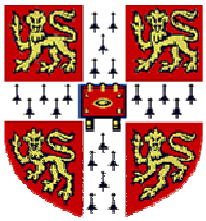
Epidemiology of Autism Spectrum Conditions in China



Xiang Sun

Clare Hall

Department of Public Health and Primary Care

School of Clinical Medicine

University of Cambridge

September 2012

This dissertation is submitted for the degree of Doctor of Philosophy at the University of Cambridge

Declaration

This research described was conducted under the supervision of Professor Carol Brayne and Professor Simon Baron-Cohen at the University of Cambridge.

I declare that this dissertation is the result of my own work and includes nothing which is the outcome of work done in collaboration except where specifically indicated in the text. I undertook all the literature work that from Chapters 1 to 5 of this dissertation. I designed the qualitative research on service provision described in Chapters 6 to 8 and was involved in the design of the pilot and validation study described in Chapters 9 to 13 of the dissertation. I was also involved in the design of the China SCORE study described in Appendix 14.1. The fieldwork was undertaken by my own. I was responsible for initial identifying possible research partners, contacting various agencies for collaboration, establishing collaboration relationships, corresponding and coordinating the project, developing service provision questionnaire, conducting interviews with parents for service provision and all the diagnostic assessments with participating families. I was responsible for data collection, data entry and analyses described in this dissertation. Where reference is made to further work of others is indicated in the acknowledgements, text and bibliography.

I declare that this dissertation is not substantially the same as any that has been, or is being, submitted for any other degree, diploma, or other qualification at any other University.

This dissertation does not exceed 60,000 words limit in length (excluding figures, tables, boxes, appendices and bibliography) set by the Degree Committee for Clinical Medicine and Clinical Veterinary Medicine.

Xiang Sun
September 2012

Acknowledgments

This work was partly funded by the Cambridge Commonwealth Trust and Clare Hall at the University of Cambridge. Project funding was provided by the Waterloo Foundation, the Cambridge Institute of Public Health, the Autism Research Centre and the Peking University First Hospital.

I am extremely grateful to my supervisor, Professor Carol Brayne, for all her help. Without her never-ending support, encouragement and enthusiasm, this work would never have been accomplished. To me, she is not only my supervisor, but my life mentor who has guided me through so many obstacles in the past four years with her wisdom and life experience. Her dedication to research, her attitude to others and her always sharp and creative thoughts enlightened me throughout my study and will continue guiding my career. I feel so lucky to have her as my supervisor since my MPhil at the University of Cambridge.

I am also deeply indebted to my co-supervisor, Professor Simon Baron-Cohen for his generous sacrifice of time to supervise me from the very beginning of this work since 2008. His excellent research, sage advice, constant encouragement and sensitiveness to others' feelings have led me to achieve what I felt was impossible. Learning from him has been a priceless experience that has enriched my life.

I would particularly like to thank Dr Carrie Allison, the advisor of my PhD, for her profound inspiration and guidance especially for her generosity of time and patience on commenting on my drafts. I will never forget that, whenever I have a problem, her door is always open for me. Without her support and encouragement, I would never have come this far. I would like to express my sincere gratitude to Professor Zhixiang Zhang for his insightful advice and great support throughout the research project as well as his hospitality during my fieldwork in Beijing. Without his dedication to his research, this project will never have been established or finished.

I would like to thank Dr Bonnie Auyeung for her great advice and encouragement during my study and also her time on reviewing my drafts. I am very grateful to Dr

Fiona Matthews, Stephen Sharp and Dr Samuel Norton for their superb statistical advice and considerable time on providing comments on my drafts. I am so grateful to Professor Sian Griffiths who supervised me during the research in Hong Kong, as described in this dissertation. I also want to express my sincere gratitude to her and Professor Huso Yi who gave me the further research opportunity to continue autism research in China. Special thanks to Dr Nina Xiong and Mr Jibin Han for their invaluable support. I would like to thank Professor Peiyu Wang, Professor Hong You, Professor Jiong Qin and his research team in Peking University First Hospital for their support and encouragement during this research.

I will always be grateful to Val Shadrack, Frances Cater, Rosemary Bell, Jenny Morris, Sarah Greenham and Sean Hickin for their excellent support with the administrative aspects of my PhD. I wish to thank friends and colleagues in the Cambridge Institute of Public Health and Autism Research Centre, for their encouragement and discussions of ideas: Dr Blossom Stephan, Matthew Prina, Dr Meng-Chuan Lai, Dr Thai Minett, Dr Riccardo Marioni, Dr Jane Fleming, Rianne Van der Linde, Jaime Perales, and Theodore Cosco. In particular, I would like to thank Yu-Tzu Wu, Yangmei Li and Bo Liu who have been my great friends and have put up with every little issue I had during the writing-up. Special thanks to Yi and his family for their hospitality and support during my fieldwork.

I cannot forget to thank Irene Hills and Bobbie Wells, who are my tutors in Clare Hall for their continuous advice and great support throughout the course of my study in Cambridge.

I would like to thank all the schools and families who participated in the research described in this dissertation, especially the Elim Training Centre for Chinese with Autism for their great support.

Finally, I would like to express my gratitude to my dearest mum and dad. Without their unconditional support and constant encouragement, I would never have completed this study.

Publications

Papers published

1. Sun, X., Allison, C., Auyeung, B., Matthews, F., Murray, S., Baron-Cohen, S., Brayne, C. Service provision for autism in Mainland China: A service providers' perspective, *Research in Developmental Disabilities,* 2012: 34(1), 440-451.

2. Sun, X., Allison, C., Auyeung, B., Baron-Cohen, S., Brayne, C. A review of healthcare and educational provision for Autism Spectrum Conditions in mainland China, *Research in Developmental Disabilities,*2012: 34(1), 469-479.

Papers under review

1. Sun, X., Allison, C., Auyeung, B., Matthews, F., Baron-Cohen, S., Brayne, C. (revision submitted) Service provision for autism in mainland China: A service users' perspective, *Social Science and Medicine.*

2. Sun, X., Auyeung, B., Allison, C., Matthews, F., Baron-Cohen, S., Brayne, C. (revision submitted) What is available for case identification in autism research in mainland China? *Journal of Autism Spectrum Disorders.*

3. Sun, X., Allison, C., Yi, H., Auyeung, B., Matthews, F., Baron-Cohen, S. Griffiths, S., Brayne, C. (under review) Pilot investigation of service provision for autism in Hong Kong: What is available? *Journal of Autism and Developmental Disorders.*

4. Sun, X., Allison, C., Matthews, F., Stephan, S., Auyeung, B., Baron-Cohen, S., Brayne, C. (under review) Autism in China, what is the evidence? A systematic review and meta-analysis of prevalence studies. *Molecular Autism.*

Papers in preparation (all in second or subsequence drafting)

1. Sun, X., Allison, C., Matthews, F., Zhang, ZZ., Auyeung, B., Baron-Cohen, S., Brayne, C. (in final preparation) Pilot and validation study of the Mandarin Childhood Autism Spectrum Test in mainland China.

2. Sun, X., Allison, C., Auyeung, B., Matthews, F., Baron-Cohen, S., Brayne, C. (in final preparation) Mandarin Childhood Autism Spectrum Test: test-retest reliability.

3. Sun, X., Allison, C., Auyeung, B., Zhang, ZZ., Matthews, F., Brayne, C., Baron-Cohen, S. (in preparation) Comparison between Mandarin Childhood Autism Spectrum Test and Clancy Autism Behaviour Scale in mainland China.

4. Sun, X., Allison, C., Yi, H., Auyeung, B., Matthews, F., Griffiths, S., Baron-Cohen, S., Brayne, C. (in preparation) Service provision of autism in Hong Kong: A service users' perspective.

5. Sun, X., Allison, C., Auyeung, B., Matthews, F., Norton, S., Brayne, C., Baron-Cohen, S. (in preparation) Psychiatry properties of Mandarin Childhood Autism Spectrum Test.

6. Sun, X., Allison, C., Matthews, F., Auyeung, B., Brayne, C., Baron-Cohen, S. (in preparation) The Mandarin Childhood Autism Spectrum Test: Sex differences.

7. Sun, X., Allison, C., Matthews, F., Auyeung, B., Baron-Cohen, S., Brayne, C. (in preparation) Comparison of service provision on autism between mainland China and Hong Kong.

8. Sun, X., Allison, C., Matthews, F., Auyeung, B., Baron-Cohen, S., Brayne, C. (in preparation) Social and communication: does culture make a difference? Brief report: a comparison between UK and China on autistic features

9. Sun, X., Allison, C., Matthews, F., Auyeung, B., Baron-Cohen, S., Brayne, C. (in preparation) Brief report: Verification of existing diagnosis of autism in mainland China using standardised diagnostic instruments.

10. Sun, X., Allison, C., Auyeung, B., Matthews, F., Baron-Cohen, S., Brayne, C. (2012) (in preparation) Brief report: an exploration of the difference in parental perspective towards behaviours related to Autism.

Abstract

Autism Spectrum Conditions (ASC) are characterised by impairments in social interaction, communication and the presence of repetitive and stereotyped behaviours, interests and activities. Previously reported prevalence estimates in mainland China focused on the extreme end of the spectrum (Childhood Autism) and the estimates were much lower than in the West. This thesis reviewed available literature regarding ASC in China, conducted interviews with parents on current service provision, and introduced and adopted new screening and diagnostic instruments for ASC to mainland China.

A systematic review examined published prevalence studies on ASC in China, which demonstrated that different research methodology has been used to estimate prevalence, in comparison to the West. A second systematic review of current screening and diagnostic instruments demonstrated a lack of validated instruments suitable for the Chinese population. A third review of current service provision demonstrated that there is an under-developed health system and a lack of support for children with ASC and their families in mainland China.

Empirical work focused on two objectives. The first was to investigate the current healthcare and education service provision in mainland China and Hong Kong. A qualitative research study was conducted with service providers in mainland China. Two other qualitative research studies were carried out using self-developed questionnaire in the form of semi-structured interviews with parents of children with ASC in both mainland China and Hong Kong. The healthcare and educational system for ASC especially in mainland China has not been well-developed. The system in Hong Kong is better developed but still needs improvement. Awareness and perception of ASC in the Chinese general population may be influenced by culture.

The empirical study focused on introducing and adopting a Mandarin Chinese version of the Childhood Autism Spectrum Test (M-CAST) for ASC screening in Chinese population. A pilot of the M-CAST confirmed the UK cut-off (≥15) was suitable for the M-CAST. A validation study was conducted in two primary schools in Beijing. The standardised diagnostic instruments, the Autism Diagnostic Observation

Schedule (ADOS) and the Autism Diagnostic Interview-Revised (ADI-R), were adopted for case identification. Verification of existing autism diagnoses was conducted in the validation using the ADOS and the ADI-R. A further test-retest reliability study and a comparison study between the M-CAST and another screening instrument that is currently used in mainland China (the Clancy Autism Behaviour Scale (CABS)) were conducted in the assessment phase of the validation study.

New findings, together with the reviews of the previous literature, support the possibility that ASC may be currently under-diagnosed in mainland China. The utility of the M-CAST is acceptable as a screening instrument for ASC in large epidemiological studies in China. The combination of using the ADOS and the ADI-R can identify children with severe autism as well as those with milder manifestations of the condition (such as PDD-NOS, Asperger Syndrome). This work lays the ground for further large scale epidemiological study of ASC in China.

Members of research team

XS Xiang Sun

CB Carol Brayne

CA Carrie Allison

SBC Simon Baron-Cohen

ZZ Zhixiang Zhang

FM Fiona E. Matthews

BA Bonnie Auyeung

Abbreviations

AAA	Adult Asperger Assessment
AAP	American Academy of Pediatrics
ABA	Applied Behaviour Analysis
ABC	Autism Behaviour Checklist
AD	Autistic Disorder
ADHD	Attention Deficiency and Hyperactivity Disorder
ADI-R	Autism Diagnostic Interview-Revised
ADOS	Autism Diagnostic Observation Schedule
ADOS-G	Autism Diagnostic Observation Schedule-Generic
AQ	Autism Quotient
AS	Asperger Syndrome
ASC	Autism Spectrum Conditions
ASDASQ	Autism Spectrum Disorder in Adults Screening Questionnaire
ASDI	Asperger Syndrome Diagnostic Interview
ASSQ	Autism Spectrum Screening Questionnaire
AUC	Area under curve
BCDPF	Beijing China Disabled Persons' Federation
CA	Chronological age
CABS	Clancy Autism Behaviour Scale
CAC	Child Assessment Centre
CARS	Childhood Autism Rating Scale
CAST	Childhood Autism Spectrum Test
CAST-1	First distribution of the Mandarin CAST in the test-retest reliability study
CAST-2	Second distribution of the Mandarin CAST in the test-retest reliability study
CBCL	Child Behaviour Checklist
CCC	Child Care Centre
CCMD-2	Chinese Classification of Mental Disorders, 2nd edition
CCMD-2-R	Chinese Classification of Mental Disorders, 2nd edition revised
CCMD-3	Chinese Classification of Mental Disorders, 3rd edition
CDFA	Categorical Data Factor Analysis
CDPF	China Disabled Persons' Federation
CFA	Confirmatory Factor Analysis
CFI	Comparative Fit Index
CHAT	Checklist for Autism in Toddlers
CHAT-23	Checklist for Autism in Toddlers-23
CI	Confidence Interval
COS	Comprehensive Observation Service
CTT	Classic Test Theory
CUHK	The Chinese University of Hong Kong
DAWBA	Development and Well Being Assessment Psychiatric Interview
DIR	Developmental, Individual-Difference, Relationship-Based model, Floor time communication development therapy
DISCO	Diagnostic Interview for Social and Communication Disorders

DSM-III	Diagnostic and Statistical Manual of Mental Disorders, 3rd edition
DSM-III-R	Diagnostic and Statistical Manual of Mental Disorders, 3rd edition, revised
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders, 4th edition
DSM-IV-TR	Diagnostic and Statistical Manual of Mental Disorders, 4th edition, revised
EASI	Early Autism Screening Items
EETC	Early Education and Training Centre
EFA	Exploratory Factor Analysis
EQ	Empathy Questionnaire
FOSPAC-R	Flinders Observational Schedule of Pre-verbal Autistic Characteristics-Revised
GADS	Gilliam Asperger Disorder Scale
GARS	Gilliam Autism Rating Scale
GFC	Geomin rotated factor correlations
GPG	Autism Spectrum Disorder Good Practice Guidance
HFA	High functional autism
HHS	Heep Hong Society
ICC	Item Characteristic Curve
ICCC	Integrated Child Care Centre
ICD-10	International Classification of Disease-10th revision
ICD-9	International Classification of Disease-9th revision
IIC	Item Information Curve
IK/G	Integrated Programme for Mildly Disabled Children in Kindergartens
IQ	Intelligence Quotient
IQR	Inter quartile range
IRT	Item Response Theory
Kiddis-SADS	Schedule for affective disorders and schizophrenia for school-age children present and lifetime version
MA	Mental age
MAA	Multidisciplinary multiagency assessment
M-CHAT	Modified Checklist for Autism in Toddlers
MCHC	Maternal and Child Health Centre
MD	Mental Disorders
MeSH	Medical Subjects Headings
MHD	Medical and Health Department
MR	Mental Retardation
NAPC	National Autism Plan for Children
NICE	National Institute for Health and Clinical Excellence
NPV	Negative Predictive Value
NSC	UK National Screening Committee
OR	Odds ratio
OT	Occupational Therapy
PASS-IT	Pictorial Autism Screening Scale for Infant and Toddler
PCA	Principle Component Analysis
PCI	Picture Communication Intervention
PDD	Pervasive Developmental Disorders

PDD-NOS	Pervasive Developmental Disorders-not otherwise specified
PECS	Picture Exchange Communication System
PPV	Positive Predictive Value
PT	Physical Therapy
PUFH	Peking University First Hospital
RBIA	Repetitive and stereotyped behaviours, interests and activities
RCT	Randomised Controlled Trail
RDI	Relationship Developmental Intervention
RMSEA	Root Mean Square Error of Approximation
ROC	Receiver operating characteristics curve
RPM	Raven's Progressive Matrices
RTT	Rett's Syndrome
SATQ	Sub-threshold Autism Trait Questionnaire
SCCC	Special Child Care Centre
SCORE study	"Social and Communication Research and Epidemiology" Study
SCQ	Social Communication Questionnaire
SD	Standard deviation
SE	Standard error
SEN	Special Educational Needs
SIB-R	Scale of Independent Behaviours-Revised
SRMR	Standardized Root Mean Square Residual
SRS	Social Responsiveness Scale
ST	Speech Therapy
TEACCH	Treatment and Education of Autistic and related Communication Handicapped Children
TIC	Test Information Curve
TLI	Tucker-Lewis Index
VABS	Vineland Adaptive Behaviour Scale
WABS	Waterville Autistic Behaviour Scales
WHO	World Health Organization
WISC-III	Wechsler Intelligence Scale for children
WLSM	Weighted least squares estimation
WLSMV	Weighted least squares estimation with mean and variance adjusted estimator
WPS	World Psychological Service
Yrs	Years

Table of Contents

List of Figures

List of Tables

List of Boxes

Chapter 1 Background

1.1 Statement of aims

This thesis explores the epidemiology of Autism Spectrum Conditions (ASC) in China. The first part focuses on the healthcare and education service provision for direction, management and support for ASC in China. The second part focuses on the screening and diagnosis of ASC in China.

This thesis covers the following aims:

1. To conduct systematic reviews on the current situation of ASC in China including service provision, prevalence, screening and diagnostic instruments.
2. To conduct qualitative research on service provision in mainland China and Hong Kong.
3. To conduct a pilot study of a Mandarin Chinese version of a UK-developed screening test, the Mandarin Childhood Autism Spectrum Test (M-CAST), in Chinese populations to determine its feasibility and cultural acceptance for the screening of ASC in primary school aged children.
4. To conduct a validation study of the M-CAST in a Chinese primary school aged sample by adopting the standardised diagnostic instruments of ASC, the Autism Diagnostic Observation Schedule (ADOS) and the Autism Diagnostic Interview-Revised (ADI-R).
5. To further examine the utility of the M-CAST by conducting studies on test-retest reliability, performance comparison between the M-CAST and the Clancy Autism Behaviour Scale (CARS), and the exploration of psychometric properties of the M-CAST.

These studies form the preliminary phase of the first large prospective epidemiological study undertaken to estimate the prevalence of ASC at a population level in primary school aged children in China.

1.2 Definition

1.2.1 Autism Spectrum Conditions

Autism Spectrum Conditions (ASC) are neurodevelopmental disorders, characterised by impairments in social interaction and communication, and the presence of repetitive and stereotyped behaviours, interests and activities[1]. Their onset usually begin before three years of age[2] and these impairments are considered to be persistent throughout life[3]. In the Diagnostic and Statistical Manual Fourth Edition (DSM-IV)[4], ASC includes three diagnoses: Autistic Disorder, Asperger's Disorder and Pervasive Developmental Disorder not otherwise specified (PDD-NOS)[5]. In this thesis, the term ASC is chosen as an overall term for all these three diagnoses and the term autism refers to classic autism including Childhood Autism or Autistic disorder.

1.2.2 Screening

Screening is the pre-diagnosis phase of disease detection. As defined by the US Commission on Chronic Illness, "screening is the presumptive identification of an unrecognised disease or defect by the application of tests, examinations or other procedures which can be applied rapidly"[6, 7]. The aim of screening is to separate those apparently well persons who are more likely to have the disease from those who are less likely to have it[8]. Screening positive does not necessarily mean the person has the disease. However, individuals with positive or suspicious screening results should be referred for further diagnosis and necessary treatment, where available[7].

1.2.3 Prevalence

Prevalence is a measure of disease occurrence. It is estimated as the total number of people who have a disease or condition at a particular time or time period divided by the total population at risk of having this disease or condition at that time or at the mid-point of that specific period of time[7].

1.3 The conditions

1.3.1 History of changing terminology of ASC

Autism was first described by Leo Kanner in 1943[9] based on the case histories and observation of 11 children who showed a similar pattern of behaviours including

language delay, social remoteness, excellent rote memory, obsessive to sameness, oversensitivity to stimuli and delayed echolalia[10]. At that time, the term autism was used to describe early infantile autism or infantile autism[11]. In 1944, Hans Asperger independently described a syndrome which is now known as Asperger Syndrome (AS)[12]. The descriptions of Kanner and Asperger shared a similarity in some autistic characteristics such as poor eye contact, stereotyped language and physical movements, resistance to change and narrowed special interests[10, 12, 13]. The important value of the identification of AS was the recognition that autistic-like syndromes can arise in individuals of normal language and cognitive development but who have often shown more subtle abnormalities in communication patterns[14-16].

With the development of research and clinical practice, more behavioural symptoms were described and categorised as autistic characteristics[10]. The term "autism spectrum" was proposed by Lorna Wing and Judith Gould in 1979 in order to capture the wider description of this condition[4, 17]. Since the publication of the third edition of Diagnostic and Statistical Manual of Mental Disorders (DSM-III) in 1980[18], a broad spectrum of disorders with similar core behavioural symptomatology has been grouped under the term "Pervasive Developmental Disorders (PDD)"[10, 17]. At that time, PDD included three subgroups: infantile autism, childhood onset PDD, and atypical PDD. In 1987, a revised edition, DSM-III-R, defined PDD with only two subgroups, Autistic Disorders and Pervasive Developmental Disorders-not otherwise specified (PDD-NOS)[11]. In 1993, the International Classification of Disease, 10th revision (ICD-10)[1] described ASC as including the following subgroups: Childhood Autism, Atypical Autism, Asperger's Syndrome and pervasive developmental disorder, unspecified. In 1994, the DSM-IV[4] adopted the term Autistic Disorders and defined the spectrum as Autistic Disorder, Asperger's Disorder and PDD-NOS. Nowadays, the categories in both ICD-10 and DSM-IV are used as diagnostic terminology in the West. The DSM-V is underdevelopment with marked changes in diagnostic categorisation[19]. With these proposed changes, the impairments in social interaction and communication will be combined together into a single subgroup. The three domains of core impairments will become two: 1) Social/communication deficits; 2) Fixated interests and repetitive behaviours. A single diagnosis of ASC might replace separate diagnostic subtypes in DSM-V[20], so the diagnosis of Asperger Syndrome and PDD-NOS may not be used. The change of terminology is shown in Table 1.1.

Table 1.1 Terminology of autism over time[11]

Diagnostic criteria	Kanner[21]	Rutter[22]	DSM-III [18]	DSM-III-R[23]	ICD-10[1]	DSM-IV[4]	DSM-IV-TR[24]	DSM-V[25] (Proposed revision)
Year	1956	1978	1980	1987	1993	1994	2000	2012
Larger category	N/A	N/A	PDD	PDD	PDD	PDD	PDD	ASD
Terminology for autism at that time	Early infantile autism, infantile autism	Infantile autism; autism; Childhood Autism	Infantile autism	Autistic disorders	Childhood Autism	Autistic disorder	Autistic disorder	Autism Spectrum Disorder
Age of onset	Not specified	By 30 months	By 30 months	During infancy or childhood	By 36 months	By 36 months	By 36 months	Early childhood
Other disorders in larger category	N/A	Other infantile psychoses	Residual state; Atypical PDD	PDD-NOS	Asperger's Syndrome; Atypical autism; PDD-NOS; Rett Syndrome	Asperger's Disorder; PDD-NOS; Rett's Disorder; Childhood disintegrative disorder	Asperger's Disorder PDD-NOS; Rett's Disorder; Childhood disintegrative disorder	None.

1.3.2 Behaviour description

As a spectrum disorder, although individuals with ASC have impairments in three main domains, their clinical phenotype, severity and frequency of symptoms are heterogeneous. Impairments usually show in a qualitative way among individuals with ASC[26]. The main characteristics are described with examples in Box 1.1&1.2[27-29].

Box 1.1 Impairments of ASC in social interaction and communication[26, 28, 30-36]

I: Impairment in social interaction:

1) The child seldomly makes eye contact or bids for others' attention with gestures or vocalisations. Lack of social smile and poor body posture to regulate interactions are often observed in the child. He/she might have difficulty in the initiation or responding to joint attention.
2) The child has a preference for being alone and shows little interests in other children, especially those of their own age, so he/she usually has very few friends.
3) The child seldomly or never spontaneously points or shows objects to others. He/she fails to follow a point to an intended direction or follow a loud voice of their name being called by others. Their hearing may seem "selective" in that children with ASC may attend well to other sounds rather than human voices.
4) The child often seems indifferent with other people's feeling. He/she rarely initiates a conversation with others or shows any comfort to others even parents. They have difficulties in understanding the perspective of others.
5) The child has inappropriate responses and facial expressions to unfamiliar persons. Usually he/she does not know how to act according to current sense or environment. The child may act as usual when his/her mother shows anger, fear or cries.

II: Impairment in communication

1) The child may have a delay in the development of receptive and expressive language. In addition, he/she may show a delay in non-verbal communication skills such as lack of eye gaze and gestures to communicate.
2) The child may constantly bring up inappropriate questions or statements to others and have problems in starting and sustaining conversations. Often the content of his/her speech is self-centred with little intention of sharing mutual interests. He/she usually does not know how to initiate or carry on with "small talk" according to proper social scenarios.
3) The child may have script speeches that are rather odd phrases or he/she seems to say the same thing repeatedly in almost exactly the same way.
4) The child may have little interest in role play or pretend play, and may take things literally and demonstrate lack of imagination.

Box 1.2 Impairments in restrictive and stereotyped behaviours[4, 16, 24, 26, 35, 37, 38]

III: Restrictive, stereotyped, and repetitive patterns of behaviours

1) The child may have unusual preoccupations such as interested in things like metal objects, lights, street lights or toilets. He/she may have special hobbies/interests that are unusual in their intensity.
2) The child may show behavioural restriction with certain non-functional rules or routines that have been set up by his/her own. He/she may show difficulty in coping with changes in the routine, environment or people.
3) The child may show repetitive hand flapping, spinning, twirling, rocking, tip-toe walking or more complex body movements which are resistant to external attempts to stop.
4) The child may be obsessed with part of the object and play with it in a way that is different from typically developing children. He/she may repetitively line up trains or other toys, and keep rolling or spinning objects. He/she may show unusual interests in some sensations such as the feeling of cloth or sniffing or mouthing non-food objects.

1.4 Screening for ASC

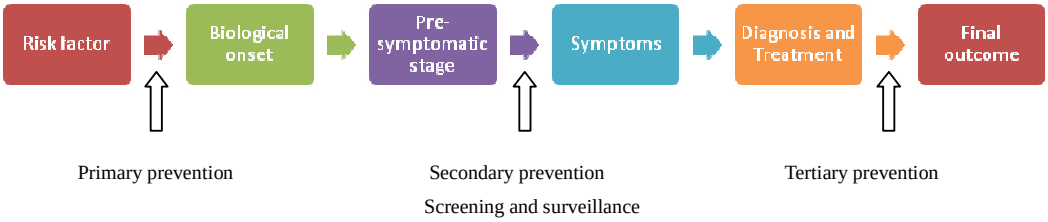
1.4.1 Natural history and time of screening

Generally, the natural history of a condition includes three stages[7]: pathological onset, pre-symptomatic and clinical manifestation. The length of this period of time varies depending on the natural history of the condition, referring to its course from pathological onset or inception to resolution[7]. Understanding the natural history of a condition can lead to appropriate actions, such as prevention and intervention, which may alter the natural history itself. Generally, according to the different stages of a condition, prevention can be conducted at three levels[7, 13]:

1) Primary prevention: intends to change behaviours of the individual or communities or reduce potential risk exposures in order to protect health before the onset of a disease, thus may reduce disease incidence.
2) Secondary prevention: interventions to slow down or stop the pathological changes in order to control the progression of disease and thus shorten the duration and reduce disease prevalence.
3) Tertiary prevention: measures aimed at alleviating or eliminating impairments, disabilities and minimising suffering in order to prolong potential life years and improve the quality of life.

The natural history of disease and prevention levels is illustrated in Figure 1.1.

Figure 1.1 Natural history and prevention



Often the existence of ASC is recognised at the time when the characteristic symptoms are manifest, so it is usually after the actual onset of this condition. Therefore, the early signs of ASC might have been missed due to various reasons such as the lack of awareness of this condition of parents[39] or physicians[8, 40]. As interventions conducted during the early phase of ASC are considered to have a potential to improve the outcomes of the effected individual[41], it is important to learn about the natural history of this condition. According to the ICD-10[1] and DSM-IV[4], autistic symptoms should be present before the age of 3 years in order to meet the diagnostic criteria within the autism spectrum[42]. A recent study indicated there are several different patterns of autism onset[43]. The most common is described as early as Kanner[9], in which children show developmental abnormality in social settings and communication in the first year of life[43]. The second is termed as regressive autism as children of this pattern usually appear to be normally developed in the first one to two years. However, in the following year, they lose certain skills that have been previously acquired, accompanied by the presence of other autistic symptoms[44]. The third is characterised by the presence of a developmental plateau or a halt after the child has achieved certain development milestones[45].

According to previous studies, the average age of first concern by caregivers is 17 months[46], while the average age of diagnosis is 41 to 60 months[47]. There is often a considerable delay between parents' recognition of abnormality and the diagnosis of autism[48]. Several possible factors may contribute to this delay such as the developmental characteristics of ASC, heterogeneous symptom presentation among individuals[46], and the impairments in social function and communication may not be noticed until the child interacts with their peers[49]. In addition, the instruments for

screening and diagnosis vary in terms of their validity and targeted age group, and many of them are newly-developed and still under investigation[50, 51].

1.4.2 Requirements of a screening programme

The UK National Screening Committee[52] (NSC) has listed the criteria for appraising the validity, effectiveness and appropriateness of a screening programme. The evaluation criteria for a screening programme by the NSC are provided in Appendix 1.1. The criteria are listed for four categories including the condition, the test, the treatment and the screening programme to examine whether a national-based screening should be put into implementation. The screening of ASC is not recommended by the current policy in the UK[52]. However, many researchers have demonstrated the importance and possibility of screening and surveillance of ASC in the UK[13, 49, 53].

1.4.3 Validation of a screening test

1.4.3.1 Validity

Clinically, validity means the ability of a test that can correctly identify a person who does or does not have the disease of interest[7]. The validity of a test can be evaluated by estimating to what degree the test can measure what it is purported to measure[7]. There are two approaches to examine the validity of a test. First, the internal validity suggests the degree to which a study is free of bias or systematic errors. Second, the external validity is the degree to which a study may apply or be generalised to populations that did not participate in the validation study.

The internal validity can be examined by interrater and test-retest reliability. The external validity can be examined by sensitivity, specificity and predictive values of the test. The definitions of indices of screening test accuracy are shown in Table 1.2. The positive predictive value (PPV) is associated with sensitivity, specificity, and prevalence of the condition. When both sensitivity and specificity of a test are high, and if the prevalence of disease in the study sample which the test is applied to is high, the PPV would be expected to be relatively high. If the same test is applied to a sample in which the disease is rare, the PPV would be low[54]. The changes of PPV and the effect of sensitivity, specificity, prevalence and sample size is shown in Table 1.3.

Table 1.2 Definitions of indices of screening test accuracy

Indices	Definition
Sensitivity	The probability that a diseased person (case) in the population tested will be identified as diseased by the test.
Specificity	The probability that a person without the disease (non-case) will be correctly identified as non-diseased by the test.
Positive predictive value (PPV)	The probability that a person with a positive test result is a true positive (e.g., does have the disease).
Negative predictive value (NPV)	The probability that a person with a negative test result is a true negative (e.g., does not have the disease).

(Quoted from A Dictionary of Epidemiology 5th Edition[7])

Table 1.3 Positive predictive value when using tests of varying sensitivity and specificity in samples from populations with different prevalence[13, 54]

Sensitivity (%)	Specificity (%)	Prevalence (%)	Sample size	Positive Predictive Value (%)
99	99	50	200	99.0
99	99	10	1000	91.7
99	99	2	5000	66.9
90	90	50	200	90.0
90	90	10	1000	50.0
90	90	2	5000	15.5
50	40	50	200	45.5
50	40	10	1000	8.5
50	40	2	5000	1.7

1.4.3.2 Validation process

In epidemiology, the purpose of validating a screening test is to apply it in the general population for early detection of a disease in the future. It has been suggested that a screening test should be tested on a demographically and geographically diverse population in order to be highly validated[55]. Greenhalgh has listed several issues that should be given attention when evaluating a validation study of a screening or diagnostic test[56]. First, "the performance of new tests should be compared against an established gold standard in an appropriate spectrum of subjects. The gold standard should have great utility in terms of validity, accuracy and reliability which merits the description to identify the disease". Second, the sample of validation study should have an appropriate spectrum of subjects which ideally are defined in terms of age, sex, current symptoms, disease severity, and special eligibility criteria[56, 57]. Thus, it is very important that the validation study has a population including responders who have mild and severe symptoms, responders who are treated and untreated, and responders with different but confused conditions[56, 58]. After the screening, those who test positive and negative will be proportionally further assessed by the gold standard which will generate the sensitivity, specificity, PPV and NPV[13]. Third, to evaluate a

screening process, the potential sources of bias should be considered, such as the work-up bias which occurs when the gold standard test is only applied to test positives[8, 57] and the volunteer bias which comes from the potential differences between the people who participated in the screening and those who did not[8]. In sum, when evaluating a screening validation, the following should be considered: target outcomes, potential sources of bias and the study design[8].

1.4.3.3 Cut-off of the test

The cut-off of a screening test is the point at which to evaluate whether the test can differentiate between the individuals who probably have the disease from those who probably do not have the disease. Usually, the subjects who score equal to or higher than the cut-off will be considered as potentially having the disease while subjects who score below the cut-off will be considered as probably not having the disease. The individuals who score at or above the cut-off are recommended to have further detailed diagnostic assessments by a gold standard measurement in order to ascertain the disease status[29]. The cut-off of a screening test is arbitrary which yields to the ideal validity of the test. The changing of the cut-off will lead to a trade-off between sensitivity and specificity[8].

1.5 Diagnosis

1.5.1 Current international diagnostic criteria for ASC

As mentioned before, there are two diagnostic classifications for ASC which have been accepted by researchers and clinicians: the ICD[1] and the DSM[23]. The most recent editions are the ICD-10[1] and the DSM-IV-TR[24]. ASC is one subgroup of the pervasive developmental disorder (PDD) within both the ICD-10 and DSM-IV-TR. The diagnostic classification of the ICD-10 and DSM-IV for PDD is shown in Table 1.4.

Table 1.4 Diagnostic classification of PDD in ICD-10 and DSM-IV

ICD-10	DSM-IV
Childhood Autism	Autistic Disorder
Atypical autism	Pervasive Developmental Disorder not otherwise specified (PDD-NOS)
Rett's Syndrome	Rett's disorder
Other childhood disintegrative disorder	Childhood disintegrative disorder
Asperger's Syndrome	Asperger's Disorder
Other pervasive developmental disorders	
Overactive disorder with mental retardation and stereotyped movements	
Pervasive developmental disorder, unspecified	

Each diagnostic category has its own characteristic symptoms. There are differences between Asperger Syndrome and autism (Childhood Autism or Autistic Disorder). Firstly, the individuals with autism usually show specific communication impairments in terms of delayed or lack of expressive language before 3 years old, while those with AS should not have any significantly general delay in language or cognitive development during early childhood[59]. Secondly, the qualitative impairments in communication of individuals with AS are not required as evidence as those with autism[15]. Thirdly, the individuals with AS have normal intelligence[60] while autism can be diagnosed in an individual with any IQ. Fourthly, the disturbances of AS must have significant impact on the individual's life in social, occupational and other functioning areas[15].

Pervasive developmental disorder not otherwise specified (PDD-NOS) is a sub-threshold diagnosis served as a residual category within the ASC for individuals that do not fulfil the full set of criteria of Autistic Disorder (AD) but who belong to a broader autism phenotype[61].

Rett's syndrome, Childhood Disintegrative Disorder as well as the overactive disorder associated with mental retardation and stereotyped movements are subtypes of pervasive developmental disorders, which are not generally considered as autistic-like disorders[13].

Rett's Syndrome (RTT) is a severe neurodevelopmental disorder which occurs predominantly in girls with a prevalence of approximately 1 in 10,000 live female births[62, 63]. Individuals with RTT apparently have normal development until 6-18 months and then experience a marked neurological decline including an early period of developmental regression[64]. The initial manifestation of RTT can present as the loss of acquired speech, head growth deceleration as well as autistic symptoms such as reduced eye contact and emotional withdrawal. The individuals may develop other features including hand-wringing behaviour, seizures, breathing abnormalities and autonomic instability[65].

1.5.2 Current practice of ASC in the UK and US

In the UK, the National Autism Plan for Children (NAPC) was issued in 2003[66], which listed strategies for identification, assessment, diagnosis and access to early intervention for preschool and primary school children with ASC. In clinical settings, there are a few stages for diagnosing a child with ASC. When the child is brought to referral to a general practitioner for developmental assessment, the following examination of the child should be included: i) general information history; ii) a physical examination; iii) necessary and appropriate medical investigations according to clinical presentation of the child. If, during these examinations a diagnosis of ASC is suspected, the child should be recommended into the next stage, which is a multidisciplinary multiagency assessment (MAA)[67] (Table 1.5). The NAPC also recommended that at least one team member should be trained in using a standardised assessment tool, the ADOS or the ADI-R. The diagnosis of school-aged children in the UK requires involvement from more agencies including the social service, health service, education service and the voluntary service.

Table 1.5 Multidisciplinary Multiagency Assessment

Multidisciplinary Multiagency Assessment (MAA) from NAPC[67]	
1.	ASD-specific developmental history by an experienced member of the team with recognised ASD training
2.	Observational assessments, includes focused observations taken across more than one setting (such as home, nursery, etc)
3.	Cognitive assessment, including individual's unique profile of skills/difficulties on subscales
4.	Communication, speech and language assessment
5.	Behaviour and mental health assessment in comorbid neurodevelopmental disorders and psychiatric disorders
6.	Family assessment, undertaken by the key worker (in some localities, allocation of a key worker during assessment and before diagnosis may provide support for families at this crucial time) to identify the strengths and needs using the Framework for the Assessment of Children in Need and their Families[68]
7.	A physical examination and medical investigations as guided by clinical presentation
8.	Other assessments, including physiotherapy and occupational therapy, should be available to identify sensory needs and problems, motor planning and coordination difficulties, and self-care problems

Recently, the Committee of National Institute for Health and Clinical Excellence (NICE) issued a new NICE guideline on the recognition, referral and diagnosis of children and young people on the autism spectrum in September 2011[52]. The NICE guideline proposed the establishment of a multidisciplinary group as the autism team in each area in the UK. The autism team should include a paediatrician and/or child and adolescent psychiatrist, a speech and language therapist as well as a clinical and/or educational psychologist. The autism team should at least have a regular consultancy with the following professionals: i) Paediatrician or paediatric neurologist; ii) Child and adolescent psychiatrist; iii) Educational psychologist; iv) Clinical psychologist; v) Occupational therapist.

In the US, the diagnosis of ASC is also recommended to be carried out by a multidisciplinary team which might be formed by paediatric neurologists, developmental and behavioural paediatricians, child psychiatrists or psychologists. Other professionals in the team are also recommended such as speech, language and occupational therapists, special educators, and social workers[42]. A recent clinical review of the diagnosis and management of ASC summarised that the diagnosis of

ASC should be established through a comprehensive evaluation which includes the following: i) information about lifetime and family history; ii) review of medical and educational records; iii) observation of behaviours; iv) physical examination; v) administration of standardised instruments such as the ADOS; vi) cognitive and adaptive assessment; vii) review of the DSM or ICD diagnostic criteria[42].

1.6 Motivations of investigating the epidemiology of ASC in China

There are several motivations for investigating the epidemiology for ASC in China.

1.6.1 Epidemiological research of ASC in China

In the UK and US, recent epidemiological studies have reported an increase in prevalence estimates of ASC. The prevalence of ASC was 4.8 in 10,000 in 1976[69] but as high as 157/10,000 in the UK in 2009[70] and 113 per 10,000 in the US in 2012[71].

Little has been known about the epidemiology of ASC in China. A recent review focused on the prevalence of ASC in Asia identified eight prevalence studies on Childhood Autism in mainland China[72]. However, different methodologies in case identification in previous studies make prevalence comparisons and the extent of the public health impact of ASC on society in the East and West impossible. Almost no data are available on other diagnostic categories relating to Pervasive Developmental Disorders (PDD), such as the Asperger Syndrome or PDD-NOS in mainland China[72].

China has a population of more than 1.37 billion people. If Western prevalence estimates for ASC are accurate and stable cross-culturally and are applied to mainland China, there would be 13.7 million Chinese people with ASC. However, the reported prevalence of Childhood Autism in China (approximately 10 per 10,000) is very much lower than the estimates in the West. No comparable estimates yet exist.

1.6.2 Public awareness

Autism was not recognised until 1943[9]. It is now highlighted as an “epidemic” by the media[73]. In the West, there has been more public attention on ASC due to more advanced autism research and improved awareness in the general population[74], which could be partly due to a few high profile celebrities and parents lobbying for

recognition. The characteristics of ASC are presented in novels and movies which have improved their recognition and acceptance by the society.

In China, the recognition of ASC was much later than the West. The first study on autism in mainland China was published in 1987[75]. During the following 13-year period, there was almost no literature available on this condition[72]. The ASC has been categorised into the domain of mental health in China since 1989[76]. After the establishment of the People's Republic of China, the first National Mental Health Meeting was held in 1958[77]. However, the development of mental health programmes almost ceased during the Cultural Revolution (1966-1976)[78]. In 1978, the Opening Policy led to the reform of the healthcare system which encouraged hospitals to be part of the market economy in order to make a profit[79]. Mental healthcare was not improved until the first National Mental Health Plan (2002-2012), when new targets were identified to develop the mental health system in mainland China[80]. The Harvard Health Policy Review in 2005 indicated the characteristics of mental health services in China: a lack of specific efforts to systematically address mental illness, slow development of specialised training and treatment of mental illness. and a lack of mental health policy to secure rights for people with mental illness[81]. Autism was been stated as one of most urgent mental illnesses for "rescue" (meaning high attention and priority) in the 12th Five-Year Development Programme for China Disabled Persons (2011-2015) issued in 2011[82]. The awareness of ASC among the public has increased following this call.

1.6.3 Possible benefits of early detection and diagnosis

Autism has been considered as one of the most severe childhood neuropsychiatric conditions, impacting on multiple aspects of life including development, learning, home life as well as integration into school and society[83]. It is generally agreed that Childhood Autism can be reliably diagnosed as early as 2 years old, while a diagnosis of Asperger Syndrome and PDD-NOS is more difficult until later in childhood[47, 84]. The possible benefits of early detection and diagnosis have been proposed as follows.

Early diagnosis may lead to the early implementation of targeted intervention, which may improve the outcome of children with ASC[48, 85, 86]. After identification, a variety of intervention approaches for ASC have been studied including pharmacotherapy,

behavioural intervention, psychosocial intervention, and educational intervention[87]. There have been a few intervention programmes for ASC which demonstrated positive outcomes in terms of IQ gains and reductions in symptom severity[85, 88-97]. There have also been several Randomised Controlled Trails (RCT) on the effectiveness of Picture Exchange Communication System (PECS) in improving the intentional communication[98-100]. Four RCTs on parent training intervention[101-104] and two RCTs using Applied Behaviour Analysis (ABA) reported the improvement in child's ability after intervention[105, 106]. A most recent review on available intervention studies by Warren and colleagues suggested that studies using Lovaas-based approaches[95], early intensive behavioural intervention[92], as well as the Early Start Denver Model[107] provided some evidence of improvements in cognitive performance, language and adaptive behaviour skills. However, it also indicated a generally poor quality and lack of methodology coherence of the available studies. In general, robust evidence for the effectiveness of intervention which can only be provided by RCT is still lacking. However, there is an increasing agreement that the age of intervention on communication is important for children with ASC as it may influence future outcome[48, 108].

Early identification of ASC is also important in order to help parents recognise and understand their child's difficulties and needs[83]. By having an diagnosis early on, parents found advantages arising from an ASC diagnosis' capacity as it helped to explain their child's difficulties to others within or outside their families[109, 110]. As a result, it may shorten the time period between first parental concern and the confirmed diagnosis, which would help parents to learn how to cope with their child's problems and also their own lives[29]. This approach can potentially release the stress experienced by parents[111, 112].

Early detection can lead to families with children having autism receiving support early from the society or government, which could reduce the financial burden on parents[113]. In the US, the annual average expenditure for special education services per children with autism at primary school was estimated to be $11,543. This was higher than children in any other category of disability and two times the average cost for a child in special education[114, 115]. In the UK, the total societal cost for a child with

ASC was estimated to be £689 per week, of which £223.82 was for education and £144.38 for early interventional therapy[116].

The risk of having a second child with ASC when the first has an ASC diagnosis was reported to be ranging from 3% to 15%[117], which is 20 to 50 times higher than the general population[118]. A recent study on the recurrence in siblings reported a rate of 18.7% studied in a number of 664 infants with an older biological sibling with ASC[119]. Early identification of autism may help with the future family planning in terms of having another child[48, 120]. Early diagnosis may lead to prevention of additional problems or conditions with the child such as anxiety, depression and antisocial behaviours[121-123]. In the US, it was recommended by the National Research Council that "children with autistic spectrum disorders require early identification and an diagnosis to equip them with the skills (e.g. imitation, communication) to benefit from educational services, with some evidence that earlier initiation of specific services for autistic spectrum disorders is associated with greater response to treatment"[124]. However, whether similar strategy and recommendations can be made in China depends on the current situation of ASC. The potential differences in culture should also be borne in mind such as stigma which might have impact on the awareness and acceptance of this condition. These issues regarding the current situation of service provision for autism in China will be investigated in the following chapters. In the next chapter, the available instruments for case identification in autism research in developed countries are reviewed.

Chapter 2 Epidemiology of ASC: What is Available for Case Identification in Autism Research in Developed Countries?

2.1 Introduction

ASC has been studied more thoroughly in developed countries such as the UK and US in the West and Japan in Asia[72, 125]. Although this work focuses on autism in China, it is important to summarise what is known in other settings. In this chapter three areas are covered: screening instruments, standardised diagnostic instruments, and prevalence estimation.

2.2 Review of screening instruments for primary school aged children with ASC in developed countries

2.2.1 Introduction

To date, the screening and diagnosis of ASC mainly depends on the observational or reported behavioural characteristics in current practice and research[126]. Since 2000, many prevalence studies have adopted a two-phase approach for case identification, which includes screening and further diagnostic assessment[125]. There has been an interest in early identification of ASC in very young children, however, the reported age of diagnosis of ASC in previous studies was around 5 years old[127] or even later for high-functional ASC[128, 129]. As a developmental disorder with heterogeneous features among affected individuals, behaviours in the context of primary school or special educational settings may not be the same as those of very young children or adults. Previous reviews have identified a number of screening instruments for case identification of ASC in developed countries[108, 130, 131]. Several of them are used in epidemiological research in primary school aged populations[70]. As suggested by Glascoe, the acceptable sensitivity of a screening test should be at least 70-80%, and the specificity should be closer to 80%[132].

The aim of the following review was to identify and summarise the screening instruments in current use and report their validity for screening of ASC in primary school aged children.

2.2.2 Method

2.2.2.1 Literature search

A literature search was conducted in two databases including PubMed and Web of Knowledge to identify the peer-reviewed studies on screening instruments. The search strategy is given in Box 2.1. Reference lists from identified papers and several reviews[130, 133, 134] were also searched by the candidate to identify articles that may have been missed by the search.

2.2.2.2 Study selection

The papers identified by the literature search were examined against the inclusion criteria (Box 2.2). The inclusion criteria were designed to ensure the instruments identified are applicable to primary school aged children for the purpose of screening but not diagnosis of ASC.

2.2.2.3 Data abstraction

The selected papers were categorised according to each identified screening instrument. The data of the characteristics of the instrument, the research methodology of the validation study and test validity were abstracted from the reviewed papers for further analysis.

Box 2.1 Search strategy for review of screening instruments for ASC within primary school aged children

PubMed (searched on 1st February 2012)
Years (1966-2011)
Step 1: "Autism"/all subheadings [MeSH] OR "Autistic Disorder"/all subheadings [MeSH] or "Autism Spectrum"/all subheadings [all fields] OR "Pervasive developmental disorder"/all subheadings [MeSH] OR "Asperger"/all subheadings [all fields]
Step 2: "Validation"/all subheadings [MeSH] OR "Screen"/all subheadings [MeSH] OR "Screening test"/all subheadings [MeSH] OR "Mass screening"/all headings [MeSH] AND results in Step 1

Web of Knowledge (searched on 1st February 2012)
Year (1950-2011)
Step 1: "autism"/ [Topic] OR "autistic disorder"/ [Topic] OR "autism spectrum"/ [Topic] OR "pervasive developmental disorder"/ [Topic] OR "asperger syndrome"/ [Topic]
Step 2: "validation"/ [Topic] OR "screen"/ [Topic] OR "screening test"/ [Topic] OR "mass screening"/ [Topic] AND results in Step 1

Box 2.2 Inclusion criteria for review of screening instruments for ASC within primary school aged children

1. An original study about a screening tool
2. The screening tool was used to identify the whole spectrum of ASC
3. The sample was from a population based or clinical or mixed setting
4. Study sample include children older than 5 years old but not adults
5. Study population in developed countries
6. Provide information about sample size
7. Provide information about the reference diagnostic method which was used as gold standard which could be diagnostic instruments, criteria or clinical judgement.
8. Should be prospective study
9. Provide information about the validity and reliability of the instrument
10. Published in English

2.2.3.1 Studies identified

The literature search in PubMed identified 253 studies and 2,577 from Web of Knowledge. After excluding the screening instruments used in children younger than 5 years old, 51 studies in PubMed and 137 studies from Web of Knowledge including duplicates were included for detailed examination. A total of 20 studies examining the validity of the screening instruments were identified.

2.2.3.2 Screening instruments identified

Seven screening instruments met the inclusion criteria for this review: (1) Childhood Autism Rating Scale (CARS) (2 studies) ; (2) Autism Behaviour Checklist (ABC) (4 studies); (3) Gilliam Autism Rating Scale (GARS) (3 studies); (4) Autism Spectrum Screening Questionnaire (ASSQ) (3 studies); (5) Social Communication Questionnaire (SCQ) (5 studies); (6) Social Responsiveness Scale (SRS) (4 studies); (7) Childhood Autism Spectrum Test (CAST) (2 studies). The characteristics for each instrument and methodology of their validations studies were summarised in Table 2.1& 2.2.

Table 2.1 Descriptions of identified screening instruments used in Western studies

Test	Year of First publication	Author	Age coverage	Behaviour Description	Informant	Domains/ subscales	Number of scales, rate scales	Level of functioning	Number of study	Screening/ Diagnosis tool (S/D)
CARS	1980	Schopler[135]	All children including preschoolers	AD symptoms	Professionals	15 domains (see blow)	15 items Rated 1 to 4	Full range	2	S/D
ABC	1980	Krug[136]	18 months-35 years	AD symptoms	Parent/teacher/ professional	Sensory; Relating; Body and object use; Language; Social; Self-help skills.	57 items Rated 1 to 4	Full range	4	S/D
GARS	1995	Gilliam[137]	3-22 years	ASD Symptoms Early history	Parent/teacher	Social interaction; Communication; stereotyped behaviours; developmental disturbances	56 items Rated 0 to 3	Full range	3	S
ASSQ	1999	Ehler & Gillberg[138]	7-16 years	AD symptoms	Parent/teacher	Social interaction; Communication; Repetitive and stereotyped behaviours.	27 items Rated 0 to 2	Mild and above	3	S
SCQ	1999	Berument[139]	>4 years CA >2 years MA	ASD symptoms	Parent/ caregiver	Reciprocal social interaction; Language; Communication; Repetitive and stereotyped patterns of behaviours.	40 items Rated 0 or 1	MA >2 years	5	S
SRS	2000	Constantino[140]	4-18 years	Reciprocal social behaviours	Parent/teacher	Social awareness; Social information processing; capacity for reciprocal; social communication; social anxiety/avoidance; autistic preoccupations and mannerisms	65 items Rated 0 to 3	Mild and above	4	S
CAST	2002	Baron-Cohen[121]	4-11 years	ASD symptoms	Parent/teacher	General development; Social interaction; Communication; Repetitive and stereotyped behaviours.	37 items Rated 0 or 1	Mild and above	2	S

CA: chronological age; MA: mental age; AD: Autistic Disorders; CARS domains: Relating to people; Imitative behaviour; Emotional response; Body use; Object use; Adaptation to change; Visual response; Listening response; Perceptive response; Fear or anxiety; Verbal communication; Non-verbal communication; Activity level; Level and consistency of intellectual relations; General impressions.

Table 2.2 Screening instruments identified according to inclusion criteria

Tool	Year	Author	Sample size	Age at screen	Sample source	Cut-off point	Diagnostic instrument	Reference diagnostic criteria	Sensitivity	Specificity	PPV
CARS	2004	Rellini[141]	65 (54 autism, 9 ASD, 1 ADHD, 1 other disorder)	1.5-11	Clinical settings	≥30 for autism	Diagnostic protocol in hospital unit	DSM-IV	100%	--	--
	2010	Chlebowski[142]	2-year-old: 376 4-year-old: 230	2 and 4	Part of large screening study in clinical settings	≥25.5 for autism	ADOS, ADI-R	DSM-IV	2 year old: 92% 4 year old: 82%	2 year old: 89% 4 year old: 95%	94% 97%
ABC	1988	Volkmar[143] *	157 (94 autism, 63 no autism)	--	Clinical settings	Confirm autism: ≥67 Suspicious autism: 53-66	--	DSM-III/DSM-III-R	57%	62%	--
	1991	Wadden[144] *	123 (67 autism, 56 other developmental disorders	5-17	Clinical settings	1. Volkmar's criteria 2. cut-off=44 3. 34 item version	--	DSM-III-R or Clinical diagnosis	1. 49% 2. 87% 3. 85%	1. 100% 2. 96% 3. 93%	--
	1996	Nordin[145] *	Group 1: 99 with learn disability and 184 with motor disability Group 2: 165 from normal schools	2-17 7-12	Clinical settings	Weighted score by Krug : ≥67	--	Clinical diagnosis	Group1: ≥67: 38% ≥45: 100% Group 2: ≥67: 29% ≥45: 65%	Group1: ≥67: 97% ≥45: 93% Group 2: ≥67: 99% ≥45: 96%	--
	2004	Rellini[141]	65 (54 autism, 9 ASD, 1 ADHD, 1 other disorder)	1.5-11	Clinical settings	≥53 for autism	Diagnostic protocol in hospital unit	DSM-IV	54%	--	--
GARS	2002	South[146]	119 with ASD	3-10.5	Five independent research samples	≥90 as probably autistic	ADOS, ADI-R VABS	DSM-IV	48%	--	--
	2005	Lecavalier[147]	284 children and adolescents	3-21	General population (local schools)	≥90 as probably autistic	GADS, SIB-R	DSM-IV	38%	--	--
	2008	Sikora[148]	109 with Autism 32 with ASD, 51 non-ASD	1.3-5.9	Autism program sample	≥90 as probably autistic	ADOS, CBCL	DSM-IV	53%	54%	--
ASSQ	1999	Ehlers[138] *	Main sample: 110 clinical referral Validation sample: 34 AS	6-17	Clinical settings	≥13 parent ≥19 parent ≥22 teacher	--	Clinical diagnosis	91% 62% 70%	77% 90% 91%	--
	2009	Posserud[149]	9,430	7-9	General population	Combined teacher and parent version: ≥17	Kiddie-SADS[150], WISC-III, DISCO	ICD-10, DSM-IV	91%	86%	36%

Tool	Year	Author	Sample size	Age at screen	Sample source	Cut-off point	Diagnostic instrument	Reference diagnostic criteria	Sensitivity	Specificity	PPV
	2009	Mattila[151]	School students: 4480 AS/autism: 47	8 7-12	General population outpatients	Combined parent and teacher: 30 Teacher version: 22	ADOS, ADI-R, WISC-III	ICD-10	100% 85%	73% 69%	35% 28%
SCQ	2006	Eave[152] *	151 clinical referral and preschool clinic	5	Clinical settings	≥15	ADOS, ADI-R	DSM-IV	71% 71%	62% 53%	--
	2007	Chandler[153]	247 from special education Two samples from general population: 411 and 247	9-10	Special education records General population	15-21: moderately high; ≥22: high	ADOS, ADI-R	ICD-10	88%	72%	64%
	2007	Charman[154]	119	9-13	Special education	≥15 for ASD	ADOS, ADI-R	ICD-10	86%	78%	74%
	2010	Johnson[155]	219	11	General population	≥15 for ASD ≥14 for ASD	DAWBA	DSM-IV-TR	82% 91%	88% 86%	32% 31%
	2011	Schanding Jr[156]	3,375: 1,663 ASD, 1,712 siblings	4-17 ≥4	Previous autism research sample	Teacher: ≥15 Parent: ≥145	ADOS, ADI-R	--	Teacher: 60% Parent: 75%	Teacher: 95% Parent: 99%	94% 99%
SRS	2007	Charman[154]	119	9-13	Special education	≥75 for ASD	ADOS, ADI-R	ICD-10	78%	67%	63%
	2007	Constantino[157]	577: 406 with PDD; 171 without PDD	4-18	Clinical settings	≥60	ADOS, ADI-R	DSM-IV	75%	96%	--
	2011	Schanding Jr[156]	3,375: 1,663 ASD, 1,712 siblings	4-17 ≥4	Previous autism research sample	Teacher: ≥60 Parent: ≥75	ADOS, ADI-R	--	Teacher: 70% Parent: 80%	Teacher: 95% Parent: 99%	93% 99%
	2011	Aldridge[158]	48	4-15	Clinical settings	Teacher :51.5; Parent: 56.5;	ADOS, ADI-R	DSM-IV-TR	Teacher: 97% Parent: 97%	Teacher: 25% Parent: 8%	--
CAST	2002	Scott[121]	1,150 mainstream students	5-11	General population	≥15	ADOS, ADI-R	DSM-IV or ICD-10	--	98%	--
	2005	Williams[159]	1,925 mainstream students	5-11	General population	≥15	ADOS, ADI-R	ICD-10	100%	97%	50%

--: not available. DAWBA: Development and Well Being Assessment Psychiatric interview. GADS: Gilliam Asperger Disorder Scale; SIB-R: Scale of Independent Behaviours-Revised. DISCO: Diagnostic Interview for Social and Communication Disorders; CBCL: Child Behaviour Checklist; Kiddie-SADS: Schedule for affective disorders and schizophrenia for school-age-children present and Lifetime version; WISC-III: Wechsler Intelligence Scale for children (3rd ed.); VABS: Vineland Adaptive Behaviour Scale. *Study details were from previous reviews.

2.2.3.3 Sample characteristics

The sample size of identified validation studies ranged from 48 to 9,430 with the median as 219. Out of 20 studies, 10 studies focused on children between 5 and 11 years old.

2.2.3.4 Childhood Autism Rating Scale

The CARS was developed by Schopler and can be applied to children of all ages[135, 160]. It was generated from five diagnostic criteria[161] including the Kanner[21], Creak[162], Rutter[163], Ritvo[164] and DSM-II-R. The CARS contains 15 domains[141] with each domain rated from 1 to 4 (1, 2, 3, 4). Thus, the total score ranges from 15 to 60. The cut-off for mild to moderate autism is 30 and 36.5 respectively, and for severe autism is higher or equal to 37, while less than 30 is non-autistic[142, 165]. It is clinician-rated, which can be based on parental interview and/or clinical observation.

Two validation studies were identified, and both were conducted in clinical settings. These studies recommended different cut-off points, one study adopted 25.5 (≥ 25.5) and the other adopted 30 (≥30). Both of them used the DSM-IV as reference diagnostic criteria. One used hospital protocol as a diagnostic schedule, while the other study used the ADOS and ADI-R as diagnostic instruments. The validity reported in those two studies was a little different from the validity reported by the author[166]. The sensitivity of the CARS was reported as 89% by the author when it was used in a clinical setting with clinical judgement as the reference diagnostic criteria[166].

2.2.3.5 Autism Behaviour Checklist

The ABC was developed by Krug and colleagues in 1980[136]. It was designed to be applied to individuals aged between 18 months and 35 years[136, 167]. The behaviour features listed in the ABC were generated from several sources[167]: the Kanner's criteria[168], Lovaas's findings[169], the British Working Party's Checklist or Creaks' Nine Points[162], Rimland's Form E-2[170], the BRLAAC[171], the Rendle-Short and Clancy's Checklist[172], and the Lotter's Checklist[173]. The ABC has 57 items and each item is rated from 1 to 4. The cut-off of the ABC was recommended as 53 (≥53). It can be administrated by the evaluator and also can be filled in by the parents without prior training[13]. The results of the ABC can be in one of the following five categories:

normal, severe emotional disturbances, deaf/blind, severe mental retardation and autistic[141].

Four validation studies were identified[141, 143-145]. All of them were conducted in clinical settings using DSM-III or DSM-IV as the reference diagnostic criteria and none of them used diagnostic instruments for case identification. The adopted cut-offs and reported validity was different in those studies. Rellini[141] reported a sensitivity of 54% and recommended a cut-off of 53. The ABC was reported to have performed not as good as the CARS in distinguishing children with mild-moderate autistic disorders from those with other developmental disorders[141].

2.2.3.6 Gilliam Autism Rating Scale

The GARS was developed by Gilliam[137] as a parent-reported behaviours checklist. The applicable age range is from 3 to 22 years old[137]. It was constructed from diagnostic criteria in DSM-IV and from the Autism Society of America's definition of autism[174]. The GARS contains 56 items to evaluate four subscales[137, 148, 174]. The score for each scale is then added up and converted to a total score which is called the Autism Quotient (AQ). The cut-off of the GARS is recommended as 90 (≥90)[175].

Three validation studies were identified, two of which were conducted in research settings[146, 148] while one was population-based[147]. The cut-off of 90 was used in all three studies. The reference diagnostic criteria were DSM-IV for three studies, and two of them used the ADOS as diagnostic instrument. The validity of the GARS was reported to be low in all three studies. Lecavalier conducted an evaluation of the GARS in a heterogeneous sample of 284 school children and adolescents. This study suggested the instrument should be used with care in higher functioning individuals and a low cut-off should be recommended[147]. The recent validation study suggested the sensitivity of the CARS was 53% and the specificity was 54%[148].

2.2.3.7 Autism Spectrum Screening Questionnaire

The ASSQ was originally developed to screen Asperger Syndrome in the general population of school aged children by Ehlers and Gillberg[138, 176]. The applicable age of the ASSQ is between 7 and 16 years old[138]. It was based on the diagnostic criteria in ICD-10 and DSM-IV[151, 177]. The ASSQ[138] contains 27 items and each item is rated from 0 to 2[151]. The score of the ASSQ ranges from 0 to 54. The ASSQ only takes

about 10 minutes to complete. It has two versions: one for teachers and the other for parents, with the cut-off of 21 and 18 respectively[138, 178].

The author reported using the cut-off of 13. The sensitivity of the parents' ASSQ was 91% and the specificity was 77%[138]. No validity was reported for the teachers' version. Three validation studies were identified, two in general populations[149, 151] and one in a clinical setting[138]. Two studies used ICD-10 or DSM-IV as reference diagnostic criteria and the other one used clinical diagnosis. Two out of three studies used diagnostic instruments either the ADOS or the ADI-R. The cut-offs in these studies were different. Two used combined teacher-parent version, while one adopted both versions as separate. Posserud conducted a validation study of the ASSQ in a total population sample and reported the ASSQ performed best as a combined version with a cut-off of 17 (sensitivity=91%, specificity=86%)[149]. Mattila conducted an epidemiological study in Finland using the ASSQ and recommended a cut-off of 30 for parents' and teachers' summed score version (sensitivity=100%, specificity=73%), and a cut-off of 22 for the teachers' version (sensitivity=85%, specificity=69%)[179].

2.2.3.8 Social Communication Questionnaire

The SCQ was originally developed by Berument and colleagues to be used in children at least aged 4 with a mental age of 2[139]. It was derived from the ADI which was an early version of the ADI-R[180].

The SCQ has 40 items, with each item rated 0 or 1. The total score ranges from 0 to 39[154]. The recommended cut-off of the SCQ was 15 by the first study[139] to differentiate PDD including autism from other disorders, whereas a cut-off of 22 was used to discriminate autism from other subtypes within PDD.

The author reported the sensitivity of the SCQ was 85% and the specificity was 75%[139]. Five validation studies of the SCQ were identified. Two studies were conducted in special education[153, 154], one in clinical settings[152], one from previous autism research sample[156] and one in general population[155]. Four studies used either ICD-10 or DSM-IV as reference diagnostic criteria and four used the ADOS and ADI-R as diagnostic instruments. The cut-off of 15 was adopted in all five studies. The recent validation suggested the sensitivity was 60%, specificity was 95% for the

teachers' version, while sensitivity was 75% and specificity was 99% for the parents' version[156].

2.2.3.9 Social Responsiveness Scale

The Social Responsiveness Scale was developed by Constantino and Gruber[181] as a quantitative measure for ASC in individuals aged between 4 and 18 years old[181, 182]. It is a 65-item questionnaire designed to be completed by a teacher or a parent[156]. Each item is rated from 0 to 3 with the total scores ranging from 0 to 195.

The author reported a sensitivity of 85% and specificity of 75% at the cut-off of 75 (≥75)[181, 183]. Four validation studies were identified. Two of them were conducted in clinical settings[154] and two were from previous autism research samples. Three of them used ICD-10 or DSM-IV as reference diagnostic criteria and all of them used the ADOS and ADI-R as diagnostic instruments. Two of them adopted a cut-off of 60 while the other two adopted 75. The recent validation suggested the sensitivity was 97% and specificity was 25% for the teachers' version, while sensitivity was 91% and specificity was 8% for the parents' version[158].

2.2.3.10 Childhood Autism Spectrum Test

The Childhood Autism Spectrum Test (CAST) was developed by Baron-Cohen and colleagues in 2002[121]. It was designed specifically for primary school aged children between 4 and 11 years old[121]. It was based on of the behavioural descriptions of ASC described in ICD-10[1] and DSM-IV[4]. The CAST consists of 37 parent-rated items, of which 31 are scorable. Each item scores 0 or 1 with the total score ranging from 0 to 31[184]. The recommended cut-off is 15 (≥15)[121].

Two validation studies were identified, both of which were conduced in the general population. Both studies used ICD-10 or DSM-IV as reference diagnostic criteria and the ADOS and ADI-R as diagnostic instruments. Using the cut-off of 15, Williams reported the sensitivity of the CAST for ASC was 100% and the specificity was 97%, justifying the potential suitability of the CAST as a screening tool for epidemiological research on ASC in primacy school aged children[159].

2.2.3.11 Summary of research methodologies

Four out of seven identified screening instruments have been validated in general populations, which were in seven out of twenty studies[121, 147, 149, 151, 153, 155, 159]. Those studies were conducted prospectively. Generally, the first phase was the distribution of screening instruments to parents or teachers. Then, after screening, the participants who scored equal to or above the cut-off were invited to further diagnostic assessment using standard instruments. Four studies adopted the ADOS and ADI-R for the diagnostic assessment, and their final diagnosis was confirmed by either ICD-10 or DSM-IV.

Six studies were conducted in the samples of children and their parents referred to clinics[138, 141, 145, 152, 157, 158]. Three of them adopted the ADOS and ADI-R as diagnostic instruments, while the other three used clinical judgement as reference diagnostic criteria. Four studies recruited the participants from other research samples[142, 146, 148, 156]. The participants were contacted again and asked to fill in the screening questionnaire and then diagnostic assessments were carried out using the ADOS and ADI-R. Three studies recruited the participants from special educational settings[153, 154]. These participants included children who already had an ASC diagnosis with special needs. All three studies distributed the screening instrument first and then invited the stratified screened sample for a further diagnostic assessment using the ADOS and ADI-R.

2.2.4 Discussion

2.2.4.1 The validity of identified screening instruments

The seven screening instruments identified by this review could all be used in primary school aged children in the detection of ASC. In both validation studies of the CARS, the CARS was used as a diagnostic instrument with other diagnostic methods. Both of them reported acceptable validity of the CARS. One study compared the performance of the CARS with DSM-IV and found complete agreement with those two[141], while the other study suggested a lower cut-off of the CARS (≥25.5) for clinical use[142]. One study compared the validity between the CARS and the ABC, and proposed to adopt the CARS but not the ABC as a standard diagnostic protocol for case identification of ASC.

All studies on the ABC were conducted in clinical referral populations and none in the general population. Although it has been suggested that the ABC has reasonable sensitivity and specificity by the author[185], the validity in reviewed studies varied and only one study reported an acceptable validity. Two studies demonstrated an increase in sensitivity of the ABC by adopting a lower cut-off[144, 145].

Regarding the performance of the GARS, all three studies indicated unsatisfactory validity and suggested cautions were needed when using the GARS as a screening instrument for ASC[146, 147]. One study found the validity of the GARS was worse than that of the Childhood Behaviour Checklist (CBCL) which is used in children who are 36 to 71 months old[148]. One possible explanation for this was that the GARS was designed with emphasis on the measurement of repetitive and stereotyped behaviours, while several social and communication areas were given less attention[147].

The validity of the ASSQ has been investigated in both clinical settings and in the general population. Two studies out of three have indicated good validity of the ASSQ as a screening instrument for ASC and two out of three studies recommended the use of both the parents' and teachers' versions of the ASSQ[149, 151].

Among the seven instruments, the validity of the SCQ has been the most thoroughly investigated. All identified studies reported good validity of the SCQ in detecting ASC either in clinical settings or in the general population. Two studies confirmed the utility of the SCQ as a screening instrument of ASC in school aged children[153, 154]. Two studies suggested using lower cut-off of the SCQ could improve the sensitivity and specificity and thus to be more adequate for screening[152, 156]. It has been suggested that the SCQ perform best within individuals who are over 7 years old[130].

The acceptable validity of the SRS was reported in two studies out of four identified studies. The SRS has been compared with the SCQ in two studies[154, 156]. One study found the teacher's SRS performed slightly better than the SCQ[156], while the other study reported the opposite result[154]. Three out of four studies confirmed the utility of the SRS as a screening instrument for ASC. One study found very low specificity of the parents' version (8%). It also suggested that caution needs to be employed when

screening children with previously identified social development problems using the SRS[158]. However, none of the reviewed studies were conducted in the general population.

Both the validation studies on the CAST were conducted in general populations[121, 159]. By using the same cut-off in both studies, the CAST showed good validity as a screening instrument for the detection of ASC in primary school aged population.

2.2.4.2 Limitation

The purpose of this review was to identify current available screening instruments for primary school aged children in the West. The limitation was that the literature search only conducted in two databases and it was not a systematic review of studies per se but the summary of what has been developed and available for epidemiological research on ASC in developed countries. As this review was only conducted in two databases with specific search terms for ASC, instruments that can detect ASC but are not exclusively used for ASC may not have been included in this review. It is also possible that not all studies on each identified screening instrument were included in this review. Thus, it is possible that studies on these screening instruments have been missed out by this review.

2.2.4.3 Conclusion and future directions

If there is an intention to screen large populations for ASC, it is crucial that the screening instrument is known to perform reliably and accurately in relevant populations. However, the majority of validation studies have not been conducted in the general population. Only the validity of the SCQ, the ASSQ and the CAST has been investigated in general populations with acceptable results. Among them, the CAST was the only screening instrument that was designed specifically for primary school aged children in a large population-based epidemiological study for the whole autism spectrum. It has achieved the highest sensitivity and specificity within the reviewed instruments. However, its validity has only been investigated in the UK. It would be valuable to have studies designed to validate the CAST in a different culture to examine whether its performance is stable across cultures.

2.3 Description of the ADOS and ADI-R

2.3.1 Introduction

The diagnostic instruments that assist identification of autistic behaviours by a standardised approach are considered crucial for diagnosis and classification of ASC. During the last two decades, a combination of observation-based and informant-based instruments has been developed for the systematic assessment of ASC: the ADOS[186] and ADI-R[27, 180, 187]. The combined usage of the ADOS and ADI-R is now viewed as a "gold standard" for diagnosing ASC[188, 189] in research and has been widely adopted in both research and clinical settings [190]. Both instruments require intensive training and high reliability levels for the administration[180, 191, 192]. The following section summarises what is known about the research on the ADOS and ADI-R.

2.3.2 Autism Diagnostic Observation Schedule

2.3.2.1 Description

The ADOS was developed by Lord[36] as a semi-structured, standardised, play-based observational instrument[186]. The assessment was designed to create a "social world" in which the subject could interact with the examiner[193]. The purpose of having different social scenarios is to elicit and observe the autistic features of the subject in terms of social and communicative behaviours, play and imagination as well as restricted and repetitive behaviours. It was developed from two previous instruments, the Pre-Linguistic Autism Diagnostic Observation Scale[194] and the Autism Diagnostic Observation Scale[36].

The ADOS which is the ADOS-generic (ADOS-G)[186] has been developed to detect the borderline spectrum of ASC which has four comparable models for administration with different individuals according to their chronological age and expressive language level[158, 195]. Module 1 is for administration with individuals who have not achieved phrase speech with a minimum of no speech and a maximum of simple phrases. Module 2 is for administration with individuals with a minimum of flexible three-word phrases and a maximum of fluent speech. Module 3 is for individuals with a minimum of fluent speech, and module 4 is intended to be used when the individuals have fluent language[195]. Generally, the higher the module, the more

language and social abilities are demanded. Most recently, there has been a new version of the ADOS, the ADOS-2 which has a Module 5 for the administration among very young children who are less than 30 months old. There are two categories of diagnosis including autism and ASC on the ADOS algorithm. The tasks of each module of the ADOS can be found in Appendix 2.1. After the assessment, the examiners should rate the performance using standardised coding in an algorithm, which should be done shortly after the administration[158]. The items for the algorithm (non-revised version) of each module of the ADOS and a sample of the algorithm in Module 2 booklet can be found in Appendix 2.2.

2.3.2.2 Reliability and Validity

The ADOS has shown substantial interrater and test-retest reliability for each item, excellent interrater reliability within domains and excellent internal consistency[186]. The author reported that algorithm items for module 1 have 100% in both sensitivity and specificity while module 2 has a sensitivity of 95% and specificity of 94% for discriminating autism (more extreme cases) from non-spectrum. Module 3 and 4 had similar sensitivity (0.94 for module 3 and 0.90 for module 4) and specificity (0.94 for module 3 and 0.93 for module 4) for differentiating individuals with autism and ASC from those without[196]. Module 5 had a sensitivity of 87% and specificity of 86% for discriminating ASC from non-spectrum among verbal children aged 12-20 months and nonverbal children aged 21-30 months. Within the same age group, the author reported a sensitivity of 87% and specificity of 91% for differentiating ASC from typical developing children. Among verbal children who were 21-30 months old, the sensitivity for the ADOS in discriminating ASC from non-spectrum was 81%, while specificity was 83%. The sensitivity of discriminating ASC from typical development children was 81%, while specificity was 90%[197].

2.3.3 Autism Diagnostic Interview-Revised

2.3.3.1 Description

The ADI-R was developed by Rutter[180], Le-Couteur[187] and Lord[27] as a standardised, face-to-face semi-structured diagnostic protocol for interviewing parents or caregivers of individuals referred for a possible ASC[27, 180]. The ADI-R is an 85-page booklet containing 111 items in three core domains of ASC[198]. The first 10 items include two

parts: the first part includes items on the medical and psychological history of the subject, while the second part contains items on key ages of developmental milestones. The remaining 101 items are categorised into four domains: Items 11-41 for communication; Items 42-69 for social development and play; Items 70-85 for interests and behaviours; and Items 70-85 for general behaviours[199]. In general, each item is rated from 0 to 3. The ADI-R takes approximately two hours to complete. After the assessment, the coding needs to be transferred into an algorithm to generate a diagnosis. The diagnosis in the ADI-R only has two categories, autism or not autism. In order to meet the ADI-R criteria of autism, the score of the subject needs to be equal to or higher than the cut-off in all three domains, and the child's development had been concerned before the age of 3[200]. The algorithm of the ADI-R is provided in Appendix 2.3.

2.3.3.2 Reliability and Validity

The author reported the sensitivity of the ADI-R was low for identifying low-functional individuals[201] and that the communication items did not perform very well in discriminating autism from low-functional mental retardation[202]. Risi and colleagues investigated the validity of the ADI-R within children under 3 years old. The sensitivity of the ADI-R was 82% and specificity was 72%[203]. Studies have reported the ADI-R can significantly differentiate children with autism from non-autistic children as well as typical developing children[27, 204], although its performance was reported as better at identifying Autistic Disorder than Asperger Syndrome[183, 205].

2.3.4 Summary of diagnostic instruments

The combination of the ADOS and ADI-R used both direct observation and interview with parents to identify children with ASC. This approach has been proven to have good validity for case identification of ASC. The adoption of those two instruments improved the comparability of studies on ASC in different regions especially in different countries in the West. However, this approach has not been well adopted in Asia, where there is a large population. This may be partly due to the language barrier.

2.4 Review of prevalence studies of ASC in developed countries

2.4.1 Introduction

The first two sections of this chapter focused on the development and usage of screening and diagnostic instruments used in Western studies. This section will review available prevalence studies on ASC in developed countries where those instruments have been adopted. There have been many reviews focusing on the prevalence studies worldwide. As most of the screening and diagnostic instruments for ASC have been applied to populations in the UK and US[125], and previous review suggested the ASC has been more thoroughly studied in Japan compared to other countries in Asia[72], this review will only focus on the UK, US and developed counties in Asia such as Japan. For studies in other countries, see an extensive review of prevalence studies worldwide[206].

2.4.2 Method

2.4.2.1 Literature search

Literature searches were conducted in two databases: PubMed and Web of Knowledge. This review focuses on prevalence studies conducted in the UK, US and Japan. The bibliographies of previous reviews[2, 125, 207] were also examined to identify published prevalence studies. The search strategy is shown in Box 2.3.

2.4.2.2 Study selection

The inclusion criteria for the review of prevalence studies are shown in Box 2.4. The abstracts of the identified papers were checked by the candidate. In cases where it was uncertain whether a study should be included, the original paper was examined where available.

2.4.2.3 Data abstraction

Within each study, the following variables were extracted: characteristics of the studied population, screen method, diagnostic method, and the prevalence estimate.

Box 2.3 Search strategy for review of prevalence studies on ASC in the UK, US and Japan

PubMed (searched on 1st January 2012)
Years (1966-2011)
Step 1: "Autism"/all subheadings [MeSH] OR "Autistic Disorder"/all subheadings [MeSH] or "Autism Spectrum"/all subheadings [all fields] OR "Pervasive developmental disorder"/all subheadings [MeSH] OR "Asperger"/all subheadings [all fields]
Step 2: "UK"/all subheadings [all fields] OR "Britain"/all subheadings [all fields] OR "USA"/all subheadings [all fields] OR "US"/all subheadings [all fields] OR "America"/all subheadings [all fields] OR "Japan"/all subheadings [all fields] AND results from Step 1
Step 3: "Prevalence"/all subheadings [MeSH] OR "Epidemiology"/all subheadings [MeSH] OR "Screening"/all subheadings [MeSH] AND results in Step 2

Web of Knowledge (searched on 26th January 2011)
Year (1950-2011)
Step 1: "Autism"/ [Topic] OR "Autistic Disorder"/ [Topic] OR "Autism Spectrum"/ [Topic] OR "Pervasive developmental disorder"/ [Topic] OR "Asperger Syndrome"/ [Topic]
Step 2: "UK"/ [Topic] OR "Britain"/ [Topic] OR "USA"/ [Topic] OR "US"/ [Topic] OR "America"/ [Topic] OR "Japan"/ [Topic] AND results from Step 1
Step 3: "Prevalence"/ [Topic] OR "Epidemiology"/ [Topic] OR "Screening"/ [Topic] AND results in Step 2

MeSH (Medical Subjects Headings), The National Library of Medicine controlled vocabulary for indexing articles in PubMed.

Box 2.4 Inclusion criteria for review of prevalence studies on ASC in the UK, US and Japan

1. An original epidemiological research
2. Conducted in a geographically and temporally defined population or clinical settings or mixed
3. A cross-sectional study or data, or first phase of a longitudinal study
4. Have defined criteria for screening and/or diagnostic criteria for autism of autism spectrum conditions
5. Provide information about sample size
6. The target population must be a wide range of children in the general population
7. Includes prevalence estimation
8. Provides clear description of screening methods for initial case identification
9. Provides information about measurements on the final identification of cases such as based on clinical or other diagnostic assessments after initial identification
10. Published in English
11. Peer reviewed paper

2.4.3 Results

2.4.3.1 Study identified

For studies in the UK and US, the literature search identified 418 studies in PubMed database and 319 studies in Web of Knowledge including duplicates. After an initial examination of titles of papers and abstracts against the inclusion criteria, 35 papers from PubMed and 25 papers from Web of Knowledge were identified for further detailed examination. In total, 24 of these studies, which focused on the UK and US met the inclusion criteria and were included in further analysis.

For studies in Japan, the literature search identified 22 studies in PubMed and 112 studies in Web of Knowledge including duplicates. After examination of abstracts, in total 13 studies were included for Japan. Another study recently conducted in South Korea was found during the literature search. Since South Korea is one of the developed countries in Asia, this study was also included in analysis.

2.4.3.2 Study methodology in the UK and US

The 24 population studies focused on the UK and US are shown in Table 2.3. The studied population ranged from 2,536 to 4,590,333 (median=45,599). The age of study samples ranged from 0 to 27 years old.

Ten (42%) studies were prospective, while 14 studies were retrospective using previous diagnostic data for case identification. In the screening phase, four approaches were used to identify possible cases: available records in health system (n=12), questionnaires as screening tool (n=7), letters to clinical settings or schools to elicit referral (n=3), and routine check (n=1). One study used both records and letter of referral for screening. In the diagnostic phase, only five of these studies conducted detailed diagnostic assessment, while the rest confirmed the case status by examining previous diagnostic records. Eight studies used the standard diagnostic instruments such as the ADOS and ADI-R, while the others were given a diagnosis based on international diagnostic criteria only. The diagnostic criteria for final case confirmation included the following: Kanner’s criteria, Lotter’s Rating Scale, DSM-III, DSM-III-R, ICD-10, DSM-IV, and DSM-IV-R.

2.4.3.3 Study methodology in Japan and South Korea

Thirteen Japanese studies and one South Korean study were identified (Table 2.4). Original papers for studies before 1980 were not available and details of these studies were abstracted from previous reviews. The sample size of prevalence studies conducted after 1980 in Japan ranged from 8,537 to 609,848 (median=34,987). The age of study samples ranged from 0 to 18 years old. Five Japanese studies identified cases from the general health examinations conducted by local health centres. This general health examination was reported to have covered the whole local population in identified studies. The Health Checklist 18 was developed as a screening instrument in Japan[208], and DSM-III/IV and ICD-10 were used the diagnostic criteria. Two studies distributed questionnaires or letters to schools and medical institutions for screening, while two studies referred to previous health records to count the number of cases without perspective screening. The studies before 1982 adopted Kanner's criteria for diagnosis of ASC. Later studies adopted ICD-10 or DSM-III/IV as the diagnostic criteria. The study in South Korea adopted a two-stage study design using the ASSQ as the screening instrument, the ADOS and ADI-R as diagnostic instruments, and the DSM-IV as diagnostic criteria[209].

2.4.3.4 Prevalence estimation

The first epidemiological study for the estimation of the prevalence of autism was conducted in England in 1966. Prevalence was reported as 4.5 per 10,000 people among children aged 8 to 10 years old. Since 1985[210], population-based studies reported an prevalence estimate of 4-5 per 1,000 within children under 18 years old[2, 11, 211, 212]. During this period of time, most studies adopted the Kanner's[213] or Rutter's diagnostic criteria. There has been an apparent rise in the reported prevalence since 2000. The median prevalence reported in the UK and US before 2000 was 4.5 per 10,000, while the median prevalence between 2000 and 2009 was 40 per 10,000[214].

In Japan, prevalence estimates increased after each change of diagnostic criteria especially from Kanner (median=2.3/10,000)[215] to DSM-III/ICD-10 (median 15.5/10,000)[216] and DSM-IV (181/10,000)[217]. The highest prevalence estimate was recently reported in the South Korea study in 2011 (264 per 10,000)[209].

Table 2.3 Prevalence studies of ASC in the UK and USA

No	Year	First author	Country	Area	Target population	Age	No. of cases	Prospective (P)/ Retrospective (R)	Screening instruments	Diagnostic criteria	Gender ratio	Prevalence /10,000	95% CI
1	1966	Lotter [218]	UK	Middlesex	78,000	8-10	32	P	Questionnaire	Kanner	2.6 (23/9)	4.5	2.7; 5.5
2	1970	Treffert [213]	USA	Wisconsin	899,750	3-12	69	R	Records	Kanner	3.06 (52/17)	0.7	0.6; 0.9
3	1979	Wing [17]	UK	Camberwell	25,000	5-14	17	R	Records	24 items rating scale of Lotter	16 (16/1)	4.8	2.1; 7.5
4	1987	Burd [2]	USA	North Dakota	180,986	2-18	59	P	Letter to elicit referral	DSM-III	2.7 (43/16)	3.26	2.4; 4.1
5	1989	Ritvo [219]	USA	Utah	769,620	3-27	241	P	Letter to elicit referral	DSM-III	3.73 (190/51)	2.47	2.1; 2.8
6	1997	Webb [220]	UK	South Glamorgan, Wales	73,300	3-15	53	P	Letter to elicit referral	DSM-III-R	6.57 (46/7)	7.2	5.3; 9.3
7	1999	Taylor [221]	UK	North Thames	490,000	0-16	427	R	Records	ICD-10	--	8.7	7.9; 9.5
8	2000	Powell [222]	UK	West Midlands	25,377	0-5	148	R	Records	ADI, ICD-10, DSM-III-R, DSM-IV	--	20.2	15.3; 26.0
9	2000	Baird [223]	UK	South East Thames	16,235	1.5	50	P	Questionnaire-CHAT	ICD-10, ADI-R	15.7 (47/3)	30.8	22.9; 40.6
10	2001	Bertrand [214]	USA	Brick Township, New Jersey	8,896	--	36	R	Records +ADOS-G	DSM-IV	2.2 (25/11)	40.0	28.0; 56.0
11	2001	Fombonne [224]	UK	England, Wales and Scotland	10,438	5-15	27	P	Questionnaire-DAWBA	DSM-IV, ICD-10	8.0 (24/3)	26.1	16.2; 36.0
12	2001	Chakrabatri [225]	UK	Staffordshire	15,500	2.5-6.5	97	P	Routine checks	DSM-IV; ADI-R	3.3 (20/6)	16.8	10.3; 23.2

No	Year	Candidate	Country	Area	Target population	Age	No. of cases	Prospective (P)/ Retrospective (R)	Screening instruments	Diagnostic criteria	Gender ratio	Prevalence /10,000	95% CI
13	2002	Croen [226]	USA	California	4,590,333	5-12	5038	R	Records	DSM-III-R, DSM-IV	4.47 (4116/921)	11.0	10.7; 11.3
14	2002	Scott [184]	UK	Cambridgeshire	43,472	5-11	196	R	Records +letter	ICD-10	8	57	--
15	2003	Yeargin-Allsopp [227]	USA	Atlanta	289,456	3-10	987	R	Records	DSM-IV	4.0 (787/197)	34.0	32; 36
16	2003	Lingam [228]	UK	North East London	186,206	5-14	567	R	Records	ICD-10	4.9 (470/97)	30.4	--
17	2004	Tebruegge [229]	UK	Maidstone district (Kent)	2,536	8-9	21	R	Records	ICD-10	6.0 (19/3)	82.8	47.5; 118.7
18	2005	Fombonne [230]	UK	Staffordshire	10,903	4-6	64	R	Record	ICD-10 ADI-R	6.1 (55/9)	22.0	14.1; 32.7
19	2006	Harrison [231]	UK	Lothian	134,661	0-15	443	P	Questionnaire-CARS,GARS,	ICD-10 ADOS	7.0 (369/53)	44.2	39.5; 48.9
20	2006	Baird [232]	UK	South Thames	56,946	9-10	158	P	Questionnaire-SCQ,DISCO	ICD-10 ADOS, ADI-R	3.3 (121/37)	116.1	90.4; 141.8
21	2007	Latif [179]	UK	South Wales	39,220	0-17	240	R	Records	ICD-10, DSM-IV, Kanner's and Gillerg's criteria	6.8	61.2	54; 69
22	2008	Williams [233]	UK	Avon	14,062	11	86	R	Questionnaire-DISCO,ASDI	ICD-10 ADOS	6.8	51.1	39.2; 62.9
23	2008	Nicholas [234]	USA	South California	47,726	8	295	R	Records	DSM-IV-R	3.1 (224/71)	62.0	56; 70
24	2009	Baron-Cohen [70]	UK	Cambridgeshire	11,700	5-9	52	P	Questionnaire-CAST	ICD-10 ADOS,ADI-R	3.6	157	111; 218

DISCO: Diagnostic Interview for Social and Communication Disorders; ASDI: Asperger Syndrome Diagnostic Interview.

Table 2.4 Prevalence studies of ASC in Japan and South Korea

No	Year	Candidate	Country	Area	Size of target population	Age	Screening instruments	Prospective(P)/ Retrospective(R)	Diagnostic criteria	Gender ratio	Prevalence /10,000
1	1971	Yamazaki [235]	Japan	--	--	2-12	--	--	Kanner	--	2.6
2	1971	Haga [236]	Japan	--	--	≤15	--	--	Kanner	--	1.7
3	1971	Nakai [237]	Japan	--	--	5-14	--	--	Kanner	--	1.1
4	1971	Tanino [215]	Japan	--	--	--	--	--	Kanner	--	2.3
5	1982	Hoshino [238]	Japan	Fukushima Ken	609,848	0-18	Questionnaire	P	Kanner	9.9:1	2.3
6	1983	Ishii [239]	Japan	--	34,987	6-12	Letter to elicit referrals	P	DSM-III		16
7	1987	Maisuishi [216]	Japan	Kurume City	32,834	4-12	Records	R	DSM-III	4.7:1 (42/9)	15.5
8	1988	Tanoue [208]	Japan	Ibaraki	507,003	≤7	Questionnaire-Health checklist-18	P	DSM-III	4.1:1	13.9
9	1989	Sugiyama [240]	Japan	Nagoya	12,263	1.5	Questionnaire-Health checklist-18	P	DSM-III	2.1:1	13
10	1992	Ohtaki [241]	Japan	Chikugo City	35,366	6-14	Records	R	DSM-III-R		11.7
11	1996	Honda [242]	Japan	Yokohama	8,537	≤5	Questionnaire-Health checklist-18	P	ICD-10	2.6:1	21.1
12	2005	Honda [243]	Japan	Yokohama	35,716	≤5	Questionnaire-Health checklist-18	P	ICD-10	2.5:1	19
13	2008	Kawamura [217]	Japan	Toyota	12,589	5-8	Questionnaire-Health checklist-18	P	DSM-IV	2.8:1	181
14	2011	Kim [209]	South Korea	Ilsan district of Goyang City	55,266	7-12	Questionnaire ASSQ	P	DSM-IV ADOS, ADI-R	2.5:1	264

2.4.4 Discussion

2.4.4.1 Prevalence estimates in the same region

Prevalence studies that were conducted in the same region in different calendar years suggested an increase of prevalence over time. Baird and colleagues conducted a prevalence study in South East Thames in 2000[223]. In this study, a population of 16,235 children aged 18 months old were screened using the Checklist for Autism in Toddlers (CHAT) to identify Childhood Autism. The prevalence for Childhood Autism in this study was 30.8 per 10,000 (95% CI: 22.9-40.6). In 2006[232], the same research group conducted another study in a target population of 56, 946 aged 9 to 10 in South Thames. This research screened all children with a clinical diagnosis of ASD through local health services as well as those at risk of being undiagnosed through the special needs registration system. This study estimated the prevalence of Childhood Autism as 38.9 per 10,000 and 116.1 per 10,000 for ASC. Similarly, Fombonne and colleagues conducted a prevalence study in 2001[225] within a population of 15,500 in Staffordshire. They reported a prevalence of 16.8 per 10,000 for Childhood Autism. This research relied on the national framework of Child Health Surveillance to screen children who were between 2.5 and 6.5 years old, followed by an assessment by a multidisciplinary team using the ADI-R. Four years later, in 2005[230], the same research group conducted another prevalence study in Staffordshire in a population of 10,903. All children aged between 4 and 6 were screened through the same Child Health Surveillance system and suspected children were assessed using the same methodology as in 2001. The estimated prevalence of Childhood Autism in this study was 22.0 per 10,000. In Cambridgeshire, Baron-Cohen and colleagues conducted prevalence studies in 2002[184] and 2009[70] using the same methodology which showed the estimated prevalence of ASC increased from 57 to 157 per 10,000. Studies that estimate prevalence of ASC in the same region in the West suggested an increase in prevalence estimates.

2.4.4.2 Preliminary comparison of prevalence estimates between the West and East

Most recent studies[70, 244] in the West estimate the prevalence of ASC to be around 100 per 10,000 (1%)[245]. In Asia, the prevalence of ASC has been investigated more thoroughly in Japan and recently in South Korea. After the DSM-III was adopted as

the diagnostic criteria[18], the reported prevalence for Childhood Autism has increased. The median prevalence before 1980 was 2.3 per 10,000[215], while it was 14.7 per 10,000 between 1980 and 2005. Five studies in Japan used similar research methodology which adopted the Health Checklist 18 for national screening in healthcare system since 1988 until now[208, 217, 240, 243]. The most recent study reported the prevalence of ASC in Japan is 181 per 10,000[217]. In 2011, Fombonne and colleagues conducted a prevalence study which focused on a total population of 55,266 aged 7 to 12 years in South Korea[209]. This research adopted comparable methodology for case identification with the Western studies, which estimated the prevalence of ASC as 189 per 10,000 in mainstream schools and 75 per 10,000 in special schools in South Korea. Both Japan and South Korea have very different culture and genetic backgrounds compared with the UK and US. Although there was variance between studies, it appears that the prevalence estimates were similar when comparable methodologies for case identification were adopted.

2.4.4.3 Possible reasons for prevalence variation

Because of the apparent increase in prevalence estimates, there has been considerable debate about whether there is an "autism epidemic" over the last two decades[11, 246]. During these discussions, besides the possibility that there has been a real increase in prevalence of ASC, several reasons have been proposed by researchers as potential explanations for the current high prevalence: 1) the broader definition of autism and possible diagnostic substitution[247]; 2) change in diagnostic criteria; 3) the development in screening and diagnostic instruments[50]; 4) change in research methodology[248]; 5) geographical differences among targeted population in different studies. A more detailed explanation of those proposed reasons can be found in Appendix 2.3.

2.5 Summary of the case identification in research on ASC in developed countries

The current situation of ASC has been investigated most thoroughly in developed countries. Recent developed screening instruments have been more age-specific and designed to identify milder cases on the spectrum. The validity of those instruments varied but few of them have been validated in the general population. The adoption of the standardised diagnostic instruments, the combination of ADOS and ADI-R, has

improved the comparability and consistency among studies in different regions. Using advanced screening and diagnostic instruments, recent prevalence studies have reported an increase in prevalence estimates than before in developed countries.

While there have been prevalence studies on ASC in Japan and South Korea, the current situation in China, which has a huge population, is largely unknown. One of the possible reasons is the lack of validated screening instruments and the standardised diagnostic instruments. It would be valuable to conduct research to investigate the reliability and validity of well-developed screening and diagnostic instruments in Chinese population in order to further investigate the prevalence of ASC in China. The results from such study could then be compared with those from other countries. In the next Chapters 3 and 4, systematic reviews were conducted to examine available prevalence studies on ASC and identify current used screening and diagnostic instruments for ASC in China.

Chapter 3 Systematic Review of Prevalence Studies on ASC in Mainland China, Hong Kong and Taiwan

3.1 Introduction

In order to investigate the available literature on the prevalence of ASC in China, this chapter presents a systematic review of studies examining the prevalence of ASC in mainland China, Hong Kong and Taiwan. The aims of this chapter are: to identify all available studies on the prevalence of ASC in these three regions; to assess the quality of this research through synthesising their characteristics; and to evaluate the effects of the chosen research methodology on the prevalence estimates.

3.2 Method

3.2.1 Literature searches

A systematic literature search for prevalence studies of ASC in China was conducted in December 2011 within four databases. Two were English databases (PubMed and Web of Knowledge). The other two were Chinese databases (China Web of Knowledge and Weipu), which were two of the biggest Chinese scientific databases. Based on previous experience with literature review in Chinese databases, in order to capture all the existing studies on this topic in Chinese databases, broader search terms were used in the second search. The search strategy is shown in Boxes 3.1&3.2. In addition, the bibliographies of previous reviews were examined to identify published prevalence studies[11, 72, 125]. All the searches were conducted twice.

Box 3.1 Search strategy for identifying prevalence studies in English databases

PubMed (searched on 16th December 2011)
Years (1966-2011)
Step 1: "Autism"/all subheadings [MeSH] OR "Autistic Disorder"/all subheadings [MeSH] or "Autism Spectrum"/all subheadings [all fields] OR "Pervasive developmental disorder"/all subheadings [MeSH] OR "Asperger"/all subheadings [all fields]
Step 2: "China"/all subheadings [all fields] OR "Hong Kong"/all subheadings [all fields] OR "Taiwan"/all subheadings [all fields] AND results from Step 1
Step 3: "Prevalence"/all subheadings [MeSH] OR "Epidemiology"/all subheadings [MeSH] OR "Screening"/all subheadings [MeSH] AND results in Step 2

Web of Knowledge (searched on 16th December 2011)
Year (1950-2011)
Step 1: "Autism"/ [Topic] OR "Autistic Disorder"/ [Topic] OR "Autism Spectrum"/ [Topic] OR "Pervasive developmental disorder"/ [Topic] OR "Asperger Syndrome"/ [Topic]
Step 2: "China"/ [Topic] OR "Hong Kong"/ [Topic] OR "Taiwan"/ [Topic] AND results from Step 1
Step 3: "Prevalence"/ [Topic] OR "Epidemiology"/ [Topic] OR "Screening"/ [Topic] AND results in Step 2

MeSH (Medical Subjects Headings) The National Library of Medicine controlled vocabulary for indexing articles in PubMed.

Box 3.2 Search strategy for identifying prevalence studies in Chinese databases

Search 1:
Weipu database (searched on 17th December 2011)
Years (1989-2011)
Step 1: "Gu Du Zheng (Autism)"/ [Key words] OR "Zi Bi Zheng (Autism)/ [Key words] OR "Gudu Zheng Pu Xi Zhang Ai (Autism Spectrum)"/ [Key words] OR "Gu Fan Xing Fa Yu Zhang Ai (Pervasive developmental disorder)"/all [Key words] OR "A Si Be Ge (Asperger)"/ [Key words]
Step 2: "Prevalence"/ [Key words] OR "Epidemiology"/ [Key words] OR "Screening"/ [Key words]) AND results in Step 1
China Web of Knowledge (searched on 18th December 2011)
Year (Until 2011)
Step 1: "Gu Du Zheng (Autism)"/ [Key words] OR "Zi Bi Zheng (Autism)/ [Key words] OR "Gudu Zheng Pu Xi Zhang Ai (Autism Spectrum)"/ [Key words] OR "Guang Fan Xing Fa Yu Zhang Ai (Pervasive developmental disorder)"/ [Key words] OR "A Si Be Ge Zheng (Asperger)"/ [Key words]
Step 2: "Prevalence"/ [Key words] OR "Epidemiology"/ [Key words] OR "Screening"/ [Key words] AND results in Step 1
Search 2:
Weipu database/China Web of Knowledge (searched on 18th December 2011)
Year (Until 2011)
"Gu Du Zheng (Autism)"/ [Key words] OR "Zi Bi Zheng (Autism)"/ [Key words]

3.2.2 Study selection

Identified papers were examined against inclusion criteria by the candidate. All the abstracts were reviewed. When it was not clear from the abstract whether the paper should be included, the paper itself was examined when possible. Where the papers were not available, the corresponding authors were contacted. If there was more than one published paper on a particular study, the paper with the most recent data was included in the review. The inclusion criteria are shown in Box 3.3.

Box 3.3 Inclusion criteria for identifying prevalence studies in China

1. An original epidemiological research
2. Conducted in a geographically and temporally defined population or clinical settings or mixed
3. A cross-sectional study or data, or first phase of longitudinal study
4. Have defined criteria for screening and/or diagnostic criteria for autism of autism spectrum conditions
5. Provide information about sample size
6. The target population must be a wide range of children in the general population
7. Includes prevalence estimation
8. Provides clear description of screening methods for initial case identification
9. Provides information about measurements on the final identification of cases such as based on clinical or other diagnostic assessments after initial identification
10. Published in English in English databases and in Chinese in Chinese databases
11. Peer reviewed paper

3.2.3 Data abstraction

Following the removal of duplicates, the following variables were extracted from each paper: sample characteristics (year of publication, sample age, sex, region, location) sampling strategy, screening methods, diagnostic criteria, instrument response rate, and prevalence estimation measures.

3.2.4 Analysis

Crude prevalence estimates, confidence intervals (CI) and study details were extracted from each paper where available. The identified studies were divided into two groups based on diagnosis: 1) Childhood Autism: included all studies that had provided a prevalence estimate for Childhood Autism, or Autistic Disorder; 2) ASC: included all

studies that estimated the prevalence for the whole autism spectrum. Forest plots were drawn to visualise the extent of heterogeneity among studies.

A random effects meta-analysis was used to estimate the overall prevalence and investigate the heterogeneity between studies. CI was calculated from the crude prevalence estimates if not available. The extent of heterogeneity was estimated by calculating I^2 (values of 25%, 50%, and 75% representing low, medium, and high heterogeneity, respectively)[249]. The proportion of between-study variance explained by the covariates was estimated using adjusted R^2 values. Meta-regression was used to estimate the effect of the following covariates on the log odds of the outcome: age group, year of publication, publication period, area, sample source, sample size, screening method, screening instrument, screening informants, diagnostic tool, diagnostic criteria, and diagnostic informant. Each covariate was included separately, and then a multivariable meta-regression model was constructed including all covariates with a statistically significant (p<0.05) association in the univariate analyses.

3.3 Results

3.3.1 Studies identified

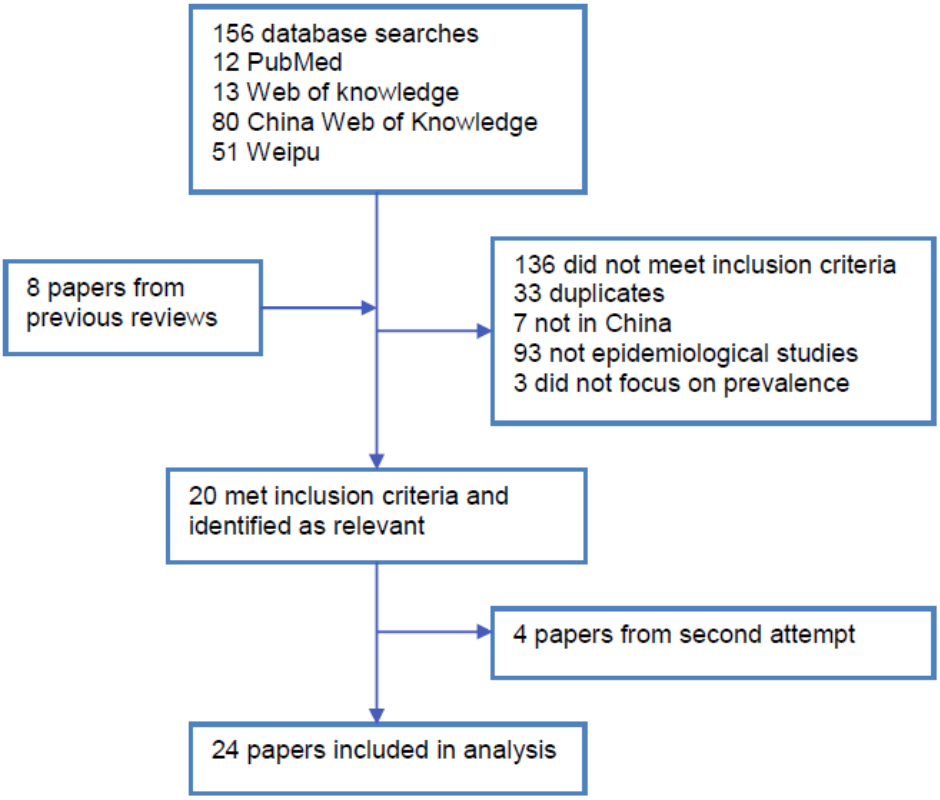
Of 6,226 abstracts, 24 papers that met inclusion criteria were identified (Figure 3.1). Twenty-one studies were conducted in mainland China, two studies in Taiwan, and one study in Hong Kong (Table 3.1). In all of the studies, information about other minority populations other than the Chinese population was generally unavailable. One paper reported two prevalence studies within two different age groups using different methodology. This paper was considered as two studies in the following analyses[250]. Thus, there were 25 studies in total identified for this review.

3.3.2 Study description

The population size of the reviewed prevalence studies ranged from 660 to 4,247,206 with a median sample size of 7,238 people. Two studies aimed to represent the whole region of Hong Kong[251] and Taiwan[252], while one study was generated from the records of the national survey for disability in mainland China[253]. The ages of the participants included in the studies ranged from 1 to 97, within which 23 studies

focused on children aged 0-6 and 12 studies on children aged 6-14 (Box 3.4 & Appendix 3.1).

Figure 3.1 Flowchart of systematic review of prevalence studies of ASC in China



Box 3.4 Study descriptions of reviewed studies

Study location:
- Mainland China: 21 studies
- Taiwan: 2 studies
- Hong Kong: 1 study

Age range;
- 0-2 years old: 6 studies
- 2-6 years old: 17 studies
- 6-12 years old: 5 studies
- 12-14 years old: 4 studies
- 14-17 years old: 3 studies

Study region:
- Urban: 14 studies
- Mixed: 10 studies
- Rural: 1 study

3.3.3 Sampling strategy

There were four sample sources: 1) Clinical case counting in psychological clinics: two studies[75, 254]; 2) Case counting from hospital records in the national health system: two studies[252, 255]; 3) Random selection from local kindergartens: five studies[256-259] and one sample was from primary schools[260]; 4) Random selection from the general population: Fourteen studies selected the sample using a two-stage approach. The first stage was stratification of the general population followed by randomized sampling from the stratified sample. There were five methods of sampling including case counting, randomized sampling, whole sample, clustered probability sampling and cluster-randomized sampling. More details of sampling are provided in Appendix 3.2.

3.3.4 Screening methodology

Other than three studies which did not conduct screening but instead identified cases from existing health records[75, 252, 255], screening was conducted using the following approaches: 1) prospective screening in clinics (n=1)[254]; 2) face-to-face interviews with a questionnaire (n=19); 3) postal questionnaires (n=1)[261]; 4) postal questionnaires followed by face-to-face interviews (n=1)[262]. Five studies conducted a second screening phase, while 17 studies only conducted one screening phase. Within the first screening phase, four instruments were used including the Clancy Autism Behaviour Scale[172] (CABS) (n=15), the Autism Behaviour Checklist[143] (ABC) (n=3), the Checklist for Autism in Toddlers[50] (CHAT) (n=3), the Autism Spectrum Disorder in Adults Screening Questionnaire[263] (ASDASQ) (n=1). For the second screening, three studies used the ABC and two used the Childhood Autism Rating Scale (CARS)[135]. Of the 25 studies, seven studies reported the validity of the screening instruments that had been previously established in other studies.

3.3.5 Diagnostic methodology

In the diagnostic phase, studies generally did not provide details about the diagnostic procedure. Three studies considered the screening results to be the final diagnosis without any additional diagnostic assessment. Twelve studies reported that the diagnosis was made according to clinical judgement using international diagnostic criteria without using any diagnostic instrument. Twelve studies adopted the CARS as the diagnostic instrument and one study adopted both the CARS and the Autism Diagnostic Interview-Revised (ADI-R)[180]. Thirteen studies confirmed the diagnosis

by clinicians conducting an interview with the parents or caregivers, of which eleven studies reported the interrater agreement between the clinicians using Kappa's agreement while the other two studies used percentage agreement. More details are provided in Appendix 3.3.

Six different types of diagnostic criteria were used for case ascertainment which determined a prevalence estimate for autism: 1) Rutter's criteria (n=1); 2) Chinese Children Mental Diagnosis, 2nd edition revised (CCMD-2-R)[264] (n=5); 3) Diagnostic and Statistical Manual of Mental Disorders, 3rd edition revised (DSM-III-R)[23] (n=1); 4) DSM-IV[4] (n=13); 5) International Classification of Disease, 10th revision (ICD-10)[1] (n=2); 6) ICD-9 (n=1). (See Appendix 3.4 for CCMD-2-R criteria for autism)

3.3.6 Response rate and participation rate

Twenty-one studies reported response rates at the screening phase. In the reviewed prospective studies, participation rates in the diagnostic phase were not directly reported since these studies conducted the screening and diagnosis during a single appointment. In these cases, when the child scored above the cut-off on the screening instrument, the diagnostic assessment was conducted immediately. Therefore, these studies only reported the final participation rate following the diagnostic phase. Where no information was provided about the children who were not assessed in the diagnostic phase, the participation rate was assumed to be 100%, which assumes that all children who screened positive completed a further diagnostic assessment during the analysis.

3.3.7 Prevalence estimation

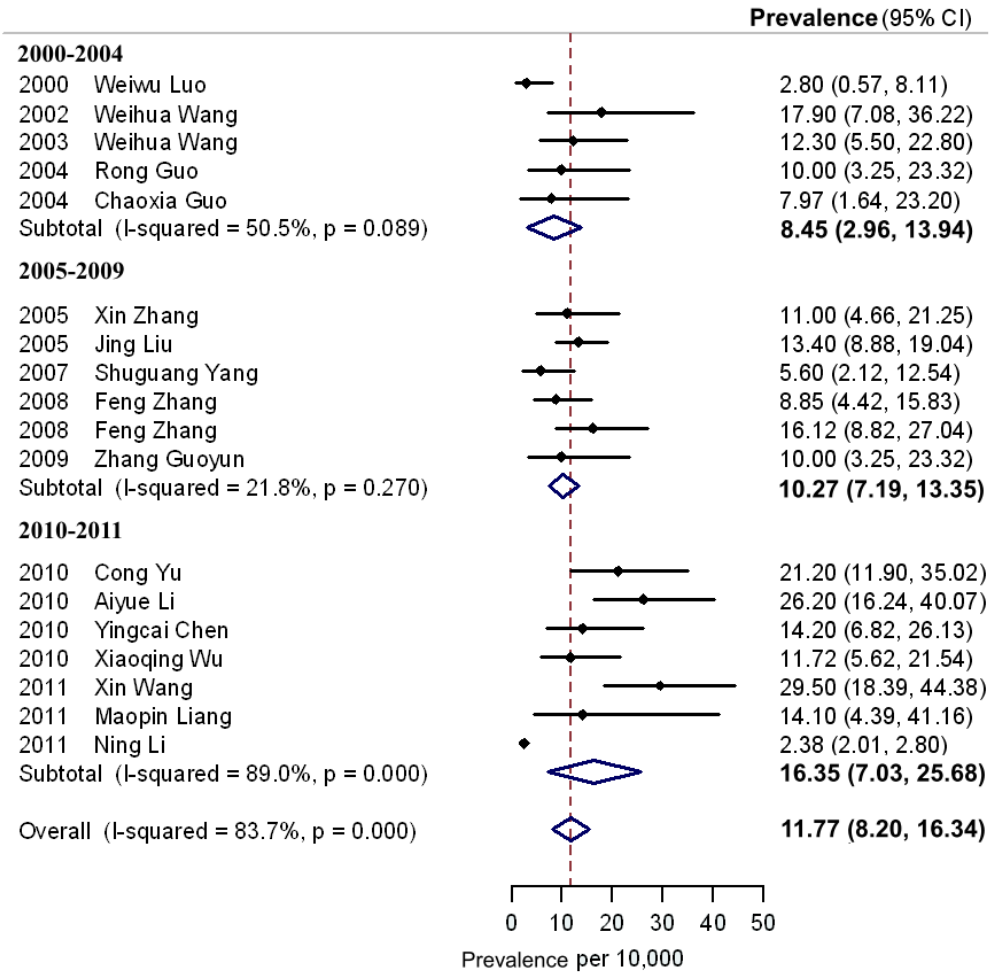
Twenty-two studies provided prevalence estimates for Childhood Autism. Seven studies provided prevalence estimates for ASC (appendix 6), of which four studies also investigated the prevalence of other subtypes, including atypical autism and pervasive developmental disorder not otherwise specified (PDD-NOS)[256, 261, 262, 265]. Eighteen studies conducted both screening and diagnostic assessments for identifying cases of Childhood Autism in mainland China (Figure 3.2). The pooled prevalence estimate for Childhood Autism among these 18 studies was 11.8 per 10,000 (95% CI : 8.2, 15.3). The pooled prevalence estimate for ASC was 26.6 per 10,000 (95% CI: 18.5, 34.6). More details are provided in Appendix 3.5.

Table 3.1 Characteristics of the populations studied in reviewed studies

No	Year	First author	Region	Sample size	Area	Age	Sample screened	Screen methods	Screen tools	Cut-off	Response rate	P/R	Diagnostic tools	Diagnostic criteria	Childhood Autism Prevalence/SE (per 10,000)	ASC Prevalence/SE (per 10,000)
1	1987	Tao[75]	Mainland	457,200	Urban	3-8	C	R	N/A	N/A	N/A	R	N/A	Rutter	0.32 (0.08)	-
2	2000	Luo [266]	Mainland	10,802	Mixed	2-14	SG	QI	ABC	31	100%	P	N/A	CCMD-2-R, DSM-III-R	2.8 (1.60)	-
3	2002	Wang [259]	Mainland	3.978	Urban	2-6	K	QI	CABS*	7	98.3%	P	CARS	CCMD-2-R	17.9 (6.70)	-
4	2002	Ren [267]	Mainland	3,559	Urban	3-5	SG	QI	CABS	14	99.1%	P	N/A	N/A	250 (2.31)	-
5	2003	Wang [268]	Mainland	7,488	Mixed	2-6	SG	QI	CABS	7	98.08%	P	CARS	CCMD-2-R	12.3 (4.05)	-
6	2003	Chang [254]	Taiwan	660	Mixed	15-93	C	C	ASDASQ	5	100%	P	N/A	DSM-IV	-	60.0 (30.06)
7	2004	Guo [269]	Mainland	5,000	Urban	0-6	WP	QI	CABS	7	99.1%	P	CARS	CCMD-2-R	10 (4.47)	-
8	2004	Guo [270]	Mainland	3,776	Rural	2-6	SG	QI	CABS	7	100%	P	CARS	DSM-IV	8 (4.59)	-
9	2005	Zhang [271]	Mainland	7,416	Urban	2-6	SG	QI	CABS	7	99%	P	CARS	DSM-IV	11.0 (3.85)	-
10	2005	Zhang [258]	Mainland	1,305	Urban	3-7	K	QI	CABS	14	100%	P	N/A	N/A	19.9 (2.47)	-
11	2005	Liu [272]	Mainland	21,866	Mixed	2-6	SG	QI	CABS	7	100%	P	CARS	DSM-IV	13.4 (2.47)	15.3 (2.64)
12	2007	Yang [260]	Mainland	10,412	Urban	3-12	PS	QI	ABC	31	100%	P	N/A	DSM-IV	5.6 (2.32)	-
13	2008	Wong [255]	Hong Kong	4,247,206	Mixed	0-14	HS	R	N/A	N/A	N/A	R	CARS, ADI-R	DSM-IV	-	16.1 (0.19)
14	2008	Zhang [250]	Mainland	8,681	Urban	2-3	SG	QI	CHAT	N/A	100%	P	CARS	DSM-IV	16.1 (4.3)	-
15	2008	Zhang [250]	Mainland	12,430	Urban	4-6	SG	QI	CABS	14	100%	P	CARS	DSM-IV	8.85 (2.7)	-
16	2009	Zhang [273]	Mainland	5,000	Urban	0-6	SG	QI	CABS	7	99.98%	P	CARS	CCMD-2-R	10.0 (4.47)	-
17	2009	Wang [257]	Mainland	4,156	Urban	2-6	K	QI	CABS	14	100%	P	N/A	N/A	19.5 (6.84)	-
18	2010	Li [274]	Mainland	8,006	Mixed	1.5-3	SG	QI	CHAT	N/A	92.99%	P	CARS	DSM-IV	26.2 (5.71)	-
19	2010	Wu [275]	Mainland	8,532	Urban	0-3	SG	QI	CHAT	N/A	100%	P	CARS	DSM-IV	8.2 (3.10)	-
20	2010	Yu [262]	Mainland	7,059	Mixed	2-6	SG	Q	CABS	7	89.7%	P	N/A	DSM-IV	21.2 (5.47)	22.7 (5.66)
21	2010	Chen [261]	Mainland	7,034	Mixed	2-6	SG	Q	CABS	7	98.78%	P	CARS	DSM-IV	14.2 (4.49)	24.2 (5.86)
22	2011	Wang [256]	Mainland	7,500	Urban	2-6	K	QI	CABS	14	87.8%	P	N/A	DSM-IV	29.5 (6.26)	75.4 (9.99)
23	2011	Liang [276]	Mainland	2,485	Urban	3-6	K	QI	CABS	14	100%	P	N/A	DSM-IV, ICD-10	14.1 (7.53)	-
24	2011	Li [253]	Mainland	616,940	Mixed	0-17	SG	QI	ABC	N/A	N/A	P	N/A	ICD-10	2.38 (0.20)	-
25	2011	Chien [252]	Taiwan	372,642	Mixed	0-17	HS	R	N/A	N/A	N/A	R	N/A	ICD-9	-	28.7 (0.88)

Sample screened: C: Clinical patients; SG: Stratified general population; K: Kindergartens; WP: Whole population; PS: Primary Schools; HS: Population in health system; Screen methods: R=Records; QI=Questionnaire based interview; C= Clinical referral; Q=Questionnaire distribution. ABC: Autism Behaviour Checklist; CABS: Clancy Autism Behavioural Scale; ASDASQ: Autism Spectrum Disorder in Adults Screening Questionnaire; CHAT= Checklist for Autism in Toddlers; CARS: Childhood Autism Rating Scale; P: Perspective; R: Retrospective.

Figure 3.2 Prevalence estimates of Childhood Autism (n=18)



3.3.8 Investigation of heterogeneity among studies on Childhood Autism

The heterogeneity of the prevalence estimates among the 22 studies on Childhood Autism was very high (I^2=93.4%). In further analyses, four studies on Childhood Autism were excluded since one was case counting of hospital records and three only conducted screening without a diagnostic phase[256, 258, 267]. The heterogeneity of 18 studies was reduced but still high (I^2=83.7%). The heterogeneity of the seven studies describing the prevalence of ASC was also high (I^2=97.4%).

The pooled prevalence estimate increased over time. Between the years 2000 and 2004, the pooled prevalence estimate was 8.5 per 10,000 (range: 3.0, 13.9), which increased to 10.3 per 10,000 (range: 7.2, 13.4) between 2005 and 2009. The estimate was the highest in the past two years (2010-2011) at 16.4 per 10,000 (range: 7.0, 25.7). The prevalence estimates were higher when using the CABS (12.8 per 10,000) and the CHAT (17.0 per 10,000) as screening instruments, rather than using the ABC (2.4 per 10,000). The heterogeneity was very low among studies using the ABC (I^2=0.0%) (Figure 3.3).

Only the studies that conducted both screening and diagnostic assessment for Childhood Autism were examined using meta-regression since the recommended minimum number of studies for inclusion in a meta-regression analysis is ten[277]. There was a significant association between the use of screening instruments and the prevalence of Childhood Autism (Table 3.2). The prevalence estimates for Childhood Autism in studies using the ABC as the screening instrument was 79% lower than those studies using the CABS (odds ratio: 0.21; 95%CI: 0.11, 0.38) (p<0.001). The prevalence estimates from studies using the CHAT were 25% higher than those using the CABS (odds ratio: 1.25; 95%CI: 0.71, 2.21), but the confidence interval was wide and included 1.0.

In three age groups (<4, 4, >4 years old), the prevalence estimates in studies with children older than 4 years old were significantly lower than estimates in younger children (odds ratio: 0.32; 95%CI: 0.16, 0.68). However, this result is dependent on three very large studies. If these three studies with the largest sample size were excluded, this association was not observed (p=0.33). No significant association was observed between the prevalence estimate and group sample size (≤5000, 5000-7500,

>7500). No other covariates were found to have a significant association with the prevalence estimates. Among 18 studies focusing on Childhood Autism in mainland China, the different choice of screening instruments explained 77% of the between-study variance (R^2=77% I^2=45%). The age group of the children explained 56% (R^2=56%, I^2=71%).

A meta-regression model was constructed which included screening instrument and age group (Table 3.3). This model explained much of the heterogeneity between the studies (R^2=81%, I^2=44%). In this model, after adjusting for the age group, the odds ratio for ASC in studies using the ABC as the screening instrument was 0.29 compared with the CABS (95% CI: 0.12, 0.69; p=0.009), whereas studies using the CHAT had higher rates (OR: 1.79; 95% CI: 0.70, 4.55; p=0.20). After adjusting for the screening instrument, age group no longer showed a significant effect.

Figure 3.3 Prevalence estimates of Childhood Autism and screening instruments

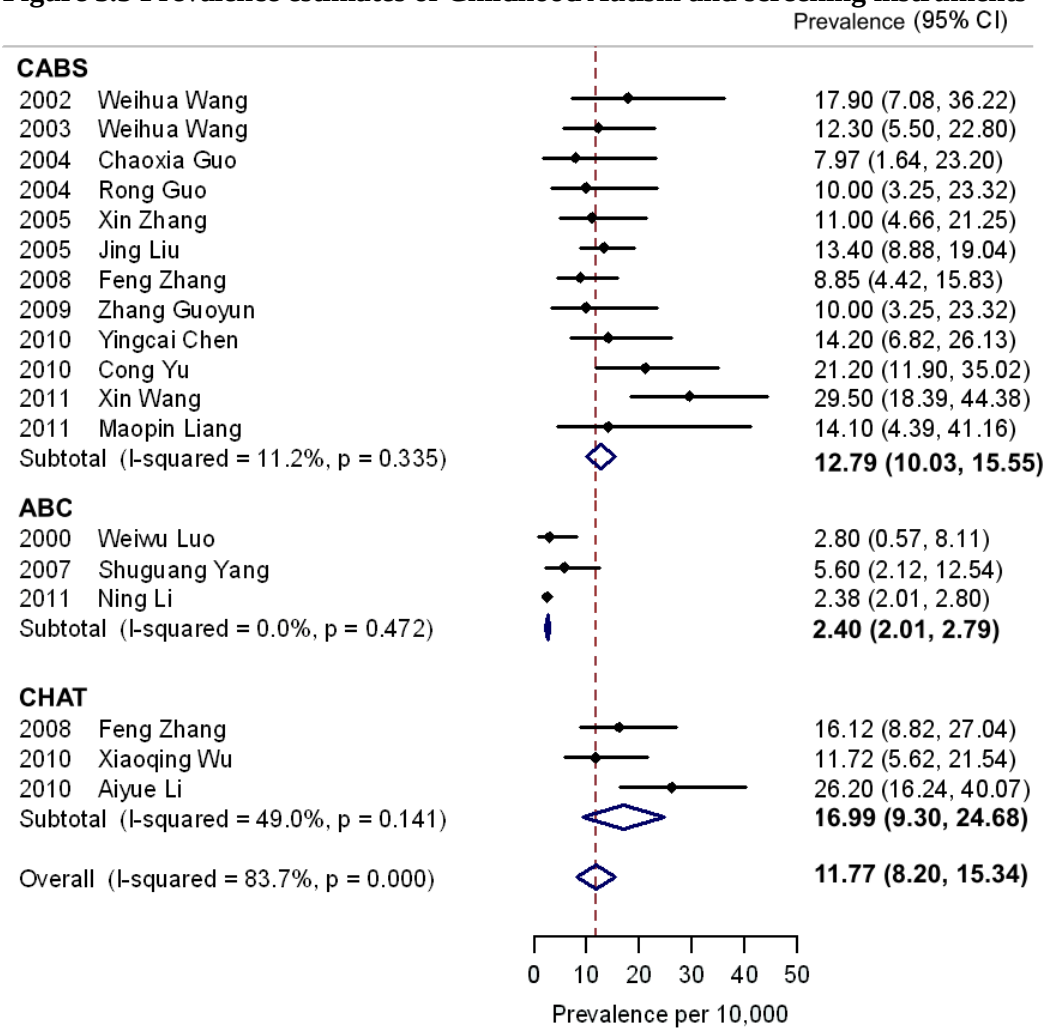


Table 3.2 Results of meta-regression for studies of Childhood Autism, univariate analysis (n=18)

Covariate	Categories of covariate	No. of studies	Odds ratio	95%CI	P-value	Variance explained (%)
No covariates		18				
Year (continuous)		18	1.04	(0.93, 1.17)	0.43	-5.09
Year (categorical)	2000-2004	5	1.00	--	--	-10.92
	2005-2009	6	1.13	(0.42, 3.08)	0.80	
	2010-2011	7	1.44	(0.55, 3.77)	0.43	
Age group	<4	5	1.00	--	--	56.00
	4	8	1.06	(0.56, 2.02)	0.84	
	>4	5	0.33	(0.16, 0.68)	0.005	
Area	Urban	9	1.00	--	--	-8.40
	Mixed or rural	8	0.81	(0.38, 1.75)	0.57	
	Rural	1	0.64	(0.09, 4.37)	0.62	
Sample group	≤5000	5	1.00	--	--	7.43
	5000-7500	5	1.43	(0.54, 3.80)	0.44	
	>7500	8	0.74	(0.30, 1.80)	0.48	
Sample source	Population-based	13	1.00	1.00		-0.19
	Schools or kindergartens	4	1.44	(0.60, 3.48)	0.39	
Screening method	Interview	15	1.00	--	--	-0.89
	Questionnaire	2	1.64	(0.54, 4.98)	0.36	
Screening tool	CABS	12	1.00	--		76.99
	ABC	3	0.21	(0.11, 0.38)	<0.001	
	CHAT	3	1.25	(0.71, 2.20)	0.42	
Time	Once	13	1.00	1.00		-2.10
	Twice	4	1.40	(0.60, 3.27)	0.41	
Screening informant	Clinician	8	1.00	--	--	-13.86
	Parent	3	0.93	(0.31, 2.75)	0.88	
	Research	6	0.90	(0.38, 2.10)	0.79	
Diagnostic criteria	CCMD-2-R	5	1.00	--	--	-5.34
	DSM-III-R/DSM-IV/ICD-10	12	1.23	(0.52, 2.87)	0.62	
Diagnostic tool	None	6	1.00	--		2.54
	CABS	11	1.51	(0.71, 3.21)	0.27	
Diagnostic informant	Clinician	13	1.00	--	--	8.19
	Researcher	4	0.47	(0.19, 1.17)	0.10	

Table 3.3 Multivariable meta-regression results for studies of Childhood Autism (n=18)

Covariate	Categories of covariate	No. of studies	Odds ratio	95%CI	P-value	Variance explained R^2 (%)
Age group	<4	5	1.00	--	--	
	4	8	1.61	(0.68, 3.81)	0.26	
	>4	5	1.03	(0.34, 3.04)	0.96	
Screening tool	CABS	12	1.00	1.00	--	80.7
	ABC	3	0.29	(0.12, 0.69)	0.009	
	CHAT	3	1.79	(0.70, 4.55)	0.20	

3.4 Discussion

3.4.1 Main findings on prevalence

There was a high degree of heterogeneity and a large amount of variation in the prevalence estimates among the reviewed studies. In mainland China, the pooled prevalence estimate for Childhood Autism was 11.8 per 10,000 (95% CI: 8.2, 15.3) and the pooled prevalence estimate for ASC was 26.6 per 10,000 (95% CI: 18.6, 34.6) in China.

3.4.2 Research methodology and prevalence estimates

The covariate most strongly associated with variation in the prevalence estimates for Childhood Autism was the choice of screening instrument. The association between screening instrument and prevalence estimates has been investigated in Western studies[131, 278, 279]. The ABC and CABS (which were developed in the 1980s from the West) were introduced to Chinese autism research much earlier than the CHAT. The studies using the ABC as the screening instrument reported the lowest prevalence estimates, while studies using the CHAT reported the highest estimates for Childhood Autism. However, there have been only three studies using either the ABC or the CHAT to date. The comparison of the effect of screening using the ABC or the CHAT on the prevalence estimates is therefore limited. In this review, the age group of the children screened was also found to be strongly associated with the prevalence estimate. However, this association disappeared when adjusting for the screening instrument. This may be due to the fact that recently developed screening instruments have specifically determined age ranges, while older measures included participants with a wider age range. After adjusting for age group, the prevalence estimates for Childhood Autism generated from studies using the ABC as the screening instrument was 70% lower than those using the CABS, and the prevalence estimates in studies using the CHAT was 80% higher than those using the CABS.

The multi-regression model including the age group and screening instrument explained the most among-study variation in studies of Childhood Autism. However, there are differences between studies in developed countries and Chinese studies. These differences might include the following: 1) Population characteristics: due to missing information of the target population, it is difficult to evaluate the

generalisability of the sample for a whole region in China and make comparisons to other countries. In addition, service development for special education and healthcare systems were different in mainland China, Hong Kong and Taiwan; 2) Administration of screening by face-to-face interview is not common in studies in developed countries; many identified studies in this review were based on samples from the stratified general population, while large population based studies in developed countries used whole population distribution of a screening questionnaire[70]; Screening using two instruments is not common in studies in developed countries and which instrument was administrated first was not clear in these reviewed studies. If a second screening test is applied only to screen positives following the first screening, it is generally considered to increase the specificity by reducing the false-positives compared with a single test[58]. If the two screenings were done simultaneously, this might lead to higher sensitivity as the children that had been missed by the first screening instrument may have been identified to be at risk for ASC by the second screening instrument[280]; the cut-off of the same screening instruments varied among studies; 3) In the diagnostic phase, four prospective studies considered the screening results to be the diagnostic results; standardised diagnostic instruments were not adopted in Chinese studies; information on the reliability and quality control of the diagnostic process was generally lacking and assessors were not blind to the screen status of the children when making a diagnostic evaluation; children whose screen results were negative were not given a diagnostic assessment.

3.4.3 Limitations

There are several limitations of this review. First, the studies reviewed were selected from two English and two Chinese databases, and no other databases were searched. Thus, it is possible that papers that were not published in mainstream journals were not identified which may have reported different results. However, the four databases were searched systematically using a consistent approach with a second attempt of one by one checking. Thus, it is unlikely that the reviewed papers are biased with respect to prevalence estimates reported. The number of studies included in the meta-analysis was limited, with only 18 for Childhood Autism and seven for ASC. Meta-regression of studies for ASC was not conducted due to the limited number of available studies. There were a limited number of studies conducted in Hong Kong and Taiwan. Due to the differences among regions, caution should be employed when

applying the results from mainland China to Hong Kong and Taiwan. Due to the limited number of studies available in rural area, it was impossible test the heterogeneity among studies for this factor. The prevalence of ASC may be lower in rural area since less diagnostic and intervention services are available in such areas in mainland China. The coding approach of covariates may have affected the detected association with prevalence estimates, such as the approach of categorising the diagnostic criteria and using the age groups. Since information on the process of screening and diagnosis was often missing, an assumption was made about the participation rate in the assessment phase. It would be helpful to have further information about the specific details where this information was missing. Only the impact of quantifiable covariates on prevalence estimates was assessed in this review. Potential qualitative influences on prevalence such as public awareness and the recognition of ASC were not included.

3.5 Conclusion and implications for further research

This review revealed major differences in research methodology for estimating prevalence between China and the developed countries. In the future, in order to make comparisons between studies cross-culturally, it would be valuable to validate more recently published screening instruments for ASC used in Western countries in China. Standardised diagnostic instruments including the ADOS[192] and ADI-R are needed to be adapted and validated in Chinese population to make robust comparison possible. Since the CCMD was developed and only used in mainland China, the criteria for autism in the CCMD-2-R focused on Childhood Autism but not the whole spectrum. It was developed according to the criteria in the ICD and DSM but revised in order to be culturally acceptable. A more universal diagnostic process for ASC should be considered. Prospective population based epidemiological studies of ASC also need to be conducted in Hong Kong and Taiwan where there are additional cultural differences to mainland China using methods which are comparable across Chinese population and with the rest of the world.

Chapter 4 Systematic Review of Screening and Diagnostic Instruments for ASC in Mainland China

4.1 Introduction

Chapter 3 reviewed available prevalence studies of ASC in China. One of the limitations of these studies was the lack of information concerning the validity and reliability of the screening and diagnostic instruments for case identification. It was not clear how these instruments had been introduced and developed in China. Learning from what is available can help to decide whether it is necessary to introduce and adopt more recently developed instruments from the West for autism research in mainland China.

This chapter has two objectives: to identify validation studies of screening and diagnostic instruments in mainland China for ASC systematically, to examine the current methodology and propose directions for future research on ASC in mainland China.

4.2 Method

4.2.1 Literature searches

A systematic literature search for publications relating to validation studies of screening and diagnostic instruments for in China was conducted in four databases: PubMed, Web of Knowledge, China Web of Knowledge and Weipu (Box 4.1& 4.2).

Box 4.1 Search strategy for identifying validation studies in English databases

PubMed (searched on 27th December 2011)
Years (1966-2011)
Step 1: "Autism"/all subheadings [MeSH] OR "Autistic Disorder"/all subheadings [MeSH] or "Autism Spectrum"/all subheadings [all fields] OR "Pervasive developmental disorder"/all subheadings [MeSH] OR "Asperger"/all subheadings [all fields]
Step 2: "China"/all subheadings [all fields] OR "mainland China"/all subheadings [all fields] AND results from Step 1
Step 3: "Validation"/all subheadings [MeSH] OR "Screen"/all subheadings [MeSH] OR "Screening test"/all subheadings [MeSH] OR "Mass screening"/all headings [MeSH] AND results in Step 2

Web of Knowledge (searched on 27th December 2011)
Year (1950-2011)
Step 1: "autism"/ [Topic] OR "autistic disorder"/ [Topic] OR "autism spectrum"/ [Topic] OR "pervasive developmental disorder"/ [Topic] OR "asperger syndrome"/ [Topic]
Step 2: "China"/all subheadings [all fields] OR "mainland China"/all subheadings [all fields] AND results from Step 1
Step 3: "validation"/ [Topic] OR "screen"/ [Topic] OR "screening test"/ [Topic] OR "mass screening"/ [Topic] AND results in Step 2

MeSH (Medical Subjects Headings) The National Library of Medicine controlled vocabulary for indexing articles in PubMed.

Box 4.2 Search strategy for identifying validation studies in Chinese databases

Search 1:
Weipu database (searched on 27th December 2011)
Years (1989-2011)
Step 1: "Gu Du Zheng (Autism)"/ [Key words] OR "Zi Bi Zheng (Autism)/ [Key words] OR "Gudu Zheng Pu Xi Zhang Ai (Autism Spectrum)"/ [Key words] OR "Gu Fan Xing Fa Yu Zhang Ai (Pervasive developmental disorder)"/all [Key words] OR "A Si Be Ge (Asperger)"/ [Key words]
Step 2: "Validation"/ [Key words] OR "Screen"/ [Key words] OR "Screening test" OR "Validity"/ [Key words] or "Reliability"/ [Key words] AND results in Step 1
China Web of Knowledge (searched on 27th December 2011)
Year (Until 2011)
Step 1: "Gu Du Zheng (Autism)"/ [Key words] OR "Zi Bi Zheng (Autism)/ [Key words] OR "Gudu Zheng Pu Xi Zhang Ai (Autism Spectrum)"/ [Key words] OR "Gu Fan Xing Fa Yu Zhang Ai (Pervasive developmental disorder)"/all [Key words] OR "A Si Be Ge (Asperger)"/ [Key words]
Step 2: "Validation"/ [Key words] OR "Screen"/ [Key words] OR "Screening test" OR "Validity"/ [Key words] or "Reliability"/ [Key words] AND results in Step 1
Search 2:
Weipu database/China Web of Knowledge (searched on 27th December 2011)
Year (Until 2011)
"Gu Du Zheng (Autism)"/ [Key words] OR "Zi Bi Zheng (Autism)"/ [Key words]

4.2.2 Study selection and data extraction

The papers identified from the systematic search were examined against the inclusion criteria (Box 4.3). After excluding the duplications using the Reference Manager, the following variables were extracted from the selected papers: screening instrument, cut-off of instrument, case characteristic, control characteristic, diagnostic instrument, diagnostic criteria, and validity of the instruments.

Box 4.3 Inclusion criteria for validation studies

1. An original study about a screening tool or diagnostic instrument
2. The sample was from a population based or clinical or mixed setting
3. Provide information about sample size
4. Provide information about the reference diagnostic method which was used as golden standard that could be diagnostic instruments, criteria or clinical judgement.
5. Should be a prospective screening study
6. Provide information about the validity and reliability of the instrument
7. Published in English in English databases and in Chinese in Chinese databases

4.3 Results

4.3.1 Studies identified

The results of the first search in each database were as follows: three papers from PubMed; 12 papers from Web of Knowledge; 44 papers from Weipu database; and 14 from China Web of Knowledge. After removing duplicates, abstracts were reviewed. One paper from English databases and 18 papers from Chinese databases met the inclusion criteria. After the second search in Chinese databases, another three papers were identified which had not been identified during the first search. In total, 22 studies on nine screening instruments and two diagnostic instruments were included for review (Figure 4.1). 15 studies focused on screening instruments, six studies on diagnostic instruments, and four studies on diagnostic criteria. Three studies investigated more than one topic. A summary of the studies and their characteristics is shown in Table 4.1.

Figure 4.1 Search results of studies on screening and diagnostic instruments

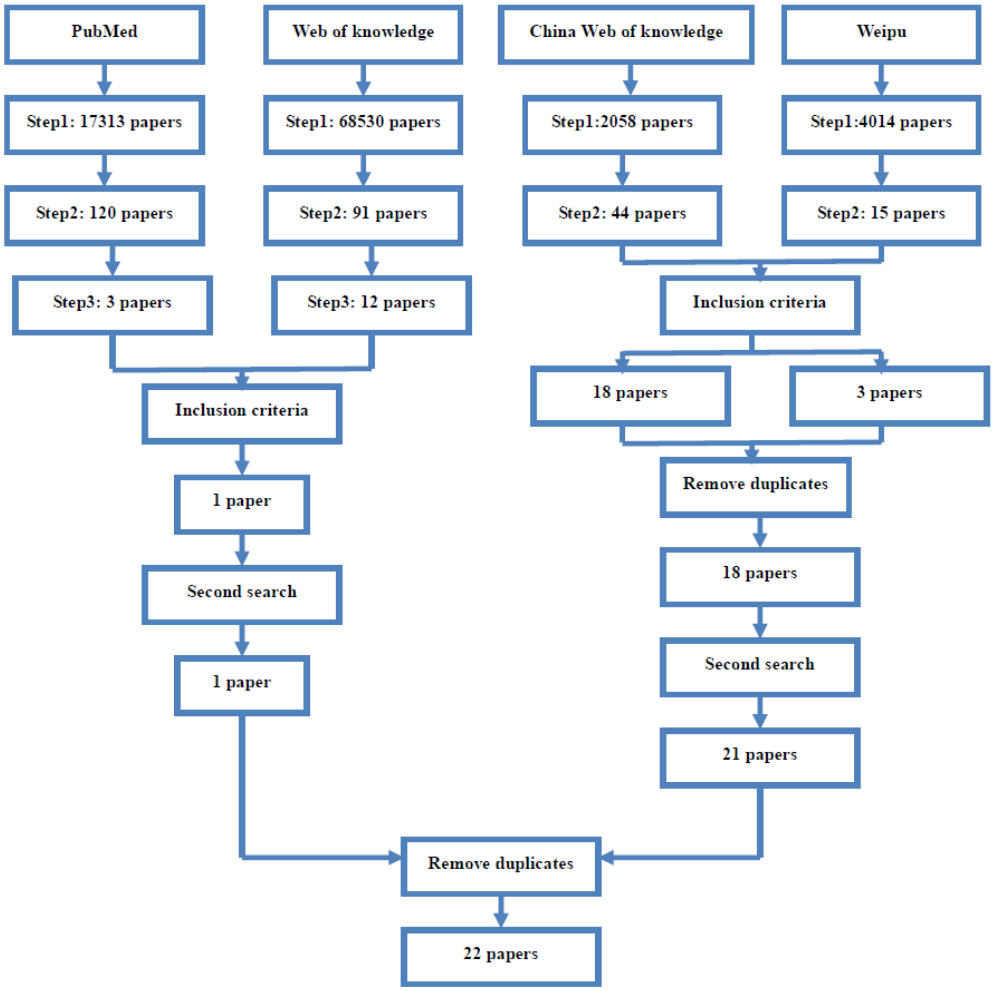


Table 4.1 Validity and reliability of screening and diagnostic instruments in mainland China

Tool	Year	Author	Case No	Cases age (mean)	Sample source	Control No	Control age	Cut-off for screening	Cut-off for diagnosis	Sensitivity	Specificity	Agreement percentage	Reference standard
ABC	1993	Yang [281]	60	2-17 (6.37)	Clinical	157 for 108 (N)	7-17 (11.7) 4-8 (6.3)	31	50	31 cut-off: 100% 50 cut-off: 97%	31 cut-off: 100% 50 cut-off: 100%	--	DSM-III-R
	2002	Wang [259]	20	2.33-11 (4)	Clinical	20(ADHD)	6-12 (8.5)	53	68	--	--	80%	ICD-10
	2003	Wang [282]	20	2-8 (4.5)	Clinical	0	--	56	72	--	--	85%	ICD-10
	2003	Wang [283]	22	2-8 (4.6)	Clinical	0	--	56	72	--	--	86%	ICD-10
	2004	Lu [284]	43	1.83-16	Clinical	31(N)	2-14	53	67	--	--	81%	ICD-10
	2005	Li [285]	28	1.5-3 (26 children) ≥7(2 children)	Clinical	34 (N)	1.5-3 (31 children); ≥7(2 children)	31	--	97%	89%	94%	DSM-IV
	2011	Yin [286]	178	--	Clinical	0	--	53	--	Cronbach's α=0.81	89%	--	CCMD-3
CABS	2003	Wang [282]	20	2-8 (4.5)	Clinical	0	--	14	--	--	--	95%	ICD-10
	2003	Wang [283]	22	2-8 (4.6)	Clinical	0	--	14	--	--	--	96%	ICD-10
	2005	Li [285]	28	1.5-3 (26 children) ≥7(2 children)	Clinical	34 (N)	1.5-3 (31 children); ≥7(2 children)	6	--	91%,	82%	87%	DSM-IV
	2006	Zhang [287]	65	2.5-4	Clinical	65 (N)	--	NA	--	88%	82%	--	Clinical judgement
CHAT-23	2010	Wu [275]	535	1.5-2	General population	0	--	1) ≥6 items positive in 23 items;2) ≥2 items positive in 7 key items	--	Either meet 1) or 2): 94%	Either meet 1) or 2): 88%	--	DSM-IV
M-CHAT	2011	Zhang [288]	25	0.96-2.92 (1.9)	Clinical	400 (N)	1.75-2.75 (2)	1) ≥3 items positive in 23 items;2) ≥2 items positive in 6 key items	--	Either meet 1) or 2): 72%	Either meet 1) or 2): 95%	94%	DSM-IV

Tool	Year	Author	Case No	Cases age (mean)	Sample source	Control No	Control age	Cut-off for screening	Cut-off for diagnosis	Sensitivity	Specificity	Agreement percentage	Reference standard
M-CHAT	2011	Gong [289]	93	1.2-3 (2.3)	Clinical	85 (N)	1-2.9 (2)	1) ≥3 items positive in 23 items;2) ≥2 items positive in 6 key items	--	96%	60%	--	DSM-IV
ASSQ	2011	Guo [290]	94	3.9-9.6 (6.75)	Clinical	120 (N) 71 (MD)	4.7-7.3 (6) 10.8-16.8 (13.8)	12	--	96%	83%	--	DSM-IV
WABS	2009	Song [291]	30	--	Special school	30 (MD) 33 (N)	-- --	51.5	--	100%	97%	--	Clinical judgement
FOSPAC-R	2010	Yang [292]	27	1-1.42	Clinical	27 (N) 27 (MD)	1-1.42 1-1.42	14	--	96%	93%	--	DSM-IV CHAT
EASI	2011	Zhang [288]	25	0.96-2.92 (1.9)	Clinical	400 (N)	1.75-2.75 (2)	40	--	80%	75%	75%	DSM-IV
PASS-IT	2011	Zhang [288]	25	0.96-2.92 (1.9)	Clinical	400 (N)	1.75-2.75 (2)	20	--	88%	64%	66%	DSM-IV
CARS*	2004	Lu [284]	43	1.83-16	Clinical	31(N)	2-14	30	36	--	--	98%	ICD-10
	2005	Li [285]	28	1.5-3 (26 children) ≥7(2 children)	Clinical	34 (N)	1.5-3 (31 children); ≥7(2 children)	30	--	100%	100%	100%	DSM-IV
	2005	Li [293]	41	2-10 (3.8)	Clinical	34 (MD)	3-11 (4.5)	--	30	100%	100%	100%	DSM-IV
	2011	Yin [286]	178	--	Clinical	0	--	30	37	Cronbach's α=0.78	97%	--	CCMD-3

*: diagnostic instrument; --: not applicable; NA: not available. CABS: Clancy Autism Behaviour Scale; ABC: Autism Behaviour Checklist; CARS: Childhood Autism Rating Scale; CHAT: Checklist of Autism in Toddlers; M-CHAT: Modified Checklist of Autism in Toddlers; ASSQ: Autism Spectrum Screening Questionnaire; WABS: Waterville Autistic Behaviour Scales; FOSPAC-R: Flinders Observational Schedule of Pre-verbal Autistic Characteristics-Revised; EASI: Early Autism Screening Items; PASS-IT: Pictorial Autism Screening Scale for Infant and Toddler: N: typical developed children; MR: mental retardation; ADHD: attention deficiency and hyperactivity disorder; MD: mental disorders.

4.3.2 Screening instruments

The screening instruments that have been used in mainland China include the following: the Autism Behaviour Checklist (ABC); Clancy Autism Behaviour Scale (CABS); Checklist for Autism in Toddlers-23 (CHAT-23); The Modified Checklist for Autism in Toddlers (M-CHAT); Autism Spectrum Screening Questionnaire (ASSQ); Flinders Observational Schedule of Pre-verbal Autistic Characteristics-Revised (FOSPAC-R); Waterville Autistic Behaviour Scales (WABS); Early Autism Screening Items (EASI); and Pictorial Autism Screening Scale for Infant and Toddler (PASS-IT).

4.3.2.1 Autism Behaviour Checklist

The ABC was developed by Krug and colleagues in 1980[136]. It was designed to be applied to individuals aged between 18 months and 35 years[136, 167]. The ABC has 57 items with each item rated from 1 to 4. The cut-off of the ABC is 53 (≥53) [13].

The ABC was first introduced into China for autism screening and diagnosis in 1989[283, 294]. The Chinese version of the ABC contains 57 items, including 10 items for tapping sensory behaviours (total score 30), 11 items for relationships (total score 35), 12 items for physical development (total score 28), 13 items for language (total score 31) and 11 items for daily living skills (total score 25).

Seven studies examined the utility of the ABC in Chinese samples. All seven studies were conducted in clinical settings. During clinical referral, the children were given a diagnosis of Childhood Autism first, and then the ABC was filled in by parents. Four of them used the ABC in both children with Childhood Autism (cases) and children without (controls)[259, 281, 284, 285], while the other three studies only recruited children with Childhood Autism[282, 283, 286]. The age range of studied samples ranged between 1.5 and 16 years old. Three diagnostic criteria were used for case identification including the ICD-10[1], DSM-III/IV[4, 18] and CCMD-3[295] (See Appendix 4.1). The percentage agreement between the ABC and diagnostic criteria was calculated in six studies to examine the utility of the ABC. The percentage agreement was the number of children who scored above the cut-off of the screening instrument divided by the total number of real cases. Four studies reported high percentage agreement between the ABC and ICD-10 (80%-86.3%)[259, 282-284]. However, the sensitivity and specificity were not provided in four studies. Two out of seven studies reported the validity of

ABC[285, 295]. The first validation study of ABC recommended a cut-off of 31 for screening[281], which reported a sensitivity of 100% and a specificity of 100%. Using a cut-off of 31, another validation study reported a sensitivity of 97% and specificity of 89%[285]. The cut-offs adopted in these studies were different: three adopted 53, two adopted 56 and two adopted 31. All seven studies recommended a score range of 50 to 70 on the ABC for the diagnosis of Childhood Autism. One study reported the ABC had good internal consistency in 178 children with Childhood Autism (*Cronbach's* α=0.81), and the percentage agreement between the ABC and CCMD-3 was 89%[286].

4.3.2.2 Clancy Autism Behaviour Scale

The CABS was first published in 1969[172]. However, no literature was found focusing on the utility of the CABS in Western population. The Chinese version of the CABS was designed to be completed by parents. It contains 14 items with each item rated on three frequency levels including 'Never (score 0)', 'Occasionally (score 1)' and 'Often (score 2)'. If the child scores equal to or higher than 14, and has less than 3 items score as 'Never' and more than 6 items as 'Often', then child should be considered as a potential case of Childhood Autism.

Six studies were identified, of which four studies met the inclusion criteria were included, while the other two were excluded since they did not report the validity or reliability. All four studies were conducted in clinical settings[282, 283, 285, 293]. Two studies recruited both cases and controls[285, 287]. The age of studied samples ranged between 1.5 and 8 years old. The ICD-10 and DSM-IV were used as diagnostic criteria. Two studies reported high percentage agreements between the CABS and ICD-10 (≥95%)[282, 283]. The agreement between the CABS and DSM-IV was 87%[285]. One study used clinical judgement for case identification without specifying the diagnostic criteria[287]. Two studies adopted a cut-off of 14 on the CABS[282] while one study adopted a cut-off of 6[285]. Both studies investigated the validity of the CABS reported a good validity of the CABS (Sensitivity: 88%, 91%; Specificity: 82%).

4.3.2.3 Checklist for Autism in Toddlers and its modified versions

The CHAT includes nine questions for parental completion and five observation tasks for the child[50]. It takes about 10 to 15 minutes to complete. The applicable age for the CHAT as a screening instrument is 18 months old[50]. It has been thoroughly validated

and evaluated in the general population in the West[83]. The CHAT had been adopted and modified by American researchers as the M-CHAT[296, 297]. Researchers in Hong Kong developed a screening instrument called the CHAT-23 by combing the M-CHAT (23 questions) with graded scores and the observational section B from the CHAT[298]. To be screened positive on the CHAT-23, the child should meet one of the following two requirements: first, the individual must score positive in more than 6 items in all 23 items; second, of the 7 core items of the CHAT-23, the individual must score positive in more than 2 items.

Only one study investigated the utility of the CHAT-23[275], while two studies investigated the M-CHAT in Chinese samples[288, 289]. All three studies were conducted in children who were no older than three years old using DSM-IV as the diagnostic criteria. The study on the CHAT-23 reported a sensitivity of 94% and specificity of 88% in the general population[275] . This study indicated the validity of the CHAT-23 in this sample was higher than the first study in Hong Kong. This might be due to the small number of cases (n=51) compared with the number of controls in this study (n=482). Two studies on the M-CHAT were conducted in clinical samples using similar methodology. However, there were great differences in the validity of the M-CHAT reported in those two studies (sensitivity=96% vs 72%; specificity=95% vs 60%)[289, 299].

4.3.2.4 Autism Spectrum Screening Questionnaire

The ASSQ is based on the diagnostic criteria in ICD-10 and DSM-IV[151, 177], which takes 10 minutes to complete. It contains 27 items with each item rated from 0 to 2: 0 indicating normal, 1 indicating maybe abnormal and 2 indicating definite abnormality[151]. The score of the ASSQ ranges from 0 to 54. The applicable age range of the ASSQ is between 7 and 16 years old[138].

In the only validation study, the Mandarin ASSQ was applied to children with ASC (n=94) and unaffected children (n=120), as well as children with other mental conditions (n=71). Using a cut-off of 12 (≥12), the sensitivity of the ASSQ was 96% and specificity was 83%. No validation of the ASSQ has been conducted in the general population in China[290].

4.3.2.5 Flinders Observational Schedule of Pre-verbal Autistic Characteristics-Revised

The FOSPAC-R was developed by researchers in Flinders University Australia[300]. It was designed for the detection of autism in children as early as 12 months of age. The FOSPAC-R contains 17 items with each rated on a 3-level scale including normal behaviours, between normal and abnormal behaviours, and abnormal behaviours. It takes 15 to 20 minutes to complete. One study validated the FOSPAC-R in clinical settings. The sample included children with Childhood Autism, typically developing children and children with Mental Retardation. This study adopted the CHAT and DSM-IV for diagnosis. Using a cut-off of 14, the validity of the FOSPAC-R was good (sensitivity=96%, specificity=93%) for identifying children with Childhood Autism[292].

4.3.2.6 Waterville Autistic Behaviour Scales

The WABS was developed from the DSM-IV and ICD-10[291]. It contains four domains including social behaviours, language and communication, behaviours and interests, and movement and cognition. One study investigated the validity of the WABS within children having Childhood Autism, children with mental disorder and typical developing children[291]. This study recommended a cut-off of 51.5 and reported a sensitivity of 100% and specificity of 97%.

4.3.2.7 Early Autism Screening Items

The EASI was developed by an American researcher, Larry Burd, and has not yet been validated in the West[288]. The validation of the Chinese EASI was the first validation study since it was developed. The Chinese EASI contains 46 items with each item rated 0 to 2 according to the frequency and degree of autistic behaviours: 0 as never or seldom, 1 as sometimes and 2 as often. A total score of less than 40 is recommended as the cut-off. The validation study applied the EASI to 25 autistic cases diagnosed by DSM-IV and 400 typically developing children. The sensitivity of EASI was 80% and specificity was 75%[288]. The percentage agreement between the EASI and DSM-IV was 75%.

4.3.2.8 Pictorial Autism Screening Scale for Infants and Toddlers

The PASS-I, which was also developed by Larry Burd, consists of 25 pictures of different facial expressions or gestures. The parents or caregivers are asked to recall

whether or not their child has the expressions or gestures in the 25 pictures shown to them. An answer of yes or no is scored as 1 and 0 respectively. A total score of less than 20 (≤20) is recommended as the cut-off. In the validation study of the EASI, the PASS-IT was applied to the same sample. The sensitivity of the PASS-IT was 88% and specificity was 64%[288]. The agreement between the PASS-IT and DSM-IV was 66%.

4.3.2.9 Screening instruments not meeting inclusion criteria for review

Three papers were excluded from this review because they did not report validity or reliability of the instruments. Two studies focused on the CABS, of which one investigated whether the CABS can distinguish children with autism from typically developing children. It reported that 13 items out of 14 items in the CABS can significantly identify autistic cases[301]. Another study reported that 6 out of 14 items on the CABS can significantly differentiate autism from other conditions, while 11 out of 14 items can significantly distinguish children with autism from typically developing children[302]. The third study introduced and evaluated the Aberrant Behaviour Checklist (ABC)[303] which was used as an evaluation questionnaire for the intervention of ASC. The findings from these excluded studies are shown in Appendix 4.2.

4.3.3 Diagnostic instruments

Studies on two diagnostic instruments were identified: the Childhood Autism Behaviour Scale (CARS) and the Autism Diagnostic Interview-Revised (ADI-R). The Autism Diagnostic Observation Schedule (ADOS) was introduced without any validation studies.

4.3.3.1 Childhood Autism Rating Scale

The Chinese version of the CARS contains 15 items and was rated by evaluating the frequency of abnormal behaviours. The rating scale 1 to 4 indicates the following: “behaviours appropriate for the child’s age”, “mildly abnormal”, “moderate abnormal”, and “severe abnormal”. The total score of the CARS is 60 and the cut-off of 30 is recommended (≥30).

Four studies investigated the utility of the CARS. All of them were conducted in clinical settings, three of which applied the CARS to both children with autism and children without. The age range of studied samples was between 1.8 and 16 years old. Three diagnostic criteria were used in identified studies including DSM-IV, ICD-10 and CCMD-3. Two studies reported a 100% agreement between the CARS and DSM-IV. The agreement between CARS and the other two criteria was also high (≥97%). All four studies adopted a cut-off of 30 for diagnosis of Childhood Autism. The validity of the CARS as a diagnostic instrument for Childhood Autism was reported as very good in two studies (sensitivity=specificity=100%). One study reported the internal consistency of the CARS was acceptable (*Cronbach's* α=0.78)[286]. The findings of studies on the CARS are shown in Table 4.1.

4.3.3.2 Descriptions of studies on the ADI and ADOS

The ADI[187] was introduced into mainland China in 1998. The results of studies on ADI are shown in Table 4.2. The Chinese ADI includes items on three core domains: social interaction, communication and repetitive and stereotyped behaviours, interests and activities (RBIA). Two studies were conducted in clinical settings to investigate the validity of ADI in Chinese populations. Both studies applied ADI in children with autism and children without autism. One study reported that 15 out of 16 items in the social interaction domain can statistically distinguish children with autism from non-autistic children ($p<0.01$). In the communication domain, 11 out of 13 items can differentiate autism from non-autism ($p<0.01$). In the RBIA domain, 4 out of 8 items produced significant differentiation of children with autism from non-autistic children ($p<0.01$)[304]. The interrater reliability of the ADI was good in 15 out of 16 items in the social interaction domain (*kappa*≥0.68) and in 10 out of 13 items (*kappa*≥0.68) in the communication domain. It was good in 3 out of 8 items in the RBIA domain ((*kappa*≥0.68)[304]. It suggested the relatively lower validity and reliability of the items in the RBIA domain was due to the low specificity of these items as reported by previous studies[305, 306], but not the cultural influence[304].

The second study investigated the reliability and validity of parts of the items from ADI that had been identified by the first study. The second study examined 17 items in the ADI: 7 items from the social interaction domain, 6 items from the communication domain and 4 items from the RBIA domain[307]. It reported the

interrater reliability of 11 out of 17 items was moderate (*kappa*: 0.43-0.58), while it was good in another 5 items (*kappa*: 0.6-0.64). The test-retest reliability was good in 9 items (*kappa*: 0.61-0.73), and moderate in the remaining 8 items (*kappa*: 0.4-0.58). This study indicated that all items can significantly distinguish children with autism from children with other mental conditions or typically developing children ($p<0.001$)[307].

The ADOS was first mentioned in the introduction report of ADI[308]. It was formally introduced in a recent report as one of the two gold standard diagnostic instruments for ASC[292]. This report provided the description of the ADOS. However, no study has yet applied the ADOS to the Chinese population.

4.3.4 Comparison of diagnostic criteria for ASC

The Chinese clinicians used four diagnostic criteria for the diagnosis of autism: ICD-10, DSM-III-R, DSM-IV and the Chinese Classification of Mental Disorders (CCMD-2/2-R/3). The first three are the same criteria used in western countries while the last one has only been used in mainland China. The CCMD categorises autism as a childhood psychiatric condition but not a developmental disorder. The CCMD-2 has been in use since 1993[264], while the CCMD-3 was issued in 2001[295]. Descriptions of studies on the comparison of diagnostic criteria are shown in Table 4.3.

Four studies were identified which investigated the agreement between different diagnostic criteria on autism in mainland China. One study investigated the performance of the ICD-10, DSM-IV and CCMD-2-R by applying them to 95 cases of autism[309]. The reference standard was clinical judgement. It reported the agreements between the clinical judgement and three diagnostic criteria, the CCMD-2-R, DSM-IV and ICD-10 were 90%, 97% and 96% respectively. This study also reported the agreement between the CCMD-2-R and the other two diagnostic criteria, the DSM-IV and ICD-10, was 48% and 59% respectively. One study investigated the agreement between the CCMD-2-R, CCMD-3 and ICD-10. It applied them to 117 autistic cases previously diagnosed using clinical judgement[310]. This study reported an agreement of 100% between the CCMD-3 and ICD-10 (*kappa*=1.00), and an agreement of 95.8% between the CCMD-2-R and ICD-10 (*kappa*=0.92). One study investigated the agreement between the CCMD-3 and DSM-IV within 255 autistic

cases and reported an agreement of 96.1%[311]. Another study examined the performance of DSM-IV for the diagnosis of autism compared with clinical judgement by clinicians within 65 autistic cases and 65 typically developing children. The agreement between the DSM-IV and clinical judgement was 100%. It also reported the sensitivity of DSM-IV was 96% and specificity was 92%[287].

Table 4.2 Studies on the ADI-R

Tool	Year	Author	Case No	Case age (mean age)	Sample source	Control No	Control age	Validity	Reliability Kappa	Reference standard
ADI	2002	Guo[304]	50	2-14 (4.9)	Clinical	32 (MD)	2-14 (9)	Domain 1: 15 items p<0.01 Domain 2: 11 items p<0.01 Domain 3: 4 items p<0.01	Domain 1: 15 items kappa≥0.68 Domain 2: 11 items kappa≥0.68 Domain 3: 4 items kappa≥0.68	Clinical judgement
ADI	2004	Liu [307]	50	2.8-12.2 (5.9)	Clinical	45 (MR) 50 (N)	4.6-13.7 (10.3) 2.6-11.5(6)	All 17 items p<0.001	5 items: kappa: 0.60-0.64; 11 items: kappa: 0.43-0.58	Clinical judgement

Table 4.3 Studies on comparison between diagnostic criteria for ASC in mainland China

Criteria	Year	Author	Case No	Case age	Sample source	Control No	Control age	Agreement P (percentage) K (kappa)	Reference standard
ICD-10 DSM-IV CCMD-2-R	1998	Tan[309]	95	3-13 (6)	Clinical	20	3-13 (6)	CCMD-2-R & Clinical judgement: P= 90%; DSM-IV & Clinical judgement: P=97%; ICD-10 & Clinical judgement: P=96%.	Clinical judgement
CCMD-3 CCMD-2-R	2002	Guo [310]	117	2-14 (6.2)	Clinical	--	--	CCMD-3 & ICD-10: K=100% CCMD-2-R & ICD-10: K=96%	ICD-10 & Clinical judgement
DSM-IV	2006	Zhang [287]	65	1.5-14 (4.5)	Clinical	--	--	Sensitivity=96% Specificity=92%	Clinical judgement
DSM-IV CCMD-3	2006	Liu [311]	255	1.6-16 (4.9)	Clinical	--	--	P=96%	Clinical judgement

4.4 Discussion

4.4.1 Availability of screening and diagnostic instruments in mainland China

This study examined the available screening, diagnostic instruments and criteria for autism in mainland China. The most frequently used instruments for screening are the CABS and the ABC. The most frequently used diagnostic instrument is the CARS. The ADI was only validated without adoption in epidemiological research, while the ADOS has not been applied to the Chinese population[292]. As mentioned before, the sensitivity and specificity of a screening instrument should be between 70-80% in order to be considered as psychometrically sound[132]. The validity of the CABS, ABC, CARS, CHAT-23 and ASSQ was reported as good in previous studies (sensitivity>80%, specificity>80%). However, most reviewed screening instruments were used to capture cases of Childhood Autism in mainland China but not the whole autism spectrum. In two prevalence studies of autism in China, the CARS as a diagnostic instrument was also used as a second-stage screening instrument[307, 312].

The CABS was developed in 1969[172] and introduced to China during the late 1980s. There have been very little updates since it was first translated and validated. It has been widely used in epidemiological research on Childhood Autism in mainland China; however, the data on its validity and reliability in the West is lacking. The CARS and ABC were also adopted early and they are still in use for ASC research in the West[161, 313]. The CHAT-23 and M-CHAT were developed recently and have been validated and adopted more thoroughly in the West[50, 83, 296], however, the research on their utility in Chinese general population is still limited. The WABS, FOSPAC-R, EASI and PASS-IT were developed most recently and have not been widely adopted or studied in the West[288].

In reviewed studies, there was limited information on the translation and back-translation process of reviewed instruments. Judging from the listed items of CABS and CARS in reviewed studies, most of the items were direct translation from English versions of the instruments. For example, in the English version of the CABS, one item is about the children try to avoid eye contact with others. The term eye contact means more about using eye to communicate in English. In Chinese version, the term contact was translated as “touch” in Chinese which means direct eye-to-eye gaze.

While direct eye-to-eye gaze might not be so common in Chinese culture as Western culture[314], such translation may cause differences in the two versions of the CABS. However, there has been limited information available on the cultural adaption of those instruments.

4.4.2 Limitations of this review

There are several limitations in this review. First, the literature search was conducted in four databases. It is possible that there are other studies which were not identified because they were not published in major journals. However, the search methodology was systematic with double-checking by a second search in all databases It was unlikely the publication and selection bias could influence the results. Second, all the papers were in Chinese and, because the data was extracted and translated into English by the candidate only, there could be language effects. Thus, it would be valuable to have a second reader for data extraction and translation. Third, the results of the validity and reliability of instruments were summarised according to the analytic methods stated in each paper. However, the detailed description of analytical approaches is generally lacking in reviewed papers, the analytic methods were assumed from the presentation of results in each paper. Thus, there might be a misinterpretation of the analytical approach of reviewed studies.

4.4.3 Critique of research methodology in reviewed studies

The limitations of reviewed studies are summarised in Box 4.4. More detailed limitations are provided in Appendix 4.3.

Box 4.4 Summary of limitations of reviewed studies

- Most studies used previous diagnosed cases, only two studies recruited cases prospectively.
- Case status was generally assumed the same as the original diagnosis without re-evaluation.
- Characteristics and background information on cases and controls were largely missing. Whether the cases and controls were drawn from the same population was unknown.
- No control group were recruited in seven studies.
- Clinicians and researchers were not blinded to case status.
- Several instruments were adopted as both screening and diagnostic instruments by use of lower and higher cut-offs.
- Most screening instruments were only used to identify children with Childhood Autism rather than the whole spectrum.
- Diagnostic instruments were generally lacking, and clinical judgement was considered as gold standard. The reliability of clinical judgement on the diagnosis of autism was largely missing.
- The development of instruments as well as their previous validity and reliability was generally not mentioned. Several instruments had only recently been developed in the West and not yet been thoroughly evaluated and validated in the West.
- Analytical methods were either not described or unclear.

4.5 Conclusion and future directions

Studies on screening and diagnostic instruments for ASC in mainland China are limited. Two screening instruments, the ABC and the CABS, had been more thoroughly studied in mainland China. Both of them were adopted from the West more than two decades ago for the case identification of Childhood Autism. The CARS have been most frequently used as a diagnostic instrument in autism research in mainland China. More standardised diagnostic instruments have not been adopted into autism research in mainland China. There is a lack of consistency in research methodology within identified studies, which made the comparison among those studies difficult. There is an urgent need to introduce more advanced and well-developed screening and diagnostic instruments to mainland China and adopt more standardised research methodology for instrument development for ASC. In Chapters 9 and 10, a pilot and a validation studies are conducted to introduce and apply a Mandarin Chinese version of CAST to the Chinese population as a screening instrument for ASC.

Chapter 5 Systematic Review of Service Provision for ASC in Mainland China

5.1 Introduction

Children with ASC and their families require a range of assessments and support services[315]. As presented in Chapter 1, in developed countries the system of service provision has been better established. In the UK, the Autism Spectrum Disorders Good Practice Guidance (GPG) has been developed[316]. The National Autism Plan for Children (NAPC) and the more recent NICE guidelines provide recommendations for service structure on the identification, diagnosis and early intervention for children with ASC[66, 317]. In the US, practice guidelines for service provision of ASC have been published regularly since 1999 by the American Academy of Child and Adolescent Psychiatry[318]. The American Academy of Pediatrics (AAP) proposed a developmental surveillance and screening algorithm for paediatric preventive care visits for ASC in 2006 in a policy statement[26]. This strategy suggested that all children's developmental progress should be formally monitored[319].

After diagnosis, intervention programmes were recommended in both the UK and the US for individuals with ASC. The NAPC recommended that intervention for autism should commence no later than six weeks following a diagnosis of autism[320]. In the US, several types of intervention programmes have been provided for children with ASC such as speech therapy, occupational therapy, behaviour management programmes, and service coordination/case management[114, 321]. The evaluation of service provision and delivery for individuals with ASC has been investigated both in the West and East[40, 322-324].

As introduced in Chapter 1.6, during the Cultural Revolution (1966-1976), the development of all critical domains such as economy, health, and education in mainland China was halted[325]. Reforms in the education began soon after the commencement of the Reform and Opening in 1978. An effort to promote integration for all children in education was launched in the mid 1990s through the introduction of a law for nine-year compulsory education[326]: a Law of the People's Republic of China to protect individuals with disabilities[327] and Regulations on education for

individuals with disabilities[328]. Those laws achieved the implementation of a compulsory nine-year education for children with disabilities[329]. In 1988, the '*Suiban Jiudu'* (attending schools in regular classroom) policy was issued to encourage children with disabilities to attend mainstream school classrooms[330]. However, children with autism were reported to have been turned away from both mainstream and special schools for a long time due to a lack of resources and knowledge about autism[325]. The situation has been slowly changing since the early 1990s partly due to the establishment of private intervention programmes for young children and the fact that the *'Suiban Jiudu'* policy increased the opportunities of mainstream classroom attendance[325]. However, to date little is known about how current service provision works for individuals with ASC in mainland China.

This chapter provides a review of the available literature on service provision for people with ASC in mainland China to learn about the current situation regarding ASC, and to identify possible directions for improvements in future research and service planning.

5.2 Method

5.2.1 Literature search

Literature searches were conducted in January 2012 in four databases for publications focusing on healthcare and education provision for individuals with ASC in mainland China. Broader search terms were adopted to capture all available studies. The search strategy is shown in Box 5.1.

5.2.2 Data abstraction and inclusion criteria

After searches, all possible relevant papers were read. The data in Chinese papers were extracted and translated into English to present in this review by the candidate. In addition, ancestral searches were conducted during the literature search where it was necessary to help understand the contexts of those articles. Inclusion criteria for this review included being an original report or a review paper focusing on the healthcare and education services for individuals with ASC in mainland China. The selected papers were categorised into several groups according to different ASC service settings that were described in the papers.

5.2.3 Materials from other source

In June 2011, the first summit conference for autism in mainland China was hosted by the China Disabled Persons' Federation (CDPF). Six out of ten provinces reported their achievements in mental health rehabilitation during the "Eleventh Five-Year programme" (2005-2010) and described the current situation with regards to autism in their provinces for the first time[82]. The contents of the reports constitute an unpublished official summary of the mental healthcare situation and achievements of service provision for mental health in ten provinces. These reports were provided to the first author by the CDPF.

Box 5.1 Literature search strategy for review of health and education service for ASC in mainland China

PubMed (searched on 27th December 2011)
Years (1966-2011)
Step 1: "Autism"/all subheadings [MeSH] OR "Autistic Disorder"/all subheadings [MeSH] or "Autism Spectrum"/all subheadings [all fields] OR "Pervasive developmental disorder"/all subheadings [MeSH] OR "Asperger"/all subheadings [all fields]
Step 2: "China"/all subheadings [all fields] OR "mainland China"/all subheadings [all fields] AND results from Step 1

Web of Knowledge (searched on 27th December 2011)
Year (1950-2011)
Step 1: "autism"/ [Topic] OR "autistic disorder"/ [Topic] OR "autism spectrum"/ [Topic] OR "pervasive developmental disorder"/ [Topic] OR "asperger syndrome"/ [Topic]
Step 2: "China"/all subheadings [all fields] OR "mainland China"/all subheadings [all fields] AND results from Step 1

Weipu database (searched on 17th December 2011)
China Web of Knowledge (searched on 18th December 2011)
Years (1989-2011)
Step 1: "Gu Du Zheng (Autism)"/ [Key words] OR "Zi Bi Zheng (Autism)/ [Key words] OR "Gudu Zheng Pu Xi Zhang Ai (Autism Spectrum)"/ [Key words] OR "Gu Fan Xing Fa Yu Zhang Ai (Pervasive developmental disorder)"/all [Key words] OR "A Si Be Ge (Asperger)"/ [Key words]

5.2.4 Data analysis

The healthcare and education systems provide services for individuals with ASC throughout the natural history of this condition from onset to treatment. In order to better understand the service provision in general, the key topics in Box 5.2 served as a guideline for data analysis.

Box 5.2 Key topics of service provision for ASC from literature

I: Healthcare: diagnosis and recognition
1) How are individuals with ASC diagnosed in mainland China?
2) Under current practice, have all individuals with ASC been identified thoroughly?
3) The awareness and knowledge among clinicians and parents about ASC.

II: Education: intervention and education inclusion
1) What happens after initial diagnosis?
2) Which settings can provide intervention for ASC? Can all diagnosed children receive intervention?
3) What do these identified intervention settings provide?
4) What are the providers' qualifications?
5) Implementation of education inclusion for children with ASC

III: Perceptions on service provision from teachers and parents
1) Teachers' and parents' attitude towards education inclusion
2) Parents' perceptions on service provision

IV: The service costs on ASC

5.3 Results

5.3.1 Study identified

Six papers were identified from two English databases and eight papers from two Chinese databases as well as six reports from the CDPF regarding the situation in six provinces. The results are provided in Table 5.1. Seven papers focused on the healthcare system, of which five were original studies, one was a summary report and one paper only had an English abstract available. Seven studies were identified for education provision, of which six were original studies and one was a review. Six reports obtained from the CDPF reported on both healthcare and education service provision on autism in mainland China.

Table 5.1 Reviewed studies of healthcare and education service for ASC in mainland China

Source	No	Year	First author	Language	Focus	Region	Research method
Healthcare system	1.	2007	Ming [331]	English abstract	Parent initiated referral for ASC	Wenzhou city	Retrospectively using hospital referral records
	2.	2011	Xiong [332]	Chinese	Healthcare and education support for autistic children	Jiangsu province	Interviews with various informants: 28 headmasters in rehabilitation centres, 36 special teachers and 216 parents
	3.	2011	Guo [333]	Chinese	Social support system for autistic children	Jiangxi province	Interviews with 100 parents
	4.	2011	Tao[334]	Chinese	Healthcare and education	Hubei province	Interviews with 60 parents
	5.	2011	Wu [335]	Chinese	Healthcare and education	Hunan province	General summary and recommendations
	6.	2011	Chen [336]	Chinese	Healthcare and education	Shanghai city	Interviews with 3 parents
	7.	2011	Zhang [250]	Chinese	Acknowledge of autism among parents and health professionals	Wuxi city	Questionnaires from 201 parents, 197 community physicians and 95 paediatricians
Education	8.	2005	Gao [337]	Chinese	Status of autistic children in ordinary schools	Beijing city	Interviews with 7 headmasters and 12 teachers in mainstream schools and 7 parents of autistic children
	9.	2003	McCabe [325]	English	Inclusion education	General	Review of policy changing
	10.	2008	McCabe [338]	English	Intervention programme at private and state-run centres	Beijing and Nanjing city	Interviews with 43 parents or caregivers
	11.	2008	McCabe [329]	English	Intervention in a state-run rehabilitation centre	Nanjing city	Interviews with 1 headmaster, 3 doctors, 6 teachers and 8 parents
	12.	2008	McCabe [339]	English	The influences of autism towards the parents and families	Beijing city	Questionnaires from74 parents and then invited 13 parents for interview
	13.	2010	McCabe [340]	English	Employment and perspective of mothers with autistic children	Beijing city	Questionnaires from 70 mothers and 12 mothers were invited for interview
	14.	2011	Xiong [341]	English	Raising burden of children with autism and other disabilities	Beijing city	Interviews with 61 parents
CDPF reports	15.	2011	CDPF [82]	Chinese	Healthcare and rehabilitation provision for autistic children	Provinces: Fujian, Guangdong, Jiangsu, Jiangxi, Hubei, Hunan	Governmental reports from provincial CDPF

5.3.2 Study methodology

Of 14 studies identified from the literature, 11 conducted interviews with various informants: a total number of 724 parents were interviewed in 11 studies; 295 physicians were interviewed in two studies; 54 teachers either in mainstream schools or special schools were interviewed in three studies; 36 school headmasters were interviewed in two studies. Two studies were general summaries or recommendations on service provision of autism in mainland China, and one study used previous hospital records to investigate the referral for autism.

5.3.3 Diagnosis of ASC

One study found that hospital referrals for autism were mostly initiated by parents in mainland China[331]. One study reported that 66.7% of parents chose a paediatric or a women and children's hospital for diagnosis while the remainder chose a psychiatric hospital or a neurological hospital[334]. In another study of 100 families, 74 children were diagnosed in hospitals while the remaining were diagnosed in rehabilitation centres[333].

Regarding the accuracy of initial diagnosis, one study interviewed 60 parents of children with autism in Jiangxi province. It reported that 75.9% of children were correctly diagnosed with autism initially while 24.1% were first misdiagnosed as other mental conditions. Prior to receiving a diagnosis of autism, 75.6% of parents had no knowledge of autism[333].

From the CDPF reports, in 2011, there were approximately 6000 children with autism and 72 mental health hospitals in the Hunan province. In Jiangxi province, the reported prevalence estimate of children with autism was between 2 and 5 per 10,000, and the total number of children with autism was approximately 40,000. In Guangdong province, the prevalence of autism was estimated to be 5 per 10,000 and the total number was 19,000. In Fujian province, the total number of children with autism was estimated to be 35,000[82].

5.3.4 The awareness and knowledge among physicians and parents on ASC

Recognition of autism among physicians varied across different regions[334]. It may partly depend on the familiarity of this condition in the local area. Since the first

diagnosis of autism was given by Dr Tao in mainland China[329], the Neurological and Mental Illness Prevention hospital (the Brain hospital) he established was receiving many children's referrals for autism. The Brain hospital therefore gained a positive reputation, and thus in this region, many doctors followed Dr Tao's footsteps and began to specialise in the diagnosis and assessment of autism[329].

One study investigated the awareness among community physicians, paediatricians in comprehensive hospitals and parents who were referred to these settings in Wuxi city[333]. This survey used a self-completion questionnaire that included 22 items related to the concept, diagnostic features, aetiology, assessment and treatment of autism. Results indicated that overall, the hospital-based paediatricians knew more about the existence of autism. However, parents were the most knowledgeable about the diagnosis of autism. The report concluded that there was a general lack of knowledge of autism among physicians and paediatricians in Wuxi city[333]. It suggested this might be due to increased access to information about autism diagnosis from the internet and media coverage about autism. However, this conclusion might be more applicable to cities where the general population have more access to internet. However, this might not be the same for the population in rural area. As there was no further information or statistic reference such as the internet coverage in this city available, the representative of the study sample or the generalizability of the statement cannot be justified. Another study reported that 44% of parental knowledge of autism was from the internet, 33% from other parents with children having autism and only 16% was from health or rehabilitation professionals[76].

5.3.5 What happened after initial diagnosis

On study reported that one in five children with autism received intervention immediately after diagnosis, while 65% received within one year post-diagnosis[76]. Another study reported 51.4% of parents accepted the initial diagnosis straight away and began to seek an intervention for their child[290]. In contrast, 48.6% of parents delayed seeking help for two main reasons. First, 23% of parents did not believe the diagnosis and took their child elsewhere for further assessments and diagnosis. Second, 12% of parents did not seek an intervention due to financial limitations in their personal circumstances[290].

5.3.6 Which settings provide intervention

One setting for intervention is the state-owned hospital such as the Brain hospital. In 1989, it began to provide language and life-skill training for children with autism. In 1994, the Rehabilitation Division of the Nanjing Centre established an intervention programme for children with autism. Another setting is the private rehabilitation centres[329].

In the CDPF reports, the available intervention services were summarised. In Hunan province**,** there were 16 rehabilitation centres for autism, and five of them were established by the Hunan CDPF. In Jiangxi province, there were eight autism rehabilitation centres, of which one was established by the Jiangxi CDPF. The others were all private centres, three of which were the main sources for autism rehabilitation in Jiangxi. In Fujian province, 20 rehabilitation centres were supported by the provincial CDPF in 2010[82] .

5.3.7 The coverage of intervention

Four studies reported the coverage of rehabilitation services for children with ASC. One study investigated the rehabilitation services in Jiangsu province[332]. This study conducted interviews with headmasters in all 28 rehabilitation centres for autism in this province. Thirty-six teachers in mainstream schools, and 216 parents of children with autism were also interviewed. Within the 28 centres, only five operated smoothly with independent financial affairs. A total of 5,100 children received special intervention programmes in Jiangsu province, which accounts for less than one quarter of the provincial estimated number of children with autism[332]. The report commented that how private rehabilitation centres could fit into the health system was unclear, given that support from the government and society was limited.

From the CDPF reports, the coverage of intervention on autism was provided as follows. In Hubei province, there were 935 children with autism who received intervention in the last five years. In 2006, the autism rehabilitation centre in Hubei province was established in Wuhan, which can serve 150 children. In Guangdong province, there were 67 rehabilitation centres: within which, there were 593 special teachers/therapists and 1,051 children with autism. It was reported to have exceeded its maximum capacity of service provision which was 1,000 children. In Jiangsu

province, there were 72 rehabilitation centres serving 533 children. Approximately 3000 children were reported to have received intervention in Fujian province from 2008 to 2011[82].

5.3.8 Intervention programmes

The intervention programmes in the state-run rehabilitation centres such as the intervention in the Nanjing Centre (established by Brain hospital), included one-to-one instruction, sensory integration therapy, group music therapy and game classes. The centre was set up for children aged 3 to 10 with autism and required the presence of one caregiver as an observer during the classes. The one-to-one instruction was attended by all children in the centre, which comprised three modules: fine-motor tasks, language exercises, and pre-academic skills. This study suggested that one of the main intervention strategies in Nanjing Centre was the parents' involvement and learning from therapists by observation, which allowed parents to continue the intervention with their child at home[329].

The intervention programmes provided in private rehabilitation centres were reported by one study[332] which included the following: 1) Comprehension therapy: the Applied Behavioural Analysis (ABA)[342]; Relationship Development Intervention (RDI)[343]; the Developmental, Individual-Difference, Relationship-Based model, Floor time communication development therapy (DIR)[344]; the Treatment and Education of Autistic and Related Communication Handicapped Children (TEACCH)[345]; Mr Liu ability development therapy; Mr Liu scenario teaching method; Picture Communication Intervention teaching method (PCI). 2) Singular therapy: sensory integration therapy, music therapy, picture exchange communication system (PECS)[346], social story therapy, computer assistant therapy. 3) Other therapy: behavioural therapy, acupuncture and massage therapy[347]. All 28 centres adopted the ABA therapy, sensory integration therapy, music therapy, and PECS therapy, while 21 centres (75%) used the TEACCH as a therapeutic method.

According to reviewed literature, there has been no specific intervention programmes or special assistant programmes provided in mainstream schools for children with autism in mainland China. The intervention programmes employed in each setting are summarised in Table 5.2.

Table 5.2 Intervention programmes in different settings for ASC[332, 338]

Setting	Details of therapy
Private rehabilitation centres	Applied Behavioural Analysis (ABA) Relationship Development Intervention (RDI) DIR Floor time therapy TEACCH (Treatment and Education of Autistic and related Communication handicapped Children) Mr Liu's ability development therapy Mr Liu's Scenario therapy PCI therapy Sensory integration therapy Music therapy Picture exchange communication system (PECS) Social story method Computer assistant therapy Acupuncture and massage Behavioural therapy
State-run rehabilitation centre	Fine motor tasks Language exercises Pre-academic skills Sensory integration therapy Group music therapy Game classes
Mainstream schools	None special intervention or special assistant programme for children with ASC but have "*Suiban Jiudu*" policy to allow children with disability to attend regular class

5.3.9 Qualification of providers

One study reported[332] the teachers and therapists in the rehabilitation centres were recruited from one of the following educational backgrounds: pre-school education, special education, psychology, and social workers with the majority (71%) were recruited from college graduates majoring in pre-school education.

5.3.10 Implementation of education inclusion for children with autism

One study reported on the policy of education inclusion for children with autism in mainland China[325]. It indicated children with more severe disabilities were still not in the mainstream or special education system (including mainstream and special schools)[348]. Since the implementation of the '*Suiban Jiudu*' policy, the situation has gradually changed. However, this policy is not mandatory but simply encourages the local government to provide nine-year compulsory education to all children. One study found whether children with autism can attend a mainstream school and have educational opportunities does not depend on the implementation of this policy itself, but rather on the parents' personal connections and the school's willingness and ability to accept children with such condition[325].

5.3.11 Teachers' and parents' attitude towards education inclusion

One study examined children with autism in mainstream schools in Beijing[337]. Interviews were conducted with parents of children with autism (n=7), the school head teacher (n=7), teachers (n=12) and parents of typical children (n=7) in seven mainstream schools. Five out of seven head teachers (70%) agreed to accept children with autism into their school. However, all the teachers interviewed were not willing to accept a child with autism in their class, but if it was imposed on them by the head teacher then they had to accept it. The main reason why teachers did not want to have children with autism in their classroom was because they believed that such child's behaviours would disturb their classes[337].

Another study focused on the acceptance of the '*Suiban Jiudu*' policy by interviewing various informants[332]. All teachers (n=36) considered that autistic behaviours were the primary reason why these children could not integrate into mainstream classroom or society in general. Only one out of seven parents (14%) of typical developing children interviewed agreed with including autistic children into the mainstream classroom with their own child. All the other parents disagreed with such integration. Several parents of typical developing children expressed very negative attitudes towards the '*Suiban Jiudu*' policy because they thought this would negatively influence their own children's education. All seven parents of children with autism expressed their willingness to let their child attend a mainstream school and to try their best to cooperate with schools and the other parents. These parents considered that their children's social environment was more important than achieving good grades at school[332].

Two studies reported the difficulties in integrating into mainstream education faced by children with autism[334, 335]. One study reported that 70% of parents would like their child to attend a mainstream school in the future[334]. Another study focused on the situation in Changsha city conducted interviews with parents and teachers in a rehabilitation centre. These two studies suggested that even when children with ASC were accepted into a mainstream school, the children were encouraged to leave once their autistic behaviours became apparent at school. Thus, children with autism aged 7 to 16 usually found themselves with no education provision due to the lack of special educational facilities[335].

5.3.12 Perceptions on current service provision

One study indicated the challenges for state-run intervention centres based on the experience of the Brain hospital[329]. It concluded that there were two main challenges. The first challenge was financial support. As the state-run centre was unable to make as much profit as the other divisions in the comprehensive hospital, the tuition fees increased. A second challenge was the limitation in the development and improvement of their intervention programmes. There was no ongoing learning programme available for therapists and special teachers, making it difficult to improve or update their intervention methods [329].

Challenges for private intervention settings were also indicated in reviewed studies as follows: 1) a shortage of funding. This included unstable support from government and society which led to the imbalance between tuition fees covered by parents and allowances from the government[341]; 2) the unstable structure of human resources for special teachers/therapists. The teachers and therapists in private centres may leave one centre for another one. This made it difficult to create or develop coordinated training and professional development within private centres[332, 349]; 3) cooperation between parents and the rehabilitation centres was not without difficulty due to a lack of knowledge of autism and the relatively low social status of parents[332]; 4) a lack of a standard qualification requirement for teachers and therapists specialising in autism interventions.

One study in Jiangsu province suggested the integration into the society for children with ASC after intervention was still difficult. It indicated that following participation in an intervention programme, less than 10% of children who received intervention were considered to be able to integrate into society, and less than 3% attended a mainstream school [332].

Two studies suggested a long waiting period between receiving a diagnosis of autism and entering an intervention programme in a rehabilitation centre. One study reported that the average time period was 10 months[334]; the other study found that 77% of children waited for more than 6 months to enter a rehabilitation centre after enrolment[333].

One study interviewed 216 parents of children with autism. The authors found that all the parents wanted better early detection and diagnostic systems for children with autism. Further, parents indicated that there was a huge financial burden on parents to provide education and intervention for their children with autism[332]. All parents expressed a desire for the availability of government-supported specialised institutions for diagnosis and intervention. Parents indicated that there should be a clear healthcare pathway for their children to follow. This study also found that parents were concerned about the future quality of life of their children with autism[332].

Another study interviewed three parents of children with autism in Shanghai city. It suggested that receiving a diagnosis of autism can be very difficult for parents to cope with. If not managed properly, further difficulties within the family may prevail. They proposed that the integration education in kindergarten should be encouraged in order to provide more opportunities for children with autism to interact with typically developing children during the period of time when it might be the optimum period for implementing interventions.

5.3.13 The cost of ASC in mainland China

One study interviewed 61 parents of children with autism. It provided estimates for the average annual costs for three service domains including rehabilitation, education and medical expenses for a child with autism. The estimated costs for those domains were £1,919.80, £642.80 and £376.70 respectively, with the total cost as £2,939.3[341]. With basic living expenses included, the cost rose to £4,099.80. However, the average annual family income was £2,056.9. Thus, the financial burden of raising a child with autism amounted to £2,042.9 annually[341]. Another study interviewed 100 parents and found 56% of the children did not have a disability certificate from the government and another 30% did not know how to obtain one[333]. As a result, 93% of the children in that sample did not receive an allowance. However, the parents who received an allowance reported that the allowance can only cover part of the fees for rehabilitation[333]. The reported cost for rehabilitation varied from £150 to £500 monthly. 96% of families had never received any financial support, and 56% of parents wanted to get financial support in the future[333]. One study investigated the employment experiences of mothers of children with autism, using questionnaires (n=70) and face-to-face interviews (n=12). This study concluded that mothers usually

sacrificed their own career in order to accompany their child to attend rehabilitation centres and to provide home-based intervention[340].

In the CDPF reports, the information on governmental support for ASC was provided. In Hunan province, 50 children with autism in low income families received financial support from a 'rescue programme' hosted by the CDPF for children with disability aged 0-6 in 2010,. In Jiangxi province, the government granted each centre with 80,000RMB (£8,000) to help them operate in 2011. In Hubei province, the Hubei CDPF supported each child in the government identified centres with 500RMB (£50) per year as an allowance, while the Wuhan government supported each child in the government identified centres with 3000RMB (£300) per year. In Jiangsu province, since 2007, the provincial financial department had distributed an allowance of 1,2000RMB (£1200) annually to each child with autism in low income families. In Fujian province, since 2010, the provincial government began to support children with autism attending the identified rehabilitation centres with 5000RMB (£500) per child per year. In 2010, 20 rehabilitation centres were supported by the Fujian CDPF[82].

5.4 Discussion

5.4.1 Summary of findings

This study has identified literature from both the West and China as well as directly from the government. The literature itself was based on both interviews with service providers and parents of children with autism. It provides a summary of current evidence on both healthcare and education service for children with ASC in mainland China. Findings suggest that most service only focused on children with autism. There are achievements as well as barriers within the health, government and education systems. There is a lack of knowledge among professionals and lack of awareness among the public on ASC. The healthcare and education systems are under-developed for ASC. The lack of support from the government and society has resulted in a substantial financial burden on parents of children with ASC in mainland China.

5.4.2 Limitations and strengths

There are several limitations of this review. First, this review is based on literature from two English and two Chinese databases, together with material from one other

source. It is possible there may be papers focused on this topic that were not published in mainstream journals and thus were not identified in this review. However, the Chinese databases were two of the biggest databases in mainland China. The systematic search strategy with broad search terms and cross-checking in four databases should have kept publication bias to the minimum. It is unlikely the other unidentified papers could influence the results substantially. Second, the data were collected and analysed by a single researcher. This may lead to the language bias since most studies were published in Chinese. However, given the nature of this review, it is unlikely that key information would have been missed or misinterpreted. Third, most of the available English papers were written by the same American author who is fluent in Chinese, since these were the only studies that were available. However, similar findings were reported by other studies in Chinese identified in this review. In addition, the representativeness of the findings should be noted since there was a limited number of publications and a high degree of heterogeneity in study design. Caution must be applied when generalising these regional results to the population as a whole.

5.4.3 Challenges for the diagnosis of ASC

This review indicated one obstacle for diagnosis is a lack of health professionals on ASC in clinical settings in mainland China. Most physicians have little knowledge and experience of autism[299]. This is because in China, paediatricians are usually the first health professionals that parents are referred to following concerns about a suspected ASC[350]. However, diagnosis and management of ASC can be a challenge for physicians since diagnosis in China mainly depends on clinical judgement. It has been suggested the clinical judgement can be supplemented by adopting standardised assessment instruments such as the ADOS and ADI-R[350]. Thus, it would be helpful to introduce more standardised instruments and provide training to improve knowledge of ASC among health professionals in mainland China.

5.4.4 Challenges for service delivery

In reviewing the literature, there are many problems within the current system: 1) an unclear pathway from diagnosis to intervention in mainland China[333]; 2) lack of standardised regulation of private training centres. It is difficult to integrate the private centres into either business services or public educational institutes; also, there

is a lack of management and monitoring by the government, and the quality of such services cannot be ensured[332]; 3) a lack of educational facilitates for older children with ASC. Current programmes mainly focus on children aged 0 to 6 years old. There has been limited educational facilities available for children outside this age range[82]; 4) Different policy and service provision from the government for autism among regions in mainland China. Because the awareness and familiarity of autism varied in different regions, the corresponding policy and support for children with autism and their families are different. There has been no standard strategy for service provision in mainland China; 5)the links within the healthcare system among the government, institutes, schools, community and families are still weak and the cooperation between these settings is under-developed[335].

5.4.5 Challenges in mainstream educational settings

Children with ASC require not only healthcare services but also special education services[114]. Many obstacles on the education pathway for children with autism were identified, including attending mainstream schools. First, the purpose of the '*Suiban Jiudu*' policy was to encourage mainstream schools to accept children with special conditions like autism, but whether accepting children with disability or not was up to the discretion of each school. Thus, there is still a long way to go to achieve a situation where children with autism can be fully accepted by mainstream schools[325]. Second, a lack of strategy and teaching methods for children with autism in mainstream schools led to confusion and frustration among the school teachers as they did not know how to help children with such condition[332]. Third, there was a lack of awareness and knowledge about autism among the general public evidenced by the attitude of parents of typically developing children in mainstream schools[332].

5.4.6 The family burden of ASC

Autism has not been included in general health insurance, therefore most of the costs for rehabilitation and medical care are paid by parents[341]. There has been limited support for families with children having autism. The annual expense for a child with autism in mainland China was reported as £4,099.80[341]. This was a conservative estimate taking into account that study also reported that the monthly tuition fees of private intervention centres range from £150 to £500[333]. In mainland China, the social stigma and misunderstanding on ASC might partly contribute to the lack of help and

concern from society and the general public towards children with autism and their families. The government allowance varied across regions and was not adequate to reimburse the parents for the true cost of supporting their child. In many families, one parent gave up their career to accompany their child in rehabilitation centre, which only served to increase the financial burden on the family due to this income loss[340].

5.5 Conclusion and recommendations for future research

The volume of literature on healthcare systems and education services for children with ASC was profoundly limited. Parents of children with autism faced many problems, partly because of the under-developed service systems. The improvement of service provision could be achieved by the following strategy: 1) providing ASC related medical training for physicians, in particular integrating it into basic psychiatric training; 2) further epidemiological research focusing on the whole spectrum to understand the underserved needs of ASC in the general population; 3) providing systematic service pathway descriptions and practice guidelines on ASC with regulation for each setting in the system; 4) issuing evidence-based unified policies by the government in regards to the support for families with autistic children; 5) enhancing public education of ASC to improve awareness and acceptance of ASC in general population; 6) thorough implementation of "*Suiban Jiudu*" policy to improve the education inclusion for children with ASC; 7) conducting further research on the service provision from both service providers' and users' perspective to provide feedback for service improvement. In Chapter 6, qualitative research was conducted to investigate the current service provision of ASC in mainland China from a service providers' perspective.

Chapter 6 Service Provision for Autism in Mainland China: Service Providers' Perspective

6.1 Introduction

In this chapter, the current available healthcare provision and education services for children with ASC and their families in mainland China was explored by learning from the views of service providers to identify future challenges for improvement in policy making and autism research.

6.2 Method

6.2.1 Preliminary identification of service settings: literature search

A literature search was conducted in two Chinese databases, the Chinese Web of Knowledge and Weipu database, to identify previous literature on service provision for ASC in mainland China. The following search terms were used: "Autism" OR "Autistic Disorder" OR "Autism Spectrum" OR "Pervasive Developmental Disorder" OR "Asperger Syndrome" AND "Healthcare" OR "Education". The inclusion criteria for study selection included: 1) It must be an original report; 2) it must focus on mainland China; 3) It must focus on the healthcare service and education provision for ASC. Information about the main settings of service provision was summarised from the identified studies.

The five papers identified from literature search were used as a preliminary source to identify existing service settings[271, 337, 351, 352]. One paper described children with autism in a primary school in Beijing city[337], which suggested that pre-school children with ASC might be educated at home or in kindergarten. For school aged children, there were four education settings: home, special education schools, rehabilitation centres and mainstream primary schools. Nine-year compulsory education (provided by the government) provided education through mainstream schools and state-owned special education schools[353]. From the national survey of disability, 62% of children with disability received the compulsory education in mainland China[351]. Of these, 3% were children classified as having mental disability, and 70% of children with mental disability received nine-year compulsory education[351]. No data were available for the

percentage of children with ASC attending compulsory education. Two papers listed available intervention methods for autism and mental retardation[271, 354]. The reported intervention included: (1) hospital treatment: medication, surgical operations and physical therapy; (2) family treatment: intervention and training by parents or special therapists at home; (3) institution treatment: special therapy and training in a rehabilitation centre; (4) educational treatment: education in a nursery or a kindergarten or a mainstream school. Another study based on interviews with 30 parents of children with autism from rural areas in China suggested that rehabilitation and education services for autism in rural areas were less available compared to urban areas due to the financial constraints and the lack of community support[352].

6.2.2 Procedure

Based on this literature, healthcare service providers for children with autism included the government, hospitals and autism research settings. Education service providers included state-owned special education schools, private rehabilitation or training centres and mainstream primary schools. Therefore, six service settings for ASC in mainland China were identified and five of them were selected for the current study. These settings included a research setting, a clinical setting, a government authority, a special education setting and a rehabilitation setting. This study was part of a collaborative research project between the University of Cambridge, UK and the Peking University First Hospital, China. This work was considered and approved by the Peking University First Hospital Ethics Committee.

6.2.3 Participants

In order to reach the appropriate informants within the identified settings, snowball sampling was used. This sampling method was used because the initial informants recommended further relevant participants[355, 356]. Figure 6.1 shows the process of identification of service providers in this study. A total of 10 informants were recruited as service providers (Table 6.1).

Figure 6.1 Snowball sampling

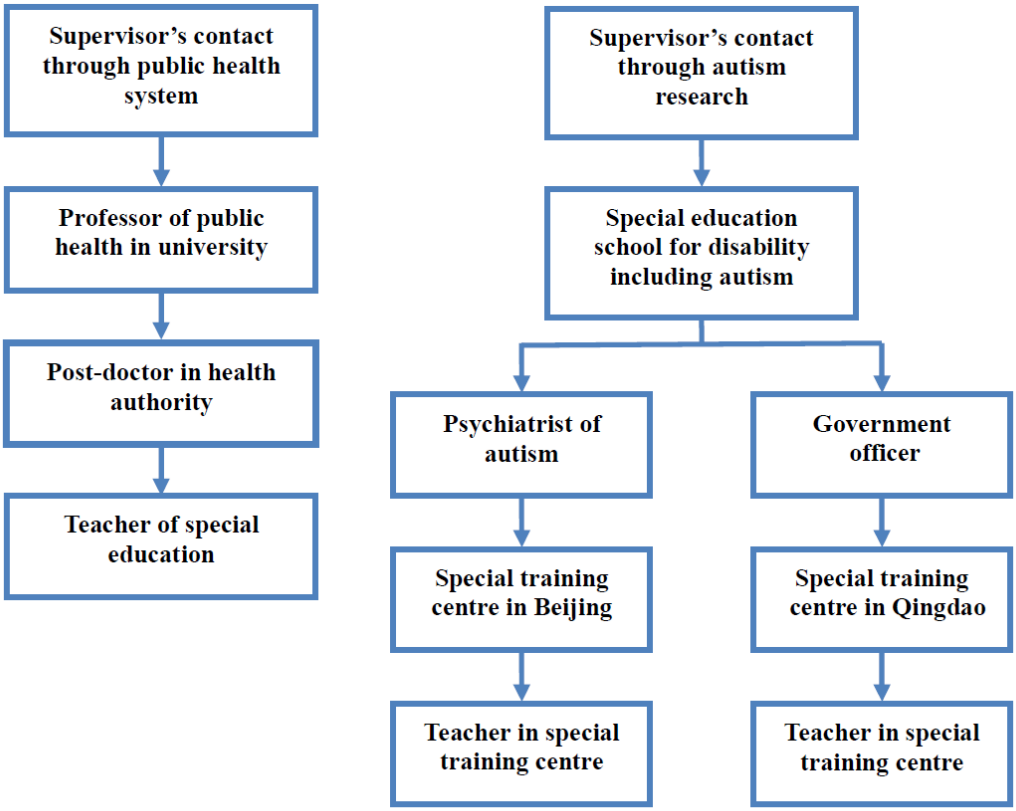


Table 6.1 Settings represented by interviewed providers

Title of informant	Setting	No	Setting for autism	Source provider represented	Years of experience related to autism
Professor of Public Health	Research institute in University	1	Research	University or medical school	30 years research experience in Public Health
Dean of special education school	Education	1	Intervention and education provision	Private owner	8 years special school for children with disability
Post-doctor in heath authority	Health authority	1	Intervention and evaluation	Government-owned Rehabilitation	7 years research experience in development of children with disability
Government officer	Policy Authority	1	Policy and service provision	Government	5 years experience in autism
Psychiatrist	Hospital	1	Diagnosis	Hospital/ Government	30 years experience in child psychiatry specialised in the diagnosis of autism
Headmaster of special centre	Special training centres	2	Intervention	Private owner	5 years experience in autism intervention
Teacher of special training centre	Special training centres	3	Intervention	Private owner	2-6 years experience in autism intervention

6.2.4 Semi-structured Interviews

Face-to-face interviews were conducted. Written transcripts of the interviews were taken, however, no audio recording of interviews was conducted as requested by the informants. The semi-structured format guided informants through the key themes of enquiry but allowed for flexibility and responsive probing when different informant-prompted topics emerged. The service provider informants in this study will be referred to as P1 to P10. The key themes of that were used to guide the interview are shown in Box 6.1.

Box 6.1 Key themes of interview with providers

- History of ASC in mainland China
- National and local level health services for ASC
- Key issues on current practice for ASC
- Healthcare differences between regions
- Local educational settings for children with ASC
- Advantages and disadvantages of the state-run and private education services

6.2.5 Data collection and analysis

A generic qualitative method was adopted. The method included participant recruitment, interviews, transcription, checking, reflection on the interviews and analysis via thematic coding[357]. The hand-recorded interview transcripts were the primary data. Key points of the transcripts from each interview were summarised and sent back to the informants to check for accuracy. The informants' comments were incorporated into the transcripts. The transcripts were then read by the candidate to note relevant ideas and identify possible text segments for further coding in Microsoft Word and Excel. The basic purpose of thematic coding is data retrieval, which is used to classify text according to theme, so that later on, when doing analysis, it is easy to retrieve all passages that relate to a given topic. Thus, when examining the transcripts, the content related to the targeted key themes listed above were identified and marked. The potential relationships among identified information were established in order to convey a meaning and comprehensive interpretation. The codes were either

inductively drawn from the data or deductively and iteratively refined. The codes were rechecked by the candidate after the first entry to ensure accuracy. In the next step, the coded data were categorised into meaningful patterns for further analysis and reporting. Qualitative analysis was conducted in such a way that the experiences and personal dimensions reflected the current healthcare system for ASC[358].

6.3 Results

6.3.1 Context

All informants had a median of 7 years experience (range: 2-30 years) working with children with ASC and their families. Their experience with ASC was established based on their roles as service providers in different service settings in mainland China.

6.3.2 The introduction of autism in mainland China

Until now, there has been no available literature either in Chinese or English about how the term 'autism' has been understood by Chinese psychiatrists. The psychiatrist indicated that the term 'autism' was most likely introduced to China by a child psychiatrist named Tao Kuo-Tai. Tao Kuo-Tai went to America to study Child Psychiatry at the Institute of Psychiatry at the University of California in 1948, sponsored by a scholarship from the World Health Organization (WHO)[75]. A year later, he came back to China in 1949 to develop the discipline of child psychiatry. He established the Nanjing Child Mental Health Research Centre on 1st June, 1984. Since then, much research on autism has been conducted with the support of this centre[359-361]. There are two literal Chinese translations of the term 'autism' ("Gudu Zheng" and "Zibi Zheng") and both mean the disease of loneliness or self-isolation. It is described as a condition in which a person usually has difficulties with communicating or forming relationships with others[266] and who has a tendency to keep to him or herself. These two terms refer to the same condition and were used interchangeably in China[76]. In medical text books, autism as a diagnostic term was first included in Child Psychiatry in the 2nd edition of Chinese Psychiatry in 1989 with a description as a comprehensive developmental disorder[362]. Over recent years, the psychiatrists and researchers in the West have tended to adopt the terms 'autism spectrum disorders' or 'autism spectrum conditions' to capture more subtypes of autism, reflecting autism as

a spectrum, with Childhood Autism at one extreme. In China, the term Childhood Autism has been used most frequently. Research on ASC has mainly focused on Childhood Autism in mainland China, rather than viewing autism as a spectrum[267] (Box 6.2: P1-1, P3-1).

Box 6.2 Quotes of the introduction of autism in mainland China

> *"The term 'Gudu Zheng' and 'Zibi Zheng' was probably generated as the translation of autism from the West by Professor Kao-tai Tao... He went to America for a year and studied Child Psychiatry and he was also the first doctor that reported the diagnosis of autism in mainland China. The term 'Childhood Autism' was used most frequently since we first heard about the existence of autism." (P1-1)*
>
> *"Most studies of autism in mainland China have focused on Childhood Autism rather than the autism spectrum since we still don't have a very clear definition and diagnostic criteria for the spectrum." (P3-1)*

6.3.3 The development of research on autism

The first research article about autism in mainland China was published in a Chinese journal by the child psychiatrist Tao Kuo-Tai in 1982[363] reporting four cases. The first publication in English about Chinese children with autism five years later was also written by Tao Kuo-Tai[75] (Box 6.3: *P5-1*).

ASC is a relatively new research topic in mainland China. Research on ASC can be found in various disciplines including Psychiatry, Psychology, Education, Social Science, Pathology, Genetics, Neuroscience, Public Health and Epidemiology[352]. Medical training in mainland China for undergraduates does not include Psychiatry. Therefore, clinicians who can give a diagnosis of autism in mainland China either learnt from a graduate supervisor whose work was related to autism, or s/he had experience in a psychiatric department in hospital in their career. Research on ASC in mainland China has mainly focused on aetiology, specifically concerning genetics[360, 364, 365] (Box 6.3: *P1, P5-2*).

Epidemiological research focusing on prenatal and perinatal risk factors[366] and autistic characteristics has usually been carried out in hospital settings. According to the informants from research institute (P1) and health authority (P3), there were almost

no epidemiological studies before the survey for autism conducted in 2001[266] (Box 6.3: *P3-2, P1-2, P3-3, P3-4*).

Box 6.3 Quotes of the development of research on autism

"…In China, the branch of developmental psychiatry has not been developed into an independent department yet, there has been no specific research team for autism in universities.…so the training of clinicians about autism largely depended on the autism referral rate to that particular hospital…" (P5-1)

"…Medical training in China for undergraduates is five years, after which medical students need to pass a practitioner examination in order to become a registered doctor. However, in the basic five-year training, we usually do not have courses in Psychiatry, rather we have courses on Internal Medicine, Surgery, Obstetrics and Gynaecology, and Paediatrics… So most students may not have heard of autism.…until they are at graduate level and learned from supervisors who had been involved in research on autism or mental health." (P1-2)

"When I was in medical school, I did not know about autism since we did not learn it.…after graduation, I became a doctor in this hospital.…I worked in the Paediatric department for a while with my attending physician was an expert of autism who was one of the earliest doctors in China that could diagnose autism.…after many years, we were transferred to the psychiatry department and opened this out-patient clinic for autism." (P5-2)

"…there have been two national surveys of disability so far. One was in 1987 and the other was in 2006. In the first national survey, autism was not included as it was barely known about in China at that time…." (P3-2)

"…in 2001, there was a survey for autism conducted in 12 cities in mainland China which was hosted by the China Disabled Persons' Federation (CDPF), Ministry of Health and Ministry of Public Security…." (P1, P3-3)

"…in 2004, the Beijing CDPF hosted a survey on autism in 18 regions in Beijing using a clinical questionnaire without further follow-up assessments.…the second national survey in 2006 included autism…"(P3-4)

6.3.4 National and local policy for autism

The informants from the health authority (P3) and special education services (P2) indicated there was no unified national policy for ASC. Many regions had local policy towards ASC which varies across China. In some regions, families with children having autism are provided with an allowance from the government. However, the amount of the allowance differed among regions.

Beijing (as the capital of China) is supposed to have a better political and economical environment than average in mainland China. Thus, a relatively better policy for children with special needs is to be expected in Beijing. Five informants indicated one requirement of having a disability certificate and allowance from the government in Beijing is that the child must be a legal resident of Beijing (Box 6.4: *P3-5, P2-1*).

When asked the main issues on autism from the policy making and management point of view, three informants indicated that there has been increased awareness about autism as a result of the media publicity and widespread information via the internet. Usually, when parents become concerned that their child may have autism, they try to find information online prior to seeking a diagnosis (Box 6.4: *P4-1, P4-2, P5-3*). Although children with autism have been given more attention than in previous years, the system of service support from the government and society is still under-developed with limited resources that cannot fulfil the needs of these children and their families (Box 6.4: *6-1, 4-3*).

Box 6.4 Quotes of national and local policy for autism

"…the local policy depends on whether the local population is familiar with this condition or not…I learnt this from parents of children with autism from other provinces, they told me about their local policies on autism…the policies vary across regions….in Beijing, the Beijing China Disabled Persons' Federation (BCDPF) provides £50 monthly as an allowance for each child who both has a "Hu Kou" (residential identification) and a disability certificate…however, the allowance is not directly accessible to parents. They obtain the money once, at the end of year, by invoicing for the special training payments in rehabilitation centres…there are certain conditions of the reimbursement…." (P3-5)

"If the child is trained outside Beijing, the £50 cannot be used to compensate the payment in this case…in Beijing, the disability certificate requires the confirmed diagnosis from a well-known Psychiatric hospital and the "Hu Kou" (residential identification) in Beijing." (P2-1)

"…there has been a marked rise in autism concerns since 2000 which requires recognition with more provision for children with autism and their families..." (P4-1)

"…much focus has been put on autism by the media since there have been many TV programmes about children with autism..." (P4-2)

"…there are many children who come from all over China to get into hospitals or institutes, all of which have become well-known in this for autism diagnosis… the parents usually can get this information through an internet search…or heard from other parents…" (P5-3)

"…as there are few government supported special training and educational institutes for autism, many private institutes have been established by parents of children with autism…because of the lack of support, once diagnosed, it is usually the parents who have to pay for the costs to support their autistic child..." (P6-1)

"…in each setting related to autism, people tend to work separately and independently…they seldom work together as a team, so there is little interaction and collaboration among Chinese researchers or officers to make any scientific or policy breakthroughs on autism…often the parents of children with autism are the ones that are suffering from this situation…" (P4-3)

6.3.5 Current practice for autism

The informant in the Psychiatric hospital described a general delay in diagnosis for autism because many parents did not seek diagnosis of their children for various reasons. Some parents did not notice there was a problem with their child until someone else pointed it out, while some parents may have noticed early on but did not think it was something serious. Some parents were simply reluctant to accept the condition (Box 6.5: *P5-4, P5-5*). Once the child was taken to a clinical setting for a diagnosis, the diagnostic process was relatively short due to limited resources and a lack of diagnostic instruments (Box 6.5: *P5-6*).

The questionnaires used in mainland China are old versions of questionnaires that were adopted from the West in the 1980s, such as the ABC[136, 281], the CABS[172, 282] and the CARS[135]. The ADOS[186] and ADI-R[180] have not been well adapted in clinical or research settings in mainland China (Box 6.5: *P5-7, P5-8*). The informant also indicated that clinicians in China often felt frustrated since it seemed there was no medication or other treatment that could act to alleviate symptoms of autism (Box 6.5: *P5-9*).

Box 6.5 Quotes of current practice for autism

"There are many children who were diagnosed many years after their parents sensed there might be something wrong with the child…" (P5-4)

"Many parents have been reluctant to accept the diagnosis of autism when they were first given it…because this means their child has a mental disorder…this is especially difficult to accept if their child appeared to have typical development in early childhood, or if the child has high-functioning autism…" (P5-5)

"The diagnosis for autism is usually no more than 30 minutes…it usually contains a time for parents to complete some questionnaires and coding…then the interview with parents…and an observation of the child by asking him or her to complete several tasks…actually in many cases by simply observing the child, you can tell whether he or she has autism or not…" (P5-6)

"There is no national screening programme for autism in clinical settings during routine developmental check-up for children…however in our psychiatric department we have adopted Chinese versions of Western screening questionnaires to initially evaluate the child at referral, such as the ABC and the CABS… after the parents fill in the questionnaires we calculate the score, and then we spend some time playing with and observing the child. On the basis of this, a decision about a suitable diagnosis is made..." (P5-7)

"We have translated the ADI and conducted a pilot study and validation…but it has not been generally used in clinical diagnosis since it is quite long…" (P5-8)

"I felt quite sad and powerless when I saw some very severe cases and they came to diagnosis too late…...following diagnosis, there is very little we can do to help the child other than recommending special training…" (P5-9)

6.3.6 Local education service for children with autism

Informants from the health authority and policy authority reported the availability of local education services for children with autism (Box 6.6: *P4-4, P3-6*). During the interviews with the headmasters of two well-known private rehabilitation centres for autism, the general operation of these centres was described as follows (Box 6.6: *P7-1, P7-2, P6-2*).

Courses in private centres included individual training in sensory integration, fine motor skills, music, video and sports. In one centre each class lasted about 45 minutes, while in the other it was 30 minutes. Each child had a fixed curriculum designed by the therapists in the centres following an evaluation. These two centres mainly used

the ABA[367], TEACCH[368] and RDI[343] as the theoretical basis for the training, adopted from the West. In general, three months was required by private centres as the minimum training period for each child. There were also other training centres which offered training courses for sensory integration, fine and gross motor skills, and language skills but they were not exclusively for children with autism. These centres were privately owned and some of these centres had become chain business. The two informants from the private centres also indicated that parents had concerns about current education services (Box 6.6: *P8-1, P8-2*).

An interview was conducted with the Dean of a private special education school. Most of the children in the school were under 13 years old and were allocated into different grades according to their intellectual ability. The curriculum was similar to that of mainstream schools with special training lessons. One of the training lessons included making ceramics, which was adopted from Japan. When the teachers were confident about the learning ability of the child, they would recommend the child to study in a higher grade. There was a mainstream primary school nearby. When the child was considered capable enough, the teacher would send him or her to this primary school to study with typically developing children. This was called the integration education programme. However, only a small proportion of the children in this special education school had autism.

Box 6.6 Quotes of local education services for children with autism

"Children with an existing diagnosis of autism usually cannot enter mainstream primary schools, since their behaviours will be easily recognised by teachers and other children…. It might be possible that children having autism with normal intelligence could stay in a mainstream school as long as their examination scores do not influence the overall academic performance of the class. But still very few of them could stay…." (P4-4)

"From the records in our department, most children who have been diagnosed and have a certificate of disability are not in mainstream schools. Some of them are in private training centres for autism, while some of them are in government-supported or private special education schools… I am not sure whether there are children that have been kept at home…" (P3-5)

"When the child enters the school, professionals in our centre will evaluate the ability of the child in the following domains: cooperation and reinforcement effectiveness, visual performance, receptive language, motor imitation, vocal imitation, requests, labelling, intra-verbal and spontaneous vocalization…all these abilities will be evaluated and updated daily by the teacher in one-to-one training class for each child."(P7-1)

"During daily training, each child has to have an adult to accompany him or her throughout the whole day". (P7-2)

"During weekdays, the training usually takes place from 9am to 4pm…the training is like a primary school from Monday to Friday with Saturdays reserved for parental training." (P6-2)

"Our centre is only able to accept children who are between 3 to 6 years old. If they have reached primary school age, we have to let them go but many parents reported that they would end up with nowhere to go and they wanted to come back…." (P8-1)

"The number of government-supported special schools is very limited. They do not provide special intervention for children with autism. So the parents are concerned that, if they send their child to such school after intervention in our school, their child might soon revert back to their original condition and therefore have wasted all the years of intervention…." (P8-2)

6.3.7 Advantages and disadvantages of state-run and private education services

6.3.7.1 Lack of resources in state-run education service

The informant from the health authority reported that the Beijing China Disabled Persons' Federation (BCDPF) has a state-run rehabilitation centre which provides several training courses for children with autism such as sensory integration, fine and gross motor skills, and the speech therapy. These courses are relatively cheap and their costs can be reimbursed from the government allowance. However, given the shortage of special teachers, there are a limited number of places available in this centre. There was no such rehabilitation facility in the state-run Psychiatric hospitals. The informant from the health authority indicated that there were state-run special education schools in Beijing (Box 6.7: *P3-7, P5-10, P2-2*).

Box 6.7 Quotes of the lack of resources in state-run education services

"The rehabilitation centre of BCDPF was small and has a limited number of therapists and special teachers…the intervention programmes are separate, which are different from private centres where the programmes are all day long and comprehensive…we offer intervention as modules…for example, once or twice a week for fine motor or sensory intervention…we can only cater for a small number of children due to a shortage of resources…" (P3-7)

"We only provide diagnosis and basic examination to children in our clinic. We don't have therapists here, so after diagnosis, the parents need to find a rehabilitation centre for intervention or other educational settings…" (P5-10)

"Generally, each district has one school run by the government which is relatively cheap…the tuition fee can be reimbursed by the government allowance if the child has a disability certificate…however, all of these schools are not specialised for children with autism…most children in those public special schools were children with other mental or physical disabilities…children in all age groups are mixed together…since each district only has one state-run special school, the number of children that can attend such school is limited, and thus not all local needs are catered for…many parents have to choose other private special schools like us in order to get their child educated…"(P2-2)

6.3.7.2 A developing structure for special teachers and therapists in private centres

Compared with the shortage of resources in state-run rehabilitation centres, certain private centres tried to develop their own structure of coordinated training and professional development for special teachers and therapists. Three informants who were teachers in two private centres reported that teachers in their special training centres were mainly recruited from special education colleges. In one centre, they were required to pay a training fee to join an ABA training programme, run by the centre. The training programme for teachers consisted of two parts: theory of ABA, and the ABA practice with children. All the trainers in the training centre were experienced special teachers of autism. There were usually 30 to 40 participants at the beginning of the training. However, after two examinations, only 10 to 13 trainees could actually graduate and become teachers in this centre. This maintained the quality and manpower of the intervention programme.

6.3.7.3 Reported improvement of children with autism by intervention in private centres

The most effective part of training was the individual training or 'one-to-one training class', according to the teachers. In one centre, this individual training must be carried out without the parents, while in the other centre, the training required the caregiver to be present. After each individual training class, the teacher reported progress to the parent. This included the improvements the child made that day and instructions on how to continue the training at home (Box 6.8: *P8-2, P9-1*).

6.3.7.4 Non-unified regulations on intervention among private centres

Although teachers reported improvements of children with autism following intervention, the regulations and training strategy in private centres are lack of coherence. They usually have different and sometimes contradicting theories regarding what is best for the child in terms of intervention. This makes it difficult for a child to adjust if the child has to be transferred from one centre to another which employing a different strategy (e.g. the presence or absence of parents during individual training sessions). (Box 6.8: *P8-3, P9-2).*

Box 6.8 Quotes of intervention in private centres

"The child with autism needs to be trained in order to foster basic daily routines…the training helps to improve the ability of the child and to make it easier for the parents to cope with their daily lives." (P8-3)

"Most children made progress within three months, especially in speech…many children who were unable to speak when they first entered the training programme began to speak during their training…"(P9-1)

"…we do request one caregiver to attend the one-to-one training…because we want the parents to learn the methods and the purpose of training…only in this way, they can continue the training at home…only one hour one-to-one training session a day is less than adequate…the child needs to be trained during daily life, not only in class…" (P8-3)

"…we don't recommend the parent to be present during the one-to-one training…we found that many autistic child behaved differently in front of their parents …they become more difficult to teach when their parent is there…every teacher reports progress and gives instructions to parents after each class." (P9-2)

6.4 Discussion

The main aim of this research was to learn the current situation of healthcare and education service for children with ASC in mainland China from the service providers' perspectives. Interviews with several key informants from the health and education system were conducted. The findings from each provider brought up several common issues on service provision in main settings for ASC.

6.4.1 Implications for professional training and research

There is a lack of trained professionals in the field of recognition and detection of ASC in China that is partly due to a lack of education among medical students during their basic training. This would be improved greatly if Psychiatry could be included in the medical training programme or become a branch of special training. Another option would be to include training about autism into the field of Paediatrics. Without the basic knowledge and awareness among the clinicians, it will be difficult to implement early detection and diagnosis for ASC in mainland China. The improvement of knowledge would encourage more researchers and clinicians to conduct research on ASC. So far, research on ASC in mainland China is limited. It would be valuable if a Chinese network for ASC research could be established to

encourage collaboration and effective resource utilisation. This research highlights the gap in government support for children with autism and their families both in service provision and research. One of the obstacles for policy making might be the lack of data on the prevalence of ASC in mainland China. It will be difficult to estimate the needs of children with autism without adopting validated screening and diagnostic instruments to help accurately determine the population prevalence of ASC. Without this information, policy making would be impossible. Thus, a prevalence study for ASC would be a good start for further research and policy making.

6.4.2 Implications for healthcare service provision

The lack of standardised diagnostic and assessment tools on ASC in mainland China was highlighted in this study. Government input could help with the introduction and adoption of more advanced assessment tools to improve the diagnosis of ASC by training professionals and developing a multi-disciplinary assessment team. The multi-disciplinary assessment model had been developed in the US[26] and UK[66, 67]. It has also been adopted in Hong Kong[369]. In a multi-disciplinary team, each health professional has their own role and responsibility. They contribute and coordinate together all of their knowledge and results from their individual evaluation of the child to make a diagnosis and to form an individual plan[370]. In order to achieve this, the gap between research and clinical practice should be closed by applying standardised methodologies for diagnosis and advanced intervention in clinical settings. This would help to support clinicians and improve their confidence in the diagnostic decision-making. Informants were aware of the time delay between the first concerns about ASC and an eventual diagnosis. Children with severe autism usually display typical autistic features around the age of 2 to 3[371]. It would, therefore, be helpful to improve public knowledge about ASC in order to assist early recognition. For example, public education on autism can begin from education for pregnant women who attend check-ups after delivery in hospital. It also can be conducted through TV, newspaper, or advertisements which may help to reduce stigma[372, 373] towards autism in the general population. There is a need to develop the healthcare system and put in place more resources in clinical settings for children with ASC and their families.

6.4.3 Implications for education service provision

Most children who had been diagnosed with ASC in mainland China were not in mainstream education but in a private rehabilitation centre or a state-owned special education school. There were a limited number of state-run special education schools and most of them were not specialised in ASC. It is also possible that there may be children with severe autism that have been kept at home. This study highlighted the concerns from service providers in mainland China towards the education system for children with ASC. Previous research reported that many children with autism attend mainstream schools because of personal connections[325] rather than the implementation of the "*Suiban Jiudu"* policy.

In the UK, each school has a Special Educational Needs (SEN) register which monitors children who require access to additional support beyond the mainstream curriculum offered by schools[70]. Children on the SEN register can apply for a 'Statement of Special Educational Needs'. This states a child's needs and the help that they should receive at school. This statement is reviewed every year to make sure the required extra help has been provided[70]. Three decades ago, the inclusion of education for children with different abilities was achieved through a great effort from the parents in the US. It is possible that China is in the middle of a transition, previously experienced in the West[325].

6.4.4 Limitations

This study has several limitations that should be acknowledged. The first is to question the reliability and generalisability of snowball sampling. The informants were approached mainly through academic links. The description of the healthcare service for autism is predominantly from their personal points of view. However, they did also describe the wider context. During these interviews, the informants reported overlapping information, which provides some confirmation of reliability of the accounts. Second, although the sample size in the current study is considered as adequate for generating sufficient in-depth data in qualitative research[374], the number of informants in each service setting was limited. The informants in this study were professionals in specific fields that might limit the representativeness of the views of each field as a whole. Thus, future studies should recruit more informants within each service setting. Third, the sources of informants and the types of service settings in

this review were limited; there may be other settings related to ASC which were not covered in this study. Fourth, the interviews were not audio-recorded, so the hand-written transcript did not capture every word reported by the informants. It is possible that some contents were missed out. However, transcripts were sent back to the informants to check for accuracy, it is reasonable to assume that the major topics should have been covered. Although all the transcripts and coding results were double-checked, the transcripts and the coding were conducted by a single researcher. This might lead to a bias in the interpretation of content.

6.5 Conclusion

There are two types of health services for autism in mainland China. One is a government-supported service that includes local government, the China Disabled Person's Federation, research institutes and hospitals. The other is parent and privately supported service which includes parent-established training centres and special schools for children with disabilities. In mainland China, these two seem to operate in parallel. Parents depend on government health services for obtaining a diagnosis. However, for intervention, parents largely depend on a service that is mainly provided and funded by their own. There is little connection between government and private services, resulting in a shortage of training centres and a huge burden on parents in the support of their children. There is an urgent need to enhance healthcare and education services for children with autism in mainland China. In Chapter 7, interviews with parents were conducted to explore the current service provision of ASC in mainland China from a service users' perspective.

Chapter 7 Service Provision for Autism in Mainland China: Service Users' Perspective

7.1 Introduction

The previous chapter presented the service provision from the providers' perspective[375]. As service users, the parents' beliefs and experiences could provide insights on current services and give feedback to policy makers and system developers for further improvement. This chapter aims to map the healthcare and education pathway of autism in mainland China and to identify potential barriers in service provision from the parents' perspective.

7.2 Method

7.2.1 Ethical approval

This research was part of a collaborative research project between the University of Cambridge and the Peking University First Hospital (PUFH). This programme of work has been approved by the Ethics Committee of Peking University First Hospital.

7.2.2 Settings

The contacts of several headmasters of special rehabilitation centres in mainland China were obtained from service providers interviewed in the study described in Chapter 6. Two of the most well-known private training centres agreed to participate. Centre 1 was in Beijing and Centre 2 was in Qingdao. A state-run training centre in Beijing (Centre 3) was also included.

7.2.3 Participants

A total number of 69 informants were recruited for face-to-face interviews. They were parents of children with autism in three rehabilitation centres described above. There were in total 45 children in Centre 1 who were all contacted through the centre administration. The parents of 35 of them agreed to participate. The total number of children in Centre 2 was 330, and the parents of 30 children were recruited. The other four informants were recruited from Centre 3.

7.2.4 Procedures

Opportunistic sampling was used to reach service users. After the consent was obtained from the three centres, the parents in those centres were contacted and invited for participation. In such centres, a parent or a caregiver is required to accompany the child throughout the day during training[375]. The interviews were carried out during the one-to-one training class of the child, when the parents or caregivers were available. In Centre 1 and 3, the parents were approached directly. In centre 2, the parents and caregivers were invited though the administration of the centre. Only after the consent was obtained from the parent, was a face-to-face interview arranged.

7.2.5 Interview procedures and self-developed questionnaire

After the permission from training centres and consents from the parents were granted, semi-structured interviews were conducted with parents or caregivers. Each interview was conducted with one informant and lasted up to 1.5 hours. A topic-guided schedule was developed from the themes that emerged from the initial seven interviews. The questions used in the interviews comprised the descriptions of 10 areas (Box 7.1). The full questionnaire is provided in Appendix 7.1.

Box 7.1 Question areas covered by the interview schedule

(1) General information about the child
(2) First signs of any difficulties
(3) Referral to hospital for diagnosis
(4) Diagnostic process
(5) Finding and entering special training centres
(6) Training courses in special training centres
(7) Burden on the family due to autism
(8) Local policy for autism
(9) Possible causes of autism
(10) General information about the parents

7.2.6 Data collection and analysis

All the interviews were recorded by hand without audio taping as requested by parents. Key points of each interview were checked with the informants at the end of

each interview. Mixed methods were adapted in the analysis for the data. The transcripts were read by the candidate to identify possible text segments for further coding. Qualitative analysis[376] was conducted to identify the most important variables and then quantitative methods were used to conduct further analysis. Mann-Whitney U tests were conducted to compare the mean age of independent groups. Systematic modelling was used to map the healthcare and education pathway of children with autism[377]. Stata 10.0 was used for the analysis.

7.3 Results

7.3.1 Characteristics of the children and parents

In total, parents of 69 children with a diagnosis of autism participated in this study. There were 55 (80%) boys and 14 (20%) girls. The mean age of the children was 4.6 years old (range: 2.2, 11). Most of the children (63/69, 91%) were the first-born child in the family.

China has 23 provinces and five autonomous regions as well as two special administrative regions[378]. In this sample, the children with autism were born in 19 regions including Beijing city and 18 provinces within mainland China. 51 (74%) children lived in the north of China and 18 (26%) lived in the south. 62 children (90%) lived in urban areas. The geographical distribution of this sample is shown in Figure 7.1. The characteristics of parents are shown in Table 7.1.

7.3.2 Results: The pathway from first awareness to diagnosis

7.3.2.1 Time delay during diagnosis and intervention

The mean age of children when their parents had first awareness of their abnormality was 2.2 years old (range: 0.5, 6). The mean age at diagnosis was 2.8 years old (range: 1.7, 6.8). The mean age of initial intervention was 3.3 years old (range: 1.3, 7) and the mean age at the commencement of current training was 3.7 years old (range: 1.7, 10.2). The mean time lag between first awareness and diagnosis was approximately 7.1 months (range: 0-30 months), while the mean time lag between diagnosis and the commencement of initial intervention was about 6.5 months (range: -15.6-48 months). Thus, the mean delay between first awareness and initial intervention was 13.6

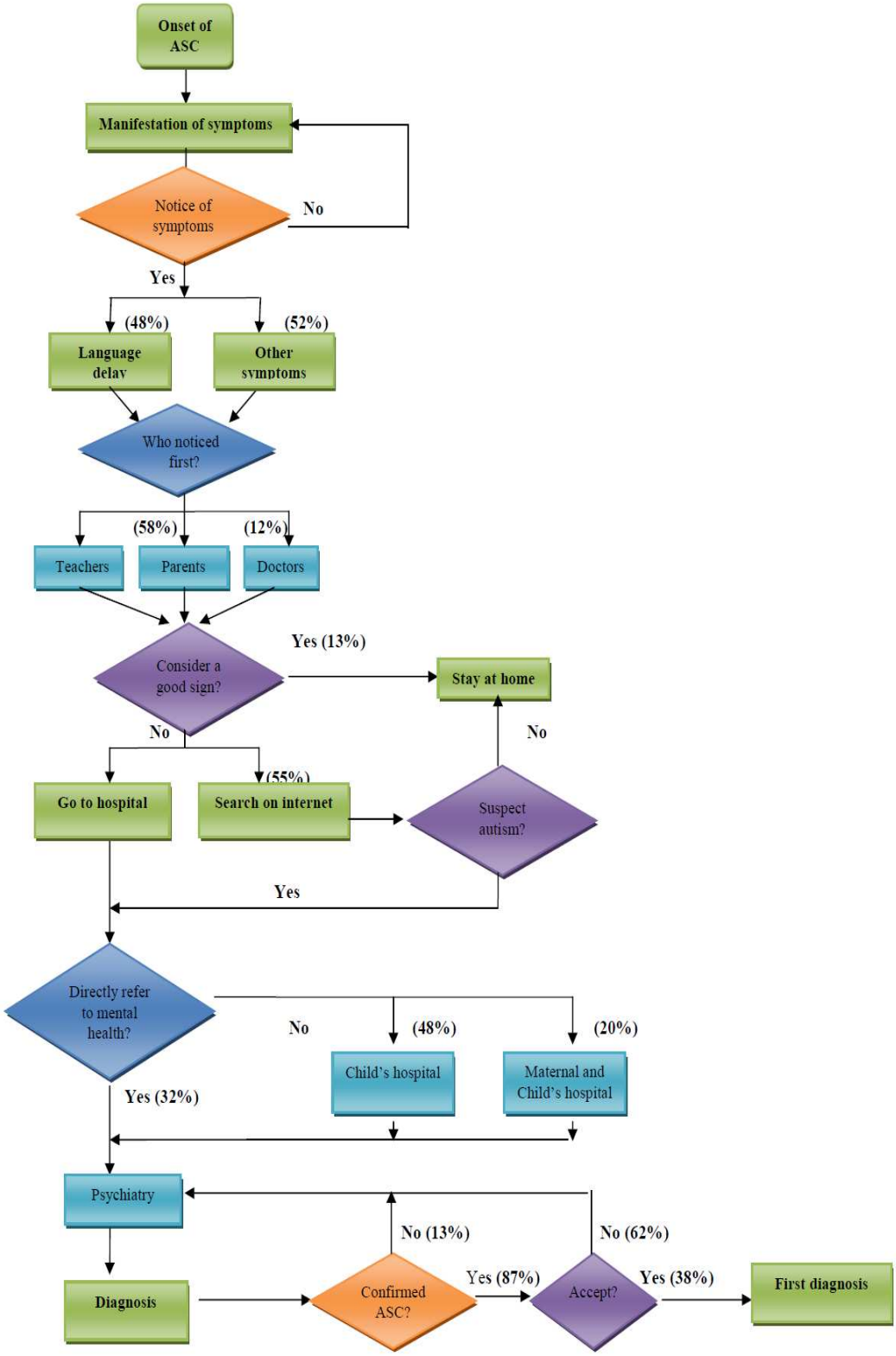
months (range: 0-51 months). The pathway from first awareness to diagnosis is shown in Figure 7.2.

Figure 7.1 Geographical distribution of children with autism in this sample

Table 7.1 Characteristics of parents

Characteristics	Categories	Number (%)
Age of mother	<=25	9 (13)
	26-30	38 (55)
	>30	22 (32)
Age of father	<=25	4 (6)
	26-30	30 (43)
	>30	35 (51)
Education of mother	Less than college	18 (26)
	College	41 (59)
	Higher than college	4 (6)
	Missing	6 (9)
Education of father	Less than college	16 (23)
	College	40 (58)
	Higher than college	7 (10)
	Missing	6 (9)

Figure 7.2 Flowchart of healthcare pathway---from onset to diagnosis



7.3.2.2 First awareness

Three patterns of recognition were identified from the interviews: (i) family numbers noticed (58%) including parents themselves, grandparents, relatives or family friends; (ii) teachers (29%) in kindergartens or private nurses; (iii) doctors (12%) who recognised symptoms during the child's referral.

When asked about the primary concern regarding the child's development that caught the parent's attention, the most obvious characteristic reported was the language delay. Thirty-three parents (48%) sensed the condition because their child could not speak, unlike other children of the same age. However, nine of the children (16%) were not taken to referral at first because the parents considered language delay as a good sign. The second obvious symptom was that the child seldomly responded to other's instructions (26%).

When the parents were asked for their opinion regarding possible causes of autism of their child, 38 mothers (56%) answered, within which the most frequent answer was depression, anxiety or anger during pregnancy (13, 34%). Thirteen (19%) parents suspected environmental exposures. Ten parents (14%) blame the personality of parents and the raising pattern which suggested the lack of knowledge of autism. The rest of parents stated that they did not know and cannot think of any possible causes. Those reported causes were considered by parents which were not necessarily the risk factors or exposures for autism.

7.3.2.3 Diagnosis

A total of 38 (55%) parents emphasised the importance of the internet in finding information about what was wrong with their child which led to further hospital referral. Both private centres had websites where the information of the courses and facilitates can be accessed.

ASD can be diagnosed in three types of hospitals in mainland China including children's hospital or children research centre, maternal and children's health hospitals, and psychiatric hospitals. Parents usually took their children to more than one hospital before they accepted the diagnosis. Thirty-three parents (48%) initially

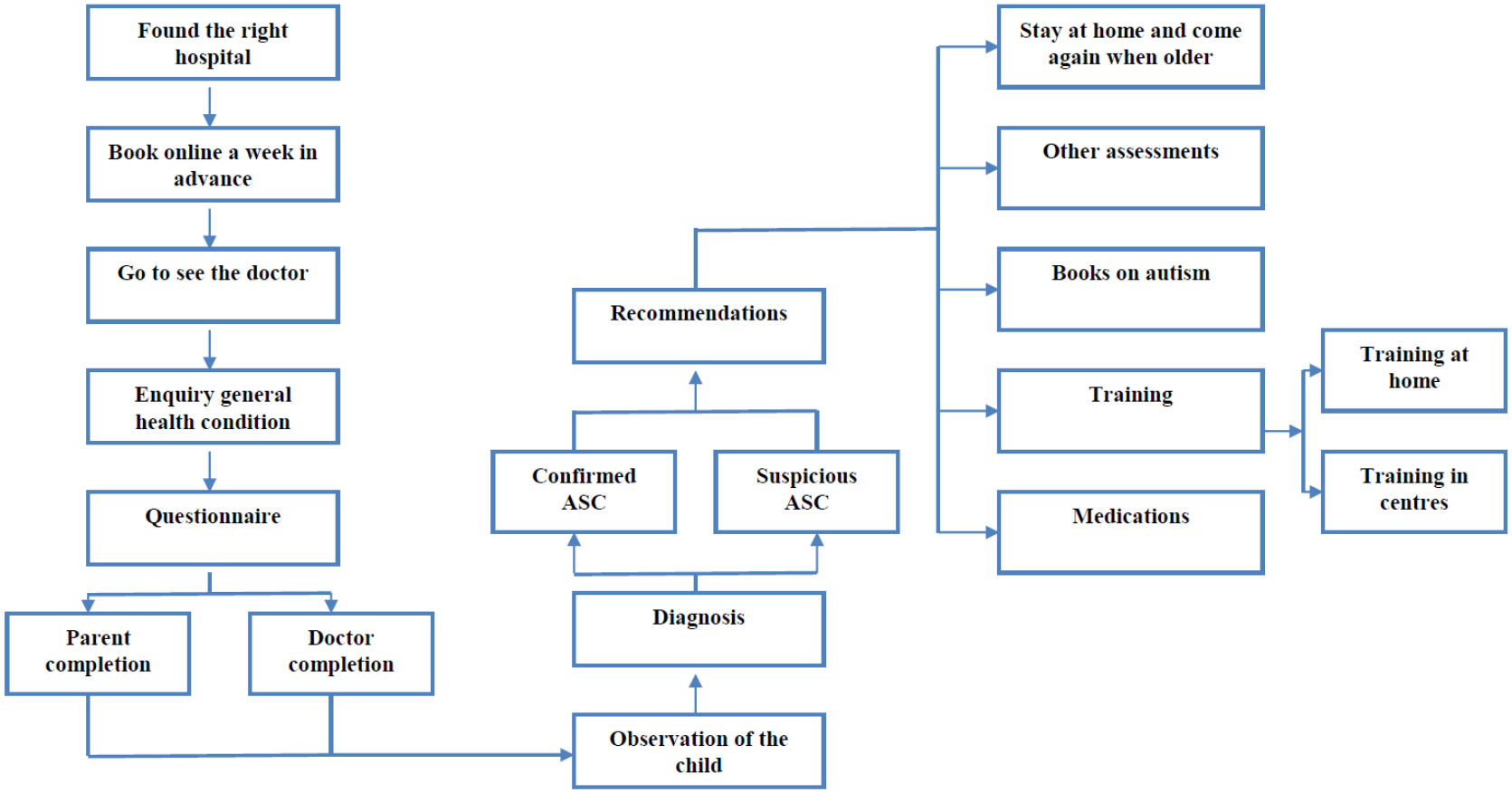
took their children the local children's hospital while 22 parents (32%) visited a psychiatric hospital. Fifteen parents (22%) sent their children to a third hospital.

Parents usually took their children to well-known psychiatrists across regions in order to obtain a confirmed diagnosis. An appointment a week in advance was usually required. Regarding the diagnosis by well-known psychiatrists at the first referral, 24 (35%) children in this study received a diagnosis of 'Autism' while 36 (52%) children were given a diagnosis of 'Tendency of autism or possible case of autism'. One child was diagnosed with Asperger Syndrome and the remaining (10%) received a diagnosis of other condition rather than autism at first. Approximately 70% of the parents reported the diagnostic process was approximately 16 to 30 minutes and 23% parents reported it to be around 60 minutes. The diagnostic process usually began with a general health enquiry, followed by a questionnaire completion and a 10-minute period of direct observation. The questionnaires used in clinical settings varied among regions, but all of them were reported as relatively easy to complete[136]. The results on healthcare pathway from first symptoms to diagnosis are shown in Table 7.2 and the diagnostic process is shown in Figure 7.3.

Table 7.2 Results of findings from first symptoms to diagnosis

Questions	Categories	Number	(%)
Symptoms of first concern	No speaking	33	(48)
	Little eye contact/response	18	(26)
	Lack of love to parents	4	(6)
	No peer relationships	13	(19)
	Stereotyped or odds behaviours	1	(1)
Who raised first concern	Family members	40	(58)
	Teachers	20	(29)
	Doctors	8	(12)
	Others	1	(1)
Consider language delay a good sign	Yes	9	(13)
	No	60	(87)
Direct to mental health	Yes	46	(67)
	No	23	(33)
Use of internet	Yes	38	(55)
	No	31	(45)
First referral hospital	Children's care/research hospital	33	(48)
	Maternal and children's care	14	(20)
	Psychiatric hospital	22	(32)
	Other	0	(0)
	Missing	0	(0)
Second referral hospital	Children's care/research hospital	16	(23)
	Maternal and children's care	1	(1)
	Psychiatric hospital	26	(38)
	Other	0	(0)
	Missing	26	(38)
Third referral hospital	Children's care/research hospital	3	(4)
	Maternal and children's care	2	(3)
	Psychiatric hospital	9	(13)
	Other	1	(1)
	Missing	54	(78)
Diagnosis	Autism	24	(35)
	Tendency of autism	36	(52)
	Other or no diagnosis	7	(10)
	Asperger Syndrome	1	(1)
	Missing	1	(1)

Figure 7.3 Flowchart of the diagnostic process



7.3.3 Intervention and other treatment

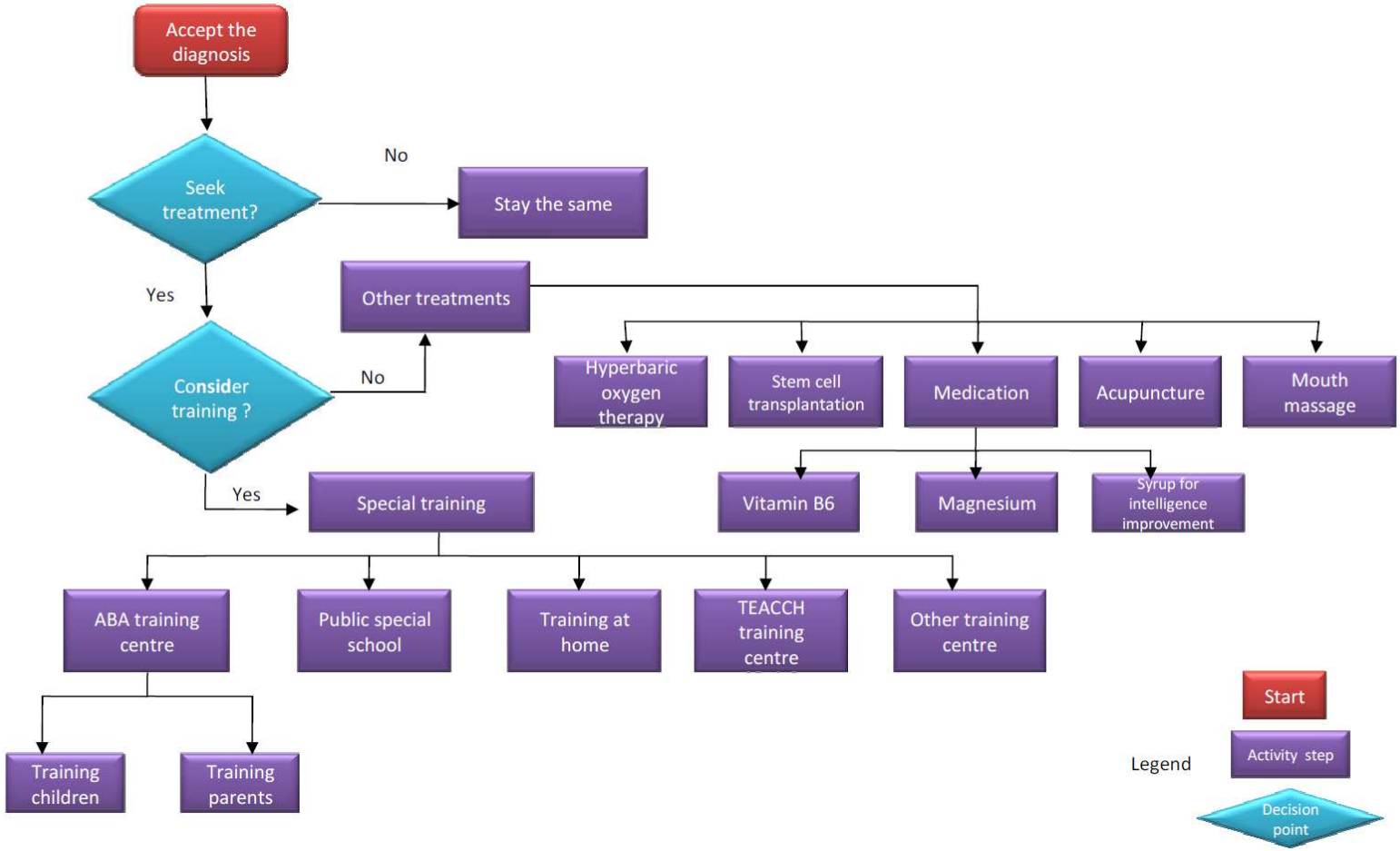
Following diagnosis, the doctor usually suggested sending the child to special rehabilitation/training centres in order to improve his/her abilities. Three types of intervention pathways after initial diagnosis were identified. Approximately 70% of children initially attended intervention programmes using several theories such as the ABA[367] and TEACCH[345], 23% of them chose the sensory integration or auditory integration training, and the rest were kept at home without intervention (7%).

A total of 44% of the children attended only one training centre, 33% attended two, and 13% attended three centres. Generally, parents booked their place in the centre and then waited for a period of time before a position became available. On average, it took a mean of 8 months to enter into private centres after booking a place.

Regarding the effectiveness of intervention, 61 parents (88%) reported a time period of 4.5 months (mean) between entering intervention centre and the obvious improvement in the child's ability noticed by parents. According to parents, the greatest improvement of their children was speech (64%) and the least improved area was the understanding (22%). The pathway from diagnosis to treatment is shown in Figure 7.4.

During interviews, parents reported other available treatments that they were aware of in mainland China including: 1) Hyperbaric oxygen therapy; 2) Stem cell transplantation; 3) Medication: Vitamin B6, Magnesium, and Syrup for intelligence improvement; 4) Acupuncture; 5) Mouth massage. However, as the number of parents who tried these treatments was unknown, it is difficult to make further recommendations (Figure 7.4).

Figure 7.4 Flowchart of healthcare pathway---from diagnosis to treatment



7.3.4 Burden related to autism

According to parents' estimation on the additional cost for treatment and caring of their children with autism, the mean expense of one child with autism in Beijing was £850 per month and £697 in Qingdao. Overall, 58% of the families spent £700-800 per month to support one child of autism and 32% of them spent between £800 and £1000 per month. All the costs were covered by the parents except those children who received £50 as government allowance per month in Beijing.

When parents were asked to quantify the degree of burden they experienced because of having a child with autism, 38% of them considered there was a certain amount of burden placed upon them, and 30% considered it as a huge burden that they were almost unable to tolerate. The results from interview are shown in Table 7.3.

7.3.5 Local policy for autism

Parents from seven provinces reported they had to apply for a disability certificate for their child in order to receive an allowance from local government. In this study, the parents of only eight children (12%) had or wanted to apply for this certificate, while the rest did not express a willingness to apply because they did not want their children to have a record in their files for the rest of their lives. The average monthly expense for autism among children who have or wanted to apply for the certificate was £618.8, while the expense was £804.9 for children whose parents did not want the certificate. The expense of the former was significantly lower than the later (Mann-Whitney U test: z=-2.314; p=0.02).

Parents from Beijing (n=21, 30%) reported that it was not easy to obtain the disability certificate even if their child met the criteria required by the government. The issue of the certificate involved various authorities including Beijing China Disabled Persons' Federation (BCDPF), the local community, or a confirmed diagnosis from well-known authorised hospitals. It was reported that officials in the local community were not familiar with autism and it took a long time for parents to find out where to apply. The evaluation arrangement was once a week, which was considered inflexible and limited by the parents. With a disability certificate, a child with autism can receive £50 per month as government allowance. The allowance was paid annually to the parents to cover training for children with autism. Receipts from the training centres

are required, and sometimes the money would go to the training centres directly as a tuition fee.

Many young mothers within this sample expressed their desire to have another child. The revised child policy allows a couple to have a second child if both parents are the only child in their families[379]. In some provinces, if the child has a disability certificate for a mental disorder, the parents can apply to the local family planning committee to have another child. The committee will seek evidence of a confirmed diagnosis and send a professional team to evaluate the child. In some provinces, a confirmed diagnosis of autism is sufficient for having another child, while in some provinces, a disability certificate is required. It was reported by a mother that the requirements of having another child by the local government also included the age of the mother and a low IQ score of the child. In certain cases, where a mother was young when her first child was diagnosed with autism, she would have to wait for several years to meet the requirement on mother's age before she could have another child. However, if, after receiving intervention programmes, her child now scored higher on the IQ test, she would not be allowed to have another child as her child's IQ would not be low enough. Thus, as the requirements vary across regions, it can easily lead to a sense of unfairness. The local policies of the other 18 regions for children with ASC are summarised in Table 7.4 with details in Appendix 7.2.

Table 7.3 Results regarding intervention and family burden

Questions	Categories	Number	(%)
Initial training method			
	Home training	5	(7)
	ABA	48	(70)
	Sensory/auditory integration/other	16	(23)
Number of centres attended			
	1	30	(44)
	2	23	(33)
	3	9	(13)
	4	6	(9)
	6	1	(1)
Waiting time			
	≤ 7 months	47	(68)
	8-10 months	14	(20)
	>10 months	8	(12)
Biggest improvement			
	Speaking	44	(67)
	Compliance with instructions/orders	13	(19)
	Play with others	3	(5)
	Concentration	0	(0)
	Stereotyped or odds behaviours	1	(1)
	Understanding	5	(8)
Least improvement			
	Speaking	9	(13)
	Compliance with instructions/orders	7	(10)
	Play with others	14	(20)
	Concentration	12	(17)
	Stereotyped or odds behaviours	4	(6)
	Understanding	15	(22)
	Missing	8	(12)
Expense (£ per month)			
	≤ 700	32	(46)
	701-800	15	(22)
	801-1000	22	(32)
Degree of burden			
	Huge burden	21	(30)
	Certain burden	26	(38)
	Little burden	21	(30)
	Missing	1	(2)
Possible causes of autism reported by parents			
	Depression/anxiety during pregnancy	13	(13)
	Exposure with computer	4	(6)
	Early childhood disease	3	(4)
	Parents' personality	5	(7)
	Spoiled way of raising child	5	(7)
	Chemical poisoning during pregnancy	9	(13)
	Don't know	30	(43)
Disability certificate			
	Yes	8	(12)
	No	61	(88)

Table 7.4 Local polices for autism in 19 regions in mainland China

Region	No of responders (%)	Have policy or not (Y/N)	Amount of allowance	Requirement of disability certificate	Have special training centre (Y/N)	Other policy
Beijing city	21 (30%)	Y	£ 50 monthly	1. BCDPF approval; 2. Local community; 3.Diagnosis from well-known psychiatrists; 4. Evaluation (once a week).	Y	--
Dongbei region	6 (9%)	Y	Very limited	--	Y	--
Shandong province	7 (10%)	Y	None	1. Diagnosis; 2. Evaluation;	Y	For a second child; 1. mother ≥32 years old; 2. child's IQ < 62.
Shanxi province	4 (6%)	Y	£1,000 in total	--	Y (but not good)	For allowance: 1. child 2-6 years old; 2. disability certificate; 3. family income at the baseline
Fujian province	5 (7%)	Y	£120 monthly	1. Diagnosis from well-known psychiatrists 2. Evaluation (twice a year)	--	For a second child: diagnosis from well-known psychiatrists
Zhejiang province	4 (6%)	N	None	--	--	For a second child: 1. child cannot speak after third birthday; 2. Evaluation.
Guangdong province	1 (1.5%)	Y	More but don't know how much	More flexible	Y	--
Sichuan province	2 (3%)	N	--	--	--	For a second child: disability certificate.
Other 11 provinces	19 (28%)	N	None	--	--	--

--: not available. Y: Yes; N: No.

7.4 Discussion

This chapter described the service pathway from first awareness, to diagnosis and then intervention drawn from the interviews with 69 parents of children with autism in special training centres in mainland China. The findings suggested several potential reasons which may lead to a delay in diagnosis and intervention for children with autism in mainland China: the lack of awareness among parents, cultural influence on mental health, old sayings for language delay, and under-developed healthcare and education systems.

7.4.1 Limitations and further research directions

It is important to note several limitations of this study. Since it was an opportunistic sample, selection bias might be introduced as the parents who did not participate in this study might have undergone a different pathway from the parents participated. The sample of this study was selected within children who already had a diagnosis of autism and were already in special rehabilitation centres for intervention. These children can be considered as part of the extreme end of all the children within the autism spectrum in mainland China. As the familiarity within the general public with autism and service provision is different across regions, the accessibility for diagnosis and intervention is different. This phenomenon may lead to different experience on the pathway, especially between rural and urban as well as between families with high and low social status. Future studies should also focus on the children with other subtypes on the spectrum, and families who do not have access to those centres due to various reasons. There might be recall bias as most of the findings were based on the memory of the parents or caregivers. The interviews were only recorded by hand. However, the key points from interview were re-checked with the parent at the end of each interview, so the effect of recall bias should have been minimised. Most of the informants were mothers of children with autism, however, it is also important to learn about the experience from the fathers' perspective. In further research, more male participants are needed in order to represent both parents' points of view. This study collected data based on semi-structured interviews with a self-developed questionnaire that limited the more in-depth information. Further study could adopt multiple interviews and a longer-term observation of families. The age of children with autism in this sample were generally between 3 to 6 years old, which only reflects the situation among children who had been diagnosed relatively recently.

There are many children beyond this age range who might have different experiences regarding the service provision. Thus, further studies should adopt multiple methods within a wider age range of children with autism.

7.4.2 Stigmatisation

In this sample, only a minority of children (12%) had the disability certificate or their parents expressed the willingness to apply for it. People with mental disorders usually experienced stigma, stemming within and outside the family influenced by societal beliefs[372]. As autism is a mental disorder categorised into the discipline of Psychiatry, many informants in this sample (especially the older generation) considered it at best as not good, and at worst as very bad. Previous studies reported that family members may feel shamed and embarrassed by their children which can trigger self-stigma[380]. Thus, some of the families interviewed preferred to keep it secret and pretended there was nothing wrong or that something else was wrong (but not a mental problem) with their child. After the diagnosis, the family may keep the child at home and avoid contacts with the other people. This could impede the child's development and make the situation even worse. When the community found out about the child's condition, stigma might arise from the community and society, which known as the courtesy stigma[380]. This might be one of the reasons why the families wanted to keep it a secret in the first place. Courtesy and self-stigma could have impacts on each other in the context of Chinese culture. The more courtesy stigma received by family members, the more negative self-evaluation, negative emotion and behavioural withdrawal may occur[381]. Children with autism sometimes present challenging behaviours and their lack of social skills leads to inappropriate behaviours which might be considered as impolite or even dangerous by others[382]. If the others are not aware of this condition, the misunderstanding from others might put a lot of pressure on the parents. The lack of knowledge and recognition of autism in the society, the more difficult the children with autism will be diagnosed and more difficult that the parents and families will get support and help they need. The stigmatisation might be an important factor for further service and policy development for autism in China.

7.4.3 Old sayings and early detection of autism

There is an old saying in Chinese culture related to language delay. It says that the child who speaks late during childhood will turn out to be smarter than others in the

future. This ancient belief has a long history in China and is rooted across generations. Even today, many grandparents still consider language delay as a good sign that predicts future success especially among boys. Thus, if the child cannot speak at the time when they should have acquired speech, the grandparents might be pleased and tell the young parents this old saying. In this sample, almost half of the children (33, 48%) who showed obvious language delay had been noticed by their family, and just over a quarter of the families took it as a good sign. This result indicated that the old saying may have partly impeded the early identification of autism. This had been suggested by a Chinese study on education provision for autism in rural areas in Jiangxi province[352]. A similar belief in India was reported to have potentially delayed the diagnosis of autism, which was "the male Indian child speaks later"[383].

7.4.4 One-child policy and seeking intervention within Chinese parents

The one-child policy has been implemented in mainland China since 1980 as a strategy for birth control and long-term development[384]. In China, many young couples who were born in the early 1980s have become new parents. Because of the one-child policy law, both parents are the only child in their own family. Their baby is therefore likely to be the only grandson or granddaughter within the two extended families. This is called the 4:2:1 phenomenon[385]. As a result, the child receives focused attention from the parents and especially from the grandparents. They anticipated all the needs of the child which makes it possible that the baby would not need to develop certain abilities on their own. This is known as the "Little Emperor Phenomenon" in mainland China[385]. In such family, the child's future is the future for the whole family.

In mainland China, the large population contributes to the competitive environment for education and career development, so a child's test scores are considered as an issue of enormous importance to parents in general. Most parents in this sample expressed their concerns about the learning potential of their children, which lead them to seek all kinds of intervention and therapy when they realise something was wrong. The implications of a child with special conditions are thus possibly even more important in mainland China where each family only have one child. In this sample, it seems that most efforts of parents were made to improve the abilities of their children with autism in mainland China.

7.4.5 Variation in policy for autism in mainland China

So far, there has been no systematic recording and monitoring system for autism in mainland China. Due to the lack of knowledge and accessible information, the awareness of autism could have been considerably impaired. The local policies for autism were found to be diverse within mainland China. The policy in one region is generally not applicable to other regions. The local policy for children with autism may depend on how familiar autism was to the local medical institutes. For example, if there are psychiatrists or paediatricians who are specialised in autism in one hospital, the referral to this hospital regarding autism would happen more often. This could lead to more confirmed cases identified in this region. As a result, in this sample, the government and local authorities of some regions were more aware of autism and paid more attention to the needs of children with autism and their families than the other regions.

7.5 Conclusion

The healthcare and education system for autism has not been well developed in mainland China. Most of the time, parents initiated the service pathway without prior knowledge or general guideline for the referral for autism. In addition, there are many culturally specific issues for children with autism in mainland China which add barriers to the pathway. As a result, the diagnosis and intervention is relatively delayed. There is a need to develop a specific autism-related service with standard policies and regulation to cater to the needs of affected children and their families. Improving public awareness of autism and increasing support from government and society could reduce stigma and ultimately reduce some of the burden on families with children having autism.

Chapter 8 Service Provision for Autism in Hong Kong from Service Users' Perspective

8.1 Introduction

Hong Kong is located in the south of China and 95% of its residents are Chinese. In 1994, the Health and Welfare Bureau adopted the prevalence of autism as 8-10 per 10,000 reported by the UK and estimated that 6, 500 children would be expected to meet a diagnosis of autism in Hong Kong[386, 387]. In 2007, an epidemiological study conducted in Hong Kong reported a prevalence estimate of ASC was 16.1 per 10,000[370]. This result was much lower than the prevalence estimates reported in recent Western studies, which were around 1%[125], but doubled the early estimate. One possible explanation for the lower estimate might be that the estimate was generated retrospectively from healthcare records rather than the prospectively conducted epidemiological studies in the general population.

As a part of China, Hong Kong has a unique history because it was a British colony between 1842 and 1997[370]. During the colonial period, Hong Kong adopted the British colonial administrative system. Autism was almost unheard of between the early 1960s and 1980s. At that time, children with autism were treated in the same way as individuals with mental handicap (MH) [370]. The milestone of the service development was a symposium on autism and children with developmental disabilities in Hong Kong in 1989[370]. After this symposium, a working group for autism was established by the Hong Kong government under the Health and Welfare Bureau in 1992 to review existing healthcare and education service provision for autism in Hong Kong. Since then, the psychological services for children with ASC in Hong Kong were gradually developed[387].

In order to learn about the current healthcare service and education provision in Hong Kong, this chapter first identified the existing service settings for ASC in Hong Kong from published literature and then investigated service provision from the parents' perspective.

8.2 Method

8.2.1 Literature search

A literature search was conducted in PubMed and Web of Knowledge databases to identify previous literature on service provision for ASC. The following search terms were used: "Autism" OR "Autistic Disorder" OR "Autism Spectrum" OR "Pervasive Developmental Disorder" OR "Asperger Syndrome" AND "Hong Kong". The inclusion criteria for study selection included: 1) the study must be an original report; 2) it must focus on Hong Kong; 3) It must focus on the healthcare service or education provision for ASC. The information of main settings of service provision was summarised from the identified studies.

8.2.2 Participants

The participants were the parents of children who already had a diagnosis of ASC in Hong Kong. They were recruited from special rehabilitation centres of the Heep Hong Society (HHS). HHS was established in 1963 as a non-governmental organisation. It was established to provide rehabilitation services to pre-school aged children with special needs and supports to their families[345]. There are 28 HHS centres in Hong Kong. The HHS was contacted and four centres agreed to participate in this study. The four centres were Chan Chung Hon Centre, Alice Louey Centre, Chun Shek Centre, and Tai Ping Centre. The first centre is located in Kowloon East and the latter three are located in New Territories East. The inclusion criteria for participants were as follows: 1) the child had an ASC diagnosis; 2) the child was currently studying in participated centres. On average, there were 60 children in each centre, and approximately half of them were children with ASC. All the parents of children in those four centres who met the inclusion criteria were contacted. In total, 34 parents (34/120, 28.3%) gave consent to participate in this study.

8.2.3 Procedure

This study was conducted through a collaboration of University of Cambridge and the Chinese University of Hong Kong (CUHK). Ethical approval of this research was obtained from the Survey and Behavioural Research Ethics Committee of the CUHK. The invitation letters and consent forms were distributed to parents through the HHS administration. The completed consent forms were collected by the centre administrators and returned to the candidate. After the consent from parent was

obtained, an interview appointment was arranged. The questionnaire used for interview was developed from previous interviews with parents in mainland China (Chapter 7). The full questionnaire is provided in Appendix 8.1.

8.2.4 Data collection and analysis

The interviews were semi-structured, each lasting for 1 or 1.5 hours. Because many parents spoke Cantonese rather than Mandarin, during each interview an interpreter fluent in Cantonese and Mandarin was present to help. All the interviews were audio-taped with permission. The transcripts were read by the candidate to identify possible text segments for coding. Both qualitative analysis and quantitative methods were used in further analysis. The parents were referred as P1 to P34. The quantitative analysis was conducted in STATA 10.

8.3 Results

8.3.1 Results from the literature

The PubMed search identified 57 articles and Web of Knowledge search identified 62 papers (including duplicates). After the removal of duplicates, the abstracts were read and examined according to the inclusion criteria. Five papers met the inclusion criteria, four of which were reports of service provision in general[369, 370, 388, 389]. The other one was an abstract of a Satellite Symposium for Child Neurology on ASC in Hong Kong[386].

8.3.1.1 Early detection of ASC

In Hong Kong, the Maternal and Child Health Centres (MCHC) provides a comprehensive range of health prevention services from birth to 5 years old through an Integrated Child Health and Development Program. A "Comprehensive Observation Service" (COS) was introduced in 1978 for early detection of developmental problems conducted in the MCHC. This service achieved its purpose by screening children from birth until the age of 3 at three age points including 3 months, 6-9 months and 3 years old. The screening provided assessments on gross and fine motor development, vision, hearing, speech and behaviour adaptability. Screening conducted by COS is a national routine check-up for all children born in Hong Kong. It is free and follows automatically from birth. However, the screening of

ASC is not part of the COS. The MCHC adopted the CHAT to screen children who are older than 18 months for ASC. Children who screened positive or are suspected of having ASC are referred to the Child Assessment Centre (CAC)[345].

8.3.1.2 General referral sources to CAC for ASC

The CAC was established by the Medical and Health Department (MHD) after the adoption of a UK model for disability assessment[369]. There are seven CAC for 18 political districts in Hong Kong in total. The MCHC can refer the children to paediatricians or clinicians of child care in hospital, clinical psychologists and doctors from private practice as well as Student Health Service[345, 369]. The recommendation from registered doctors or psychologists is required for the referral to CAC.

8.3.1.3 Multi-disciplinary assessment and afterward referral

In each CAC, the child is assessed by a multi-disciplinary assessment team consisting of developmental paediatrician, clinical psychologist, child psychiatrist, speech therapist, occupational therapist, physiotherapist, audiologist, orthopaedist or optometrist, medical social worker and a nurse. Besides assessment, a management plan for each child is provided by the team after discussion. The multi-disciplinary team then refers the child to possible agencies for intervention and education. The team also provides developmental guideline and counselling for parents[369].

8.3.1.4 Pre-school therapy and training programme for ASC

A special autism training programme was developed by the HHS for children aged 2-6 years old with ASC in Hong Kong. The training provided in HHS centres was adopted and adapted for local use from the intervention programme called TEACCH[345]. HHS has in total 28 training centres scattered in different regions of Hong Kong to cater to the needs of local children and their families. After the referral to CAC, the assessment team refer the child to a HHS centre for training and also helps the child to get onto the waiting list for identified centre.

The other training service for pre-school children includes the Early Education and Training Centre (EETC), Integrated Child Care Centre (ICCC), Special Child Care Centre (SCCC), Integrated Programme for Mildly Disabled Children in Kindergartens

(IK/G) and Preparatory Class in Special School. These schools provide training for children with developmental disabilities, but not specifically for ASC[345, 369].

8.3.1.5 Education service for primary school aged children

In Hong Kong, there has been no uniform education programme specifically for primary school aged children (7-12 years old) with ASC. At the age of 6, each child is required to be evaluated, the results of which will divide them into either mainstream or special schools. The child with an IQ≥70 reported by the evaluation can enter mainstream schools, while those with IQ<70 are placed in special schools for children with all kinds of mental disabilities. It was reported that there had been no specialised programmes for children with Asperger Syndrome in Hong Kong [369, 370].

8.3.2 Quantitative results from closed questions

8.3.2.1 Children's characteristics

There were in total 34 children whose parents participated in this study, of which 27 were boys (79%) and 7 were girls (21%). Two centres had 10 participants each and the other two centres had 8 and 6 respectively. The centres provided services for children aged 2 to 6 years old. The mean age of children in this study was 4.5 years old (range: 2.5-5.9). All the children were born in Hong Kong, 20 of them (59%) were the first child of their parents, 12 were the second (35%) and two were the third (6%).

8.3.2.2 Parents' characteristics

Among 34 families, both parents in two families attended the interview, while in five families only fathers attended. The interviews with the remaining 27 families were all with mothers only. There were 8 mothers within each of the following three age ranges: ≤25, 25-29, and 30-34. The remaining 10 mothers gave birth to their children with ASC when they were 35 years old or older. In terms of the education background of parents, 20 mothers (58.8%) and 19 fathers (56%) did not go to college and the remaining completed college education.

8.3.2.3 First notice to diagnosis of ASC in Hong Kong

The mean age of the child was 1.8 years old (range: 1.4-3) when the first awareness of abnormal development arose. In 19 families (56%), the condition was first noticed by

parents and 10 children (29.4%) were detected by doctors during check-ups in government health hospitals. Among 34 families, 18 families (53%) took their children to hospital because of the language delay. Six families (17.7%) recognised the language delay in their child but considered it to be a good sign for future success of the child and did not seek help at that time.

Thirty children (88.2%) attended governmental health hospitals and three families (8.8%) took their children to private clinics. After initial referral, 29 families (85.3%) were given the diagnosis in CAC, while the others were diagnosed in private clinics. The mean age of diagnosis was 2.4 years old (range: 0.25-4). Twelve parents (35.3%) recalled the diagnostic process during referral lasted for 31 to 60 minutes and another 12 parents recalled it to be less than 30 minutes. Sixteen children were given a diagnosis of "Autism", and 11 were given a diagnosis of "Tendency of autism" or "Suspicion of autism". Five children (14.7%) were given a diagnosis of "Autistic features", and two (5.9%) did not receive a diagnosis at first but received the diagnosis before this study. The assessment process from hospital referral to diagnosis in CAC took an average of 4.7 months. The average (mean) time from first noticing a problem until diagnosis was 9.3 months.

8.3.2.4 The role of routine screening for ASC

It was reported that there was usually a time period of 12 to 24 months from onset, through presentation of autistic features to the notice of abnormality, until referral for children with ASC in Hong Kong[370, 390]. The COS did not conduct compulsory screening between 9 months and 3 years old, and the COS screening process did not include screening for ASC. In this sample, the mean age of first awareness was 1.8 years old and 71% of the children's condition was not recognised by doctors at first. Twenty-eight (82.3%) children were diagnosed before the compulsory assessment took place. The findings suggested the majority of children with ASC in this sample were not detected by the compulsory screening but by their parents.

8.3.2.5 Intervention of ASC in Hong Kong

Following suspicion of autism or related developmental condition, many parents took their children to attend a variety of intervention programmes while they were waiting to enter the HHS centres. The mean time period between diagnosis and the initiation

of intervention was 3.5 months. The mean age of initial intervention after diagnosis was 2.8 years old. However, the mean time on the waiting list to enter an HHS centre was 14.8 months and the mean age of children when entered an HHS centre was 3.7 years old.

Fifteen children (44.1%) received integrated intervention in private centres that was similar to the training in HHS centres. Another 15 children (44.1%) attended private intervention courses such as speech therapy or occupational therapy before entering HHS centres. Within various private intervention courses, the following three courses were the most frequently attended: speech therapy (ST) (73.5%), occupational therapy (OT) (71%) and the one-to-one training (67.7%). Other therapy included group therapy (50%), physical therapy (35.3%), and early routine training. Sixteen children (47%) also attended normal kindergarten besides special intervention. In total, 32 families (94%) still sent their child to other intervention courses besides the training in HHS centres. There were 22 children (64.7%) who only attended one integrated centre while 8 children (23.6%) had been to two and four children had been to three. Nineteen families (56%) wanted their child to improve language skills through training and in reality, 11 families (32.4%) considered the greatest improvement of their children was language and six families (17.7%) considered the daily routine was the biggest improvement.

8.3.2.6 Burden related to ASC and suspicious causes

Seventeen families (50%) considered having a child with ASC as a huge burden while 9 parents (26.5%) considered it as certain burden. Twenty-six parents (76.5%) described their lives as currently stable. The reported monthly costs for autism varied among families. 21 families (61.8%) spent less than 5000HK$ (£406) to support one child with ASC and 10 families (29.4%) spent more than 5000HK$ (£406). The mean percentage of costs for ASC in monthly family income was 21%. Twenty-six parents (76.5%) reported they had a disability certificate that provided free entry to zoos or other children's facilities in Hong Kong, while the others did not.

When asking the parents about possible reasons for ASC, half of the parents (50%) could not think of any particular reasons, 6 parents (17.7%) mentioned depression

during pregnancy and 4 parents (11.8%) suggested the possibility of chemical exposures during pregnancy.

8.3.2.7 Parents' awareness and participation in training

Among 34 parents of autistic children, only 19 (56%) used the internet to search for information about autism and possible training opportunities after first awareness of autism or diagnosis. All the parents were familiar with the procedure of daily training in HHS centres, although only ten of them (29.4%) were aware of the training theories such as the ABA, TEACCH or RDI which were current theories of intervention for children with ASC[343, 345, 367]. Only 15 of them (44.1%) had ever attended training courses for parents to learn about how to help their children outside the classroom. The healthcare and education pathway is shown in Figure 8.1. The time delay from first notice to intervention is shown in Figure 8.2. The parents' responses to the closed questions during the interview are shown in Table 8.1.

Figure 8.1 Healthcare and education pathway of ASC in Hong Kong

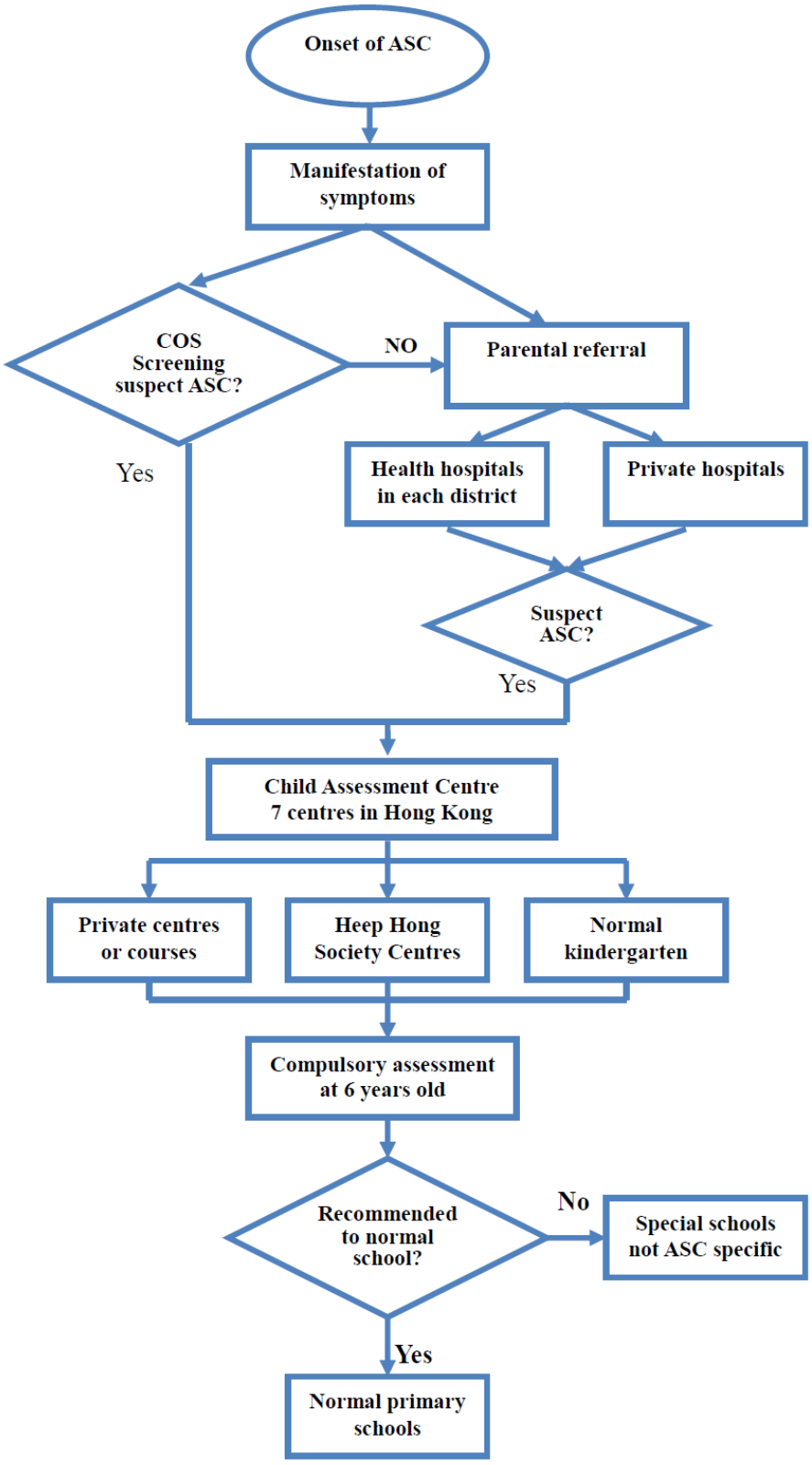


Figure 8.2 Time delay in the healthcare pathway of ASC in Hong Kong

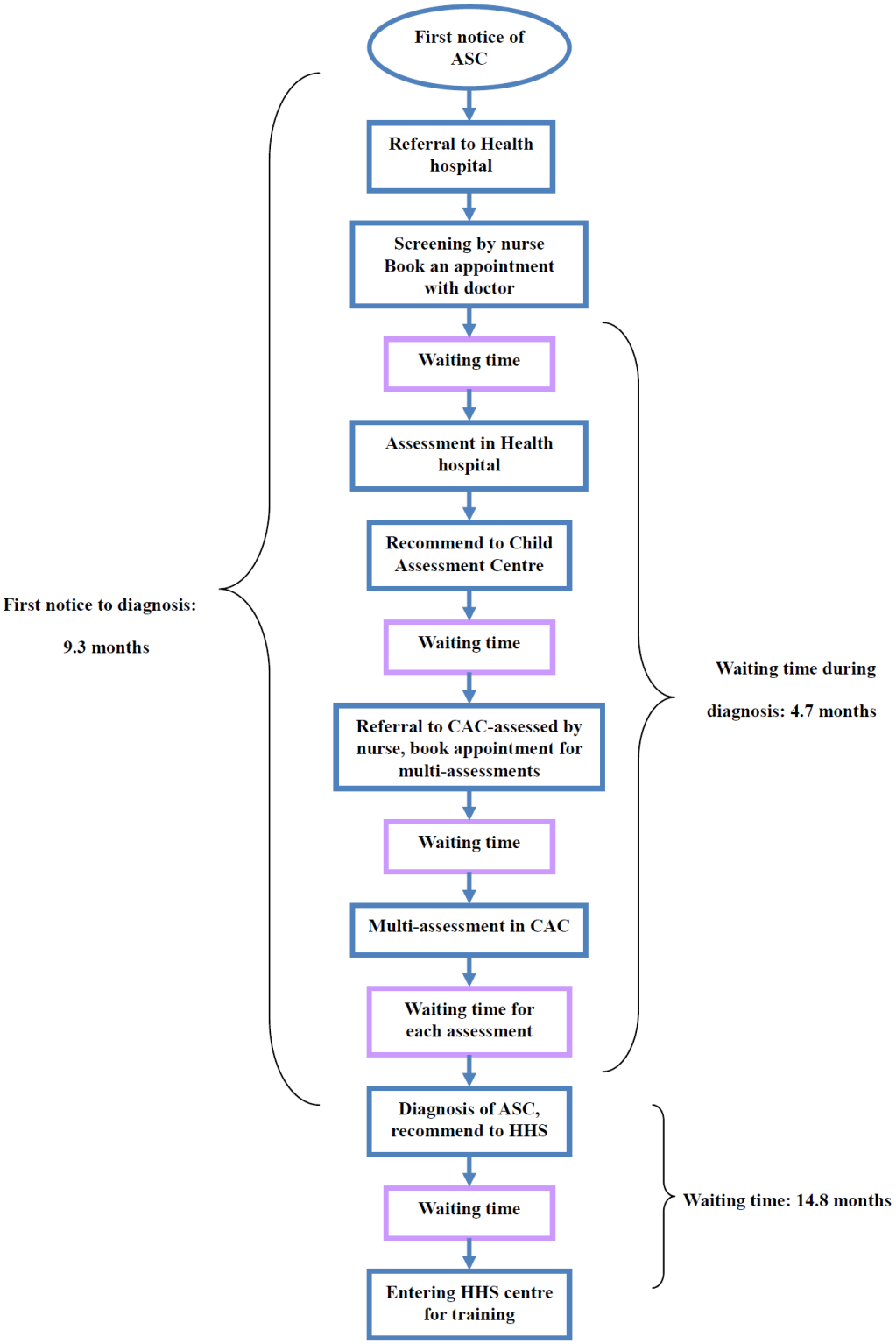


Table 8.1 Parents' responses to closed questions on service provision for ASC in Hong Kong

Characteristics	Number (%)	Characteristics	Number (%)	Characteristics	Number (%)	Characteristics	Number (%)	Characteristics	Number (%)
Maternal age		**Direct to CAC**		**Group therapy**	17(50)	**1st referral hospital**		**Percentage of monthly**	
≤25	8 (23.5)	Yes	32(94.2)	**One-to-one training**	23(67.7)	Health hospital	30(88.2)	**expense**	21%
25-30	8 (23.5)	No	1(5.9)	**Music therapy**	6(17.7)	Private hospital	3(8.8)	**Suspicious causes**	
31-35	8 (23.5)	**Use internet**		**Acupuncture**	8(23.5)	Psychiatric hospital	1(2.9)	Maternal depression	6(17.7)
>35	10 (23.5)	Yes	19(55.9)	**Brain massage**	5(14.7)	**Assessment hospital**		Computer	1(2.9)
								Early childhood	
Mother's education		No	8(23.5)	**Detoxification**	1(2.9)	CAC	29(85.3)	disease	3(8.8)
Secondary school	12 (35.3)	Missing	7(20.1)	**Normal kindergarten**	16(47)	Private assessment	1 (5.9)	Chemical during	
High school	8(23.5)	**Age of diagnosis**	2.4 yrs	**Other therapy than HHS**	32(94.1)	Psychiatric	3(8.8)	pregnancy	4(11.8)
College	14(41.2)	**Age of initial training**	2.8 yrs	**Know training theory**	10(29.4)	**Diagnosis**		Vaccine	1(2.9)
Graduate student	0	**Age of training in HHS**	3.7 yrs	**Parent therapy**	15(44.1)	Autism	16(47.1)	None	17(50)
Father's education		**Time delay**		**Symptom of notice**		Autistic features	5(14.7)	Others	3(8.8)
Secondary school	7(20.6)	Waiting for diagnosis	4.7 months	No speaking	18(52.9)	Tendency of autism	11(32.3)	**Disability certificate**	26(76.5)
High school	12(35.3)	Waiting time to HHS	14.8 months	No eye contact	4(11.8)	Other diagnosis	2(5.9)	**Stable**	26(76.5)
College	11(32.4)	Notice to training	12.1 months	No response	5(14.7)	**Time of diagnosis**			
Graduate student	3(8.8)	Diagnosis to training	3.5 months	No peer relationship	1(2.9)	≤15 minutes	1(2.9)		
Missing	1 (2.9)	Notice to diagnosis	9.3 months	Repetitive behaviours	6(17.6)	16-30 minutes	11(32.3)		
Caregiver		**Initial training method**		**Biggest improvement**		31-60 minutes	12(35.3)		
Parents only	13(38.2)	Daily routine	3(8.8)	Speaking	11(32.4)	<60 minutes	8(25.5)		
Grandparents	10(29.4)	Integrated training	15(44.1)	Daily routine	6(17.7)	Missing	2(5.9)		
Housemaid	11(32.4)	Private training	15(44.1)	Concentration	2(5.9)	**Degree of burden**			
Age of notice	1.8 yrs	Government training	1(3.0)	Stereotyped behaviours	2(5.9)	Huge burden	17(50)		
Language delay good		**Number of centre**		Understanding	3(8.8)	Certain burden	9(26.5)		
Yes	6(17.7)	1	22(64.7)	Sensory Integration	3(8.8)	No burden	8(23.5)		
No	28(82.3)	2	8(23.6)	Missing	7(20.6)	**Expense of autism**			
Way of notice		3	4(11.8)	**Expect improvement**		<1000HK$	1(2.9)		
Parents suspicion	19(55.9)	**Private ST**	25(73.5)	Speaking	19(55.9)	1000-2000HK$	11(32.4)		
Government doctor	10(29.4)	**Private OT**	24(71)	Play with others	4(11.8)	2000-5000HK$	10(29.4)		
Private doctor	3(8.8)	**Private PT**	12(35.3)	Stereotype behaviours	4(11.8)	>5000HK$	10(29.4)		
Teacher or others	2(5.9)	**Early routine training**	10(29.4)	Missing	7(20.6)	Missing	2(5.9)		

8.3.3 Qualitative results: Description of service provision by parents

8.3.3.1 Compulsory assessment for ASC in Hong Kong

At the age of three, when the child is ready to go to kindergarten, the social workers in local health hospitals contact the parents to bring their child to have assessments for developmental disabilities. Once the child is suspected for autism, the health hospital refers the child to the CAC in their residential region. Once the child has an ASC diagnosis from the CAC, the health hospital will recommend the child to wait in line to enter a HHS centre for intervention. The child can still go to normal kindergarten as long as the kindergarten accepts the child. The report provided by the doctors will be in the child's health record.

When the child is six years old, the child is contacted to have a compulsory assessment in CAC. After the assessment, if the doctor recommends that the child can go to mainstream school, then he/she can go with or without informing the school of the previous diagnosis. However, the recommendation will be in the education system as a record and the school can track it anytime they want. If the doctor recommends the child to attend special school, the child cannot attend a mainstream school. Thus, their education pathway will be totally different from typically developing children. Education and a career are not guaranteed for mature individuals with ASC in Hong Kong. There are sheltered workplaces for people with disability. However, since there are limited places available, the waiting time is also long.

8.3.3.2 Diagnosis of ASC in Hong Kong

If parents are concerned about their children, they can take them to doctors either in government-owned hospitals or private clinics, as they are equally positioned in the health system. Their recommendations for CAC referral follow the same procedure. The parents can take their children to CAC for diagnosis and they can also pay to get diagnosis in private clinics. During the hospital referral for ASC, it is usually a nurse who asks parents the screening questions and then makes an appointment with a doctor for the child. There is a waiting period for the doctor's appointment. During the appointment, the doctor conducts direct observation of the child and other examinations such as hearing, sight, and brain scan. When the result suggests the possibility of ASC, the doctor refers the child to the CAC for further assessment.

There is usually another waiting period before the CAC appointment. During the CAC referral, the nurse asks screening questions and probably observes the child for about 15-20 minutes before referring the child to the doctor. The doctor will observe the child, asking parents regarding the child's behaviours as well as recommending other assessments. The parents need to wait for another period of time to complete all assessments required by the doctor. After gathering all the results from assessments, the doctor provides a diagnosis. The diagnosis will be put into the records in the health system as a statement.

8.3.3.3 Intervention courses in governmental health hospitals after diagnosis

According to the parents' report, after the diagnostic assessment in CAC, social workers provide parents with the options of available services. There are usually two governmental supported services: 1) HHS training centre if between 3 and 6 years old; 2) Early Development Training centre if under 3 years old. They can be placed on the waiting list for both if the child is under 3 years old as both services have long waiting lists. However, once the child is accepted by one government supported service, the waiting on the other service will be terminated automatically.

The social workers also provide information of intervention programmes in health hospitals. The health hospital in their residential district is usually the first option. The appointments of special intervention programmes in health hospitals need to be booked by parents. The training programmes in health hospitals usually include ST, OT and/or Physical Therapy (PT). There is a waiting time before receiving the therapy since there is a general shortage of therapists in such hospitals. During the waiting period, the parent can consult doctors on general problems of the child such as eating and sleeping. The training programmes in health hospitals are relatively cheap if recommended by the doctors in these hospitals. The first class of each course costs 100HK$ (£8), and then 60HK$ (£5) per class for the rest of the training. Each class lasts for 45 minutes. The social worker also provides information about the other private training centres but it is limited. In general, it is the social worker's responsibility to contact the parents and assist them to complete all the assessments required by the doctor of each child. One parent suggested the doctor in the health hospital could recommend new programmes for children with ASC during the consultation. They suggested those courses would be cheaper if recommended by

doctors but the doctors wouldn't do so voluntarily. Most of the time, the parents needed to ask for themselves first.

8.3.3.4 Description of training in HHS centres

Every year there are two evaluations in HHS centres in September and January respectively. After evaluation, the therapists discuss the ability of the children and re-categorise them into three to four groups. New schedules are set up for each group according to their ability as follows: 1st group: severe autism (TEACCH group); 2nd group: less severe autism and other global delay; 3rd group: other severe disability such as the Down Syndrome, severe physical disability, Mental Retardation and other developmental disability. The daily schedule in HHS centres for autism is provided in Appendix 8.2. The one-to-one training can be ST, OT and PT with each course once a week or twice a month for each child. The whole day training starts from 9:00am to 3:30pm, Monday to Friday.

The cost of general training in HHS centres is 354HK$ (£28) per month. Besides this, the HHS has a five-day preparation course in the summer vacation for children who will enter in the new term. This pre-class has to be fully paid for by parents. In HHS, there is a non-government support training programme called "Green Plan" for children with ASC. The training includes ST, OT, sensory integration therapy, social class and one-to-one training class. The cost is 650-680HK$ (£53-55) for each 50-minute class once a week. The parents have to pay for it themselves.

8.3.3.5 Description of the training in private centres for ASC

Private centres in Hong Kong usually provide 3-hour training per day from Monday to Friday. Information about those centres is available through the internet or through the HHS parents' resource centres. The course includes ST and OT with ratios of one therapist to six children. The cost is around 8,000-10,000HK$ (£648-810) per month.
Several private centres provide training once a week. Each class is one hour at the price of 450HK$ (£37). It was reported to help the child to improve their recognition such as "small and big, colour, recognize objects and so on". They also provide a full-day course which costs 9,000-10,000HK$ (£731-812) per month without the presence of parents. Several private centres for ASC are non-profit organisations. They provide

45-minute class on ST and OT once a week. Normally it is 300HK$ (£25) per class. However, if the child is waiting to get into a HHS centre with parents only relying on governmental baseline living support, the courses will be free of charge or at a very low price of 50HK$ (£4) per class until the child gets into a HHS centre.

8.3.3.6 Other therapy for ASC in Hong Kong

Besides the intervention in HHS centres, many parents tried to find other therapy in order to get more intervention for their children. The private therapy includes group therapy, ST OT, PT, music therapy, individual training, acupuncture, brain massage, holistic therapy and detoxification therapy.

Private ST or OT is usually 400-900 HK$ (£32-73) per class for 45 minutes in a profit organisation and 300HK$ (£24) per class in a non-profit organisation. One-to-one training usually costs 300-400HK$ (£24-32) per hour. Acupuncture therapy was suggested by eight parents to be effective for the speech development of their children. It is 30 minutes per session with approximately 15 needles on the forehead and side head of the child. One parent reported the cost was 15,000HK$ (£1,215) per month in private setting and 1000-2000HK$ (£81-162) per month in a governmental hospital. One parent took the child to acupuncture 2-3 sessions a week at a price of 300HK$ (£24) per session. Music therapy 30 minutes per week was reported by one parent to be good for temper control at a price of 1,740HK$ (£141) per month. The brain skull massage was mentioned by five parents as good for sleeping at a price of 400-650HK$ (£42-53) per 1-hour session.

8.3.3.7 Support and training for parents

The HHS holds three regular seminars and lectures for parents. Each HHS centre has a parent resource centre that provided information and organised social events for parents. In some mainstream kindergartens, neighbourhood advisory consultation is provided to support parents. There is a parent training programme held by a Hong Kong parent. The mother learnt the training method for ASC in Australia and she started this course to teach parents to train their children at home. This programme runs once or twice a year. It usually has two to three classes a week for one month. The tuition of this course is 2000-3000HK$ (£162-243). Each course hosts 20 to 30 parents.

8.3.3.8 Disability certificate and disability allowance for ASC

The parent of a child with ASC can apply for a registration card of disability that lists the condition of the child on its back side. This card can help the parents to explain the child's condition to other people if necessary and also can be used as a free or discounted ticket to certain parks in Hong Kong. Once the child's record is in the health system for ASC, the government will provide a disability allowance of around 1,288-1,315HK$ (£105-107) to each child monthly. The allowance is transferred to the parents' personal bank account. The government supported baseline living allowance for an adult who doesn't have a job is 2000HK$ (£162) monthly, and 3000HK$ (£243) for a child with ASC in such a family.

8.3.4 Qualitative results: Parents' perspective on service provision in Hong Kong

8.3.4.1 Parents' perception from early detection to diagnosis

Several parents expressed their frustration regarding the early detection. After the child was referred to hospital for ASC, there were three separate periods of waiting time before a diagnosis was made: from first referral to health hospital to actually seeing the doctor in hospital, from recommendation to CAC for assessment to first referral to CAC, and from first referral to CAC to actually having the assessments in CAC. During the waiting time, the parents reported they were anxious and struggling with what was going on with their child and did not know what to do (Box 8.1: *P3-1, P9-1*).

8.3.4.2 Parents' perception from diagnosis to training

After the diagnosis, parents indicated that there should be more therapists and governmental centres in the future, so children can receive training earlier and would not waste previous time on waiting (Box 8.1: *P1-1, P21-1*). While waiting to enter HHS centres, many parents tried to find other possible training courses for their child. However, most of the private training in Hong Kong was expensive. Thus, many children received very little training until they entered HHS centre since their family could not afford it (Box 8.1: *P3-2, P27-1, P2-1*).

Box 8.1 Quotes of experience from early detection to training

"I did not know what was going on with my child at first and I felt really upset… I went to the Child Assessment Centre… at the first referral we only saw the nurse… the nurse recommended me to read some books in their library and I found all those books were about autism…This was before the examination of the doctor in CAC… From those books I learnt about autism and I felt really disappointed and hopeless…after a while, when I saw the doctor in CAC, I had been prepared to accept the diagnosis since I figured it out during the waiting time…" (P3-1)

"I took my child to CAC many times for different assessments…once for hearing…then another appointment for brain…at last we got the diagnostic results…"(P9-1)

"I hope our child would have entered the centre earlier…. it took so long only for waiting to get in…if he had received the training earlier, he could be much better now…" (P1-1, P21-1)

"My husband and I were reluctant to accept the diagnosis…we know there is no cure to autism…we never stopped trying and took my son to any possible training courses we could find and also we could afford…" (P3-2)

"I think as parents of a child with autism, we are very vulnerable and blind… We do not know which therapy is good and which will not help…so we worked hard to let the child try everything that is available…" (P27-1)

"Our family depends on the government's basic living allowance… There are three persons in my family, my mother, my son and me…We live in a governmental house and receive the basic allowance of 2000HK$ (£162) per person per month…My son is autistic, so he gets 3000HK (£243)… we can barely live on this allowance. I want him to get training but the private centre costs 10,000HK$ (£810) per month…even private speech therapy and occupational therapy cost 450-600HK$ (£36-49) per class…I simply cannot afford those…" (P2-1)

8.3.4.3 Parents' perception on training in HHS centres

Most parents were happy with the training in HHS centres since it was cheap and of good quality. The therapists and social workers in HHS were reported to be very kind and helpful. When asked about the suggestions for improvement of the HHS centre, the most common suggestions were to have more such centres and more special therapists. Since the ST, OT and PT courses were only once a week or twice a month for a child, parents wished the courses could be more intensive. Some parents suggested the classes in HHS could be more complicated and applicable to children with different levels of ability. The parents suggested there could be more space in each centre to separate autistic children according to different levels of severity (Box 8.2: *P6-1, P32-1, P10-1, P13-1, P32-2, P20-1*).

8.3.4.4 Parents' perception towards the government policy for ASC

Parents suggested there was not much support for parents other than the appointments with doctors and the arrangement of getting into HHS centres. Many of them learnt about autism only when their child was diagnosed. During the waiting period from first referral to intervention, there was no other information about the basic knowledge or general strategy for autism available. The parents needed to find such information mainly by themselves. Some parents wanted more training for parents to help their children at home and to cope with their lives after the diagnosis. Some parents suggested the disability allowance was too low to cover the private training costs. Some parents suggested the private training were too expensive and the government should establish some unified standards to control the price and provide some vouchers to release the burden. They hoped the people who were working in this field could have shown more compassion than just wanting to make profits. Some parents hoped there will be more non-governmental private centres to help low-income families (Box 8.2: *P27-1, P22-1, P15-1, P15-2, P17-1, P13-1, P12-1*).

8.3.4.5 Parents' stress and concerns

Many parents especially mothers expressed their concerns and became distressed during interviews. They described their feelings when they first got the diagnosis. Some parents felt hopeless and did not recover for a long time. Even those parents that coped better at present, showed great concern about the child's future after 6 years old. (Box 8.3: *P27-1, P13-3*)

Box 8.2 Quotes of training in HHS centres and policy for ASC

"I am satisfied with the courses here because it is an all day long course…the training in the private centre was only three hours per day…" (P6-1)

"The people here are very nice to our child and to us…very helpful…they have many materials for parents to borrow as well…" (P32-1)

"The ST, OT and music therapy here are very good, but only once a week is not intensive enough…if there are more therapists here, we can have more classes per week…otherwise we still need to go to private training centres or find a special therapist besides the training in HHS…those private training costs a lot…" (P10-1)

"I hope the one-to-one training such as speech therapy, occupational therapy, and integrated sensory could be at least once a week…" (P13-1)

"The training here is more suitable for a child who improved slowly…my son had improved a lot and he can handle most of the courses because those courses are quite simple…we need more complicated courses for children whose conditions are not that severe…maybe include some other courses…" (P32-2)

"I think they should group the autistic children according their ability…I know this must be difficult...there is not enough room and also not enough teachers to take care of so many children…" (P20-1)

"I felt there was very limited support from the government and from the society…" (P27-1)

"For a long time I only sent my child to normal kindergarten while waiting to get into this centre…because I knew nothing about autism…I did not know we needed to take him to other training early on…I only heard the term' autism' from the doctor…the government should have more publicity on autism..." (P22-1)

"Many people still have no idea about autism…when we went out to public places and my child showed autistic behaviours, some people around judged me as I did not raise and teach him well… " (P15-1)

"I did not know about autism before…even now I still do not understand why my child has it…they told us our child is not normal, but we did not know how we could help him…I don't know whether he will get any better or can support himself in the future…" (P15-2)

"I thought he just spoke late which I did not pay attention since my parents told me to wait…" (P17-1, P13-2)

"I am very grateful to a non-profit training centre…we live on basic living allowance from the government…they provided free training for our child until we got in this HHS centre…They had helped many children who cannot go to governmental centres and who cannot afford other private training…" (P12-1)

Box 8.3 Quotes of parents' stress and concerns

"When I first learnt that my child had autism, I did not know how this could happen and I felt everything was falling apart…I had a nervous breakdown…I cried a lot and was very unhappy…" (P27-1)

"It took me a year to accept the situation…Next year, he will have an assessment to decide whether he can go to mainstream school…if he fails, we have to send him to special school..." (P13-3)

8.4 Discussion

Having been adopted from the UK model since 1977[369], there has been an increase in services for children with ASC in Hong Kong following improved public awareness and acceptance[370]. However, several problems of the system were identified from interviews with parents.

8.4.1 The lack of government-supported training centres and special therapist

The waiting time for diagnosis and entrance to the HHS centres suggested an imbalance between service supply and the needs of children with ASC. There is a general shortage of government-supported centres. Thus, even if the child's condition was detected early, the long waiting time would still delay intervention which could be crucial to future outcome. Further, because of the shortage of special therapists, private therapy without governmental support is very expensive and almost unaffordable for many families in Hong Kong. The prices for private training vary, which puts parents in a difficult and vulnerable position. As a result, in rich families, the parents took their children to intervention as much as they could find and afford, while in poor families, they could only wait to get into the HHS centres. Regarding other therapies other than educational intervention, although some of them were suggested to be helpful to some children, there was no reliable evidence to show the effectiveness of these therapies. Therefore, this situation could lead to that a profit of private business and a waste of money and time of children and their families. Certain regulation and guideline for the choice of alternative therapies should be provided.

8.4.2 The government policy on ASC for children older than six

Compulsory assessment at the age of six decides the future education pathway of the child in Hong Kong. If the child is not recommended to go to mainstream school, he

or she can only attend special schools. Before 6 years old, children with ASC can receive intervention in HHS centres to improve their ability. However, there has been no such centre or school that could provide intervention for primary school aged children with ASC in Hong Kong. The lack of specific strategy of education provision for children after 6 years old has triggered concerns from parents on their children's future outcome.

8.4.3 Cultural influence and stigma

Although Hong Kong is metropolitan with a unique, mixed Eastern and Western culture[369], during this study several Eastern cultural issues still showed their influences on people's beliefs and attitudes towards children with ASC. One example is an old saying in Chinese culture, which indicates that the child who speaks late during childhood will turn out to be smarter than others in the future[352]. This was also found in the interviews with parents in mainland China described in Chapter 7. A study in mainland China found that people from the older generation in China tend to believe boys usually speak later than girls[352]. A similar belief was also reported with Indian parents of autistic children that have delayed the diagnosis of autism in Indian studies[383]. Some parents took the older generation's advice and waited until the child showed more autistic behaviours, thus, causing the delay in diagnosis and intervention.

8.4.4 Limitations

The literature search was only conducted in two English databases. There might be other papers about this topic in other databases that were not identified in this study. All five studies were the reports from the service providers' perspective and four of them were published by the same author[369, 370, 386, 388, 389]. There might be different points of view from other researchers on the service provision for ASC in Hong Kong. The participants were recruited from only four centres of HHS. The opinions from these 34 parents might be different from other parents of autistic children in Hong Kong especially those who were not in HHS centres but in other settings. Most of the parents spoke Cantonese, which was not the native language of the interviewer. Although the interviews were assisted by an interpreter, there might be misinterpretation due to language barriers. The interviews and the analysis were conducted by the candidate only which might lead to bias during the reading and coding of the transcripts. Only seven interviews were conducted with fathers, and the

perspectives on the service provision from fathers might be different from those of the mothers.

8.5 Implications and conclusion

In Hong Kong, the healthcare and education service specifically for ASC in Hong Kong has been developed since 1990s[370]. The service pathway for children with ASC is clear from the early identification to intervention in the current system. However, it still needs improvement in order to be sufficient to meet the needs of children with ASC and their families from the parents' perspective.

The findings from the present study have implications for the service provision on ASC in Hong Kong. The findings can inform service providers about the disadvantages of the current system for children with ASC. This study found the needs and supply of service for children with ASC is unbalanced. The lack of professionals and intervention centres partly contributed to the considerable delay from diagnosis to intervention. The current detection of ASC largely depends on the recognition and initiation by parents but not clinicians. The national screening for disabilities does not include ASC which if added could potentially improve the early diagnosis and intervention of ASC in Hong Kong. The findings can improve the public awareness and understanding of autism and thus reduce the stigma towards children with autism and their families. This study identified the confusion of this condition and the frustration on the service pathway, which indicated the lack of knowledge of this condition in the general public. Reports from this study can help to conduct further public education and campaign for ASC. It can also improve the communication among parents with children having ASC as they may be now aware that they share similar experience with each other. It can also inform other parents of possible strategies and solutions in terms of seeking help on diagnosis and intervention for ASC in the future. Most importantly, these findings may help to establish the communication between parents of children with ASC and those of typically developing children. It can be used to inform other parents of the existence of this condition especially during compulsory screening in health hospitals before the age of 3. The increase of knowledge of ASC in parents of typically developing children would help to reduce the stigma towards this condition in the general population.

Chapter 9 Pilot Study of the Mandarin CAST

9.1 Introduction

Chapter 3 and 4 revealed that the research methodology in the previous Chinese studies was different from the West which led to incomparable results[72, 292]. One of the differences between Chinese and Western studies was the adoption of screening instruments. Mainland China has a large population and most of the screening instruments used were developed in the West more than three decades ago[281, 282]. Thus, the application of up-to-date and well-developed screening instruments from the West to a Chinese population would be very helpful for further prevalence investigation. This chapter introduced and applied a Mandarin Chinese version of the Childhood Autism Spectrum Test (M-CAST) in a Chinese population as a pilot phase followed by a validation study in the next chapter.

9.2 Method

9.2.1 Ethical approval

Ethical approval for this research was sought from the Ethics committee in PUFH and the Cambridge University Psychology Research Ethics Committee.

9.2.2 Development of the M-CAST

The CAST was translated from English to Mandarin Chinese by the candidate, a native Chinese speaker. The M-CAST was back-translated into English by two Chinese-English bilingual speakers, not involved with autism research. The validated Taiwanese version of CAST was used as a reference version during adjustments of the translation of the M-CAST. Both the UK CAST and Taiwanese CAST have some examples in brackets after certain items. All those examples were adopted into the M-CAST. In order to be culturally appropriate, the language adjustments were conducted first through discussion within a group of professionals in autism in Beijing. It was further reviewed by an experienced psychiatrist in autism in Beijing. The translation aimed to be culturally appropriate for Chinese parents. The examples were given which tried to give direct description of what the items on the M-CAST are looking

for. For example, the item on eye contact was translated as eye communication in the M-CAST other than "touch" which was used in Chinese CABS.

9.2.3 Confirmation of the M-CAST

The M-CAST was initially piloted with Chinese parents. The participants were 10 opportunistically selected outpatients in the Paediatric department of PUFH, aged 5-10 years old. The purpose was to confirm the translation and the examples of the M-CAST. Parents were asked to fill in the M-CAST and provide feedback of their understanding and interpretation of each item to the candidate. The feedback was collected and then discussed by the professional group. The final version of the M-CAST (items and affiliated examples) was then back-translated and the approval of the final version was obtained from the UK authors of the CAST.

9.2.4 Scoring of the M-CAST

The M-CAST is a 37-item parental self-completion questionnaire, of which 31 items are scorable. Scoring of the M-CAST was identical to the original CAST (Chapter 2.2.3.10 & Appendix 9.1). For each scorable item, 1 point is assigned for an ASC-positive response and 0 for an ASC-negative response. Thus, the total score ranges from 0 to 31[70]. Additional information was also collected by the M-CAST: age of the child, date of birth, sex, birth order, number of siblings, school year number, class number, parental occupation, parental education background, contact information and any parental concerns about the child.

9.2.5 Participants

Participants included two groups of children and their parents. Group 1 were 20 children with an existing diagnosis of ASC. They were recruited from the database held by the Beijing China Disabled Persons' Federation (BCDPF) and the state-owned special rehabilitation centre in Xicheng district. BCDPF is a local branch of the China Disabled Persons' Federation (CDPF). It serves children with all kinds of disabilities in Xicheng district. The inclusion criteria for Group 1 included: 1) child aged 4 to 10 years; 2) child with an existing diagnosis of ASC prior to the start of this study made by a well-known psychiatric hospital in Beijing; 3) child living in Beijing at the time of the study.

Group 2 were 20 randomly selected typically developing children attending a primary school in Xicheng district in Beijing. The age of children in primary school in mainland China ranges from 6 to 12. The inclusion criteria for Group 2 included: 1) child aged 6 to 11 years (in grades 1 to 4); 2) child in a mainstream primary school; 3) child with no existing diagnosis of any developmental condition.

9.2.6 Procedure

All participants in Group 1 and Group 2 were sent an M-CAST pack by the candidate through their educational institution. Each pack included four parts: an information sheet; an M-CAST; a consent form; and an envelope for the return of the questionnaire. In total, 40 packs were distributed. The M-CAST pack is provided in Appendix 9.2.

9.2.7 Data analysis

Data entry of the M-CAST was conducted using Epidata[391, 392], coded in Excel and analysed using STATA 10.0. The distribution of scores on the M-CAST was examined for each group separately, and then compared. The distribution of scores on the M-CAST was described using means, standard deviations, 95% confidence intervals (CI) and ranges. The distribution normality was examined by using the Skewness-Kurtosis test. If the distribution was normal, differences in score distributions between two groups were investigated using an Independent Sample *t*-test. If the score distribution was not normal, the Mann-Whitney U test was used for comparison. The difference in age between two groups was examined using the Kolmogorov-Smirnov test. The association between age and score distribution was examined using linear regression. An item analysis was also conducted. Differences in item response between the two groups were examined using a Chi-square test. The UK cut-off of 15 was examined in the score distribution to investigate its applicability to the Chinese population.

9.3 Results

9.3.1 Characteristics of children

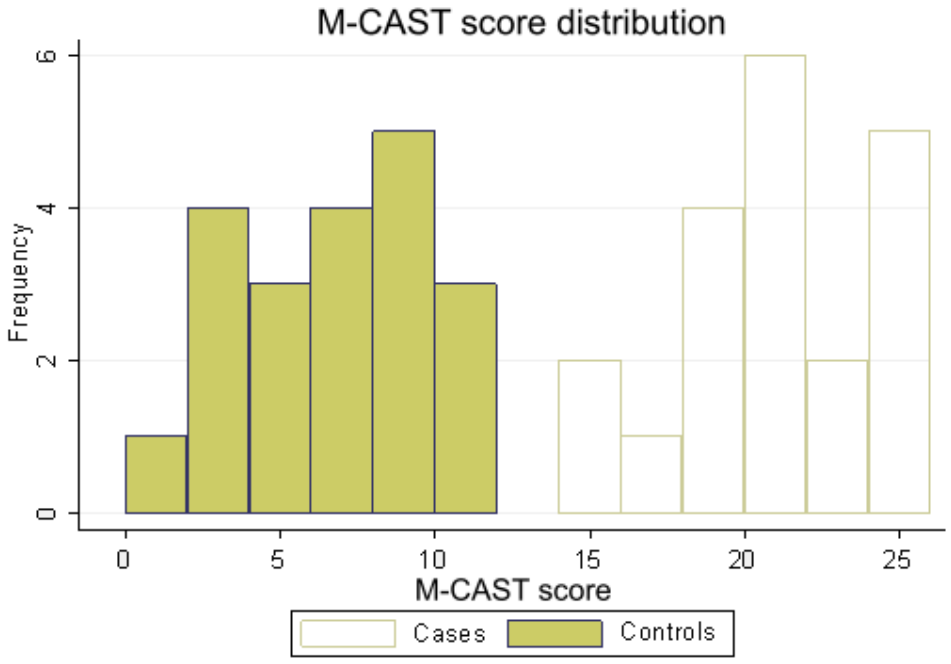
There were 20 children in Group 1 and 20 children in Group 2. The mean age of children with ASC in Group 1 was 5.4 years old (range: 4.1-8.7, SD=1.4). The mean age of typical developing children in Group 2 was 8.2 years old (range: 6.3-10.6,

SD=1.3). There were 15 boys and 5 girls in Group 1 and 13 boys and 7 girls in Group 2. The difference in age between two groups was significant (*Kolmogorov-Smirnov Test:* $p<0.001$). Using linear regression, there was no significant difference in the association between age and M-CAST score (Group 1: $p=0.92$; Group 2: $p=0.16$).

9.3.2 Score distribution

The mean score of the M-CAST in Group 1 was 20.7 (SD=3.2; 95% CI: 19.2, 22.1), ranging from 15 to 26. The mean score in Group 2 was 6.4 (SD=2.9; 95% CI: 5.0, 7.7), ranging from 1 to 11. The score distribution in Group 1 was normal (*Skewness-Kurtosis test:* $p=0.86$). The score distribution of Group 2 was also normal (*Skewness-Kurtosis test:* $p=0.27$). The Independent Sample *t*-test showed there was a significant difference in the mean score of the M-CAST between two groups ($t=14.9$; $p<0.001$). The score distributions of Group 1 and Group 2 are shown in Figure 9.1.

Figure 9.1 Histogram of score distributions of the M-CAST in cases and controls



9.3.3 Item validity

Percentage of participants in each group who scored ASC-positive on each item was calculated (Table 1). The Chi-square analyses revealed that there were eight items (item 6, 7, 9, 14, 19, 20, 34, 37) which showed no significant response differences between Groups 1 and 2. All the other items discriminated the two groups ($p<0.05$).

Table 9.1 Question responses on the items of the Mandarin CAST in pilot study

No	Question	Case (%)	Control (%)	X^2	P-value
1	Does s/he join in playing games with other children easily?	80	0	26.7	0.000
2	Does s/he come up to you spontaneously for a chat?	95	0	36.2	0.000
5	Is it important to him/her to fit in with the peer group?	60	10	11.0	0.001
6	Does s/he appear to notice unusual details that others miss?	45	60	0.9	0.342
7	Does s/he tend to take things literally?	40	15	3.1	0.077
8	When s/he was 3 years old, did s/he spend a lot of time pretending (e.g., play acting being a superhero, or holding teddy's tea parties)?	95	20	23.0	0.000
9	Does s/he like to do things over and over again, in the same way all the time?	30	50	1.7	0.197
10	Does s/he find it easy to interact with other children?	80	5	23.0	0.000
11	Can s/he keep a two-way conversation going?	90	0	32.7	0.000
13	Does s/he mostly have the same interests as his/her peers?	65	20	8.3	0.004
14	Does s/he have an interest that takes up so much time that s/he does little else?	65	40	2.5	0.113
15	Does s/he have friends, rather than just acquaintances?	90	30	21.6	0.000
16	Does s/he often bring you things s/he is interested in to show you?	60	0	17.1	0.000
17	Does s/he enjoy joking around?	80	30	10.1	0.001
18	Does s/he have difficulty understanding the rules for polite behaviour?	50	20	4.0	0.047
19	Does s/he appear to have an unusual memory for details?	45	50	0.1	0.752
20	Is his/her voice unusual (e.g., overly adult, flat, or very monotonous)?	45	30	1.0	0.327
21	Are people important to him/her?	45	5	8.5	0.003
23	Is s/he good at turn-taking in conversation?	95	15	25.8	0.000
24	Does s/he play imaginatively with other children, and engage in role-play?	90	10	25.6	0.000
25	Does s/he often do or say things that are tactless or socially inappropriate?	75	20	12.1	0.000
27	Does s/he make normal eye-contact?	70	15	12.4	0.000
28	Does s/he have any unusual and repetitive movements?	60	15	8.6	0.003
29	Is his/her social behaviour very one-sided and always on his/her own terms?	90	20	19.8	0.000
30	Does s/he sometimes say "you" or "s/he" when s/he means "I"?	40	10	4.8	0.028
31	Does s/he prefer imaginative activities such as play-acting or story-telling, rather than numbers or lists of facts?	80	35	8.3	0.004
32	Does s/he sometimes lose the listener because of not explaining what s/he is talking about?	65	20	8.3	0.004
34	Does s/he try to impose routines on him/herself, or on others, in such a way that it causes problems?	35	10	3.6	0.058
35	Does s/he care how s/he is perceived by the rest of the group?	95	15	25.9	0.000
36	Does s/he often turn conversations to his/her favourite subject rather than following what the other person wants to talk about?	60	15	8.6	0.003
37	Does s/he have odd or unusual phrases?	40	50	0.4	0.525

9.4 Discussion

Results from this study replicated the previous pilot study of the UK CAST[121]. The M-CAST was found to differentiate children with a diagnosis of ASC from typically developing children in a primary school. The cut-off of 15 appeared to be a suitable cut-off for the M-CAST. Item responses to certain items were found to be different on the M-CAST compared with the UK CAST.

9.4.1 Limitations

The sample sizes in each group were relatively small and therefore not likely to be representative of the population of children with ASC or typically developing children. The purpose was to purely replicate the methodology used in the UK pilot and to determine the translation of the M-CAST was appropriate. The total sample size of the China pilot was the same as the UK pilot (N=40). However, the UK pilot recruited more typically developing children (37) than children with ASC (13). The current study recruited an even number of cases (20) and controls (20). This approach can serve to reduce selection bias due to the different number of participants in each group. In addition, no information on the language level, cognitive abilities and other ability profiles of the cases was available for the case group. Such information would help to examine whether the differences reported between two groups were due to the presence of autistic symptomatology or other differences.

There was a significant difference between the mean ages of the two groups, with the children with ASC being 2.8 years younger than the typically developing children. The age of children in primary school in mainland China ranges from 6 to 12, while the cases recruited from the BCDPF and Elim centres were younger. Since the original CAST was designed to detect children who were 4-11 years old, the age range of the current sample was within the applicable age range. In addition, this study found no difference in association between age and score distribution in each group. Thus, it was unlikely this could invalidate the results.

The ASC status of Group 1 was not verified in this study. Only children with a diagnosis of ASC from a well-known psychiatric hospital in Beijing were invited to participate in this study. A previous review[72] has suggested that children with a

diagnosis of ASC in mainland China are mainly children with a diagnosis of Childhood Autism (rather than milder manifestations of the condition, such as Asperger Syndrome). To address this point, the verification of diagnosis status of a group of children already diagnosed with ASC in mainland China will be described in the validation study.

Finally, although the items on the M-CAST were the same as the UK CAST, certain items were adapted to the Chinese culture. For example, the pretending game for item 8 in the UK CAST was play-acting as a superhero. In the Mandarin version, the superhero was replaced by a familiar figure for Chinese children. However, the examples were generated from the validated Taiwanese version of the CAST, group discussion and the initial piloting with parents. Thus, the differences in the items due to translation should not have influenced the results.

9.4.2 Differences in score distribution between UK and China pilot studies

There was a clear difference in score distribution between the two studies. In the UK pilot study, the score range of the children with ASC was between 15 and 31, and the score range of the typically developing children was between 0 and 13. The mean score of children with autism in the Chinese sample (20.6, SD=3.2) was a little lower than the UK pilot (21.1, SD=5.5). The mean score of the typically developing children in the Chinese data (6.4, SD=2.9) was higher than the UK pilot (4.7, SD=3.6). This might be due to differences in sampling, since there were more typically developing children and fewer children with ASC in the UK study[121].

9.4.3 Differences in item response between UK and China pilot studies

More items on the M-CAST failed to differentiate children with ASC from typically developing children. In the UK pilot study, four items (item 6, 7, 9, 30) did not differentiate cases from controls. In the Chinese pilot study, 8 items (item 6, 7, 9, 14, 19, 20, 34, 37) failed to differentiate cases from controls. In both the Chinese and UK pilot samples, items 6, 7 and 9 did not differentiate the two groups.

There are several possible reasons as to why these items did not discriminate between cases and controls on the M-CAST. The awareness of ASC in study samples might be different: the UK sample was from Cambridge, where local parents were potentially

more educated and aware about ASC compared to the parents in the Chinese sample. Possible cultural influences may affect the way in which Chinese parents interpreted and answered some items on the M-CAST. For example, both items 6 and item 19 focus on attention to details. In the Chinese culture, noticing details or recalling an event from the past is considered as something good. It might be possible that parents in Group 2 wanted to show that their children were smart, so more parents in Group 2 provided an ASC-positive response on these items than Group 1. Similarly, item 20 aims to detect the oddness of speaking of the child with one example asking whether the child speaks like an adult. Since speaking in an overly adult way may be considered as a sign of maturity in Chinese culture. Chinese parents may interpret this as a way of saying that their child has linguistic talents that may lead them to endorse this item with an ASC-positive response. The detailed interpretations of each item that did not meet the significance are provided in Appendix 9.3.

9.5 Conclusion

This chapter described a pilot study aimed to develop a Mandarin Chinese version of the CAST, to apply this in a Chinese sample and establish a preliminary cut-point. The M-CAST was able to distinguish children with ASC from typically developing children at a cut-point of 15 in mainland China. The M-CAST is therefore suitable to be considered as a candidate screening instrument for ASC in epidemiological research in Chinese population. Cultural influences may be operating on certain items on the M-CAST which need further investigation.

Chapter 10 Validation Study of the Mandarin CAST

10.1 Introduction

The previous chapter illustrated that the M-CAST can distinguish children with ASC from typically developing children in a Chinese population. This chapter presented a validation study of the M-CAST to investigate the validity of this instrument as a screening instrument for ASC in the Chinese general population.

10.2 Method

10.2.1 Procedure

In order to generate comparable results with the UK studies of the CAST, the same version of the M-CAST in the pilot was used in the validation study without further adjustment to test its utility in a Chinese population. The validation study of the M-CAST had two distinct phases: screening and diagnostic assessment. In the screening phase, the CAST was distributed to the parents of primary school aged children in two mainstream schools in Beijing. The questionnaires were collected back from the children by the class teacher and then collected by the candidate. The M-CAST pack used in this validation study was the same as the M-CAST pack in the pilot study. In the assessment phase, two diagnostic instruments for ASC were applied, the ADOS and the ADI-R. The examiner was blind to screen status. The child's IQ was examined using the Raven's Progressive Matrices (RPM)[393]. Each family who participated in further assessment was provided with a report regarding the social and communication ability of the child and recommendations of referral to services where appropriate. At the end of this study, a general feedback was provided to both schools regarding the overall development of students.

In addition, in order to verify existing diagnoses of ASC, 50 children who already had an existing diagnosis of ASC (along with their parents/caregivers) were invited to complete the M-CAST, and take part in the further assessments using the ADOS and the ADI-R. Where possible, the RPM was also applied to children who already had a diagnosis. This group of children were examined separately from the validation study sample.

10.2.2 Participants

Two mainstream primary schools in Xicheng district in Beijing were invited to participate in this research. They were asked to distribute a questionnaire pack to each child who was in grade 1 to 4 (aged 6-11). There were in total 737 children in grade 1 to 4 in those two schools who were all invited. Fifty children who had a diagnosis of ASC were recruited from the database of Beijing CDPF (n=29) and the Elim Training Centre for Chinese with Autism in Qingdao (n=21).

10.2.3 Sampling strategy

Following the pilot study, a cut-off of 15(≥15) was used on the M-CAST in this validation. Where there were missing items, these items were firstly given an ASC-negative score (0) to generate a minimum score. The missing items were secondly given an ASC-positive score (1) to generate a maximum score. The M-CAST maximum scores were grouped into three bands: a high score group (≥15) (of which 100% of those who have consent were invited), a borderline group (12-14) (100% of those who have consent were invited) and a low score group (≤11) (5% randomly selected for invitation). The randomisation of children in the low score group was carried out using a random number table. All 50 children with an existing diagnosis of ASC were invited to undergo a diagnostic assessment.

10.2.4 Data entry and cleaning

A database for the M-CAST was set up in Epidata[392] after the questionnaires were collected back from schools. The data were checked and cleaned. Each entry had a unique ID number. 20% of questionnaires were double-entered to audit the accuracy. After the completion of data entry, a random 10% of the questionnaires were selected to be checked for data entry errors. 100% agreement was found between the two entered sets of data and another agreement of 100% was found in the random selected 10% of questionnaires. Participants were excluded if they did not give consent to participation or if the M-CAST was returned blank.

10.2.5 Assessment battery

The combination of the ADOS[192]and the ADI-R[180] was adopted as the assessment instruments. The Taiwanese versions of the ADOS and the ADI-R provided by the

publisher (World Psychological Service, WPS) were used. In this study, module 3 was chosen for children who had fluent expressive language. For children who already had an ASC diagnosis, module 2 was generally chosen except when the child was non-verbal, in which case module 1 was chosen. Administration of each ADOS module usually took about 45 minutes. The administration of the Taiwanese ADI-R took around 1.5 hours.

Prior to assessment, parents were asked to provide consent, including consent for the examiner to video-record the ADOS and tape-record the ADI-R assessments. Assessments were conducted by the candidate due to no other Chinese trained examiners being available. The candidate is a medical doctor and fully-trained examiner by a UK trainer in English in Cambridge for the ADOS and a reliable examiner for both the ADOS and ADI-R. Reliability of the assessments was checked by reviewing the tapes of the ADI-R and videos of the ADOS assessments twice, first by the candidate the day after initial coding, and next during consensus diagnostic discussions with the Chinese child psychiatrist. At this point the ADOS video was reviewed by the child psychiatrist and the researcher together.

The Raven's Progressive Matrices (RPM) is frequently used in clinical neuropsychology for assessing general intellectual abilities[394]. The Chinese RPM was adopted as an IQ test which was validated and applicable to individuals from the ages of 5 to 75 in mainland China[395].

10.2.6 Case identification

Cases of ASC were defined in two ways: first, using the outcome on the diagnostic assessment instruments, and second, using a consensus case definition. For the assessment diagnostic outcome, if the child scored above the cut-off for autism or ASC (in the case of ADOS) on both the ADOS and the ADI-R, the child was recorded as a case of ASC. A child was recommended to have consensus diagnosis if they reached the cut-off on either the ADOS or the ADI-R. The child was then referred to the clinical child psychiatrists in PUFH using clinical judgement based on diagnostic criteria of ICD-10 and DSM-IV. The consensus diagnosis was made by a Chinese child psychiatrist and the candidate together. There were several reasons for also

using a consensus diagnosis for case identification. First, studies have suggested that the algorithms for the ADOS and the ADI-R are too stringent and are likely to miss children with an autism spectrum diagnosis or with PDD-NOS[13, 120, 159]. Second, the UK CAST validation study adopted a consensus diagnostic outcome to determine cases[159]. Therefore, to be consistent in methodology, a consensus diagnosis was used as the final diagnosis in the analysis for this study.

10.2.7 Feedback to parents and recommendations

Following the diagnostic assessment, a summary report of each child to parents and a general summary report to two schools about the study were provided by the candidate. When the researcher had concerns about a child's development, a recommendation was made at the end of the summary report. In such situations the recommendation provided suggestions for further referral to psychiatrists to explore the issues in more detail. If the parents were concerned about the child's development while the researchers were not, parents were encouraged to seek advice about further referral.

10.2.8 Analysis and missing values

The score distribution of the M-CAST was described by median, the inter quartile range (IQR) and range. The normality of score distribution was examined using the Skewness-Kurtosis test. The hypothesis of this test is that the distribution is normal, so a non-significant result indicates a normal distribution ($p>0.05$). The characteristics of participants who took part in the further assessment and those who refused to participate were compared to assess whether systematic bias was introduced through non-participation in the assessment phase. The characteristics of responders in the low score group (≤ 11) who participated in the further assessment were compared with those who did not participate in the assessment. Statistical tests for significant differences between groups were adopted for this analysis. The Kolmogorov-Smirnov test examined for equality of distributions. The Median test was used to investigate whether the two samples were from populations with the same median. The Kruskal-Wallis H test was used to examine the difference between medians across multiple groups. Unpaired t-tests and one-way ANOVA were used to compare means, and Chi-square test was used to examine differences in proportions. Whenever the numbers were small, a Fisher's exact test was used. Since the characteristics of non-responders

in the screening phase were not available, it was not possible to assess the effect of non-response on the score distribution. Test accuracy of the M-CAST was examined by calculating the sensitivity, specificity, and PPV using the minimum score. Inverse probability weighting using sampling weights was used to adjust the estimates for the known non-response to the invitation for assessment within each sampling score group[70, 159]. This strategy was used because of the two-phase sampling strategy. The inverse probability was the empirical weights generated according to the response to the screen and to the participation rate in the further assessment phase. A raw prevalence estimate was generated by using inverse probability weighting first. Then the missing data were imputed and an adjusted prevalence was provided after adjusting for age, sex and the non-response differences. The 95% confidence intervals were calculated accordingly by applying the weighed count. A sensitivity analysis was conducted to investigate the effect of missing data. The analysis was re-run using the maximum score. If by using the maximum score, a change of score led to a change in the score group (from ≤11 to ≥12, or <15 to ≥15), the analyses were re-run without those individuals who changed score group. The data management and analyses were conducted in Microsoft Excel[396] and STATA 10.0[397].

10.3 Results

10.3.1 Response rate and missing value in screening

The total number of children was 737. One school had 165 students and the other had 572. None of the students had a previous existing diagnosis of ASC. After excluding the questionnaires that were returned blank, a total of 714 questionnaires were available for analyses (response rate=97%). A number of 655 had complete data while 59 had missing values for some items. The extent of missing data in the whole sample is shown in Table 10.1, and the response of each M-CAST item is shown in Table 10.2.

Table 10.1 The number of missing items on the M-CAST in screening

No. of missing items	Frequency	(%)
0	655	(91.7)
1	45	(6.3)
2	8	(1.1)
3	4	(0.6)
4	1	(0.1)
5	0	(0.0)
6	0	(0.0)
7	1	(0.1)
Total	714	(100)

Table 10.2 Responses and missing values on items of the M-CAST in screening

Item No.	ASC-negative (%)		ASC-positive (%)		Missing (%)		Item No.	ASC-negative (%)		ASC-positive (%)		Missing (%)		Item No.	ASC-negative (%)		ASC-positive (%)		Missing (%)	
1	671	(94.0)	42	(5.9)	1	(0.1)	15	526	(73.7)	183	(25.6)	5	(0.7)	28	574	(80.4)	140	(19.6)	0	(0.0)
2	648	(90.8)	65	(9.1)	1	(0.1)	16	666	(74.1)	48	(6.7)	0	(0)	29	548	(76.8)	165	(23.1)	1	(0.1)
5	664	(93.0)	50	(7.0)	0	(0.0)	17	529	(74.1)	182	(25.5)	3	(0.4)	30	617	(86.4)	97	(13.6)	0	(0.0)
6	225	(31.5)	468	(68.1)	3	(0.4)	18	427	(60.0)	287	(40.2)	0	(0.0)	31	505	(70.7)	207	(29.0)	2	(0.3)
7	546	(76.5)	163	(22.8)	5	(0.7)	19	185	(25.9)	525	(73.5)	4	(0.6)	32	514	(72.0)	195	(27.3)	5	(0.7)
8	516	(72.3)	193	(27.0)	5	(0.7)	20	524	(73.4)	187	(26.2)	3	(0.4)	34	478	(67.0)	230	(32.2)	6	(0.8)
9	465	(65.1)	247	(34.6)	2	(0.3)	21	627	(87.8)	81	(11.3)	6	(0.8)	35	502	(70.3)	207	(29.0)	5	(0.7)
10	656	(91.9)	58	(8.1)	0	(0.0)	23	517	(72.4)	193	(27.0)	4	(0.6)	36	520	(72.8)	191	(26.7)	3	(0.4)
11	672	(94.1)	41	(5.7)	1	(0.1)	24	634	(88.8)	79	(11.1)	1	(0.1)	37	411	(57.6)	301	(42.1)	2	(0.3)
13	625	(87.5)	89	(12.5)	0	(0.0)	25	520	(72.8)	184	(25.8)	10	(1.4)							
14	365	(51.1)	346	(48.5)	3	(0.4)	27	582	(81.5)	129	(18.1)	3	(0.4)							

10.3.2 Population characteristics

Date of birth was provided for 687 children. The mean age of the sample was 8.4 years old (SD=1.2). Information on gender was missing for 13 children (1.8%). The distribution of age and sex is shown in Table 10.3. 544 children (76.2%) were the only child in the family, and 124 children had a brother or sister (17.4%). Information about siblings was missing for 46 (6.4%) children. The occupation and education level of the parents was also collected and divided into five categories. According to avaliable statistics of education background in Beijing from the National Bureau of Statistics, the educational level of the parents in this sample is higher than average in Beijing. The characteristics of the parents are shown in Table 10.4.

Table 10.3 Age and sex distribution of the children in screening

	Sex				
Age	**Boys**	**Girls**	**Missing**	**Total**	**(%)**
6	66	68	0	134	(18.8)
7	61	52	0	113	(15.8)
8	100	95	2	197	(27.6)
9	105	84	0	189	(26.5)
10	28	23	0	51	(7.1)
11	2	1	0	3	(0.4)
Missing	9	7	11	27	(3.8)
Total	371	330	13	714	(100)

Table 10.4 Characteristics of the parents

Characteristics	**Category**	**Number**	**(%)**	**Beijing average (%)**
Father's occupation	Worker or farmer	121	17.0	--
	Clerk	211	29.6	--
	Technical staff	153	21.4	--
	Manager	31	4.3	--
	Own-business	119	16.7	--
	Missing	79	11.1	n/a
Mother's occupation	Worker or farmer	178	24.9	--
	Clerk	165	23.1	--
	Technical staff	168	23.5	--
	Manager	11	1.5	--
	Own-business	118	16.5	--
	Missing	74	10.4	n/a
Father's education	Junior high school	113	15.8	30.8
	High school	182	25.5	22.6
	College	316	44.2	33.2
	Master or higher	49	6.9	4.9
	Missing	54	7.6	n/a
Mother's education	Junior high school	130	18.2	26.3
	High school	197	27.6	23.2
	College	308	43.1	34.4
	Master or higher	32	4.5	4.2
	Missing	47	6.6	n/a

--: not available; n/a: not applicable.

10.3.3 Participants in assessment

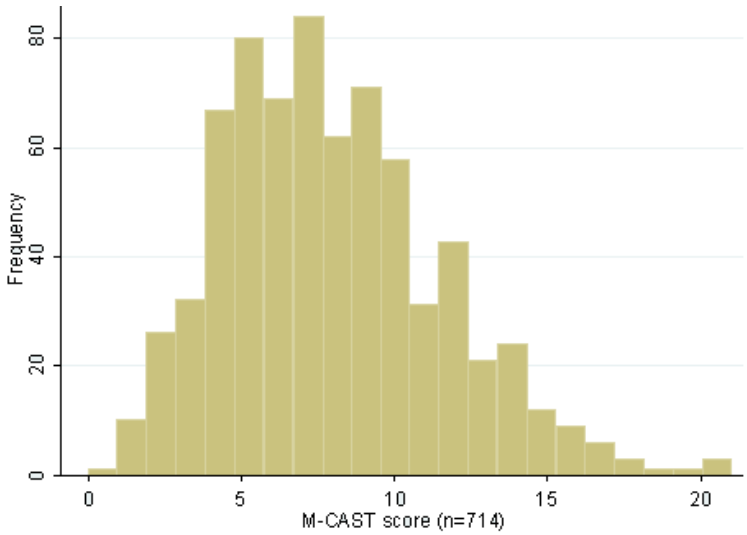
Of the 714 screened children, 35 (4.9%) were in the high score group (≥15), 94 (13.2%) were in the borderline group (12-14) and 585 (81.9%) were in the low score group (≤11). All the children in the high and borderline groups were invited for further diagnostic assessment as well as a randomly selected 5% of children from the low score group. In total, 103 children completed the assessment, of which 23 (66%) were in the high score group, 57 in the borderline group (61%) and 23 (79%) in the low score group. The overall participation rate for the diagnostic assessment was 65%. All the 103 ADOS assessments were completed using Module 3 since all those children had fluent speech.

The characteristics of those that completed assessment and those refused to participate are shown in Table 10.5. Analyses were conducted to examine whether there were significant differences among those who were assessed and those who refused to participate in the assessment according to which score group they were in. There were significant differences in ages among children in the high score group according to whether they completed assessments, were not invited or refused to participate in the assessment (*Fisher's exact test*, p=0.01). Significant differences were also found in the mothers' education among children in the low score group (*Fisher's exact test*, p=0.039). No other differences among those assessed and those who refused to participate were significant.

10.3.4 Distribution of the M-CAST score

The score distribution of the M-CAST is shown in Figure 10.1 (n=714). The median score on the M-CAST was 7 (IQR: 5, 10; range: 0, 21). 4.9% of children were in the high score group (≥15), 13.2% were in the borderline group (12-14), and the remaining were in the low score group (≤11). The distribution was positively skewed (*Skewness-Kurtosis Test*: p<0.005).

Figure 10.1 Distribution of observed score on the M-CAST (n=714)



10.3.5 Sampling and differential verification

The assessment status of each child who was selected for assessment was assigned into three categories: not-invited, invited and completed, and invited but refused further participation in the low score group (≤11). Within the low score group, no significant differences were found among children who were invited and completed the assessment, who were not invited for an assessment, and those who refused to participate (*one-way ANOVA*, $p>0.05$).

10.3.6 Diagnostic assessment

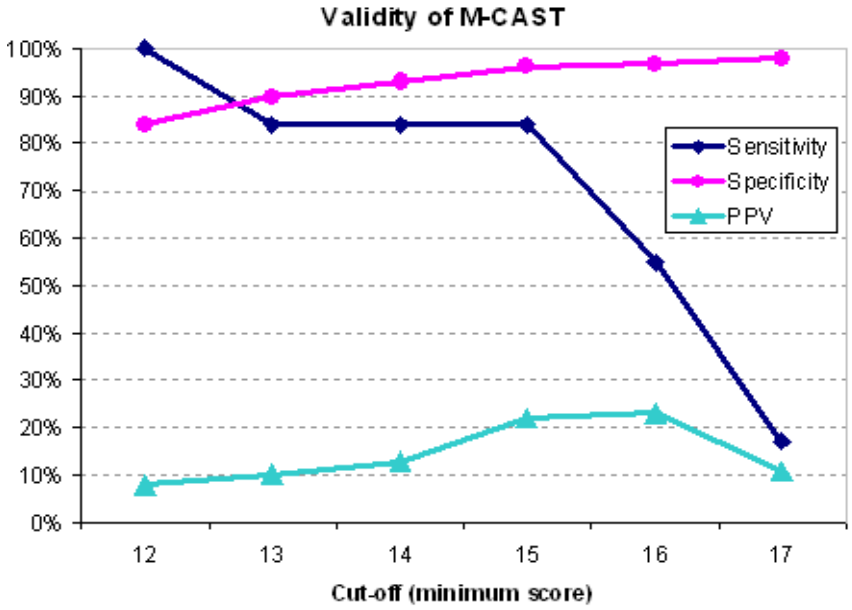
The examiner was blind to the CAST status during diagnostic phase. Three children in the high score group met cut-offs on both the ADOS and ADI-R. Four children met the cut-off of ASC or autism on either the ADOS or ADI-R. The characteristics of the seven children are shown in Table 10.6. The child that only met ADI-R cut-off missed 1 point on the ADOS. The two children that met the cut-off of the ADOS missed the cut-off of Qualitative Abnormalities in Communication and Repetitive Behaviours on the ADI-R. All seven children were examined by a child psychiatrist. After the consensus diagnosis, those children who only met the cut-off on either the ADOS or the ADI-R and were scored in high or borderline groups were all given a consensus diagnosis of ASC. It seemed that the child in the low CAST score group did not want to engage in a few activities during the ADOS due to unknown reasons. There were limited responses during the interaction which led to a high score on the social and communication scale of the ADOS. The child did not meet the cut-off on the ADI-R.

Moveover, the child behaved cooperatively during the consensus diagnosis with the child psychiatrist. Thus, this child was given a consensus diagnosis of not having ASC. Thus, in total, there were six cases of ASC identified during the assessment phase. The inverse probability weighting was used adjust the estimates for the known non-response to the invitation for assessment within each score group. Using the weightings of 35/23 (35 children scored ≥15 on the Mandarin CAST and 23 completed the assessment) and 94/57 (94 children scored 12-14 on the Mandarin CAST and 57 completed the assessment), the overall directly observed prevalence estimate for all ASC is (5×(35/23))+(1×(94/57)), which corresponds to 9.3 (95% CI: 1.9, 16.7) new (undiagnosed) cases from the screened population. As the total screened population was 714, the raw prevalence of ASC in this Chinese sample was 130 per 10,000 (95% CI: 58, 286). After imputing the data for missing value and adjusting for age, sex and non-response differences, the number of new case was 8.5 (95% CI: 1.6, 15.4) and the prevalence was 119 per 10,000 (95% CI: 53, 265). The results of diagnostic assessment of the 103 children in primary schools are provided in Appendix 10.1.

10.3.7 Test accuracy of the M-CAST

Test accuracy was calculated at different cut-offs on the M-CAST using the observed CAST (minimum) score and the consensus diagnosis. At a cut-point of 15, the sensitivity of the M-CAST was 84% and the specificity was 96%. When using higher cut-offs, sensitivity dropped greatly. Positive predictive value (PPV) was relatively low. The highest PPV was 23% at a cut-off of 16. However, sensitivity decreased to 55% at this cut-off (Table 10.7 & Figure 10.2).

Figure 10.2 Accuracy indices at each cut-off using a consensus diagnosis



10.3.8 Missing data and sensitivity analysis

A sensitivity analysis was conducted by using the maximum score to calculate the test validity. The indices of test accuracy were similar with the original calculation using the observed score. The sensitivity, specificity as well as PPV at the cut-off of 15 did not change. There was only a slight difference in the indices of test accuracy between the original analysis and the sensitivity analysis (Table 10.8).

10.3.9 Case verification of children with an existing diagnosis of ASC

Fifty children with an existing diagnosis of ASC by Chinese psychiatrists were assessed using the ADOS and the ADI-R. 48 children (96%) met all the cut-off of both the ADOS and ADI-R, while only two missed the cut off of the ADI-R (Table 10.9). The results suggested that most of the children who were diagnosed as autism in mainland China are children with Childhood Autism. The children who may be having Asperger Syndrome or high-functioning autism may be still unidentified in the general population. The procedure and results of the pilot and validation study are shown in Figure 10.3.

Table 10.5 Comparison of the characteristics of participants according to assessment status in different score groups

		Group 1: CAST≤11						Group 2: 12-14				Group 3: ≥15			
Total	**N (%)**	**Invited and assessed**		**Not invited**		**Invited but no consent**		**Invited and assessed**		**Invited but no consent**		**Invited and assessed**		**Invited but no consent**	
CAST score	Median (IQR)	6	(3.9)	7	(5,9)	7	(6,8)	13	(12,14)	12	(12,13)	16	(15,17)	16	(16,18.5)
Age	Mean (SD)	8.4	(1.2)	8.4	(1.2)	8.6	(1.1)	8.5	(1.2)	8.5	(1.4)	8.1	(1.1)	8.4	(1.6)
Sex: Boys	N (%)	8	(35)	280	(51)	4	(67)	38	(67)	21	(60)	38	(67)	21	(60)
Girls		15	(65)	267	(49)	2	(33)	19	(33)	14	(40)	19	(33)	14	(40)
Single child: Yes	N (%)	21	(68)	429	(82)	5	(83)	41	(76)	23	(66)	12	(52)	8	(67)
No		1	(3)	84	(18)	1	(17)	13	(24)	10	(29)	10	(43)	3	(25)
Missing		9	(29)	0	(0)	0	(0)	0	(0)	2	(6)	1	(4)	1	(8)
Father's occupation															
Worker or farmer	N (%)	4	(17)	86	(15)	1	(17)	14	(25)	6	(16)	6	(26)	4	(33)
Clerk		8	(35)	179	(32)	1	(17)	12	(21)	5	(14)	4	(17)	2	(17)
Technical staff		6	(26)	119	(21)	2	(33)	10	(18)	8	(22)	5	(22)	3	(25)
Manager		1	(4)	26	(5)	1	(17)	2	(4)	0	(0)	0	0	1	(8)
Own-business		3	(13)	90	(16)		(17)	13	1(23)	8	(22)	3	(13)	1	(8)
Missing		1	(4)	56	(10)	0	(0)	6	(11)	10	(27)	5	(22)	1	(8)
Mother's occupation															
Worker or farmer	N (%)	6	(26)	135	(24)	1	(17)	16	(28)	8	(22)	7	(30)	5	(42)
Clerk		4	(17)	133	(24)	1	(17)	13	(23)	10	(27)	3	(13)	1	(8)
Technical staff		7	(30)	137	(25)	1	(17)	9	(18)	5	(14)	6	(26)	3	(25)
Manager		1	(4)	9	(16)		(0)	0	(0)	0	(0)	0	0	1	(8)
Own-business		4	(17)	86	(15)	2	(33)	14	(25)	7	(19)	4	(17)	1	(8)
Missing		1	(4)	56	(10)	1	(17)	5	(9)	7	(19)	3	(13)	1	(8)
Father's education															
Junior high	N (%)	1	(4)	84	(15)	1	(17)	14	(25)	4	(11)	4	(17)	5	(42)
Senor high		6	(26)	143	(26)	2	(33)	14	(25)	10	(27)	5	(22)	2	(17)
College		14	(61)	256	(46)	2	(33)	21	(37)	10	(27)	10	(43)	3	(25)
Graduate		1	(4)	39	(7)	1	(17)	2	(4)	2	(5)	2	(9)	2	(17)
Missing		1	(4)	34	(6)	0	(0)	6	(11)	11	(30)	2	(9)	0	(0)
Mother's education															
Junior high	N (%)	0	(0)	102	(18)	1	(17)	13	(12)	6	(9)	5	(22)	3	(25)
Senor high		9	(7)	145	(26)	3	(50)	20	(18)	11	(17)	5	(22)	4	(33)
College		112	(91)	252	(45)	1	(17)	17	(15)	11	(17)	10	(43)	5	(42)
Graduate		1	(1)	26	(5)	1	(17)	3	(3)	0	(0)	1	(4)	0	(0)
Missing		1	(1)	31	(6)	0	(0)	57	(52)	37	(57)	2	(9)	0	(0)

Figure 10.3 Flowchart of the pilot and validation study of the M-CAST

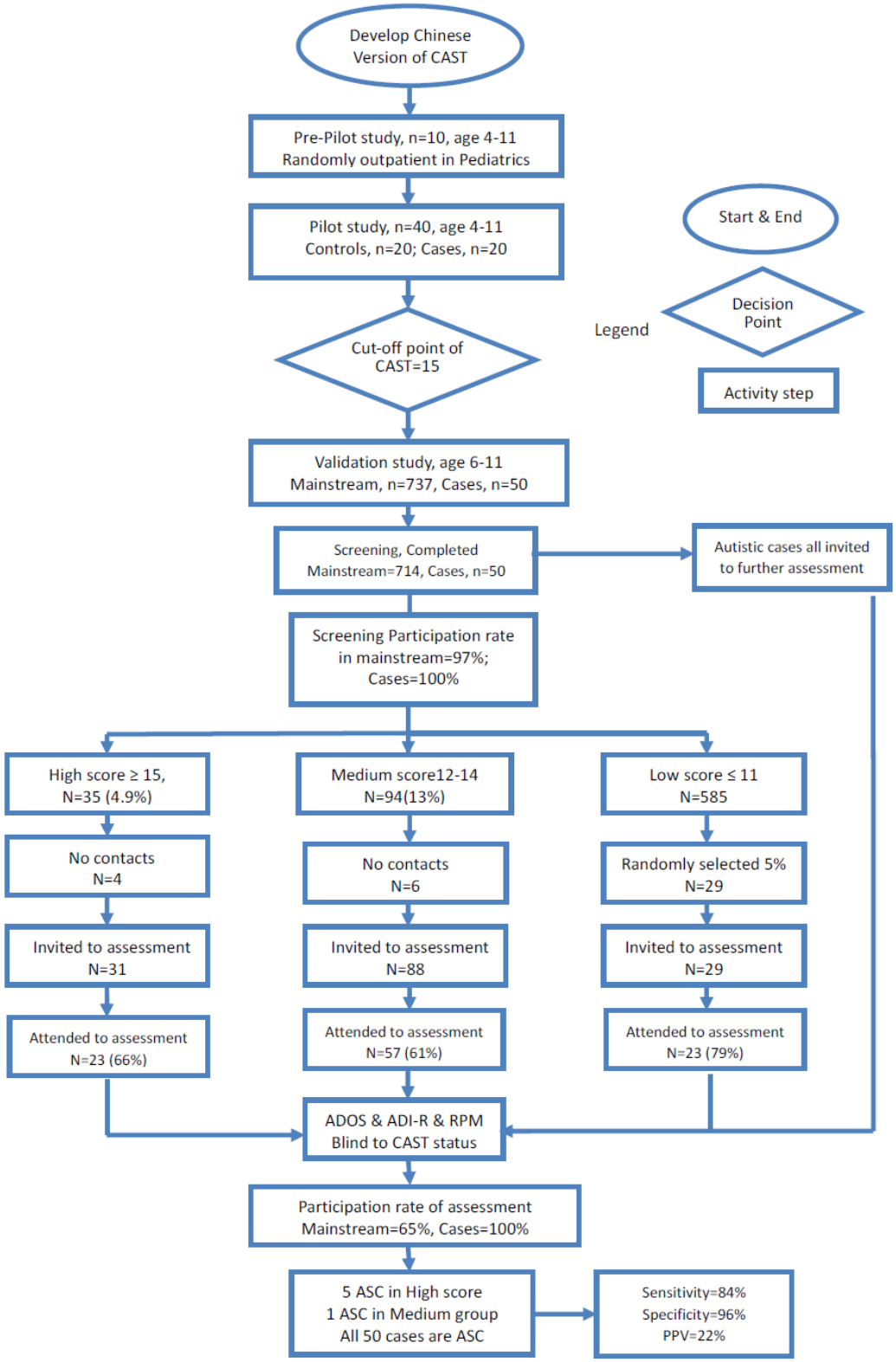


Table 10.6 Characteristics of participants meeting diagnostic criteria

No	CAST		Previous diagnosis	Assessment diagnosis		Consensus diagnosis	IQ	ADOS algorithm					ADI-R algorithm				
	Observed score	Maximum score	Y/N	ADOS	ADI-R			A	B	A+B	C	D	A	B1	B2	C	D
A	16	16	N	Y	Y	Y	118	3	4	7	0	0	18	10	--	5	1
B	17	17	N	Y	Y	Y	127	5	8	13	2	0	10	8	--	3	1
C	15	15	N	Y	Y	Y	117	2	8	10	2	0	14	9	--	4	2
D	16	16	N	N	Y	Y	119	2	4	6	1	0	15	15	--	3	1
E	15	15	N	Y	N	Y	105	4	6	10	0	0	11	6	--	2	2
F	12	12	N	Y	N	Y	114	2	5	7	1	0	12	7	--	2	1
G	2	2	N	Y	N	N	137	4	7	11	2	0	2	7	--	0	0

[a] Previous diagnosis of ASC, at the time of interview; [b] Above all cut-offs on the assessment instrument; [c] Met a research diagnosis of ASC. Y=Yes, N=No.
ADOS algorithm: A: Communication; B: Reciprocal Social Interaction; C: Imagination/Creativity; D: Stereotyped Behaviours and Restricted Interests. ADI-R algorithm: A1: QualitativeAbnormalities in Reciprocal Social Interaction; B1: Qualitaitve Abnormalities in Communication-Verbal; B2: Qualitaitve Abnormalities in Communication-Nonverbal; C: Restrcted, Repetitive, and Stereotyped Patterns of Behavours; D: Abnormality of Developmental Evident at or before 36 months.

Table 10.7 Test accuracy of the M-CAST for consensus diagnosis (minimum score)

Score	Sensitivity (95%CI)	Specificity (95%CI)	PPV (95%CI)	NPV (95%CI)
12	100% (65%, 100%)	84% (81%, 86%)	8% (4%, 14%)	100% (99%, 100%)
13	84% (46%, 98%)	90% (87%, 92%)	10% (4%, 19%)	100% (99%, 100%)
14	84% (46%, 98%)	93% (90%, 94%)	13% (6%, 25%)	100% (99%, 100%)
15	84% (46%, 98%)	96% (94%, 97%)	22% (10%, 39%)	100% (99%, 100%)
16	55% (23%, 83%)	97% (96%, 98%)	23% (9%, 46%)	99% (98%, 100%)
17	17% (23%, 55%)	98% (97%, 99%)	11% (1%, 41%)	99% (98%, 99%)

Table 10.8 Sensitivity analysis of test accuracy of the M-CAST for consensus diagnosis (maximum score)

Score	Sensitivity	Specificity	PPV	NPV
12	100% (65%, 100%)	83% (80%, 86%)	8% (4%, 14%)	100% (99%, 100%)
13	82% (45%, 98%)	90% (87%, 91%)	9% (4%, 18%)	100% (99%, 100%)
14	82% (44%, 98%)	92% (90%, 94%)	12% (5%, 23%)	100% (99%, 100%)
15	84% (46%, 98%)	96% (94%, 97%)	22% (10%, 39%)	100% (99%, 100%)
16	53% (22%, 82%)	97% (96%, 98%)	21% (8%, 43%)	99% (98%, 100%)
17	17% (2%, 55%)	98% (97%, 99%)	11% (1%, 41%)	99% (98%, 99%)

Table 10.9 Verification of existing diagnosis of ASC in mainland China

No	Age	ADOS module	Previous diagnosis	Diagnosis	ADOS algorithm					ADI-R algorithm					IQ
					A	B	A+B	C	D	A	B1	B2	C	D	
1	6.4	3	Autism	Autism	7	14	21	1	4	21	18	--	10	2	97
2	6.5	1	Autism	Autism	8	12	20	4	3	28	15	--	--	3	N/A
3	6.2	3	Autism	Autism	7	14	21	1	0	11	9	--	3	5	98
4	3.8	2	Autism Tendency	Autism	7	12	19	0	1	13	12	--	6	5	N/A
5	4	2	Autism Tendency	Autism	8	6	14	0	1	20	19	--	6	4	N/A
6	5	1	Autism Tendency	Autism	8	13	21	4	1	27	--	14	6	4	N/A
7	6.7	2	Autism	Autism	6	13	19	1	2	15	16	--	3	2	N/A
8	8.8	2	Autism Tendency	Autism	8	14	22	2	5	20	11	--	7	5	N/A
9	6.7	1	Autism Tendency	Autism	7	12	19	4	6	19	11	--	8	5	N/A
10	9.11	2	Autism Tendency	Autism	9	13	22	2	1	21	12	--	5	5	N/A
11	3.9	2	Autism Tendency	Autism	7	12	19	0	1	18	16	--	6	3	N/A
12	4.8	1	Autism Tendency	Autism	5	10	15	4	2	16	13	--	3	5	N/A
13	6.5	1	Autism	Autism	5	11	16	4	4	23	18	--	10	4	N/A
14	6.8	1	Autism Tendency	Autism	4	11	15	1	2	22	--	11	2	3	N/A
15	4.5	1	Autism	Autism	5	12	17	4	3	27	--	10	3	5	N/A
16	5.4	1	Autism	Autism	4	7	11	1	4	29	20	--	9	5	N/A
17	5.1	1	Autism Tendency	Autism	4	7	12	1	0	22	15	--	4	5	N/A
18	9.7	1	Autism Tendency	Autism	5	12	17	4	5	28	--	12	8	5	N/A
19	8.1	3	Autism Tendency	ASC	3	6	9	1	1	11	8	--	5	3	86
20	5.1	1	Autism	Autism	6	9	15	2	1	26	16	--	5	5	94
21	4.6	1	Autism	Autism	7	13	20	4	1	24	8	--	5	4	N/A
22	6	2	Autism	Autism	4	13	17	0	0	26	20	--	4	4	N/A
23	9.9	2	Autism	Autism	5	12	17	0	5	22	20	--	8	1	54
24	5.7	1	Autism	Autism	5	12	17	4	0	21	--	13	5	5	N/A
25	6.4	3	Autism Tendency	Autism	6	11	16	2	2	21	14	--	6	4	N/A
26	4.8	1	Autism	Autism	3	10	13	3	3	24	--	9	9	5	N/A
27	4.6	1	Autism	Autism	8	11	19	4	5	21	15	--	6	3	N/A
28	6.3	2	Autism	Autism	8	13	21	1	1	26	22	--	10	5	N/A
29	6	2	Autism	Autism	7	8	15	0	0	25	18	--	9	5	97
30	6.6	3	Atypical Autism	ASC	2	4	6	0	0	8	8	--	6	2	104
31	8.2	3	Autism Tendency	Autism	5	14	19	1	1	29	20	--	8	5	98
32	8.1	2	Autism	Autism	7	14	21	1	4	25	21	--	10	5	93
33	5.9	2	Autism Tendency	Autism	7	13	20	2	3	22	20	--	3	3	>146
34	6	3	High-functioning Autism	Autism	4	10	14	0	1	12	15	--	1	0	128
35	6.9	2	Autism	Autism	4	12	16	2	2	10	9	--	2	4	99
36	5.1	2	Autism?	Autism	5	13	18	2	0	23	18	--	10	5	123
37	5.6	2	Autism?	Autism	4	10	14	1	5	19	16	--	5	5	83

No	Age	ADOS Module	Previous diagnosis	Diagnosis	ADOS algorithm					ADI-R algorithm					IQ
					A	B	A+B	C	D	A	B1	B2	C	D	
38	6.8	2	Autism Tendency	Autism	4	13	17	2	2	20	11	--	8	5	101
39	5.8	2	Autism?	Autism	4	10	14	0	1	22	15	--	4	4	110
40	5.2	1	Autism	Autism	8	13	21	3	5	25	17	--	12	5	124
41	6.5	1	Autism Tendency	Autism	10	14	24	4	6	23	19	--	6	5	108
42	5.2	3	Autism Tendency	Autism	3	9	12	0	0	5	8	--	3	3	124
43	5.9	2	Autism	Autism	3	10	13	2	1	17	10	--	10	3	110
44	10.7	3	Autism Tendency	ASC	2	6	8	0	1	20	12	--	11	3	105
45	5.3	2	Autism	Autism	5	12	17	1	0	27	18	--	8	1	116
46	5.9	2	Asperger	Autism	6	12	18	2	3	21	20	--	2	1	93
47	6	2	Autism Tendency	Autism	5	8	13	2	3	28	21	--	8	4	108
48	5.2	2	Autism?	Autism	8	17	25	2	5	25	17	--	8	5	N/A
49	6.2	2	Autism Tendency	Autism	3	9	12	1	0	26	15	--	5	4	124
50	5	1	Autism Tendency	Autism	8	12	20	4	4	24	16	--	4	5	N/A

ADOS algorithm: A: Communication; B: Reciprocal Social Interaction; C: Imagination/Creativity; D: Stereotyped Behaviours and Restricted Interests. ADI-R algorithm: A1: Qualitative Abnormalities in Reciprocal Social Interaction; B1: Qualitative Abnormalities in Communication-Verbal; B2: Qualitative Abnormalities in Communication-Nonverbal; C: Restricted, Repetitive, and Stereotyped Patterns of Behaviours; D: Abnormality of Developmental Evident at or before 36 months.

10.4 Discussion

10.4.1 Main findings

The cut-off of 15 on the M-CAST had good accuracy as a screening instrument for ASC in primary school aged children (sensitivity=84%; specificity=96%)[132]. The drawback of the M-CAST is the low PPV. The children who already had a diagnosis of autism in mainland China all met the research criteria of ASC using standardised diagnostic instruments.

10.4.2 Limitations

There are several limitations of this study. The sample was drawn from two primary schools according to availability. Beijing is not a nationally representative region of China. Therefore, the results from this study may not be representative of the population at a national level. The response rate of screening was high, but the sample size was still limited. Only 66% of children in the high score group (≥15) took part in the assessment phase which may partly have contributed to the low PPV[159, 398]. Previous research suggested that non-responders in epidemiological studies on mental health may have higher prevalence and more severe features of mental disorders[399, 400].

A recent study on the effect of non-responders towards the prevalence estimate of ASC indicated the effect of non-response could vary within a study from phase to phase. It found that non-responders were likely to experience a higher rate of problems relating to ASC than responders[248].

In the future, a large population-based sample is needed to replicate this validation. Only 5% of children in the low score group (≤11) were randomly selected for a further assessment. This could lead to verification bias of the screening results. Verification bias occurs when only data from participants who received a gold standard test are used to assess diagnostic accuracy[401, 402]. In this study, the sampling strategy for a further assessment was adopted from the UK study on the CAST for the following reasons: first, in the previous UK studies, no cases were found in the low score group[70, 121, 159]; second, in the M-CAST pilot study, non-cases scored less than or equal to 11; third, due to resource limitations, it was not possible to assess all children in the low score group; fourth, the analysis of those invited and those not invited for an assessment revealed similar sample characteristics. There was no difference between those invited and not invited in the sample. Thus, it is unlikely that verification bias was introduced by the sampling strategy.

Another limitation of the study is that the ADOS and the ADI-R had not previously been validated in the general population in mainland China. Despite this, the Taiwanese versions of the instruments were approved and provided by the publisher (WPS). However, differences between the English and Taiwanese versions may affect the assessment results. Feedbacks following this research regarding the administration and translation of these instruments were submitted to the publisher in order that they can be further updated.

Finally, all the ADOS and the ADI-R assessments were conducted by the candidate within a relatively short period of time. Due to the limitation of resources, interrater reliability was not conducted. However, the candidate was a reliable examiner with technical support from senior examiners in Cambridge during the assessment phase. Future research should ensure that consensus coding meetings to establish reliability will be conducted throughout the assessment phase.

10.4.3 Comparison between the M-CAST and the UK CAST

The study design was adapted from the UK validation study conducted in Cambridge in 2003[159]. The questions on the M-CAST were the same as the UK CAST. The test accuracy of the M-CAST was lower than that in the UK validation (sensitivity=100%, 95% CI: 74%, 100%; specificity=97%, 95% CI: 93%, 99%)[159]. The distribution of CAST scores in each score group were different between the Chinese and UK studies[159]. The proportion of children who scored ≥15 in the UK study (5.8%) was higher than the China study (4.9%), while the proportion of children who scored 12-14 in the China study (13%) was 2.7 times higher than the UK study (4.8%).

These differences in score distributions between the two countries might be due to the subtle differences in the designs of the two studies. First, the population frame of these two studies was different. The UK study was conducted in five schools in a larger geographical area including both urban and rural areas. The China study was conducted in two schools located in the same district in the urban area of Beijing. Differences in geographical characteristics of these two samples may lead to differences in score distributions. Second, response to the screen in the China study (97%) was much higher than that of the UK study (26%). There were more missing data in UK study (77% complete) than in the China study (97% complete). Third, the M-CAST was translated from the UK CAST. Some of the questions on the M-CAST provided examples after each item to assist parents in their understanding of what the items were asking for. These examples were generated from the Taiwanese version of the CAST as well as from feedback during the initial piloting phase. It is possible that understanding of certain items was different between the Chinese and UK parents. Fourth, there are different education policies for children with ASC between the UK and China. Most children with a diagnosis of ASC in mainland China do not attend mainstream primary schools[325]. In the China study, no child in the two primary schools was reported to have a previous diagnosis of ASC or any other psychiatric conditions. In the UK study, six children had a previous diagnosis of ASC and three children were identified as new cases in the assessment phase. Social stigma towards children with mental illness or disability has been reported in previous studies in China[372, 381]. It is possible that parents might not want their child to be found having difficulties of any kind during this research in order to avoid potential social stigma. If this was the case, it is possible that the M-CAST was rated by parents very

conservatively, leading to lower M-CAST scores. Fifth, the diagnostic assessments were conducted by one examiner in the China study, while there were three examiners in the UK study. Having only one examiner in the assessment phase is not ideal, but this was balanced by the fact that the identified cases were discussed with experienced Chinese psychiatrists to reach a consensus case status for each child.

The M-CAST showed good sensitivity and specificity but low PPV. Low PPV is inevitable since this study was conducted in a general population where the prevalence of ASC will be low[8] (Chapter 1.4.3.1). Low PPV will generate a large number of false positives screen results. This could lead to negative consequences in a population screening setting such as causing stress and anxiety to families whose child's screen result is positive but does not have ASC. However, in a research context, parents are reassured that a proportion of children across the score distribution are invited for a further assessment to assess social and communication development in general. They were told that being invited for an assessment is not an indication that the research team think there is a problem with their child.

10.5 Conclusion and future directions

This chapter has demonstrated that the M-CAST has acceptable validity and thus can be used as a candidate screening instrument for ASC in Chinese primary school aged children for epidemiological research. Due to possible differences between Chinese and UK parents in understanding of the items on the CAST, it would be useful to examine the psychometric properties of the M-CAST in comparison to the UK CAST. In order to obtain results that could be generalised to the Chinese population, it would be helpful to apply the M-CAST to a larger and more representative population in China. The findings also suggested the potential under-diagnosis of children with Asperger Syndrome and high-functioning autism in Chinese population in mainland China.

Chapter 11 Test-retest Study of the Mandarin CAST

11.1 Introduction

When examining the utility of a screening instrument for ASC, both validity and reliability should be taken into account. Reliability can be examined by conducting a test-retest study.

The test-retest reliability of screening instruments for ASC has been reported in previous studies. The descriptions of previous studies on the screening instruments introduced in Chapter 2 are shown in Table 11.1. The reliability studies of these instruments used different approaches for the analyses. Reliability of the CARS was firstly investigated by examining the interrater agreement across the cut-off using Cohen's kappa[403, 404]. Then it was examined by calculating the descriptive statistic intra-class correlation to assess the consistency of quantitative measurements made by observers[405]. Cohen's kappa was also used in a reliability study on the GADS[406]. The test-retest reliability of the ABC[407], the SCQ[408] and the SRS[188] was examined by calculating the intra-class correlation coefficient. The SCQ[409] and the SRS[410] were also analysed using a Pearson's correlation coefficient as well as the ASSQ[176]. One ASSQ[138] study also used a paired t-test to detect whether the disagreement was systematically random.

The test-retest reliability of the UK CAST was investigated in two studies[411, 412]. The first study was conducted in children aged 1-6 in five mainstream schools in Cambridgeshire. The reliability of the CAST (<15 versus ≥15) within 136 respondents was good (*Cohen's kappa*= 0.70)[411]. The correlation between the two test scores was 0.83 (*Spearman's rho*). The second study was conducted in a high-scoring sample[412], which was an assessment sample of a prevalence study in Cambridgeshire[70]. The second study reported a moderate agreement (<15 versus ≥15) (*Cohen's kappa*=0.41) within 73 respondents. The correlation between two test scores was 0.67 (*Spearman's rho*). In order to apply the M-CAST to a future population-based epidemiological study in China, this chapter adopted the methodology of the second test-retest reliability study of the UK CAST[412] to investigate reliability of the M-CAST in a high-scoring assessment sample in mainland China.

Table 11.1 Reported test-retest reliability of screening instruments for ASC in primary school aged children

Screening Instrument	Candidate	Year	Sample size and age	Sample source	Time interval	Method	Result
Childhood Autism Rating Scale (CARS)	Pereira[404]	2008	50 with autism: 3-17 years old	University hospital patients	Minimum 4 weeks	Kappa statistic	r=0.90
	Russell[358]	2010	103 with autism: 22-44.5 years old	Clinical patients	12 months	Intra class correlation coefficient	ICC=0.81
Autism Behaviour Checklist (ABC)	Goodman[407]	1995	17 blind children: 4-11 years old	Clinical patients	11 weeks	Intra class correlation coefficient	ICC=0.65 for teachers; ICC=0.21 for parents
Gilliam Asperger's Disorder Scale (GADS)	Gilliam[406]	2003	468	n/a	2 weeks	Kappa statistic	r=0.93
Autism Spectrum Screening Questionnaire (ASSQ)	Ehlers[176]	1993	139: 7-16 years old	Epidemiological study sample	8 months	Pearson's correlation coefficient	r=0.90
	Ehlers[138]	1999	65 (teacher version); 86 (parent version): 6-17	Clinical patients	2 weeks	Pearson's correlation coefficient	r=0.94 (teacher) r=0.96 (parent)
Social Communication Questionnaire (SCQ)	Gau[408]	2011	86 with ASC : 2-18 years old	Clinical patients	2 weeks	Intra class correlation coefficient	ICC= 0.77-0.78
	Bolte[409]	2000	17 with ASC	N/A	12-24 months	Pearson's correlation coefficient	r=0.74
Social Responsiveness Scale (SRS)	Pine[410]	2006	22 with ASC; 51 normal	Preschool children	1 month	Pearson's correlation coefficient	r=0.75
	Bolte[188]	2008	838 normal	Preschool children	3-6 months	Intra class correlation coefficient	ICC=0.84-0.97
Childhood Autism Spectrum Test (CAST)	Williams[411]	2006	136: 5-9 years old	Primary school students	2 weeks	Kappa statistic; Pearson's correlation coefficient	Kappa 0.70. r=0.83
	Allison[412]	2007	73: 5-9 years old	Primary school students	2 months	Kappa statistic; Pearson's correlation coefficient	Kappa 0.41; r=0.67

LFA: low functioning autism; HFA: high functioning autism; ADHD: attention deficit hyperactivity disorder. N/A: not available.

11.2 Method

11.2.1 Participants

The first M-CAST (CAST-1) was distributed to 737 parents of children aged 6-11 years in two mainstream schools. In total, 714 questionnaires of the CAST-1 were available for analyses. As per the sampling strategy in Chapter 10, a proportion of the responders were contacted two months after the distribution of CAST-1 and invited to further assessment. The second M-CAST (CAST-2) was distributed to participants who took part in the assessment. The time lag between the completions of the two tests was two to four months. In total, there were 103 respondents who completed both CASTs. In order to encourage participation, the CAST-2 was not required to be completed by the same parent/caregiver who completed the CAST-1. Only those children with the same informant who completed the two CASTs were included in the analyses.

11.2.2 Procedure

During the screening phase of the validation study reported in Chapter 10, parents were asked if they would like to be contacted for further research. After the screening, all children who scored ≥12 and a random 5% of children who scored ≤11 were invited to a further assessment. When the children and their parents came to assessment, the parents were asked to complete the CAST-2 which was identical to the CAST-1. The CAST-2 was completed before the other assessments using the ADOS, the ADI-R and the RPM.

11.2.3 Data analysis

All analyses were conducted using STATA 10.0. For each individual, the maximum score was calculated by recoding missing items to one (ASC-positive score). The minimum score was calculated by recoding missing items to zero (ASC-negative score). Initial analyses were undertaken using the minimum score. Agreement between scores from the CAST-1 and CAST-2 was assessed by treating the data in three ways:

1. in two score categories (<15 versus ≥15)
2. in three score categories (≤11, 12-14, ≥15)
3. as a whole scale

The main outcome for test-retest reliability was a measure of agreement, Cohen's kappa, which investigates the extent to which there is agreement other than that expected by chance expressed as a ratio to the maximum possible agreement[413]. Cohen's kappa=$(P_o-P_e)/(1-P_e)$, where P_o is the observed agreement and P_e is the expected agreement which is calculated by multiplying the row total by the column total divided by the grand total[413]. Standard interpretations of kappa are shown in Table 11.2.

Table 11.2 Standard interpretations of the Cohen's kappa[414, 415]

Value of kappa	Strength of agreement
<0.20	Poor
0.21-0.40	Fair
0.41-0.60	Moderate
0.61-0.80	Good
0.81-1.00	Very good

Overall agreement of classification was calculated into a binary categorisation (<15 versus ≥15) as: $P_o=(a+d)/N$ (letters refer to Table 11.5) and P_e =((a+b)/N*(a+c)/N+(c+d)/N*(b+d)/N)/N. Agreement was calculated for scoring positives on ASC (≥15): P_{s+} =2d/(2d+b+c), as well as both negative on ASC: P_{s-} =2a/(2a+b+c). This is the conditional probability, given that one of the scores was ≥15 or <15, while the other would be as well[412]. Exact binomial confidence intervals were calculated for these proportions. Marginal heterogeneity was assessed using an exact binomial test. The null hypothesis of the exact binomial test was that the marginal proportions were equal, which indicated that the children had the same marginal probability to move down a score group as well as up a score group over time. This is to test whether the proportion of b out of b+c or the proportion of c out of b+c equals to 0.5. Since a two-sided exact binomial test was applied, the probability was doubled.

The next analyses were conducted to evaluate the reliability of the M-CAST using three score groups (≤11, 12-14 and ≥15). Both the kappa coefficient and weighted kappa coefficient were calculated. The latter took into account that movement across two score groups as a result of the change in CAST-2 was more important than movement across one score group. Standard weights for agreement were applied using linear weights: 1 for no change of score group, 0.5 for change of one group, and 0 for change of two score groups[413].

Because the cut-off for the sampling of the M-CAST is still provisional, it was sensible to analyse the reliability of the M-CAST as a whole scale. The M-CAST score was treated as a continuous variable. Descriptive statistics were provided on the score distribution at the CAST-1 and the CAST-2. Since the distribution of scores did not follow a normal distribution, non-parametric statistical tests were used for analyses. The association between CAST-1 and CAST-2 scores was examined by calculating a Spearman's rank correlation coefficient. The difference between the scores on the CAST-1 and CAST-2 was examined by the Wilcoxon Signed Rank Test to verify the association between two scores. This approach was adopted because the correlation coefficients and their significance can only justify that the two measures are related but do not necessarily agree with each other. Therefore, there may be perfect correlation but no agreement [416]. Thus, the correlation coefficients provide limited information because two measures can be perfectly correlated but biased with respect to one another[417]. In this study, because the CAST-1 and the CAST-2 were used to measure the same quantity, they would be expected to be highly related. Thus, both Spearman's rank and Wilcoxon Signed Rank tests were adopted.

The differences between scores of the two tests were calculated with their mean and standard deviation. The limits of agreements are the mean difference between the test scores plus or minus 1.96 standard deviations.

Three sensitivity analyses were carried out to investigate the effect of missing data:

1. All missing data at CAST-1 and CAST-2 were recoded as one to give a maximum score.
2. A mid-point score for each individual was generated, which was the average of the maximum and minimum score (round up to the nearest whole number). The analyses were conducted using the mid-point score.
3. The analyses were repeated using minimum score of CAST-1 and maximum score of CAST-2. This approach was to investigate the most extreme effect of missing data on the observed difference in scores.

11.3 Results

11.3.1 Informants

There was no requirement that the two CASTs must be completed by the same informants. Information on the informants of the two tests is shown in Table 11.3. Seventy informants (68%) at the time of the CAST-1 were the same informants at the time of the CAST-2. Nine informants (8.7%) changed from the father at CAST-1 to the mother at CAST-2, while eight informants (7.8%) changed from the mother to the father.

Table 11.3 Changes of informants in test-retest reliability study

	CAST-2				
CAST-1	**Father**	**Mother**	**Others**	**Missing**	**Total**
Father	20	9	2	1	32
Mother	8	49	7	0	64
Others	0	2	1	0	3
Missing	2	2	0	0	4
Total	30	62	10	1	103

11.3.2 Characteristics of the study sample

The study sample was 70 children with the two CASTs completed by the same informant. Parents of 59 children (84.3%) completed both CASTs with no missing data, nine children (12.9%) had one item missing, and another two children had three or four items missing. The median age of the 70 children was 8.4 years old (IQR: 7.7, 9.3; range: 6.3, 11.2). The mean IQ was 114 (IQR: 106, 125; range: 84, 143). Forty-four children (64%) were born in Beijing while the others were born in other cities in mainland China. Fifty-three children (76%) were an only child while 13 children (19%) had one brother or sister. The distribution of age and sex is shown in Table 11.4.

Table 11.4 Age and sex distribution of the study sample

	Sex			
Age	**Boys**	**Girls**	**Total**	**%**
6	8	5	13	18.6
7	4	3	7	10.0
8	15	11	26	37.0
9	7	12	19	27.1
10	0	2	2	2.9
11	2	1	3	4.3
Total	36	34	70	100.0

11.3.3 Minimum score

11.3.3.1 Two score categories

Agreement between the minimum score on the CAST-1 and CAST-2 was examined first by categorising children into two score groups (<15 and ≥15) (Table 11.5). The kappa statistic for the binary categorisation showed that there was good agreement between the scores (*kappa*=0.64, *p*<0.001) when applying Landis's categorisation[415]. The overall agreement of categorising an individual in the high score group (≥15) at two tests was 88.6% (95% CI: 79%, 95%). The specific agreement P_{s+} in the ≥15 category was 71% (95%CI: 59%, 82%). The specific agreement P_{s-} in the <15 score group was 93% (95%CI: 84%, 98%). Marginal heterogeneity was indicated (X~Bin (8, 3)) two-sided, *p*=0.73. This suggested that the differences in marginal proportions were not significant, so children were not more likely to move down a score group as they were to move up a score group.

Table 11.5 Agreement between CAST-1 and CAST-2 (<15 versus ≥15)

		CAST-2		
		<15	≥15	Total
CAST-1	<15	52 (a)	3 (b)	55 (a+b)
	≥15	5 (c)	10 (d)	15 (c+d)
	Total	57 (a+c)	13 (b+d)	70 (N)

11.3.3.2 Three score categories

Examining all score groups separately, 44 children (63%) did not move score groups, while 22 children (31%) moved down a score group. Among these, four children (6%) moved from the ≥15 to the 12-14 score group and 18 (26%) children moved from 12-14 to the ≤11 score group. Three children (4%) moved up a score group and all of them moved from the ≤11 to 12-14 score group. One children (1%) moved two score groups, from ≥15 to ≤11 score group (Table 11.6).

The overall agreement in the categorisations among three score groups (≤11, 12-14, ≥15) was 62.9% (95%CI: 50%, 74%). The weighted kappa showed there was moderate test-retest reliability (*kappa*=0.53, *p*<0.001).

Table 11.6 Agreement between the CAST-1 and CAST-2 (≤11, 12-14, ≥15)

		CAST-2			
		≤11	12-14	≥15	Total
CAST-1	≤11	17	0	0	17
	12-14	18	17	3	38
	≥15	1	4	10	15
	Total	36	21	13	70

11.3.3.3 Whole score

The median score on the CAST-1 was 13 (IQR: 12, 14; range: 2-21). The median score on the CAST-2 was 11 (IQR: 8, 13; range: 2-24) (Figure 11.1&11.2). The Spearman's correlation coefficient between the two scores was 0.73 (p<0.001). The Wilcoxon Signed Rank Test treated the scores of the CAST-1 and CAST-2 in each individual as a test pair. The test hypothesis was that the difference between the CAST-1 and CAST-2 in each individual was equal to zero. The test statistic showed there was a significant difference between test pairs (p=0.0002). The median difference between two test scores was -0.5 (IQR: -4, 0; range: -7, 3). More children (50.0%) scored lower at the time of the CAST-2 than at the CAST-1 (Table 11.7).

Figure 11.1 Distribution of minimum scores on the CAST-1

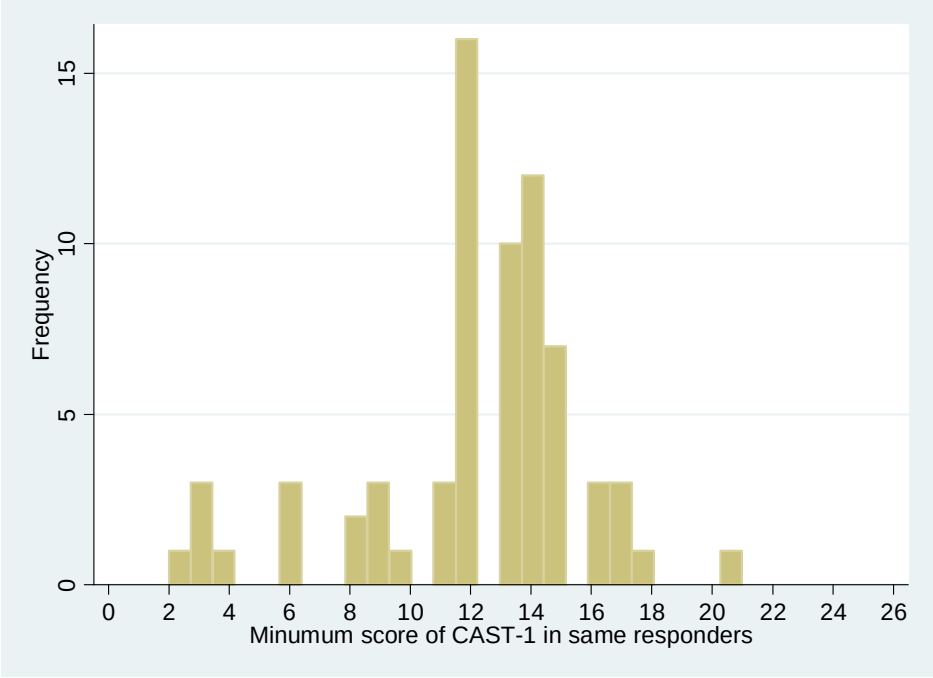


Figure 11.2 Distribution of minimum scores on the CAST-2

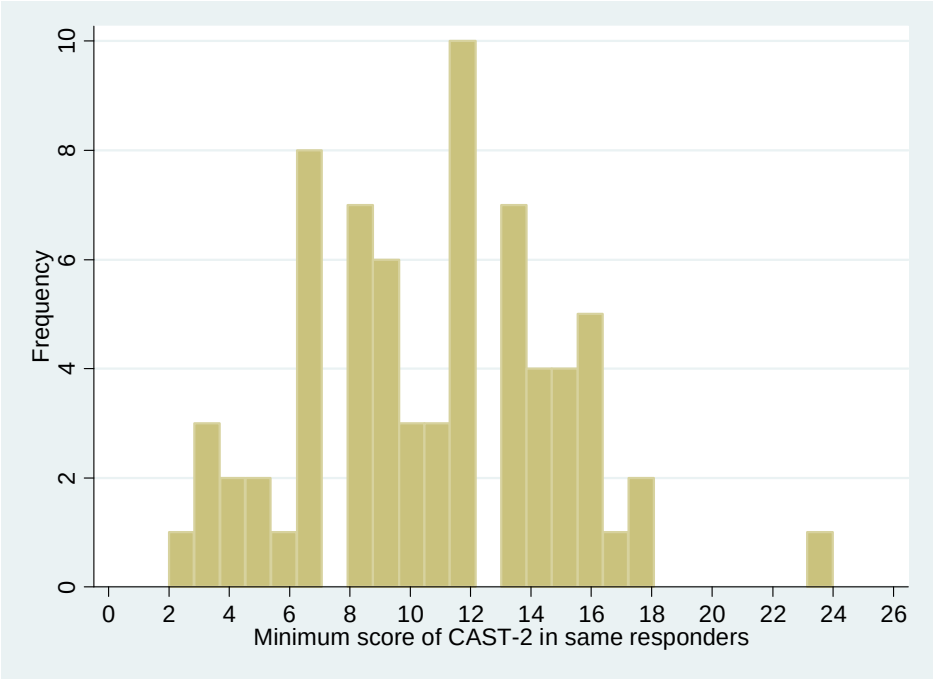


Table 11.7 Score difference: minimum CAST-2 minus minimum CAST-1

Score difference	Frequency	Percentage %	Cumulative %
-17	1	0.97	0.97
-12	1	0.97	1.94
-10	2	1.94	3.88
-9	3	2.91	6.80
-8	1	0.97	7.77
-7	3	2.91	10.68
-6	6	5.83	16.50
-5	12	11.65	28.16
-4	9	8.74	36.89
-3	6	5.83	42.72
-2	6	5.83	48.54
-1	12	11.65	60.19
0	23	22.33	82.52
1	10	9.71	92.23
2	2	1.94	94.17
3	5	4.85	99.03
8	1	0.97	100.00
Total	103	100.00	

11.3.4 Sensitivity analysis-maximum score

After treating all missing item as ASC-positive (score one), the agreement between the maximum score on the CAST-1 and CAST-2 in two score groups was the same as using the minimum score. The kappa statistic for agreement in two groups was 0.64 (p<0.001) and the overall agreement was 88.6% (95% CI: 79%, 95%). Children were

no more likely to move down a score group than to move up a score group. The overall agreement in the categorisations among three score groups (≤11, 12-14, ≥15) was 58.6% (95%CI: 46%, 70%). The weighted kappa showed the test-retest reliability was moderate (*kappa*=0.48, $p<0.001$). The median score on the CAST-1 was 13 (IQR: 12, 14; range: 2-21). The median score on the CAST-2 was 11 (IQR: 8, 14; range: 2-24). The Spearman's correlation coefficient between the two scores was 0.70. The Wilcoxon Signed Rank Test showed there was a significant difference between test pairs ($p=0.0001$). The median difference between scores was -1 (IQR: -4, 0; range: -8, 3).

11.3.5 Sensitivity analysis-midpoint score

When using the average score between the minimum and maximum scores of each child, the agreement in two score groups (<15 and ≥15) was the same as using the minimum score. The overall agreement in the categorisations among three score groups (≤11, 12-14, ≥15) was 61.4% (95%CI: 49%, 73%). The weighted kappa showed there was moderate test-retest reliability (*kappa*=0.52, $p<0.001$). The median score of midpoint CAST-1 was 13 (IQR: 12, 14; range: 2-21). The median score of midpoint CAST-2 was 11 (IQR: 8, 13.5; range: 2-24). The Spearman's correlation coefficient between the two scores was 0.72. The Wilcoxon Signed Rank Test showed there was a significant difference between test pairs ($p<0.001$). The median difference between scores was -0.5 (IQR: -4, 0; range: -7.5, 3).

11.3.6 Sensitivity analysis-minimum and maximum scores

When using the minimum score at CAST-1 and maximum score at CAST-2, the agreement between the CAST-1 and CAST-2 for two score groups (<15 and ≥15) was the same as using the minimum score. The overall agreement in the categorisations among three score groups (≤11, 12-14, ≥15) was 62.9% (95%CI: 50%, 74%). The weighted kappa showed the test-retest reliability was moderate (*kappa*=0.53, $p<0.001$). The median score of minimum CAST-1 was 13 (IQR: 12, 14; range: 2-21). The median score of maximum CAST-2 was 11 (IQR: 8, 14; range: 2-24). The Spearman's correlation coefficient between the two scores was 0.73 ($p<0.001$). The Wilcoxon Signed Rank Test showed there was a significant difference between test pairs ($p=0.0004$). The median difference between scores was -0.5 (IQR: -4, 0; range: -7, 3).

11.3.7 Score difference and informants

Among 103 responders, the changes in each scorable item on the M-CAST are shown in Table 11.8. Thirty-three informants (32%) on the CAST-2 were different from the informants of the CAST-1 for the same child. For the same children, the mean score of the CAST-1 rated by fathers was higher than the mean score of the CAST-2 rated by mothers (mean: 13.9, SD: 5.1). Similarly, the mean score of the CAST-1 rated by mothers (mean: 13.3, SD: 3.8) was higher than the mean of the CAST-2 rated by fathers (mean 8.9, SD: 3.0). The results are shown in Table 11.9.

Using the minimum score, the Spearman's test showed the correlation of the two CAST scores of the same child whose father completed CAST-1 and mother completed CAST-2 was 0.12 (p=0.76). The paired samples were independent. The Wilcoxon Signed Rank Test suggested there was a significant difference between the father's and the mother's response to the CAST items towards the same child (p=0.02). The Spearman's test showed the correlation of the two test scores of the same child whose mother filled in the CAST-1 and father filled in the CAST-2 was 0.35 (p=0.40). The paired samples were independent. The Wilcoxon Signed Rank Test showed there was a significant difference in the two CAST scores for the same child between mothers' (at CAST-1) and fathers' judgement (at CAST-2) (p=0.02).

Using either minimum or maximum score, the kappa statistic showed the agreement between fathers (at CAST-1) and mothers (at CAST-2) was fair *(kappa*=0.18, p=0.171). The kappa statistic showed the agreement between mothers (at CAST-1) and fathers (at CAST-2) was fair (*kappa*=0.38, p=0.084). However, the observed agreement could be due to chance since these results were not statistically significant.

Table 11.8 Frequency of change in scorable items on the M-CAST

No	Question	No of changes	(%)
1	Does s/he join in playing games with other children easily?	4	(5.7)
5	Is it important to him/her to fit in with the peer group?	7	(10.0)
16	Does s/he often bring you things s/he is interested in to show you?	7	(10.0)
10	Does s/he find it easy to interact with other children?	9	(12.9)
13	Does s/he mostly have the same interests as his/her peers?	12	(17.1)
17	Does s/he enjoy joking around?	12	(17.1)
2	Does s/he come up to you spontaneously for a chat?	13	(18.6)
11	Can s/he keep a two-way conversation going?	14	(20.0)
27	Does s/he make normal eye-contact?	14	(20.0)
21	Are people important to him/her?	15	(21.4)
6	Does s/he appear to notice unusual details that others miss?	16	(22.9)
24	Does s/he play imaginatively with other children, and engage in role-play?	16	(22.9)
19	Does s/he appear to have an unusual memory for details?	17	(24.3)
30	Does s/he sometimes say “you” or “s/he” when s/he means “I”?	17	(24.3)
14	Does s/he have an interest which takes up so much time that s/he does little else?	18	(25.7)
34	Does s/he try to impose routines on him/herself, or on others, in such a way that it causes problems?	19	(27.1)
36	Does s/he often turn conversations to his/her favourite subject rather than following what the other person wants to talk about?	20	(28.6)
28	Does s/he have any unusual and repetitive movements?	22	(31.4)
35	Does s/he care how s/he is perceived by the rest of the group?	22	(31.4)
20	Is his/her voice unusual (e.g., overly adult, flat, or very monotonous)?	23	(32.9)
37	Does s/he have odd or unusual phrases?	23	(32.9)
8	When s/he was 3 years old, did s/he spend a lot of time pretending (e.g., play acting being a superhero, or holding teddy’s tea parties)?	25	(35.7)
25	Does s/he often do or say things that are tactless or socially inappropriate?	25	(35.7)
15	Does s/he have friends, rather than just acquaintances?	26	(37.1)
31	Does s/he prefer imaginative activities such as play-acting or story-telling, rather than numbers or lists of facts?	27	(38.6)
7	Does s/he tend to take things literally?	28	(40.0)
29	Is his/her social behaviour very one-sided and always on his/her own terms?	28	(40.0)
9	Does s/he like to do things over and over again, in the same way all the time?	29	(41.4)
18	Does s/he have difficulty understanding the rules for polite behaviour?	29	(41.4)
32	Does s/he sometimes lose the listener because of not explaining what s/he is talking about?	31	(44.3)
23	Is s/he good at turn-taking in conversation?	33	(47.1)

Table 11.9 Score difference and different informants

Informants of same child	Statistic tests	Score			
		Minimum	Maximum	Mid-point	Extreme*
CAST-1 father CAST-2 mother	Spearman's rho	0.12	0.09	0.12	0.14
	Wilcoxon Signed Rank Test: p-value	0.02	0.03	0.02	0.03
CAST-1 mother CAST-2 father	Spearman's rho	0.35	0.68	0.51	0.68
	Wilcoxon Signed Rank Test: p-value	0.02	0.02	0.02	0.02

*extreme: using the minimum of CAST-1 and the maximum of CAST-2

11.4 Discussion

11.4.1 Main findings

This study is the first to investigate the reliability of the M-CAST as a screening instrument for ASC in Chinese population. Within an average of three months between the two tests, the test-retest reliability of the M-CAST among two score groups (<15 versus ≥15) was good (*kappa*=0.64, $p<0.001$) among the questionnaires completed by the same informants. The test-retest reliability across three categories by the same informants was moderate (*weighted kappa*=0.53, $p<0.001$). In addition, when the M-CAST was treated as a whole scale, this study found a good correlation between the scores of the CAST-1 and CAST-2 (*Spearman rho*=0.73). The Wilcoxon tests found that there was a possible difference in score distributions of the CAST-1 and the CAST-2.

11.4.2 Limitations

One limitation of this study was that the same informant for two CASTs cannot be ensured in this study. As a result, only 68% of the informants were the same for the two CASTs (n=70). Thus, the sample was relatively small. However, the sample was drawn from two mainstream primary schools with the response rate at 97% in the screening phase and 65% in the further assessment. The high participation rate should have ensured the representativeness of the study sample for the population in those two schools. However, the results cannot represent the general population in China as Beijing may not be considered as a national representative population for China due to its special political and economic status[378]. Second, it was possible that there has

been response bias. Because the parents who agreed to participate in further assessment may be those who were more concerned about their children's social and communication ability than the non-responders in the two schools. Third, the time gap between the CASTs was between two to four months but was not precisely known for each child, however, being such a short enough period of time one would not expect major changes due to child development or other external factors. Fourth, two administrations of the CAST were conducted in different settings in this study. The CAST-1 was completed at home while the CAST-2 was completed during an assessment setting in a hospital. When the parents were invited to a formal assessment, they may have re-evaluated the severity of their child's behaviours and gave different scores to some items on the CAST. The change of settings may contribute to the change of score on CAST. However, this could not be measured since the candidate was conducting assessments when the parent was filling in the CAST-2. Fifth, there were missing data in both CASTs. They were handled by different approaches in order to explore the impact of the missing values. Similar results were found which indicated it was unlikely that the missing data had affected the overall test-retest reliability.

11.4.3 Comparison between the M-CAST and other instruments

The test-retest reliability of the M-CAST reported in this study was lower than the first UK study conducted in the general population. However, by using similar research methodology, this study found the test-retest reliability of the M-CAST was higher than the UK CAST in the high scoring sample[412]. The differences in those two study samples should be acknowledged. Although both studies were conducted in a high scoring sample, the UK sample did not recruit children who scored ≤11 while this study recruited children from all three score groups.

The reported test-retest reliability of some screening instruments for ASC was higher than the M-CAST (Table 7.1). For the instruments used in children of primary school age, the ASSQ had good reliability (r=0.96)[138], as did the SCQ (r=0.74)[409]and SRS (r=0.75)[410]. However, the previous studies of other instruments adopted different sampling strategy from this study. This study was conducted in a high scoring sample within which 78.6% of the children scored above or around 15 (12-14). The difference

in research methodology as well as the analytical methods between this study and previous studies made it difficult to compare their results directly[412].

11.4.4 Possible cultural influence

Despite the differences in study samples, this study found similar results with the UK study conducted in high scoring group. Both studies found that children were no more likely to move down a score group than move up in the CAST-2 compared with the CAST-1. This may partly due to a statistical phenomenon, regression to the mean, which occurs when repeated measurements are tested on the same subject[418]. Generally, due to the random error of observed values, when observing repeated measurements in the same subject, relatively high or low observations are likely to be followed by less extreme ones rather nearer the subject's true mean[418]. Thus, the score in CAST-2 was less than CAST-2 in some children. However, it was also possible that the child's behaviours rated as ASC-positive by the parents at CAST-1, were not noticed or found out to be not obvious later on when they completed the CAST-2. It was also possible some parents may have learnt about the purpose of the assessment from other parents whose children had completed the assessment. It has been suggested that children with mental disorders in mainland China may experience stigma from the society[372, 373]. Thus, it is possible that parents tried to score lower on the CAST-2 to show that their children have no problems. Adapting screening instruments developed in one culture for another culture is not without difficulties. This is because the recognition of autistic features in the original culture may have a specific set of behavioural norms and expectations, which are not necessarily the same as the culture in the adapted country[419]. In addition, the possible difference in the perception of children's behaviours between fathers and mothers might influence the reliability of the M-CAST. The difference may be due to the potential different roles of father and mother in a family. Since in China, mother is generally the carer of the family while father focuses on provide financial support. Thus, it is possible that the time and occasions that father spends with the child is different from mother and expectations of the child's social behaviours are different between two parents.

11.5 Conclusion and future directions

The test-retest reliability of the M-CAST was found to be moderate to good in a Chinese population. This result demonstrated some evidence for the M-CAST to be recommended as a candidate screening instrument for ASC in epidemiological studies in mainland China. Cultural aspects may be important in the adoption of screening instrument for the Chinese population.

Chapter 12 Comparison of Performances between the Mandarin CAST and the Clancy Autism Behaviour Scale

12.1 Introduction

Chapter 4 showed that previous studies in mainland China adopted varied research methodologies for case definition. The most frequently used screening instrument is the CABS[271], which was first developed in the West in 1969[172]. However, there has been almost no research on the CABS in western population after the 1970s. No data are available on the utility of the CABS in the West. Thus, it is difficult to compare the prevalence estimates from previous studies in mainland China with more recent estimates in other countries. The M-CAST demonstrated acceptable validity as a screening instrument for ASC in the Chinese population (Chapter 10), as well as good test-retest reliability in same responders (*kappa*=0.64) (Chapter 11). This chapter aims to compare the utility of the M-CAST with the CABS as ASC screening instruments for ASC in a Chinese population.

12.2 Method

12.2.1 Participants

The participants of this study were drawn from two samples in the validation study of the M-CAST described in Chapter 10. The first sample comprised children who already had an ASC diagnosis in clinical settings in mainland China (n=50). The second was the assessment sample of the validation study (n=103). Thus, a total number of 153 children completed a diagnostic assessment using the ADOS, the ADI-R and the RPM. At the beginning of the assessment, the parents of children with an existing diagnosis were asked to fill in both a M-CAST and a CABS, while the parents of children from primary school was only asked to fill in a CABS for this study. Three children were excluded from the analyses because only the children who completed both the M-CAST in screening phase and the CABS in assessment phase were included for this study. Thus, the data of 150 children were available for analyses.

12.2.2 Statistical analysis

Missing items on the M-CAST and the CABS were given a value of 0 (ASC-negative value) to generate the observed score for further analysis. The score distribution of the M-CAST and the CABS was described by mean, median and the IQR. The performance of the M-CAST and the CABS were examined by the following analytical strategy: 1) Agreement between the screening instrument and standardised diagnostic assessment was examined using the Cohen's kappa[413]; 2) Validity was examined by calculating the sensitivity, specificity, PPV and NPV[8]; 3) Differences in score distribution of two instruments between children with ASC and typically developing children: the independent samples t-test was used if the distribution was robust normal, while the Mann-Whitney U test was used if the distribution was highly skewed. The normality of the distribution was examined by the Skewness-Kurtosis test. The null hypothesis of the Skewness-Kurtosis test is that the distribution is normal. Thus, a non significant test result suggests the distribution is normal ($p>0.05$); 4) Correlation of scores on the two screening instruments and the scores on the ADOS and the ADI-R algorithms: Spearman's rank correlation coefficient. The score of the ADOS and the ADI-R was the sum of all categories in the algorithm of each instrument; 5) Discriminant power in differentiating children with ASC from typically developing children: the receiver operating characteristic (ROC) area-under-curve (AUC) analysis was used[154, 420]. The analyses were conducted in STATA 10.0.

12.3 Results

12.3.1 Participants' characteristics

In total, 150 children took part in this study, of which 46 children with an existing clinical diagnosis of ASC and another 6 children received a research diagnosis of ASC after the diagnostic assessment. The mean age of this sample was 7.7 years old (SD=1.6). The mean age of the autistic cases was 8.4 years old (SD=1.2) while the mean age of the typically developing children was 6.5 years old (SD=1.6). There were 98 (66%) boys and 52 (34%) girls in this sample with a sex ratio of 1.9:1 (male: female). Among 52 children with ASC, the sex ratio was 6.3:1 (male: female).

12.3.2 Overall distribution of the M-CAST and the CABS

125 questionnaires of the M-CAST (83.3%) were fully completed while the remaining (n=25) had missing items. Using the cut-off of 15, 66 children (44%) scored equal to or greater than 15 on the M-CAST. The mean score on the M-CAST was 14.7 (SD=5.7) and the median was 14 (IQR: 12, 18; range: 2-19). All 150 questionnaires of the CABS (response rate: 100%) were fully completed. Using the cut-off of 14, 46 children (31%) scored equal to or greater than 14 on the CABS. The mean score on the CABS was 10.7 (SD=5.4) and the median score was 10 (IQR: 7, 15; range: 0-25).

12.3.3 Test accuracy

Using the cut-off of 15, the overall agreement between the M-CAST and the consensus diagnosis was 83% (95%CI: 76, 88). The kappa statistic suggested the agreement was good (*kappa*=0.64, $p<0.001$). The sensitivity of the M-CAST was 89% (95%CI: 77, 96). The specificity was 80% (95%CI: 70, 87). The association between the M-CAST and the consensus diagnosis is shown in Table 12.1.

Table 12.1 Agreement between the M-CAST (<15, ≥15) and consensus diagnosis

		Consensus diagnosis		
		ASC	**Non-ASC**	**Total**
CAST	≥15	46	20	66
	<15	6	78	84
	Total	52	98	150

The overall agreement between the CABS and the consensus diagnosis was 75% (95%CI: 67, 81). The kappa statistic suggested the agreement was moderate (*kappa*=0.43, $p<0.001$). The sensitivity of the CABS was 58% (95%CI: 43, 71). The specificity was 84% (95%CI: 75, 90). The PPV was 65% (95%CI: 50, 79). The NPV was 79% (95%CI: 70, 86). The association between the CABS and the consensus diagnosis is shown in Table 12.2. The test accuracy of two screening instruments overall and in three different subgroups including normal IQ group (IQ≥70), boys and girls is shown in Table 12.4.

Table 12.2 Agreement between the CABS (<14, ≥14) and consensus diagnosis

		Consensus diagnosis		
		ASC	**Non-ASC**	**Total**
CABS	≥14	30	22	52
	<14	16	82	98
	Total	46	104	150

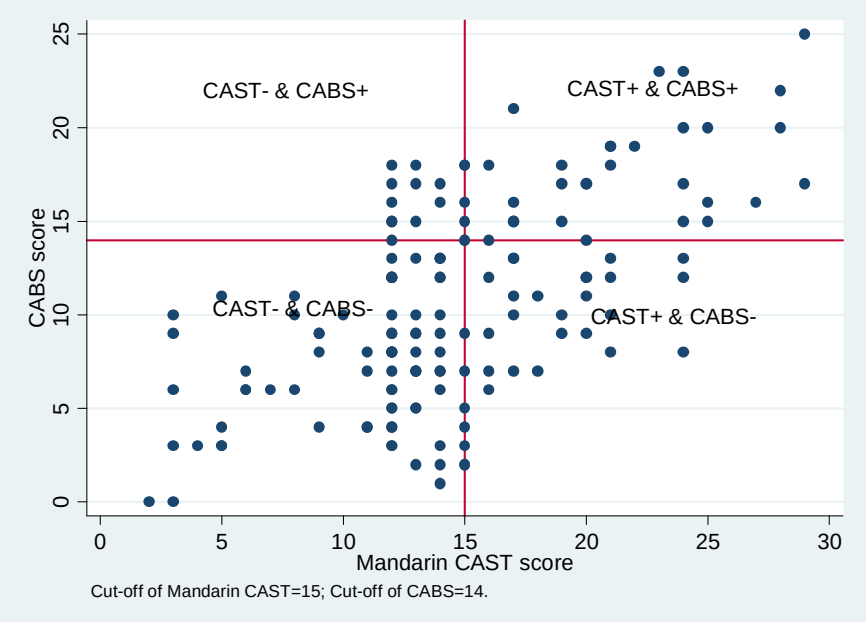
12.3.4 Score distributions and ASC status

Figure 12.1 shows the scores on the M-CAST and the CABS of the same individuals. The mean scores on the M-CAST and the CABS within children with ASC and typically developing children are shown in Tables 12.3. The Skewness-Kurtosis test showed the score distribution of the M-CAST was normal (p=0.42), and the score distribution of the CABS was also normal (p=0.06). Thus, the independent t-test was performed to compare mean scores on the two instruments between children with ASC and typically developing children. The mean scores on both the M-CAST and the CABS in children with ASC were significantly higher than those of typically developing children (p<0.001). The correlation between scores on the M-CAST and the CABS was moderately correlated (*Spearman's rho*=0.57, p<0.001). In the clinical sample, the correlation between the scores on the two instruments was moderately correlated (*Spearman's rho*=0.52, p<0.001). However, in the population sample, the correlation was weak (*Spearman's rho*=0.28, p=0.0036). The score distributions of the M-CAST and the CABS in children with ASC and typically developing children are shown in Figure 12.2 & 12.3.

Table 12.3 Scores on the two screening instruments by ASC status

	ASC (n=52) Mean (SD)	Non-ASC (n=98) Mean (SD)
CAST	11.9 (15.8)	19.9 (4.7)
CABS	14.3 (5.1)	8.7 (20.7)

Figure 12.1 The M-CAST and CABS scores in the same child*



*Each Point may represent more than one child.

Figure 12.2 Score distribution of the M-CAST in children with and without ASC

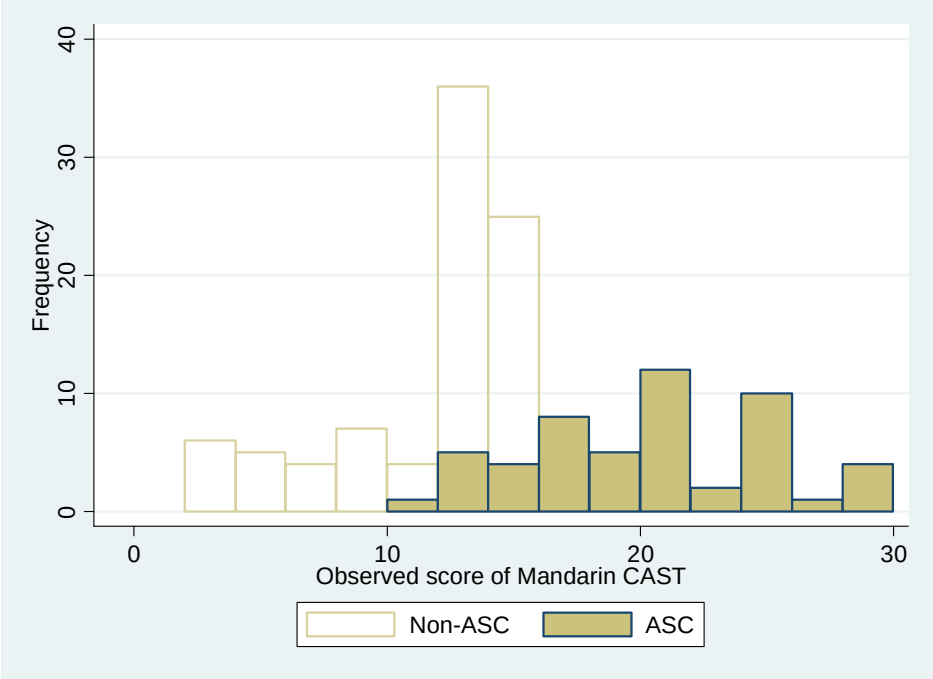
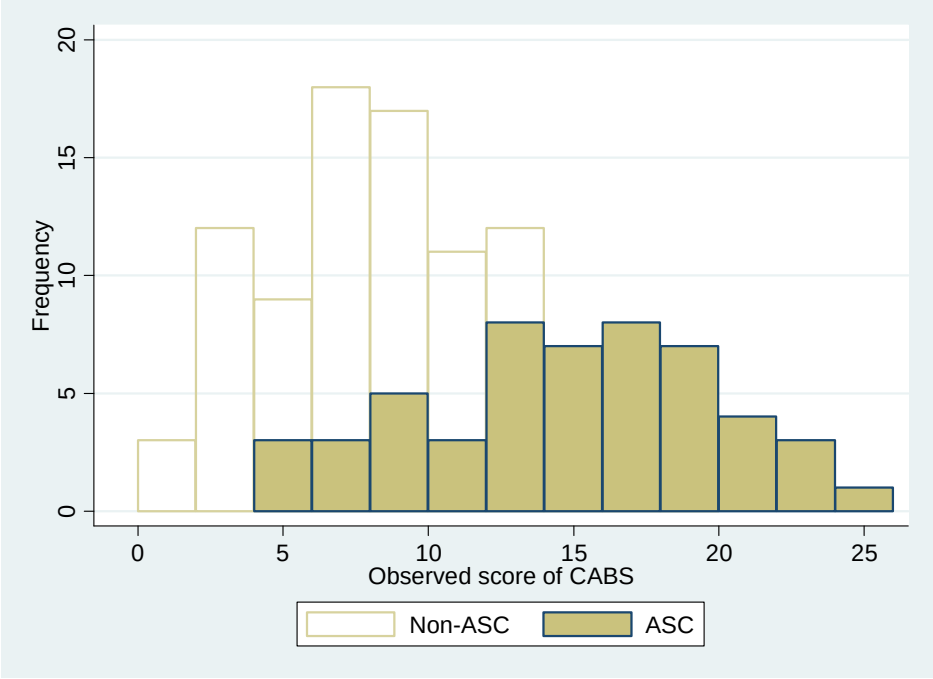


Figure 12.3 Score distribution of the CABS in children with and without ASC



12.3.5 Correlations with scores on the ADOS and the ADI-R algorithms

During ADOS assessments, 18 participants were administered using module 1 (12%), 21 participants were administered using module 2 (14%) and 111 participants were administered using module 3 (74%). The mean score on the ADOS was 7.54 (SD=10.0). The median score on the ADOS of children with ASC was 20 (IQR: 15, 25; range: 3-34), while the median of typically developing children was 0 (IQR: 0, 1; range: 0-13). The median score on the ADI-R of children with ASC was 54.5 (IQR: 42.5, 65; range: 5-77), while the median of typically developing children was 3 (IQR: 1, 7; range: 0-59). The Skewness-Kurtosis test showed that the distribution of scores on both the ADOS and the ADI-R were highly skewed. Thus, the Mann-Whitney U Test was used which showed that the median score on the ADOS algorithm of children with ASC were significantly higher than that of typically developing children (p=0.0061). The Mann-Whitney U Test showed the median score on the ADI-R algorithm of children with ASC was significantly higher than that of typically developing children (p=0.0084). The correlation between scores on the M-CAST and scores on the ADOS and the ADI-R algorithms was examined. The score on the M-CAST was significantly correlated with both scores on the ADOS (*Spearman's rho*=0.64) and the ADI-R (*Spearman's rho*=0.59). The score on the CABS was also significantly correlated with the scores on the ADOS (*Spearman's rho*= 0.44) and the ADI-R (*Spearman's rho*=0.49).

12.3.6 Comparison between the M-CAST and the CABS

The performance of the M-CAST and CABS was compared using the receiver-operating-characteristic (ROC) area-under-curve (AUC) analysis. The M-CAST had a significantly higher AUC (0.90) than the CABS (0.79) (p=0.0002) (Figure 12.4 & Table 12.4). The performance of the two instruments was also further compared in three subsamples of children with normal IQ (IQ≥70), and in boys and girls separately. The M-CAST had a significantly higher AUC (0.88) than the CABS (0.79) (p=0.008) in children with normal IQ. Within boys, the M-CAST had a significantly higher AUC (0.92) than the CABS (0.80) (p=0.0025). Similarly within girls, the M-CAST had a significantly higher AUC (0.92) than the CABS (0.67) (p=0.0106). Those results suggested the M-CAST performed significantly better than the CABS in distinguishing children with ASC from typically developing children.

Figure 12.4 Receiver operating characteristics (ROC) curves for the M-CAST and CABS

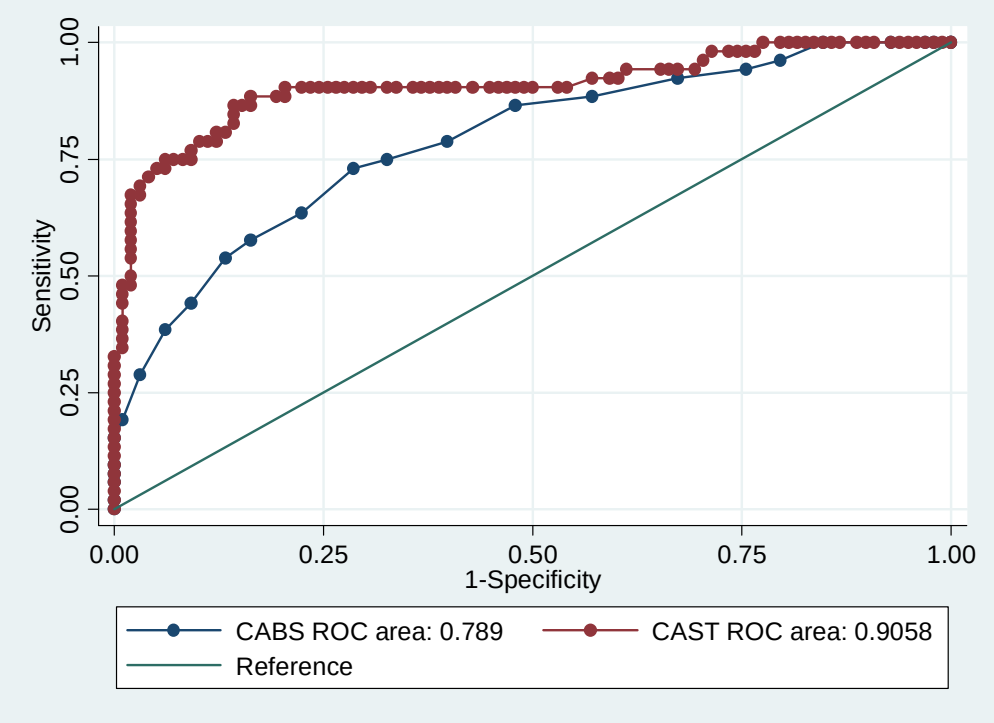


Table 12.4 Performances of the M-CAST and the CABS

	CAST cut-off ≥ 15	CABS cut-off ≥ 14
Whole sample (n=150)		
AUC (95%CI)	0.90 (0.84-0.96)	0.79 (0.71-0.87)
Sensitivity (95%CI)	0.89 (0.77-0.96)	0.58 (0.43-0.71)
Specificity (95%CI)	0.80 (0.70-0.87)	0.84 (0.75-0.90)
PPV (95%CI)	0.70 (0.57-0.80)	0.65 (0.50-0.79)
NPV (95%CI)	0.93 (0.85-0.97)	0.79 (0.70-0.86)
Normal IQ (n=127)		
AUC (95%CI)	0.88 (0.80-0.96)	0.79 (0.69-0.88)
Sensitivity (95%CI)	0.88 (0.71-0.97)	0.56 (0.38-0.74)
Specificity (95%CI)	0.79 (0.70-0.87)	0.84 (0.75-0.90)
PPV (95%CI)	0.58 (0.43-0.72)	0.53 (0.35-0.70)
NPV (95%CI)	0.95 (0.87-0.99)	0.85 (0.77-0.92)
Boys (n=99)		
AUC (95%CI)	0.92 (0.85-0.98)	0.79 (0.71-0.89)
Sensitivity (95%CI)	0.89 (0.76-0.96)	0.60 (0.44-0.74)
Specificity (95%CI)	0.80 (0.67-0.89)	0.83 (0.71-0.92)
PPV (95%CI)	0.78 (0.65-0.89)	0.75 (0.58-0.88)
NPV (95%CI)	0.90 (0.77-0.97)	0.71 (0.59-0.82)
Girls (n=51)		
AUC (95%CI)	0.92 (0.82-1.00)	0.67 (0.42-0.91)
Sensitivity (95%CI)	0.86 (0.42-1.00)	0.43 (0.10-0.82)
Specificity (95%CI)	0.80 (0.65-0.90)	0.84 (0.70-0.93)
PPV (95%CI)	0.40 (0.16-0.68)	0.30 (0.07-0.65)
NPV (95%CI)	0.97 (0.86-1.00)	0.90 (0.77-0.97)

12.4 Discussion

12.4.1 Main findings on test utility

This chapter examined and compared the utility of the M-CAST and the CABS as screening instruments for ASC in primary school aged children in mainland China. Both the M-CAST and CABS can distinguish children with ASC from typically developing children. The performance of the M-CAST as a screening instrument for ASC was found to be better than the CABS illustrated by calculating test validity and conducting the ROC-AUC analysis. The score of the M-CAST was more correlated with the scores on both the ADOS and the ADI-R algorithms. Overall, the M-CAST demonstrated better utility of distinguishing children with ASC from typically developing children than the CABS.

12.4.2 Limitations

Limitations of this study included: 1) The children with an existing diagnosis of ASC were younger than those from primary schools; however, the children were within the applicable age range of the CAST (4-11 years old). In mainland China, the applicable age range for the CABS covers all ages[302]. The difference in age is unlikely to influence the performance of two instruments since they were applied to the same sample; 2) The sample size was limited, especially the subsample of girls, which led to relatively wide confidence intervals of the test accuracy. 3) The examiner of the ADOS and the ADI-R was aware of the ASC status of children with an existing diagnosis before their completion of the M-CAST and the CABS. However, the examiner was blind to the M-CAST scores of the children from primary schools until the completion of the assessment. Thus, this difference in administration was unlikely to influence the performances of the two instruments; 4) This sample was drawn from two groups including a clinical sample and a school population sample. It might not be representative for the general population. Since 30% of the sample were children with an existing diagnosis of ASC whose parents may have more knowledge on autism, and thus they might be clearer about what the items on the questionnaire were looking for than parents in the general population in China. Thus, when applying those figures to a population level, some caution should be applied. In future study, larger clinical or population sample should be explored to test the utility of the two instruments.

12.4.3 Validity of the M-CAST and CABS

When applied to the whole sample, the sensitivity of the M-CAST was higher than that of the CABS. The sensitivity of the M-CAST was the similar in boys and girls, while the CABS had a higher sensitivity in boys than in girls. The lower sensitivity of the CABS suggested that using the CABS as the screening instrument for ASC would potentially have more false negatives and miss more children who actually have ASC than using the M-CAST. This could potentially delay referrals to further diagnosis and appropriate intervention of those individuals[146]. The specificity of the M-CAST and the CABS were both good with the latter showing slight better results than the former. The PPV of the M-CAST was higher than the CABS. However, both of them were quite low. This result might be partly due to the fact that the value of PPV depends on the prevalence of the condition. The prevalence estimates of ASC in girls were generally reported as much lower than that of boys[421, 422] which led to the much lower PPV of both instruments within girls.

12.4.4 Possible explanations for the better performance of the M-CAST

There several possible reasons for the better performance of the M-CAST than the CABS: 1) The CABS was developed in 1969 for identifying children with infantile autism which definition was much narrower than that of ASC[172]. It was introduced to China during the 1980s as a screening instrument for Childhood Autism[76]. The M-CAST was developed in 2002 as a screening instrument for identifying children on the whole autism spectrum in the general population. Thus, it was possible that the children with less obvious autistic features which could be picked up by the M-CAST would be missed by the CABS. 2) The test accuracy and validity of the CABS was examined mainly in clinical samples but not in the general population[282, 301], while the UK CAST has been piloted and validated twice in the general population[159], and it has been used in recent large population epidemiological research[70]. 3) The usage of the CABS is also non age-specific in China. Although it was designed for infantile autism, it has been used for all age groups in the Chinese population in previous studies[72, 271]. Thus, it is possible that the items on the CABS have not covered the subtle autistic features of individuals on the border autism spectrum. The M-CAST was designed to be used in primary school aged children from the very beginning.

12.5 Conclusion

The adoption of recent-developed screening and standardised diagnostic instruments for case identification in autism research in mainland China led to the results more comparable with the results in Western countries. The M-CAST showed acceptable performance in the identification of children with ASC in this sample drawn from both clinical settings and the general population. It performed better in distinguishing children with ASC from typically developing children than the CABS, a currently-used screening instrument for ASC in mainland China. The scores on the M-CAST were better correlated with scores on the standardised diagnostic instruments, the ADOS and the ADI-R than the CABS. This study provided some evidence to recommend the M-CAST as a candidate screening instrument for ASC in primary school aged children in mainland China.

Chapter 13 Psychometric Properties of the Mandarin CAST

13.1 Introduction

Due to the lack of biomarker, the diagnosis of ASC still depends on behaviour descriptions[423]. ASC were previously conceptualised as a discrete category, qualitatively different from other subgroups within the PDD[424]. However, there has been an emerging consensus that ASC are dimensional disorders representing the upper extreme of one or more quantitative traits, which traits are likely to be continuously distributed in the population samples[425-427]. Early evidence for this proposed dimensional concept was collected from studies on the association between genetic liability for ASC and the milder, non-psychopathological features within the relatives of individuals with ASC[120]. Further population studies provided evidence that autistic traits are continuously distributed in large general population[178, 426]. Debates have emerged as to whether there is one single dimension that could capture the three impairment domains of the condition or whether there would be more[428]. Factor analysis has been used to explore the possible dimensions of ASC with the data collected using screening and diagnostic assessment instruments in different samples[429, 430].

Constantino and colleagues[431] suggested a single autism dimension to explain all the behaviours in the autistic trait. It was based on findings from the factor analysis of the psychometric structure of the ADI-R and the SRS in both clinical and population samples[426, 431]. Other researchers using factor analysis suggested that the impairments of ASC might be multidimensional[432], which meant the conditions may have more than one continuous latent trait. Three studies using the data from the ADI-R proposed three-factor solution for the structure of ASC. Although the structure of these proposed factors were different among studies, these factors roughly covered the three core domains of impairment of ASC[432-434]. Another two studies based on the ADI-R suggested a two-factor solution was sufficient to explain the autism continuum including Social/Communication and Restricted/Stereotyped Behaviours[435, 436]. One study proposed a four-factor solution on data from the ADI-R and a five-factor solution on data from the ADOS[437]. Reviews on the exploration of ASC dimensions have suggested the possible reasons for the lack of consistency regarding the number

and structure of factors identified by previous studies[425, 428]. This inconsistency could be partly explained by the heterogeneous research designs. The results could be influenced by the sample characteristics, the nature of the assessment instruments, and also by the subjective interpretations when naming the identified factors in factor analysis[428]. Most the exploration of autistic traits was conducted in clinical samples with individuals of ASC. It should be borne in mind that, the underlying autistic traits identified from such studies might be different from studies conducted in general population within which there is a large proportion of individuals without ASC. A recent study examined the factional nature of ASD in a general population of 13,138 in the UK indentified 7 factors including verbal ability, language acquisition, social understanding, semantic-pragmatic skills, repetitive-stereotyped behaviour, articulation and social inhibition[438]. Although there has been no agreement on the number or structure of latent factors for ASC, the exploration of the dimensional approach can help with the evaluation of screening and diagnostic instruments for ASC. This process could indicate which possible dimensions of ASC have been reflected by the items on the instrument. Such research has been conducted using several instruments for ASC: the ASSQ[408, 439], the SRS[431], the AQ[440-442], the Sub-threshold Autism Trait Questionnaire (SATQ)[443], the Child Behaviour Checklist (CBCL)[444], the Adult Asperger Assessment (AAA)[445], the GARS[147] and the CARS[424]. A summary of those previous studies on factor analysis[446] is shown in Table 13.1. Most investigation of the psychometric properties of screening instruments for ASC was conducted in Western population. Little research has been done in the Chinese population. One exception is the SCQ. The SCQ was translated into Traditional Chinese and applied to 317 parents of children recruited from clinical settings in Taiwan[408]. A three-factor solution was proposed based on the data from the Chinese SCQ including Social Interaction, Repetitive Behaviours and Communication. Previous chapters demonstrated that the M-CAST can be considered as a candidate screening instrument for ASC in mainland China. This chapter is to explore the factor structure of the M-CAST in Chinese population.

Traditional factor analytical methods uses the continuous observed data to explore the underlying continuous latent variable[446]. Factor analysis provides a linear factor combination or principle components for observed scores on the tests based on continuous data[13, 447]. However, these methods are not appropriate to tests with binary

item response (yes/no), such as the M-CAST, due to the fact that the factor analysis assumption of item responses is on a continuous metric[448, 449]. If categorical data are treated as continuous data in factor analysis, the true factor structure might be distorted in a multi-dimensional analysis and the factor loading might be biased in uni-dimensional models[448, 450]. When applying linear models to binary data, the predictions generated may not be within the plausible range (<0 or >1)[448, 451]. Figure 13.1 shows the unfitness of a linear predictor model when it is applied to categorical data[452]. The red dots were the true association between the observed categorical variables and the continuous latent variable. When the categorical data were treated as continuous, a linear model was generated to illustrate the association which was the black line. The red dots cannot be well captured by the black line provided by the linear model, so the association suggested by the model was not appropriate for such data.

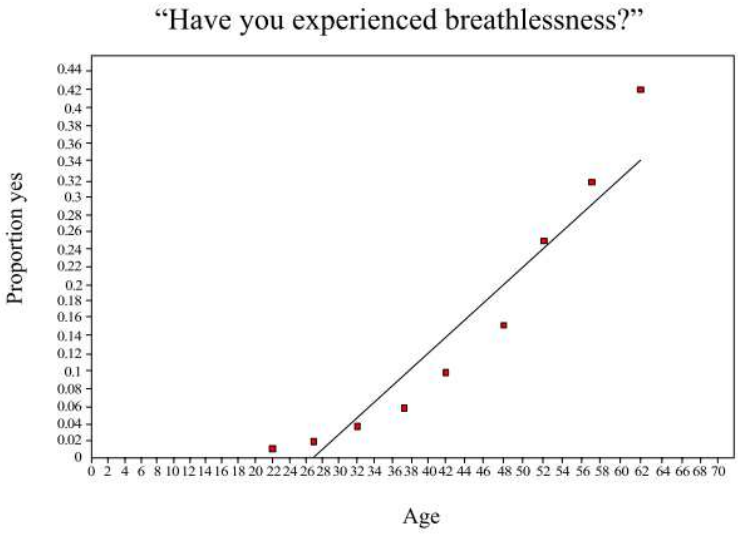


Figure 13.1 Unfitness of linear predictor model applied to categorical data[452]
Note: This figure was generated from the British coal miner data. The red dots illustrated the true association between observed categorical variables and the continuous latent variable in the sample. The black line showed the model generated from linear predictor model if the categorical variable was treated as continuous.

To highlight this point, a combination approach has been adopted to evaluate the factor structure of screening instruments with binary response[448]. This approach consists of the Categorical Data Factor analysis (CDFA) and the Item Response Theory[453] (IRT). Following this method, the exploration of potential factors of the M-CAST is conducted by the exploratory CDFA and then the confirmatory CDFA using the IRT model in the same Chinese population.

Table 13.1 Description of studies on factor analysis of screening instruments for ASC

Screening instrument	Author & year	Sample size	Sample source	Age (SD)	Analytical methods	No. of factors	Proposed factors
Autism Spectrum Screening Questionnaire (ASSQ)	Posserud[439] 2008	6,229	General population	7-9	PCA & EFA	3	1. Social function 2.Autism-associated problems 3. Cognitive style associated with HFA/AS
Social and Communication Questionnaire (SCQ)	Gau [408] 2011	736	Clinical ASC and relatives	2-18	CFA	3	1.Social interaction 2. Communication; 3. Repetitive behaviour
Social Responsiveness Scale (SRS)	Constantino[431] 2004	226	Clinical PDD and other disorders	4-18	CA & PCA	1	Single underlying 'autism' factor
Autism Quotient (AQ)	Auyeung[442] 2008	1,765	General population and clinical ASC	4-9	PCA	4	1. Mind-reading 2. Attention to detail 3. Social skill 4. Imagination
	Stewart[440] 2009	536	University students	Mean 24.3 (10.5)	EFA & CFA	4	1. Socialness 2. Pattern 3. Understanding others/communication 4. Imagination
	Hoekstra[441] 2008	1,299	University students and general population	Mean: 21.9(3.69); 35.68(6.33)	CFA	2	1. Social interaction 2. Attention to detail
Child Behaviour Checklist (CBC)	Pandolfi[444] 2009	128	Clinical ASC	1.5-5	CFA	3	1. Internalizing 2. Externalizing 3. Total problems
Gilliam Autism Rating Scale (GARS)	Lecavalier[147] 2005	284	ASC students	Mean: 9.3(3.9)	PCA & EFA	3	1. Stereotyped and repetitive behaviours 2. Social interaction 3. Communication
Adult Asperger Assessment (AAA)	Kuenssberg[445] 2011	153	Clinical AS and HFA	Mean: 33(11)	CFA	2	1. Social communication 2. RIBA
Childhood Autism Rating Scale (CARS)	Magyar[424] 2007	164	ASC students	Mean: 43.27 months (19.78)	PCA & PAF	4	1. Social communication 2. Relating to people and visual response 3. Stereotypy and sensory abnormalities 4. Emotional regulation
Sub-threshold Autism Trait Questionnaire (SATQ)	Kanne[443] 2011	1,709	University students	Mean: 18.4 (0.99)	EFA & CFA	5	1. Social interaction & Enjoyment 2. Oddness 3. Reading facial expressions 4. Expressive language 5. Rigidity

PCA: Principle component analysis; HFA: High functional autism; AS: Asperger syndrome; EFA: Exploratory factor analysis; CFA: Confirmatory factor analysis; RIBA: Repetitive/ restricted interests behaviours and activities.

13.2 Method

13.2.1 Participants

This sample was drawn from the validation study described in Chapter 10. The data of both samples from mainstream schools and clinical settings were used for this study. 714 M-CAST questionnaires of children from primary schools and 50 questionnaires from children with autism were available. Only fully-completed M-CAST questionnaires were used in the factor analysis.

13.2.2 Data analysis

13.2.2.1 Data description

All the reverse-phrased items were converted before analysis. The prevalence of item endorsement was cross-tabulated as well as the bivariate endorsement probabilities which indicated the frequency of endorsement of pairs of items. This analysis was calculated from the raw data in MPlus 6.0 using the "TYPE=BASIC" command[452].

13.2.2.2 Factor exploration: Categorical data factor analysis

The investigation of a possible non-linear relationship between the binary item response and the latent trait was investigated using the exploratory CDFA. The whole analysis was conducted in MPlus 6.0[452]. Due to the fact that the item responses are binary, the correlation matrix used in the CDFA is a tetrachoric correlation. The factor structure of the M-CAST was estimated by the weighted least square estimation (WLSM). This estimator uses a diagonal weight matrix with standard errors and mean-adjusted Chi-square test statistic that uses a full weight matrix[452].

The analysis was carried out using the following command: "VARIABLE: CATEGORICAL; ANALYSIS: "TYPE=EFA 1 6; PLOT: TYPE=PLOT3". This indicated a factor structure with up to six factor solutions to be examined one by one. The number of potential factors was determined by three approaches: 1) the eigenvalues of the sample correlation matrix: to indicate the potential number of factors for the M-CAST. The Kaiser criterion was adopted that the number of factors with eigenvalues higher than 1.0 could be recommended as the appropriate number of factors for further consideration[454]; 2) the Scree plot: to identify the number of

eigenvalues that are present before the ‘elbow’. The number of factors that starts the elbow indicates how many factors that may be appropriate for best explaining the correlation between items; 3) the criteria for model fit indices of the CDFA provided by MPlus: the Chi-square Test of Model Fit, Root Mean Square Error of Approximation (RMSEA), the Comparative Fit Index (CFI), the Tucker-Lewis Index (TLI), and Standardized Root Mean Square Residual (SRMR). Statistical tests such as the Chi-square test are dependent on, and sensitive to sample size. This leads to a situation that large samples with high statistical power can increase the probability of rejecting a true model[444, 455]. In order to avoid rejecting a suitable model due to a single significant Chi-square value, the Chi-square was not used on its own to determine model fit in this study. The remaining psychometric indices of model fit were less sample size dependent and therefore were also considered. The recommended cut-off for the good fit is shown in Table 13.2. In the CDFA, the criteria for indices of a model of good fit were as follows: RMSEA≤0.06, CFI≥0.95, TLI≥0.95 and SRMR≤0.08[456, 457]. The criteria for indices of an adequate fit model were RMSEA ≤0.08, CFI ≥0.90, TLI ≥0.90, and SRMR≤0.10[456, 457].

As the default in MPlus, the oblique Geomin factor rotation was performed for factor loading. The Geomin rotation is recommended when factor indicators have cross-loadings which indicate that some factors extracted may be correlated[417, 452]. Factor loadings for each rotated solution were examined to ensure that the items loading on to each factor make theoretical sense[417]. In each proposed model, factor loadings were examined for each item loading on to each factor in order to ensure they were salient. The minimum factor loadings which can be considered as salient were suggested as between 0.30 and 0.40 by Floyd and Widaman[458]. In this study, factor loadings that were ≥0.35 were considered as salient. Once the factor solution was chosen, items that did not load saliently on to any of the factors or cross-loaded on more than one factor were removed from further analysis. In addition, the factors that only had one to two items saliently loaded on were also removed since it requires at least three items on each factor to ensure this factor is well-measured[459].

Table 13.2 The recommended cut-off of model of good fit in CDFA[460]

	Yu 2002[461]	Hu & Bentler 1999[457]
RMSEA	≤0.05	≤0.06
CFI	≥0.96	≥0.95
TLI	≥0.95	≥0.95
SRMR	≤0.07	≤0.08

13.2.2.3 Factor confirmation: Item response theory

To confirm the factor structure identified by the exploratory CDFA, a multidimensional IRT model was used to test the model fit for identified latent traits. Since the item responses were binary, the remaining items for each factor were put into a 2-parameter, multidimensional IRT model[462].

In the IRT model, each item was described by two parameters: item discrimination and item difficulty[462]. Item discrimination indicates the extent to which the item is related to the underlying latent trait. It demonstrates the change in the probability of endorsing the item due to the change in the underlying latent trait[13]. The item difficulty parameter is related to the prevalence of an item which indicates how commonly an item is endorsed[13, 448]. It is also referred to as "commonality" in epidemiological studies since it reflects the prevalence of the described symptoms[448]. The lower the difficulty parameter, the higher the probability of an individual endorsing the item, and then the behaviour measured is considered as common[13].

To test the fitness of the model, the IRT model used robust weighted least squares estimation with mean and variance adjusted estimator (WLSMV). This estimator has been found to work well for categorical data in confirmatory factor analysis[463, 464]. Since the factor structure was estimated by the WLSMV, a 2-parameter probit model was estimated[13]. The criteria for indices of a model of good fit were as follows: RMSEA≤0.06, CFI≥0.95, TLI≥0.95 and the Weighted Root Mean Square Residual (WRMR) close to or ≤1.0[456, 457]. The criteria for indices of an adequate fit model were RMSEA ≤0.08, CFI ≥0.90, TLI ≥0.90, WRMR close to 1.0[456, 457]. In addition, the internal consistency of items was examined using Cronbach's alpha.

13.2.2.4 Graphical presentation of IRT

The psychometric performance of the M-CAST was represented graphically using the Item Characteristic Curve (ICC) and the Test Information Curve (TIC). The graphs for each factor were presented separately. The ICCs provide the trace line of IRT models which are defined by the two parameters of the IRT, item difficulty and item discrimination. The item discrimination which is the slope parameter (α) indicates the steepness of the slope of the ICC curve at the inflexion point of the S-shaped curve[448]. A steeper slope indicates a closer relationship to the construct and so this item is more discriminating[462]. The item difficulty as the location parameter (β) is the point on the trait dimension at which a respondent has a 50% probability of endorsing the item[448]. The higher the location parameter of an item, the more likely that this item will be endorsed only among individuals with more severe autistic trait[448].

The TIC is a function of standard error, which provides a graphical representation of the variations in the precision of the measurement. It indicates the reliability of the latent trait scores provided by the instrument over the full range of the latent trait scores[448]. The TIF takes the reciprocal of variance or standard deviation generating a humped plot with higher value indicating regions of precise measurement (small standard errors compared with other regions)[448]. It is the sum of the item information curves (IIC). An item information curve is computed from the inverse of the standard error of the measurement which shows the inverse of the standard error of the latent trait estimated at that point on the latent trait[13].

13.3 Results

13.3.1 Descriptive statistics

All the questionnaires with missing items (n=20) were excluded from the sample. There were 694 questionnaires available for analysis, of which 655 were from the mainstream sample and 39 from the clinical sample. The mean age of children was 8.2 years old (SD=1.33, range: 4-11.4). The data on the age of 25 children (3.6%) were missing. There were 387 (56%) boys and 307 girls (44%). The prevalence of item endorsement of the M-CAST is shown in Table 13.3.

Twenty items (64.5%) were endorsed by 15% or more of the sample (item 6,7,8,9,13,14,15,17,19,20,23,27,28,29,31,32,34,35,36,37). Only three items were endorsed by less than 10% (item 5,11,16). The tetrachoric correlation matrix between items and the proportion of the sample that endorsed pairs of items is shown in Table 13.4.

Table 13.3 Item wording and prevalence of item endorsement (n=694)

No	**Items on the CAST**(* items are reverse scored)	**Yes (%)**	**No (%)**	**Score (%)**
1	Does s/he join in playing games with other children easily?	624 (89.9)	70 (10.1)	70 (10.1)
2	Does s/he come up to you spontaneously for a chat?	614 (88.5)	80 (11.5)	80 (11.5)
5	Is it important to him/her to fit in with the peer group?	627 (90.3)	67 (9.7)	67 (9.7)
6	Does s/he appear to notice unusual details that others miss?	475 (68.4)	219 (31.6)	475 (68.4)
7*	Does s/he tend to take things literally?	169 (24.4)	525 (75.6)	169 (24.4)
8	When s/he was 3 years old, did s/he spend a lot of time pretending (e.g., play acting being a superhero, or holding teddy's tea parties)?	481 (69.3)	213 (30.7)	213 (30.7)
9*	Does s/he like to do things over and over again, in the same way all the time?	246 (35.4)	448 (64.4)	246 (35.4)
10	Does s/he find it easy to interact with other children?	607 (87.5)	87 (12.5)	87 (12.5)
11	Can s/he keep a two-way conversation going?	632 (91.1)	62 (8.9)	62 (8.9)
13	Does s/he mostly have the same interests as his/her peers?	586 (84.4)	108 (15.6)	108 (15.6)
14*	Does s/he have an interest which takes up so much time that s/he does little else?	341 (49.1)	353 (50.9)	341 (49.1)
15	Does s/he have friends, rather than just acquaintances?	489 (70.5)	205 (29.5)	205 (29.5)
16	Does s/he often bring you things s/he is interested in to show you?	634 (91.4)	60 (8.6)	60 (8.6)
17	Does s/he enjoy joking around?	498 (71.8)	196 (28.2)	196 (28.2)
18*	Does s/he have difficulty understanding the rules for polite behaviour?	291 (41.9)	404 (58.1)	291 (41.9)
19*	Does s/he appear to have an unusual memory for details?	507 (73.1)	187 (27.0)	507 (73.1)
20*	Is his/her voice unusual (e.g., overly adult, flat, or very monotonous)?	193 (27.8)	501 (72.2)	193 (27.8)
21	Are people important to him/her?	601 (86.6)	93 (13.4)	93 (13.4)
23	Is s/he good at turn-taking in conversation?	482 (69.5)	212 (30.5)	212 (30.5)
24	Does s/he play imaginatively with other children, and engage in role-play?	596 (85.9)	98 (14.1)	98 (14.1)
25*	Does s/he often do or say things that are tactless or socially inappropriate?	194 (28.0)	500 (72.0)	194 (28.0)
27	Does s/he make normal eye-contact?	549 (79.1)	145 (20.9)	145 (20.9)
28*	Does s/he have any unusual and repetitive movements?	148 (21.3)	546 (78.7)	148 (21.3)
29*	Is his/her social behaviour very one-sided and always on his/her own terms?	192 (27.7)	502 (72.3)	192 (27.7)
30*	Does s/he sometimes say "you" or "s/he" when s/he means "I"?	99 (14.3)	595 (85.7)	99 (14.3)
31	Does s/he prefer imaginative activities such as play-acting or story-telling, rather than numbers or lists of facts?	471 (67.9)	223 (32.1)	223 (32.1)
32*	Does s/he sometimes lose the listener because of not explaining what s/he is talking about?	211 (30.4)	483 (69.6)	211 (30.4)
34*	Does s/he try to impose routines on him/herself, or on others, in such a way that it causes problems?	232 (33.4)	462 (66.6)	232 (33.4)
35	Does s/he care how s/he is perceived by the rest of the group?	474 (68.3)	220 (31.7)	220 (31.7)
36*	Does s/he often turn conversations to his/her favourite subject rather than following what the other person wants to talk about?	206 (29.7)	488 (70.3)	206 (29.7)
37*	Does s/he have odd or unusual phrases?	296 (42.7)	398 (57.3)	296 (42.7)

Table 13.4 Prevalence of item endorsement, bivariate endorsement probabilities, and tetrachoric correlations (below diagonal)

Item*	1	2	5	6	7	8	9	10	11	13	14	15	16	17	18	19
1	**0.101**	0.040	0.046	0.061	0.037	0.069	0.050	0.078	0.043	0.046	0.056	0.068	0.026	0.055	0.048	0.050
2	*0.563*	**0.115**	0.046	0.061	0.050	0.065	0.061	0.045	0.048	0.046	0.065	0.063	0.029	0.063	0.065	0.068
5	*0.701*	*0.655*	**0.097**	0.048	0.036	0.048	0.039	0.055	0.033	0.045	0.053	0.063	0.030	0.055	0.045	0.056
6	*-0.131*	*-0.249*	*-0.281*	**0.684**	0.164	0.192	0.241	0.076	0.046	0.088	0.357	0.182	0.050	0.164	0.290	0.563
7	*0.213*	*0.323*	*0.213*	*-0.022*	**0.244**	0.079	0.118	0.046	0.045	0.043	0.131	0.086	0.024	0.084	0.125	0.184
8	*0.531*	*0.387*	*0.275*	*-0.145*	*0.041*	**0.307**	0.107	0.075	0.061	0.081	0.144	0.122	0.046	00137	0.115	0.209
9	*0.213*	*0.258*	*0.072*	*-0.015*	*0.262*	*-0.017*	**0.354**	0.055	0.043	0.050	0.199	0.117	0.027	0.108	0.159	0.256
10	*0.901*	*0.535*	*0.725*	*-0.124*	*0.221*	*0.445*	*0.131*	**0.125**	0.048	0.055	0.073	0.079	0.036	0.063	0.061	0.073
11	*0.694*	*0.702*	*0.566*	*-0.244*	*0.385*	*0.506*	*0.184*	*0.675*	**0.089**	0.045	0.049	0.063	0.030	0.056	0.049	0.049
13	*0.526*	*0.465*	*0.527*	*-0.208*	*0.070*	*0.358*	*-0.054*	*0.533*	*0.562*	**0.156**	0.082	0.086	0.043	0.075	0.084	0.101
14	*0.094*	*0.106*	*0.086*	*0.148*	*0.092*	*-0.048*	*0.166*	*0.144*	*0.079*	*0.059*	**0.491**	0.128	0.037	0.137	0.222	0.368
15	*0.530*	*0.389*	*0.507*	*-0.164*	*0.131*	*0.252*	*0.093*	*0.510*	*0.561*	*0.435*	*-0.123*	**0.295**	0.052	0.115	0.138	0.203
16	*0.437*	*0.442*	*0.531*	*-0.149*	*0.068*	*0.321*	*-0.057*	*0.531*	*0.558*	*0.557*	*-0.080*	*0.424*	**0.086**	0.049	0.042	0.042
17	*0.387*	*0.411*	*0.414*	*-0.233*	*0.136*	*0.393*	*0.063*	*0.359*	*0.483*	*0.347*	*-0.014*	*0.261*	*0.402*	**0.282**	0.137	0.183
18	*0.075*	*0.212*	*0.062*	*0.019*	*0.187*	*-0.098*	*0.068*	*0.098*	*0.179*	*0.192*	*0.102*	*0.106*	*0.089*	*0.138*	**0.419**	0.300
19	*-0.351*	*-0.236*	*-0.233*	*0.489*	*0.064*	*-0.129*	*-0.020*	*-0.245*	*-0.275*	*-0.155*	*0.206*	*-0.109*	*-0.359*	*-0.201*	*-0.051*	**0.731**
20	*0.151*	*0.277*	*0.239*	*0.035*	*0.319*	*-0.003*	*0.198*	*0.264*	*0.192*	*0.203*	*0.152*	*0.098*	*0.113*	*0.032*	*0.206*	*0.147*
21	*0.373*	*0.429*	*0.391*	*-0.257*	*0.148*	*0.256*	*0.140*	*0.433*	*0.399*	*0.278*	*0.239*	*0.260*	*0.437*	*0.334*	*0.201*	*-0.276*
23	*0.551*	*0.473*	*0.338*	*-0.246*	*0.254*	*0.393*	*0.161*	*0.539*	*0.700*	*0.375*	*0.039*	*0.413*	*0.345*	*0.355*	*0.054*	*-0.084*
24	*0.713*	*0.559*	*0.564*	*-0.107*	*0.229*	*0.717*	*0.188*	*0.557*	*0.652*	*0.478*	*0.046*	*0.340*	*0.488*	*0.496*	*0.176*	*-0.211*
25	*0.429*	*0.311*	*0.171*	*-0.196*	*0.304*	*0.148*	*0.248*	*0.445*	*0.428*	*0.118*	*0.210*	*0.177*	*0.159*	*0.114*	*0.356*	*-0.086*
27	*0.445*	*0.531*	*0.468*	*-0.392*	*0.134*	*0.421*	*0.153*	*0.437*	*0.547*	*0.431*	*-0.041*	*0.374*	*0.445*	*0.402*	*0.228*	*-0.358*
28	*0.378*	*0.366*	*0.338*	*-0.018*	*0.304*	*0.105*	*0.250*	*0.341*	*0.214*	*0.227*	*0.238*	*0.075*	*0.178*	*0.117*	*0.259*	*0.090*
29	*0.524*	*0.421*	*0.423*	*-0.158*	*0.357*	*0.346*	*0.180*	*0.541*	*0.568*	*0.401*	*0.158*	*0.342*	*0.212*	*0.298*	*0.325*	*-0.080*
30	*0.163*	*0.338*	*0.318*	*0.004*	*0.325*	*0.029*	*0.149*	*0.183*	*0.350*	*0.162*	*0.166*	*0.189*	*0.283*	*0.146*	*0.309*	*0.073*
31	*0.305*	*0.239*	*0.333*	*-0.052*	*0.047*	*0.507*	*-0.044*	*0.324*	*0.466*	*0.360*	*-0.056*	*0.248*	*0.321*	*0.263*	*0.026*	*-0.083*
32	*0.408*	*0.286*	*0.174*	*-0.085*	*0.258*	*0.174*	*0.207*	*0.386*	*0.410*	*0.276*	*0.188*	*0.182*	*0.167*	*0.171*	*0.253*	*-0.076*
34	*0.204*	*0.199*	*0.125*	*-0.086*	*0.305*	*0.109*	*0.315*	*0.217*	*0.170*	*0.015*	*0.188*	*0.028*	*0.048*	*0.064*	*0.128*	*-0.006*
35	*0.272*	*0.264*	*0.279*	*-0.018*	*-0.033*	*0.217*	*-0.076*	*0.194*	*0.349*	*0.236*	*0.120*	*0.183*	*0.239*	*0.151*	*0.131*	*-0.105*
36	*0.305*	*0.281*	*0.229*	*-0.149*	*0.389*	*0.215*	*0.207*	*0.383*	*0.421*	*0.134*	*0.133*	*0.200*	*0.082*	*0.246*	*0.236*	*-0.129*
37	*0.024*	*-0.002*	*-0.100*	*0.160*	*0.218*	*-0.135*	*0.196*	*0.069*	*0.013*	*-0.032*	*0.188*	*-0.069*	*-0.157*	*-0.171*	*0.121*	*0.154*

Note: Column 1(item) refers to the 31 Mandarin CAST items. Diagonal in bold refers to the proportion of the sample that endorsed each item (prevalence of item endorsement). The lower left triangle (italic text) denotes the tetrachoric correlations between items. The upper right triangle (plain text) denotes the proportion of the sample that endorsed both items (bivariate endorsement).
*31 items: Only scorable items on the M-CAST were analysed.

Item*	20	21	23	24	25	27	28	29	30	31	32	34	35	36	37
1	0.037	0.032	0.071	0.059	0.058	0.049	0.045	0.065	0.022	0.053	0.059	0.048	0.050	0.050	0.045
2	0.052	0.039	0.072	0.050	0.055	0.062	0.049	0.063	0.035	0.055	0.056	0.053	0.056	0.055	0.049
5	0.042	0.032	0.052	0.045	0.037	0.049	0.040	0.055	0.029	0.053	0.040	0.040	0.049	0.043	0.035
6	0.195	0.071	0.177	0.088	0.167	0.099	0.144	0.170	0.098	0.213	0.197	0.218	0.215	0.184	0.314
7	0.104	0.043	0.104	0.052	0.102	0.063	0.082	0.108	0.061	0.084	0.104	0.118	0.073	0.118	0.131
8	0.085	0.062	0.146	0.112	0.104	0.111	0.076	0.128	0.046	0.169	0.115	0.117	0.125	0.118	0.112
9	0.124	0.059	0.130	0.066	0.131	0.091	0.104	0.121	0.063	0.108	0.135	0.163	0.102	0.133	0.180
10	0.055	0.042	0.084	0.053	0.071	0.058	0.050	0.079	0.027	0.066	0.069	0.059	0.055	0.068	0.059
11	0.036	0.030	0.075	0.049	0.052	0.052	0.030	0.062	0.029	0.059	0.053	0.040	0.050	0.053	0.039
13	0.061	0.037	0.082	0.055	0.053	0.068	0.050	0.079	0.032	0.084	0.072	0.053	0.071	0.058	0.063
14	0.157	0.086	0.156	0.073	0.166	0.098	0.133	0.157	0.085	0.150	0.176	0.192	0.173	0.164	0.239
15	0.094	0.061	0.144	0.071	0.104	0.102	0.071	0.124	0.058	0.127	0.112	0.102	0.117	0.112	0.117
16	0.030	0.032	0.048	0.036	0.033	0.043	0.027	0.036	0.024	0.048	0.036	0.032	0.042	0.030	0.027
17	0.082	0.065	0.131	0.084	0.092	0.102	0.072	0.114	0.052	0.124	0.107	0.102	0.108	0.114	0.098
18	0.144	0.073	0.135	0.075	0.166	0.114	0.120	0.160	0.088	0.138	0.163	0.159	0.151	0.157	0.197
19	0.219	0.076	0.213	0.086	0.195	0.115	0.164	0.193	0.110	0.225	0.213	0.244	0.219	0.202	0.331
20	**0.278**	0.040	0.089	0.045	0.111	0.049	0.101	0.112	0.065	0.091	0.120	0.127	0.091	0.110	0.160
21	*0.042*	**0.134**	0.071	0.043	0.063	0.066	0.035	0.065	0.026	0.068	0.061	0.052	0.066	0.061	0.059
23	*0.037*	*0.356*	**0.305**	0.089	0.143	0.120	0.091	0.140	0.052	0.127	0.148	0.124	0.115	0.153	0.128
24	*0.070*	*0.401*	*0.512*	**0.141**	0.065	0.073	0.049	0.075	0.035	0.098	0.072	0.055	0.075	0.073	0.052
25	*0.279*	*0.323*	*0.445*	*0.307*	**0.280**	0.092	0.097	0.156	0.073	0.101	0.150	0.134	0.107	0.151	0.147
27	*-0097*	*0.497*	*0.492*	*0.542*	*0.323*	**0.209**	0.055	0.098	0.045	0.102	0.094	0.085	0.095	0.098	0.085
28	*0.386*	*0.092*	*0.239*	*0.260*	*0.346*	*0.118*	**0.213**	0.112	0.066	0.072	0.107	0.110	0.068	0.104	0.130
29	*0.298*	*0.344*	*0.433*	*0.420*	*0.600*	*0.379*	*0.482*	**0.277**	0.073	0.105	0.143	0.137	0.114	0.169	0.150
30	*0.303*	*0.130*	*0.102*	*0.250*	*0.393*	*0.210*	*0.453*	*0.398*	**0.143**	0.045	0.082	0.068	0.049	0.059	0.085
31	*0.012*	*0.296*	*0.221*	*0.569*	*0.090*	*0.320*	*0.034*	*0.133*	*-0.015*	**0.321**	0.101	0.110	0.133	0.102	0.107
32	*0.284*	*0.245*	*0.420*	*0.339*	*0.497*	*0.282*	*0.377*	*0.456*	*0.437*	*0.025*	**0.304**	0.166	0.105	0.161	0.167
34	*0.266*	*0.088*	*0.167*	*0.091*	*0.315*	*0.141*	*0.338*	*0.345*	*0.232*	*0.016*	*0.465*	**0.334**	0.094	0.160	0.195
35	*0.022*	*0.288*	*0.145*	*0.347*	*0.147*	*0.267*	*0.001*	*0.212*	*0.046*	*0.233*	*0.070*	*-0.096*	**0.317**	0.105	0.120
36	*0.223*	*0.258*	*0.468*	*0.368*	*0.524*	*0.335*	*0.369*	*0.639*	*0.203*	*0.055*	*0.528*	*0.447*	*0.089*	**0.297**	0.166
37	*0.306*	*0.023*	*-0.015*	*-0.096*	*0.207*	*-0.036*	*0.329*	*0.238*	*0.267*	*-0.217*	*0.267*	*0.352*	*-0.112*	*0.281*	**0.427**

Note: Column 1(item) refers to the 31 Mandarin CAST items. Diagonal in bold refers to the proportion of the sample that endorsed each item (prevalence of item endorsement). The lower left triangle (italic text) denotes the tetrachoric correlations between items. The upper right triangle (plain text) denotes the proportion of the sample that endorsed both items (bivariate endorsement).
*31 items: Only scorable items on the M-CAST were analysed.

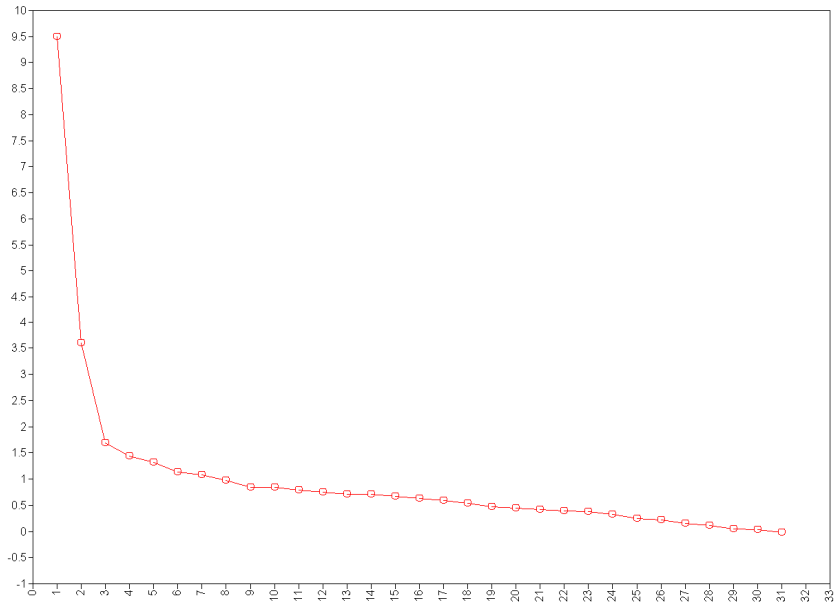
13.3.2 Categorical data factor analysis model

All the 31 items that are scorable on the M-CAST were included in the CDFA to explore the psychometric properties of the M-CAST. Based on the Kaiser criteria, the eigenvalues suggested a factor solution up to seven factors, while the Scree plot suggested a solution between three and six factors (Figure 13.2). Thus, in the following analysis, the factor structures were examined from three-factor solution until the acceptable model was identified. However, one-factor and two-factor structures were also included to gain more evidence. The eigenvalues above 1.0 obtained from the tetrachoric matrix are summarised in Table 13.5.

Table 13.5 Eigenvalues by CDFA

	1	2	3	4	5	6	7
Eigenvalue	9.496	3.601	1.687	1.434	1.323	1.137	1.082

Figure 13.2 Scree plot for 31-item M-CAST



The models provided by the CDFA were examined according to the salience of item loadings (≥ 0.35) on each factor and the indices of goodness of model fit. The goodness of model fit statistics of factor solutions from CDFA are summarised in Table 13.6.

Table 13.6 Model of good fit statistics by factor solutions from CDFA (31 items)

Factors	Chi-square			RMSEA	CFI	TLI	SRMR	Negative residual variances
	X^2	*df*	*p*					
1	1475.091	434	0.000	0.059	0.783	0.767	0.115	No
2	684.626	404	0.000	0.032	0.941	0.933	0.068	No
3	546.210	375	0.000	0.026	0.964	0.956	0.060	No
4	446.310	347	0.0002	0.020	0.979	0.972	0.052	No
5	366.505	320	0.0374	0.014	0.990	0.986	0.045	No
6	320.408	294	0.1389	0.011	0.994	0.991	0.041	No
7	272.966	269	0.4212	0.005	0.999	0.999	0.037	No

Note: Indices criteria for a model of good fit: RMSEA ≤0.06, CFI ≥0.95, TLI ≥0.95, SRMR ≤0.08.

The model fit statistics of the one-factor solution did not meet the model fit criteria and eight items did not have salient loadings on this single factor. Thus, this solution was discarded. In the two-factor solution, the first factor included items concerning Social Interaction and Communication (Factor 1), while the second factor included items concerning Inflexible/Stereotyped Language and Behaviours (Factor 2). Sixteen items (item 1,2,5,8,9,10,11,13,15,16,17,21,22,24,27,31,35) loaded on the first factor and thirteen items loaded on the second factor. There were two items, Notice unusual details (item 6) and Unusual memory (item19) that did not have salient loadings on either factor. The model fit statistics for the two-factor solution meet the criteria for an acceptable model.

The three-factor solution proposed a third factor, Attention to detail (Factor 3). The third factor only included the two items (item 6 and 19) that did not load on either factor in the two-factor solution. The same fifteen items loaded on the Factor 1 as in the two-factor solution except item 23, which cross-loaded on both Factor 1 and Factor 2. The same eleven items loaded on Factor 2 as in the two-factor solution except item 14, which did not have a salient loading on either factor, and item 20 which cross-loaded on both Factor 2 and Factor 1. The model fit statistics for this three-factor solution met the indices criteria for a good model.

The four-factor solution proposed the same three factors as model three and a fourth factor. However, other than the cross-loaded items (item 8, 24, 31), none of the other items had loaded saliently or solely on the fourth factor. These three cross-loaded items loaded most saliently on Factor 1. So the four-factor solution was discarded. Compared with the two-factor solution, the model statistics of the three-factor solution were better. Thus, the three-factor solution was chosen for further

investigation. The model fit statistics for the five-factor and six-factor solutions were good. However, as the three-factor fulfilled the criteria, those two solutions were not examined further. The Geomin factor loadings for two to four-factor solutions are shown in Table 13.7-13.9.

Regarding the two-factor solution, before removing any item from the analysis, the 31 items were either loaded saliently on Factor 1 or Factor 2. The correlation between these two factors was moderate (Geomin rotated factor correlations (GFC)=0.402). In the three-factor solution, the correlation between Factor 1 and Factor 2 was still moderate (GFC=0.511). The correlation between Factor 2 and Factor 3 was very weak (GFC=0.058) which indicated those two factors were very likely to be independent. There was a negative correlation between Factor 1 and Factor 3 (GFC=-0.185).

When examining the three-factor solution, item 20 (Unusual voice) cross-loaded on Factor 2 and Factor 3. Item 23 (Turn-taking conversation) cross-loaded on Factor 1 and Factor 2. Item 14 did not have a salient loading on any of the three factors. Therefore, item 14, 20 and 23 were removed from further analysis. The CDFA was re-run with the remaining 28 items. The model of fit indices of the 28-item version of the M-CAST met the criteria of a good fit model (RMSEA=0.026, CFI=0.967, TLI=0.958, SRMR=0.059). As it is recommended, in order to have the factors well-measured, each factor should have at least four or five indicators (observed items)[460]. In this three-factor model with 28 items, the third factor only had two items, indicating the third factor cannot be well measured in this model. Thus, the third factor was also removed from further analysis[460]. The CDFA was re-run with the remaining 26 items for a two-factor solution. The model was still stable and met the goodness of fit indices criteria (RMSEA=0.029, CFI=0.962, TLI=0.954, SRMR=0.063). The correlation between the two factors was moderate (GFC=0.447). The factor loading of a three-factor model with 28 items and a two-factor model with 26 items are shown in Table 13.10 & 13.11.

Table 13.7 Geomin rotated factor loadings for a two-factor solution from CDFA (31 items)

Item	Social Communication	Inflexible/Stereotyped Language and Behaviours
1. Play game with others	**0.818**	0.175
2. Spontaneous for a chat	**0.617**	0.213
5. Fit in peer group	**0.721**	0.059
6. Notice unusual details	*-0.385*	*0.106*
7. Take things literally	0.015	**0.506**
8. Pretending play	**0.704**	-0.153
9. Do same thing over and over	-0.046	**0.398**
10.Easy to interact	**0.763**	0.221
11. Keep two-way conversation	**0.767**	0.196
13. Same interests as peers	**0.641**	-0.007
14. Preoccupied by an interest	-0.136	**0.365**
15. Have friends	**0.561**	0.002
16. Show others things of interest	**0.705**	-0.128
17. Enjoy joking around	**0.574**	-0.051
18. Difficulty in understanding the rule of polite behaviours	0.024	**0.361**
19. Unusual memory	*-0.453*	*0.214*
20. Unusual voice	-0.099	**0.526**
21. Consider people important	**0.504**	0.091
23. Turn-taking conversation	**0.550**	0.217
24. Engage in role-play	**0.824**	-0.006
25. Tactless language and social inappropriate behaviours	0.149	**0.616**
27. Eye contact	**0.674**	0.019
28. Unusual and repetitive movements	0.001	**0.633**
29. One-sided social behaviours	0.304	**0.611**
30. Pronominal reversal	0.021	**0.546**
31. Prefer imaginative activities	**0.607**	-0.237
32. Lose listeners	0.112	**0.626**
34. Impose routines	-0.107	**0.612**
35. Care about the perception by others	**0.387**	-0.085
36. Turn conversation to his/her own interests	0.143	**0.633**
37. Odd or usual phrases	-0.385	**0.632**

Note: Figures in bold indicate the items saliently loaded on this factor without cross-loading.
Figures in italic text indicate the items did not saliently load on either factor.

Table 13.8 Geomin rotated factor loadings for a three-factor solution from CDFA (31 items)

Item	Social Communication	Inflexible/Stereotyped Language and Behaviours	Attention to Details
1. Play game with others	**0.930**	0.013	0.271
2. Spontaneous for a chat	**0.608**	0.197	-0.025
5. Fit in peer group	**0.803**	-0.047	0.124
6. Notice unusual details	-0.093	-0.147	**0.594**
7. Take things literally	0.009	**0.495**	0.090
8. Pretending play	**0.750**	-0.210	-0.002
9. Do same thing over and over	-0.077	**0.414**	0.030
10.Easy to interact	**0.880**	0.061	0.299
11. Keep two-way conversation	**0.738**	0.198	-0.090
13. Same interests as peers	**0.704**	-0.085	0.066
14. Preoccupied by an interest	*-0.048*	*0.280*	*0.248*
15. Have friends	**0.586**	-0.038	0.004
16. Show others things of interest	**0.718**	-0.157	-0.058
17. Enjoy joking around	**0.525**	-0.021	-0.151
18. Difficulty in understanding the rule of polite behaviours	-0.020	**0.387**	-0.009
19. Unusual memory	-0.218	0.010	**0.523**
20. Unusual voice	*0.014*	*0.413*	*0.334*
21. Consider people important	**0.413**	0.158	-0.196
23. Turn-taking conversation	*0.471*	*0.267*	*-0.156*
24. Engage in role-play	**0.870**	-0.072	0.026
25. Tactless language and social inappropriate behaviours	0.041	**0.689**	-0.083
27. Eye contact	**0.506**	0.155	-0.393
28. Unusual and repetitive movements	0.083	**0.540**	0.293
29. One-sided social behaviours	0.254	**0.626**	0.005
30. Pronominal reversal	0.058	**0.495**	0.175
31. Prefer imaginative activities	**0.691**	-0.323	0.050
32. Lose listeners	0.043	**0.662**	-0.007
34. Impose routines	-0.174	**0.655**	0.015
35. Care about the perception by others	**0.421**	-0.123	0.009
36. Turn conversation to his/her own interests	-0.014	**0.751**	-0.165
37. Odd or usual phrases	-0.355	**0.595**	0.217

Note: Figures in bold indicate the items saliently loaded on this factor without cross-loading.
Figures in italic text indicate the items did not saliently load on either factor

Table 13.9 Geomin rotated factor loadings for a four-factor solution from CDFA (31 items)

Item	Social Communication	Factor 4	Inflexible/Stereotyped Language and Behaviours	Attention to Details
1. Play game with others	**0.912**	0.008	0.088	0.212
2. Spontaneous for a chat	**0.589**	-0.124	0.213	-0.054
5. Fit in peer group	**0.777**	-0.255	-0.040	0.082
6. Notice unusual details	-0.027	0.320	-0.096	**0.632**
7. Take things literally	0.037	-0.006	**0.487**	0.094
8. Pretending play	*0.708*	*0.548*	*-0.054*	*-0.039*
9. Do same thing over and over	-0.057	-0.022	**0.400**	0.032
10.Easy to interact	**0.859**	-0.066	0.124	0.238
11. Keep two-way conversation	**0.712**	0.065	0.255	-0.120
13. Same interests as peers	**0.688**	-0.072	-0.054	0.044
14. Preoccupied by an interest	*-0.009*	*0.054*	*0.283*	*0.258*
15. Have friends	**0.564**	-0.107	-0.017	-0.024
16. Show others things of interest	**0.686**	-0.176	-0.147	-0.087
17. Enjoy joking around	**0.490**	0.067	0.027	-0.176
18. Difficulty in understanding the rule of polite behaviours	0.003	-0.134	**0.351**	0.004
19. Unusual memory	-0.151	0.319	0.053	**0.564**
20. Unusual voice	*0.068*	*-0.130*	*0.385*	*0.354*
21. Consider people important	**0.385**	-0.061	0.171	-0..218
23. Turn-taking conversation	*0.444*	*0.139*	*0.322*	*-0.186*
24. Engage in role-play	*0.840*	*0.434*	*0.077*	*0.014*
25. Tactless language and social inappropriate behaviours	0.056	-0.020	**0.677**	-0.087
27. Eye contact	**0.455**	-0.032	0.179	-0.423
28. Unusual and repetitive movements	0.131	-0.067	**0.528**	0.298
29. One-sided social behaviours	0.271	0.042	**0.640**	-0.004
30. Pronominal reversal	0.009	-0.170	**0.458**	0.191
31. Prefer imaginative activities	*0.654*	*0.355*	*-0.205*	*0.027*
32. Lose listeners	**0.065**	0.030	**0.660**	-0.008
34. Impose routines	-0.148	0.037	**0.644**	0.016
35. Care about the perception by others	**0.406**	0.076	-0.081	-0.002
36. Turn conversation to his/her own interests	-0.020	0.140	**0.780**	-0.186
37. Odd or usual phrases	-0.298	-0.048	**0.555**	0.236

Note: Figures in bold indicate salient loading on this factor.

Figures in italic text indicate items did not saliently load on either factor or cross-loaded.

Table 13.10 Geomin rotated factor loadings for a three-factor solution from CDFA (28 items)

Item	Social Communication	Inflexible/Stereotyped Language and Behaviours	Attention to Details
1. Play game with others	**0.953**	0.013	0.237
2. Spontaneous for a chat	**0.576**	0.188	-0.146
5. Fit in peer group	**0.781**	-0.041	-0.022
6. Notice unusual details	-0.002	-0.144	**0.666**
7. Take things literally	0.020	**0.491**	0.078
8. Pretending play	**0.779**	-0.242	0.035
9. Do same thing over and over	-0.070	**0.408**	0.022
10.Easy to interact	**0.898**	0.057	0.232
11. Keep two-way conversation	**0.724**	0.163	-0.123
13. Same interests as peers	**0.684**	-0.094	-0.045
15. Have friends	**0.572**	-0.038	-0.024
16. Show others things of interest	**0.679**	-0.156	-0.170
17. Enjoy joking around	**0.505**	-0.036	-0.189
18. Difficulty in understanding the rule of polite behaviours	-0.034	**0.401**	-0.070
19. Unusual memory	-0.153	0.004	**0.561**
21. Consider people important	**0.373**	0.142	-0.292
24. Engage in role-play	**0.889**	-0.099	0.025
25. Tactless language and social inappropriate behaviours	0.036	**0.676**	-0.091
27. Eye contact	**0.460**	0.146	-0.410
28. Unusual and repetitive movements	0.099	**0.549**	0.226
29. One-sided social behaviours	0.263	**0.625**	-0.010
30. Pronominal reversal	0.056	**0.519**	0.098
31. Prefer imaginative activities	**0.709**	-0.346	0.036
32. Lose listeners	0.052	**0.652**	0.004
34. Impose routines	-0.154	**0.651**	0.031
35. Care about the perception by others	**0.412**	-0.135	-0.059
36. Turn conversation to his/her own interests	0.001	**0.726**	-0.102
37. Odd or usual phrases	-0.324	**0.606**	0.224

Note: Figures in bold indicate the items saliently loaded on this factor without cross-loading.

Table 13.11 Geomin rotated factor loadings for a two-factor solution from CDFA (26 items)

Item	Social Communication	Inflexible/Stereotyped Language and Behaviours
1. Play game with others	**0.806**	0.189
2. Spontaneous for a chat	**0.606**	0.215
5. Fit in peer group	**0.740**	0.043
7. Take things literally	-0.011	**0.507**
8. Pretending play	**0.723**	-0.153
9. Do same thing over and over	-0.079	**0.408**
10.Easy to interact	**0.763**	0.215
11. Keep two-way conversation	**0.731**	0.212
13. Same interests as peers	**0.666**	-0.033
15. Have friends	**0.553**	0.015
16. Show others things of interest	**0.708**	-0.118
17. Enjoy joking around	**0.560**	-0.028
18. Difficulty in understanding the rule of polite behaviours	0.007	**0.374**
21. Consider people important	**0.478**	0.113
24. Engage in role-play	**0.834**	-0.003
25. Tactless language and social inappropriate behaviours	0.071	**0.657**
27. Eye contact	**0.597**	0.104
28. Unusual and repetitive movements	-0.005	**0.607**
29. One-sided social behaviours	0.252	**0.649**
30. Pronominal reversal	0.016	**0.543**
31. Prefer imaginative activities	**0.661**	-0.267
32. Lose listeners	0.043	**0.660**
34. Impose routines	-0.168	**0.647**
35. Care about the perception by others	**0.424**	-0.110
36. Turn conversation to his/her own interests	0.043	**0.701**
37. Odd or usual phrases	-0.401	**0.619**

Note: Figures in bold indicated the items saliently loaded on this factor without cross-loading.

13.3.3 Item response theory model

The confirmation of the two-factor solution was conducted in the same sample. A multidimensional IRT model was employed to examine the two-factor solution of the 26-item M-CAST.

13.3.4 IRT model fit

Using WLSMV, the indices of model the fit approved the model was acceptable. RMSEA was 0.039 and both CFI (0.922) and TLI were high (0.915). The WRMR was 1.272. The Chi-square value was 618.751 (df =298, p<0.001).

13.3.5 Graphical presentation of IRT

The Item Characteristic Curve (ICC) and Test Information Curve (TIC) of the IRT model were generated for the two factors. The ICC for Factor 1 is shown in Figure 13.3, and Figure 13.4 shows the ICC for each item loaded on Factor 1. The TIC for

Factor 1 is shown in Figure 13.5. The ICC for Factor 2 is shown in Figure 13.6, and Figure 13.7 shows the ICC for each item loaded on Factor 2. The TIC for Factor 2 is shown in Figure 13.8.

With regards to Factor 1, all 15 items functions are roughly at the same level on the social and communication trait, and all items are located to the right of the figures which indicated they are located towards the more severe end of the continuum. The ICC and TIC of Factor 1 indicates a child located between 1 and 2 standard deviations above the population mean on the latent trait would have a 50% probability of endorsing the M-CAST items. Figures also show that children at the mean latent trait value (0) had a low probability of endorsing any item of Factor 1 on the M-CAST. The shapes of the ICC curve of 15 items are similar with sharp slopes, which indicated a high discriminating power of these items with respect to the social and communication trait. The TIC of Factor 1 shown that most information that indicate the highest precision of measurement is provided by the M-CAST at around 1.8 standard deviations above the mean (0) on this factor.

In terms of the Factor 2, all 11 items are located towards the more severe end of the continuum (the right of the figure). Both the ICC and TIC of the Factor 2 indicate that a child located around 1 standard deviation above the population mean (0) on this factor would have a 50% probability of endorsing the M-CAST items. The highest precision of measurement is provided by the M-CAST at around 1.0 standard deviation above the mean (0) on Factor 2.

One items (item 35) on Factor 1 and three items (item 9, 18, 37) on Factor 2 shown more shallow slopes which suggested these items had lower discrimination power with respect to the latent trait. However, the TIC for both factors is very sharp which showed the factor structure of the M-CAST as a whole had very good discriminating power. Meanwhile, the curve is high on the trait which indicated the two subscales are discriminating at an extreme end of the population. The M-CAST has high precision on the trait, as demonstrates by the high value on the TIC (Figure 13.5&13.8).

Figure 13.3 Item Characteristic Curve for the Social and Communication factor

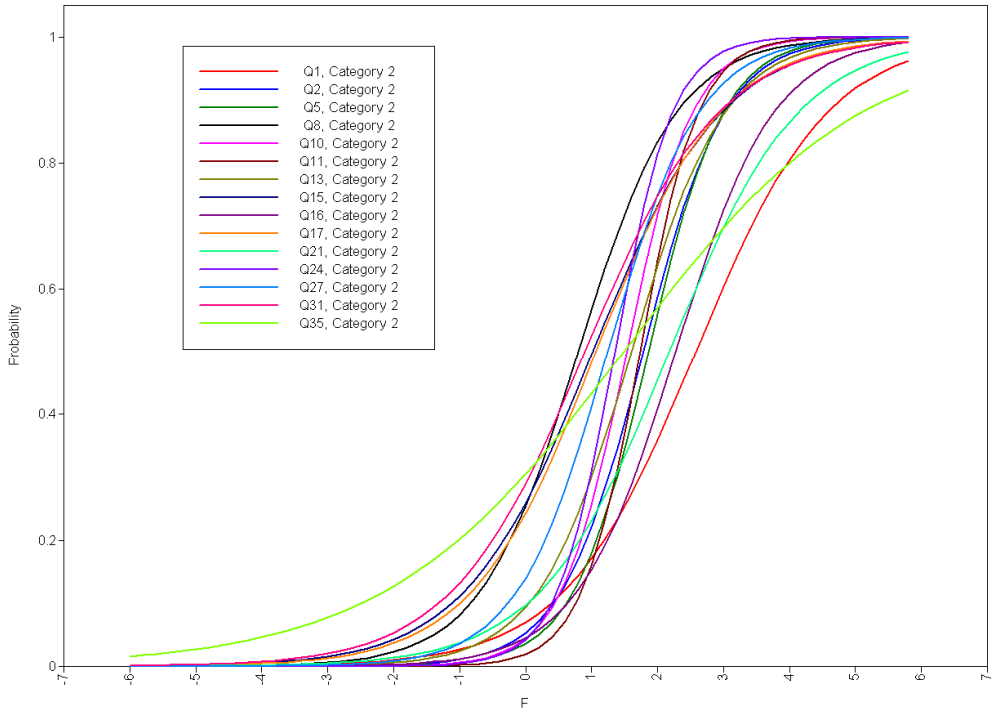
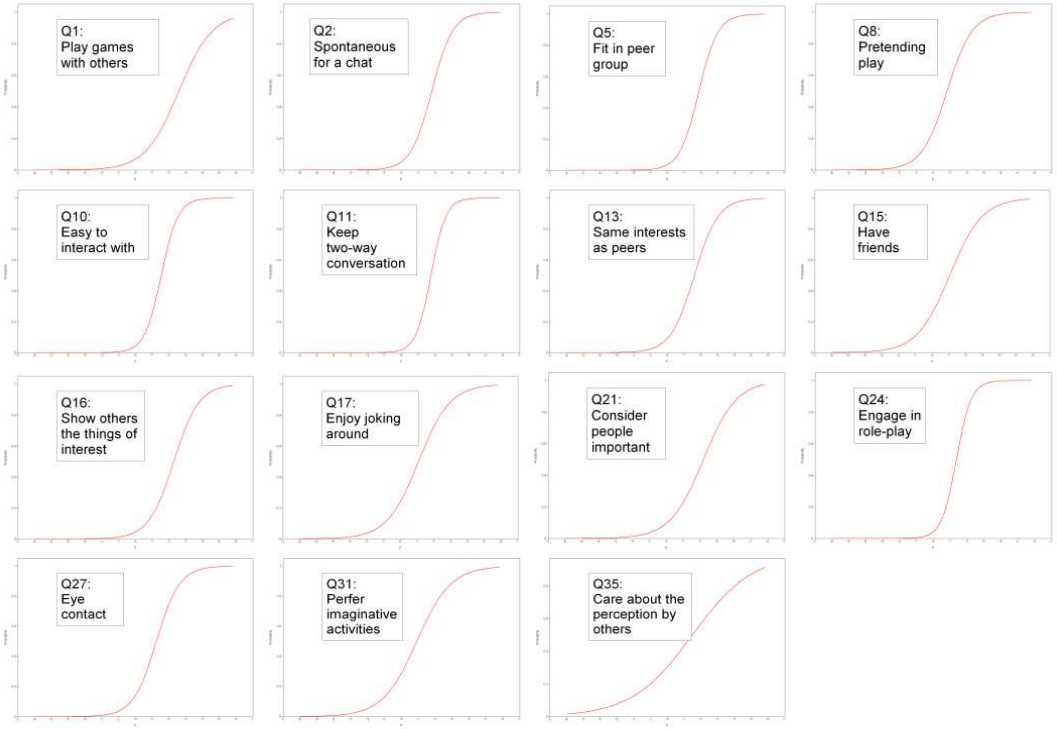


Figure 13.4 Item Characteristic Curves for the 15 items on Social and Communication factor



Note: The x-axis is the estimated latent trait score which is distributed as a standard normal distribution; the x-axis ranges from -7 to +7. The y-axis is the probability that the autistic feature on Mandarin CAST is endorsed; the y-axis ranges from a minimum value of 0 to maximum value of 1.

Figure 13.5 Test Information Curve for the Social and Communication factor

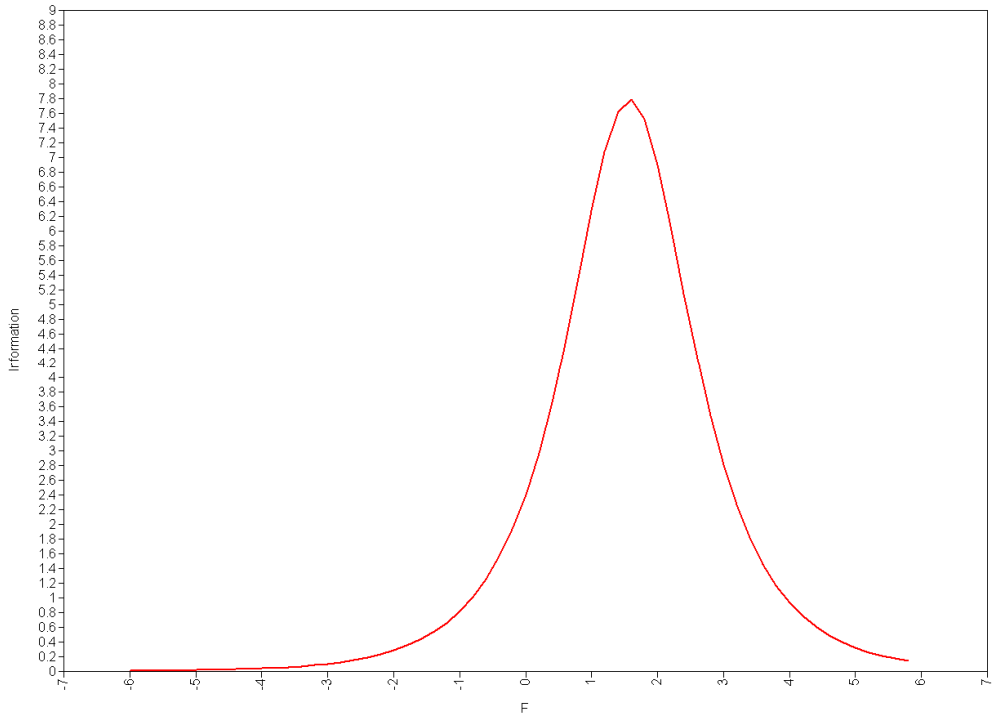


Figure 13.6 Item Characteristic Curve for the Inflexible/Stereotyped Language and Behaviours factor

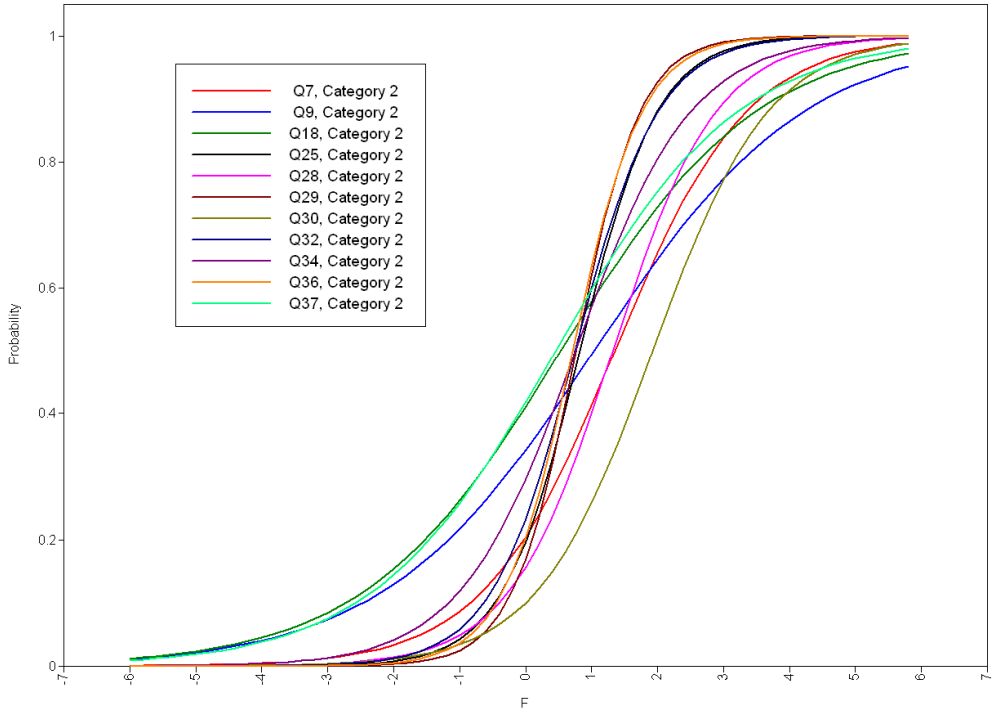
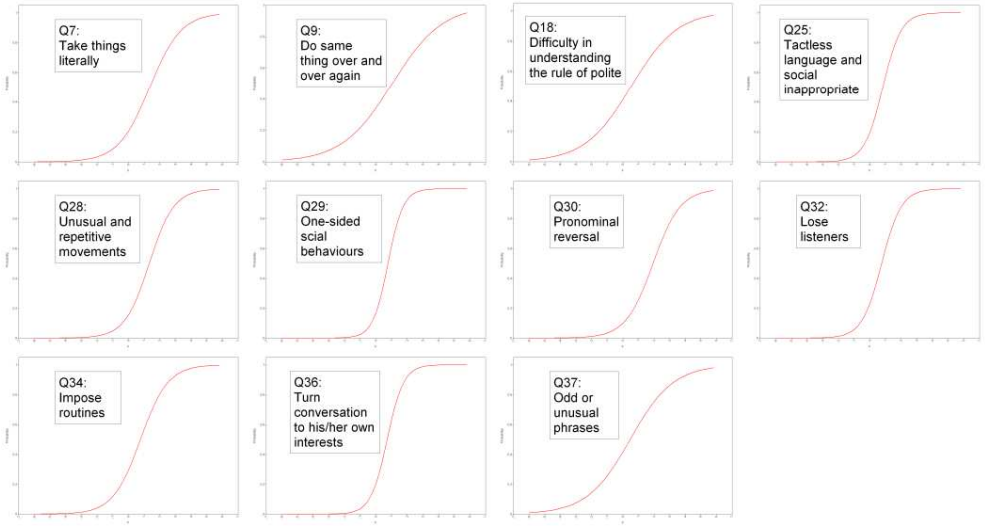
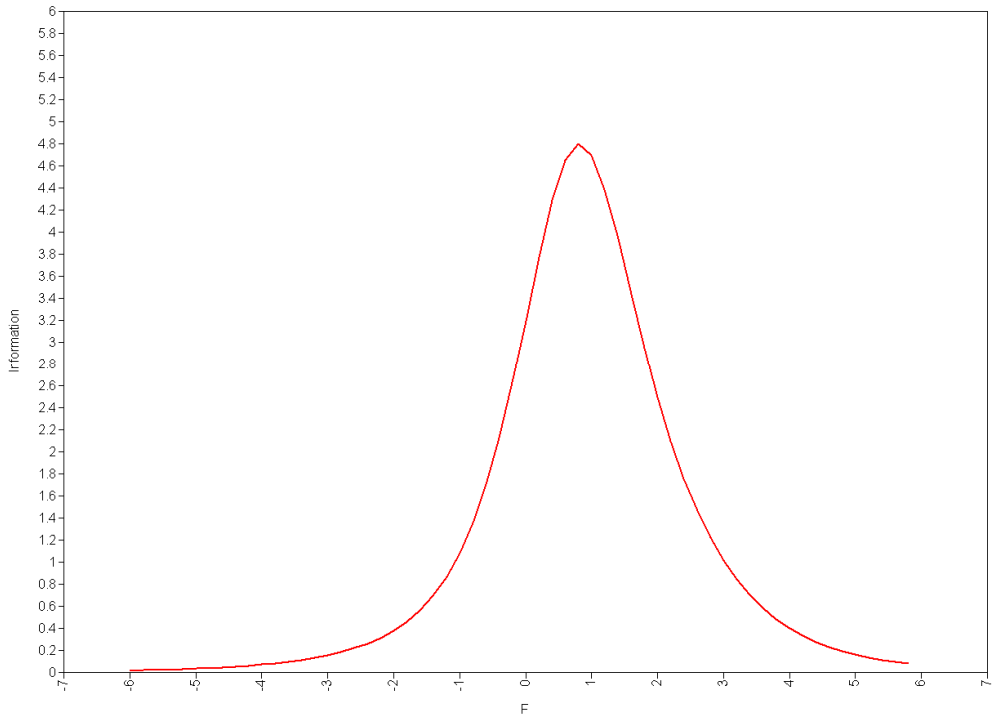


Figure 13.7 Item Characteristic Curve for the 11 items on the Inflexible/Stereotyped Language and Behaviours factor



Note: The x-axis is the estimated latent trait score which is distributed as a standard normal distribution; the x-axis ranges from -7 to +7. The y-axis is the probability that the autistic feature on Mandarin CAST is endorsed; the y-axis ranges from a minimum value of 0 to maximum value of 1.

Figure 13.8 Test Information Curve for the Inflexible/Stereotyped Language and Behaviours factor



13.3.6 IRT parameters: item discrimination and item difficulty

The labels for the values of item discrimination parameter are shown in Table 13.12. The values of item discrimination and item difficulty parameter are given in Table 13.13 and Table 13.14 for the two factors separately. On the Social and Communication latent trait, item 24 (engaging in role-play; α=1.346) showed the highest discrimination value. Three items (item 1, 31, 35) had low item discrimination value, while the other 11 items had moderate discrimination value. Item 1 (play game with others; β=2.578) and item 16 (show others things of interest to parents; β=2.276) had the highest item difficulty value. Item 8 (pretending play; β=0.799) had the lowest item difficulty value. On the Inflexible/Stereotyped Language and Behaviours trait, item 29 (one-sided social behaviours; α=1.217) and item 36 (turn conversation to his/her own interests; α=1.119) showed the highest item discrimination values while item 18 (difficulty in understanding the rule of polite behaviour; α=0.369) showed the lowest. Among a total of 11 items on this trait, 7 items had moderate item discrimination values while the rest had low discrimination values (item 7, 19, 18, 37). In terms of item difficulty parameter, item 30 (pronominal reversal; β=1.927) and item 7 (take things literally; β=1.353) had the highest discrimination values while item 37 (odd or unusual phrases; β=0.456) had the lowest value.

The IRT model suggested the item discrimination and item difficulty ability of three items (item 1, 31, 35) on Factor 1 and four items (item 7, 9, 18, 37) on Factor 2 were low. If those seven items were removed from the model, the model fit improved and achieved a good model fit for the remaining 19 items (Chi-square=268.174. *df*=151, p<0.001, CFI=0.960, TLI=0.955, RMSEA=0.055, WRMR= 1.052). This new model of a two-factor solution best explained the latent traits of ASC using the M-CAST. Figure 13.9 depicts the two-factor model of 26-item M-CAST from the multidimensional IRT.

Table 13.12 Labels for item discrimination parameter values under probit model[465]

Label	Range of values of item discrimination
None	0
Very low	0.01-0.34
Low	0.35-0.64
Moderate	0.65-1.34
High	1.35-1.69
Very high	>1.70
Perfect	+ infinity

Table 13.13 Item Response Theory model results for items on the Social and Communication factor (15 items)

	CDFA				IRT	
Item	**Threshold**	**Standardized Loading (lambda)**	**Residual Variance (1-lambda^2)**	**Z test for loading***	**Discrimination parameter *a***	**Difficulty parameter *b***
1. Play game with others	1.25	0.48	0.77	999.00	0.59	2.58
2. Spontaneous for a chat	1.19	0.67	0.56	13.50	0.95	1.78
5. Fit in peer group	1.30	0.70	0.51	13.90	1.04	1.86
8. Pretending play	0.48	0.60	0.65	12.09	0.79	0.80
10.Easy to interact	1.14	0.74	0.45	17.15	1.18	1.53
11. Keep two-way conversation	1.35	0.78	0.39	17.90	1.33	1.74
13. Same interests as peers	0.99	0.61	0.62	12.67	0.83	1.60
15. Have friends	0.50	0.49	0.76	9.94	0.60	1.02
16. Show others things of interest	1.35	0.60	0.65	9.80	0.79	2.28
17. Enjoy joking around	0.54	0.51	0.74	9.88	0.63	1.07
21. Consider people important	1.07	0.49	0.76	8.68	0.60	2.18
24. Engage in role-play	1.06	0.78	0.39	20.22	1.35	1.35
27. Eye contact	0.78	0.63	0.61	13.17	0.86	1.25
31. Prefer imaginative activities	0.43	0.48	0.77	9.36	0.58	0.90
35. Care about the perception by others	0.43	0.29	0.92	5.67	0.33	1.49

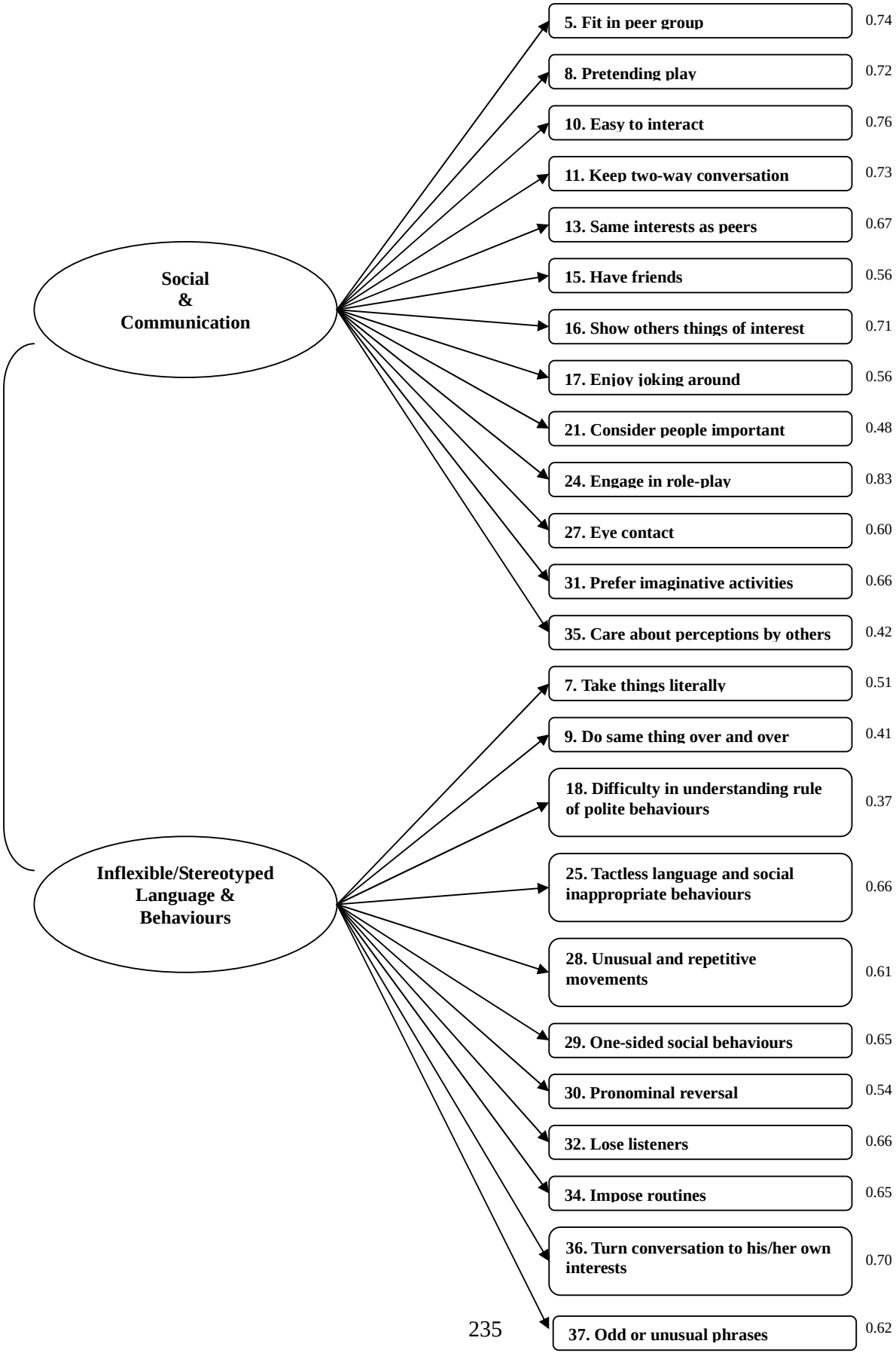
* all significant: $p<0.001$

Table 13.14 Item Response Theory model results for items on the Inflexible/Stereotyped Language and Behaviours factor (11 items)

		CDFA			IRT	
Item	**Threshold**	**Loading ((lambda)**	**Residual Variance (1-lamdda^2)**	**Z test for loading***	**Discrimination parameter**	**Difficulty parameter b**
7. Take things literally	0.65	0.48	0.77	999.00	0.59	1.35
9. Do same thing over and over	0.34	0.33	0.89	6.40	0.37	1.04
18. Difficulty in understanding the rule of polite behaviours	0.19	0.35	0.88	6.80	0.40	0.53
25. Tactless language and social inappropriate behaviours	0.56	0.68	0.53	15.23	1.00	0.82
28. Unusual and repetitive movements	0.76	0.58	0.67	11.20	0.75	1.32
29. One-sided social behaviours	0.58	0.75	0.43	17.38	1.22	0.77
30. Pronominal reversal	1.03	0.53	0.72	9.18	0.67	1.93
32. Lose listeners	0.49	0.66	0.57	14.63	0.93	0.75
34. Impose routines	0.40	0.53	0.72	10.58	0.67	0.76
36. Turn conversation to his/her own interests	0.52	0.72	0.48	17.17	1.12	0.72
37. Odd or unusual phrases	0.17	0.37	0.86	7.41	0.43	0.46

* all significant: $p<0.001$

Figure 13.9 Factor model of the M-CAST resulting from IRT (26 items)



13.3.7 Internal consistency

The internal consistency reliabilities of the 26-item version M-CAST were good (*Cronbach's alpha*=0.81)[466, 467]. The internal consistency of the items on Social and Communication factor was good (*Cronbach's alpha*=0.80) and was acceptable on Inflexible/Stereotyped Language and Behaviours (*Cronbach's alpha*=0.71).

13.4 Discussion

13.4.1 Overall findings

This chapter explored the psychometric properties of the M-CAST using a combined CDFA/IRT analysis within 4-11 years old children from both the general population and clinical settings in mainland China. The exploratory CDFA suggested a two-factor solution for the M-CAST with 26 items. This solution was then confirmed as adequate by a multidimensional IRT model. The two factors identified were Social and Communication, Inflexible/Stereotyped Language and Behaviours.

13.4.2 Limitations

The first limitation of this study is the representativeness of the study sample. Both children with existing diagnosis of ASC and children in the general population were recruited. Most of the children with an existing diagnosis were children with Childhood Autism who were at the more severe end of the spectrum. This sampling approach has been adopted in a previous study in the UK[442]. The combined sample will not be representative of the general population in mainland China. Thus, the item endorsement on the M-CAST had limited power to represent the distribution of each item in the general population. Within the population sample, there were only six cases, which had not adequate power to identify the psychometric properties for the M-CAST which has 31 items. However, the CAST was developed in the general population in the UK where children with ASC are integrated into mainstream schools. In mainland China, children with ASC were found to have been turned away from mainstream schools[468]. Thus, the mainstream school population in mainland China may not be comparable to the mainstream population in the UK. This sampling strategy was to produce a more

heterogeneous sample with an appropriate proportion of individuals with ASC and typically developing children. Although most studies on factor analysis were conducted in clinical samples, it was suggested by previous study on factor analysis using the ADI-R that studies examining measurement factor structure should also be performed in more heterogeneous samples with a greater proportion of individuals who do not meet diagnostic criteria for the disorder[436]. In addition, due to the missing values, not all the questionnaires originally collected back were used for this analysis. However, 91% of questionnaires were fully completed and it is unlikely that the excluded questionnaires would affect the results of the factor structure.

The second is the study design. The total sample size used in this study was not large enough to be separated for an exploratory and an external confirmatory analysis. Therefore, the underlying latent traits of the M-CAST was identified by the CDFA and then confirmed in the same sample. Thus, this study was to explore the factor structure of the M-CAST but not an external validation. In order to validate the identified latent traits, the confirmation CDFA needs to be conducted in another Chinese population.

Personal judgements were required in the factor analysis during the reduction of items which may influence the results[29]. Those judgements included choice of criteria for salient loading, the factor extraction, and the criteria for indices of model fit. However, the choices of inclusion criteria adopted in this study were consistent with previous studies[436, 443, 444]. Although the model of best fit comprised 19 items, the model with 26 items was considered as acceptable. However, seven items had low item discrimination or item difficulty values. This indicated future revisions of the M-CAST should improve those items in order to better reflect the underlining latent trait.

13.4.3 Item characteristics on the M-CAST

During the exploratory analysis, item 20 and item 23 were found cross-loaded and item 14 did not saliently load on either factor. This might be due to the fact that those items were related to both factors. Item 14 (Preoccupation by an interest) could be considered as the combination of item 13 (Same interests as peers) and item 9 (Do same thing over

and over again). The former belongs to factor 1 and the latter belongs to factor 2. Item 23 (Turn-taking conversation-factor 1) could be reflected by item 11 (Keep two-way conversation-factor 1) and item 36 (Turn conversation to his/her own interests-factor 2). The autistic features described by item 20 (Unusual voice) may related to both factors. These findings suggested two issues about the current M-CAST. First, several items on the M-CAST may capture the same or similar autistic features that reflect the same underlying latent trait. Second, several items may contribute useful information about more than one latent traits of ASC. In addition, three items (item 1, 31, 35) on Factor 1 and four items (item 7, 9, 18, 37) on Factor 2 had poor item discrimination parameters which indicated those items might not discriminate well at the extreme end of the latent trait. It would be worth examining those items further to determine whether the translation of wording or the content of those items needs revision.

13.4.4 Psychometric properties of the M-CAST

A three-factor solution was suggested by the CDFA. Factor 3 included two items (16 and 19) focusing on the unusual ability of remembering details that children with ASC might have. This ability could be considered as one of the unusual talents that have been observed in children with Asperger Syndrome[469-472]. This potential factor had been proposed by two studies based on the data from AQ[441, 442]. However, there has been a move towards combining the social deficits and communication deficits together as a social-communication factor, and considering the repetitive behaviours, interests and activities (RBIA) as another separate factor[445]. The two-factor solution indentified in this chapter was in line with other previous studies as well as the proposed changes of diagnostic categorisation in the development of DSM-V[19]. One study investigated the factor structure of the ADI-R algorithm and suggested a two-factor solution: Stereotyped Language and RBIA, and Impairments in Social Interaction and Communication[436]. Another study on the ADI-R algorithms also identified two factors including Social/Communication and Restricted/Repetitive Behaviours[435]. A similar factor solution was also proposed by one study based on another screening questionnaire, the AAA[15, 445]. Although there were differences in study design, study sample, and the study instruments between this study and the previous studies, similar results were found, which can

provide some evidences to the two-factor solution of latent autistic traits. However, as mentioned before, most of the other studies were conducted in clinical samples and previous studies using population samples have identified more latent autistic traits in general populations[438]. Due to the sample size of this study is limited and it was an exploratory rather than confirmatory, further research is needed to investigate the latent traits in larger sample of Chinese population. In addition, it would be valuable to incorporate the findings from current study into the revision of the M-CAST since the understanding of certain items by Chinese parents was found to be potentially different from Western parents.

13.5 Conclusion

The factor structure of the M-CAST items was explored using a combination of the CDFA and the IRT. A two-factor solution was proposed, which comprised Social Communication and Inflexible/Stereotyped Language and Behaviours. The IRT analysis demonstrated the M-CAST measured the two latent traits adequately. In addition, the two factors measured by the M-CAST provided some evidence to support that symptom manifestation of ASC in Chinese children shared some similarity with Western populations.

Chapter 14: Discussion

Little has been known about the situation of ASC in China. The few available studies mainly focused on one type of ASC (Childhood Autism), which have reported much lower prevalence estimates than those from developed countries. However, direct comparison is difficult partly due to the screening and diagnostic instruments used in previous Chinese studies were different from those in developed countries. It has been suggested that ASC has been understudied in China[72]. This thesis set out to investigate current service provision for children with ASC in China and to begin to assess the utility of a Mandarin Chinese version of a UK-developed screening instrument, the Mandarin Childhood Autism Spectrum Test (M-CAST), in the Chinese population. A number of aims were outlined at the beginning of this thesis. A summary of these aims is set out in Box 14.1, followed by chapters that have achieved to address them.

Box 14.1 Aims and corresponding chapters of this thesis

- To systematic review the existing literature on the prevalence of ASC in mainland China, Hong Kong and Taiwan (Chapter 3)
- To systematic review screening and diagnostic instruments of ASC in mainland China (Chapter 4)
- To review literatures on service provision for ASC in mainland China(Chapter 5)
- To investigate the service provision for ASC in mainland China from service providers' perspective (Chapter 6)
- To investigate the service provision for ASC in mainland China from service users' perspective (Chapter 7)
- To investigate the service provision for ASC in Hong Kong from service users' perspective (Chapter 8)
- To pilot the M-CAST in Chinese population (Chapter 9)
- To validate the M-CAST using standardised instruments (Chapter 10)
- To investigate the test-retest reliability of the M-CAST (Chapter 11)
- To compare the utility of the M-CAST with the CABS (Chapter 12)
- To examine the psychometric properties of the M-CAST (Chapter 13)

14. 1 Overview of results

14.1.1 Systematic review of prevalence studies for ASC in mainland China, Hong Kong and Taiwan

Pooled prevalence of Childhood Autism was 11.8 per 10,000 (95% CI : 8.2, 15.3) in mainland China. Pooled prevalence of ASC was 26.6 per 10,000 (95%CI: 18.5, 34.6) in mainland China, Hong Kong and Taiwan. The choice of sreening instruments explained the most of the change in prevalence estimates. After adjustment for age, the prevalence estimates for Childhood Autism in studies using the ABC as the screening instrument was 71% lower than those using the CABS (odds ratio: 0·29; 95% CI: 0·12, 0·69, p<0·001). The prevalence estimates from studies using the CHAT were 79% higher than those using the CABS (OR: 1·79; 95% CI: 0·70, 4·55; P=0·20). No population-based prospective prevalence studies on ASC have yet been published in Hong Kong and Taiwan. Studies in mainland China have methodological weaknesses and, cannot be easily compared with those from developed countries.

14.1.2 Systematic review of screening and diagnostic instruments for ASC in mainland China

The CABS, the ABC as screening instruments and the CARS as a diagnostic instrument were the most frequently used for case identification for ASC in mainland China. They were adopted from the West more than two decades ago for detecting Childhood Autism. The concept of the autism spectrum had not yet been more generally introduced and standardised instruments for case identification of ASC have not been adopted in autism research in mainland China.

14.1.3 Systematic review of service provision for ASC in mainland China

Four service settings for ASC, largely focused on autism, were identified including healthcare settings, mainstream educational settings, private special intervention settings, and state-run special educational settings. Shortage of resources in educating health professionals and the general public was reported to have contributed to the delay in identification and diagnosis of ASC and, subsequently, the implementation of

interventions. A lack of awareness and misunderstanding about autism in society was reported to aggravate obstacles to the education inclusion for children with ASC.

14.1.4 Service providers' perspective on service provision in mainland China

Providers perceived that children with ASC were an important but under-served group in mainland China. Two levels of service provision related to ASC were identified: 1) healthcare services mainly provided by government authorities; and 2) education services mainly provided by the parents of children with autism. Little cooperation was reported between the two types of providers. The structure of service provision for ASC is under-developed.

14.1.5 Service users' perspective on service provision in mainland China

Parents and caregivers reported an average of 7.1 months' delay between first developmental concerns about their children and receiving a diagnosis of ASC. There was an average 6.5 months' delay between receiving the diagnosis and commencing interventions. Several cultural issues were identified which could contribute to the delay, such as the perception of mental illness, and folk beliefs equating delayed development of language skills in early childhood as an indication of future high intelligence, and the state-imposed one-child policy. Delay in recognition of ASC and lack of support was considered to be associated with considerable burden parents reported.

14.1.6 Service users' perspective on service provision in Hong Kong

The long waiting period due to lack of professionals and potential cultural influence contributed to the delay in early detection and intervention of ASC. Screening programme and multi-disciplinary assessments are available for the identification of ASC in Hong Kong. However, the identification of ASC did not depend on the screening but more on the parental recognition and referral to hospital. Most children under six years old with ASC attend specific intervention programmes in non-profit rehabilitation centres supported by the government. Parents expressed concerns about their children's education after six years old since no specific facilitates for ASC are available for children older than six.

14.1.7 Pilot study

Using the UK cut-off of 15, the M-CAST was able to distinguish children with ASC from typically developing children in mainland China. Eight items out of 31 on the M-CAST did not have any significant difference in item endorsement between cases and controls. Cultural influences may be operating on certain items on the M-CAST.

14.1.8 Validation study

The sensitivity of M-CAST was 84%, and the specificity was 96%. The PPV was expected to be relatively low (22%) due to the fact that the prevalence of the condition in the general population was low[8, 473]. There were gender differences in the score distribution of the M-CAST. The verification of 50 children who already had an autism diagnosis showed all cases met research diagnostic criteria for ASC using the ADOS and the ADI-R. Most of the cases were given an autism diagnosis.

14.1.9 Test-retest reliability

Over a period of two to four months, using a cut-off of 15, the test-retest reliability of the M-CAST was good by same responders (*kappa*=0.64). The test-retest reliability of three categories (≤11, 12-14, ≥15) was moderate (*weighted kappa*=0.48-0.53). Correlation between the scores at CAST-1 and CAST-2 was good (*Spearman rho*=0.70-0.73).

14.1.10 Comparison between the M-CAST and the CABS

Within the comparison sample, using the cut-off of 15, the sensitivity of M-CAST was 89%, the specificity was 80%, and the PPV was 70%. Using the cut-off of 14, the sensitivity of CABS was 58%, the specificity was 84%, and the PPV was 65%. The M-CAST showed a better association with standardised instruments (ADOS & ADI-R) than the CABS. The AUC of the M-CAST was 0.90, which was significantly higher than the CABS (AUC=0.79). These findings suggested the M-CAST performed significantly better than the CABS in distinguishing children with ASC from typically developing children in mainland China.

14.1.11 Psychometric properties of the M-CAST

The M-CAST was found to have a multi-dimensional structure. The final model from the CDFA was a two-factor solution with 26 items on the M-CAST. The two factors were Social and Communication, and Inflexible/Stereotyped Language and Behaviours. This two-factor solution was further confirmed as adequate by the IRT analysis. Items on the 26-item M-CAST discriminated well at the more extreme end of the autistic latent trait. The internal consistency reliability of the 26-item version of the M-CAST was good.

14.2 Strengths and limitations of these studies

14.2.1 Strengths

The qualitative study on service provision provided insight on the situation of ASC in China which has seldomly been investigated so far. One strength was the study design which investigated the perceptions from both service providers and users to reflect the whole picture of how the system worked for children with ASC and their families. The sample for service provision in mainland China was drawn from 19 different regions to generalise the service pathway from first awareness to intervention. The sample from Hong Kong enhanced the representation of the whole country of China. In terms of method, the questionnaire of service mapping was developed as the study proceeded through face-to-face interviews with parents/caregivers from different regions. This approach provided an opportunity to collected data using unified protocol which allowed further comparison of results.

The main strength of the validation study was the population-based approach. It achieved a high participation rate in screening and further assessment. In previous UK studies, the participation rate has been generally under 30% for population-based studies[70]. The Chinese validation had a 97% participation rate, which ensured the representative of the general population in the studied region.

Another strength of the validation study is of the methodology of case identification. Verification of autistic cases that had been diagnosed by Chinese clinicians prior to this

study ensured the diagnostic status of the cases and also verified the assumption that previously diagnosed cases were mainly cases of an extreme end on the spectrum. Second, the diagnostic assessment adopted the ADOS and the ADI-R, which was the method that has been used in recent epidemiological studies in the West. Thus, the assessment results can be compared with those from Western countries directly. In addition, the RRM was used as an IQ test to supplement the final research diagnosis of the ASC, which was lacking in previous studies of the UK CAST.

The quality of results in validation study was ensured by the following approaches: 1) Possible areas of bias were minimised. The examiner of diagnostic assessments was blind to the child's M-CAST score. In the diagnostic assessment phase, the sampling of a proportion of children who scored in the low score group reduced assessor bias, since not all the children assessed were likely to have developmental problems. 2) The missing data were handled by using both ASC-positive and ASC-negative scores to generate maximum and minimum score. The analysis was conducted for both scores in order to achieve maximum capture of potential cases in the assessment phase. The difference in results by using different scores was also examined to ensure the missing data did not influence the general findings.

Another strength is the comparison between the M-CAST and the CABS which demonstrated the utility of the M-CAST in Chinese population from another angle. The M-CAST demonstrated better validity and association with standardised diagnostic instruments than the CABS. This approach gave some evidence of how the M-CAST may be more suitable to be used in large epidemiological studies in China than the instrument that is currently used.

14.2.2 Limitations

One source of limitation in service provision study was the representativeness of the sample in mainland China. The sample of parents was recruited from two of the most well-known private intervention centres. The parents from those centres are unlikely to be nationally representative for mainland China. In order to enter those centres, one parent

needed to give up their jobs and accompany the child in the centres. Some of them need to leave their hometowns. As the centres are private, the parents needed to pay the tuition fees themselves. These actions required a financial sacrifice. Thus, not all the parents in mainland China can afford to do this. In general, these were the families that had gone through the most service pathway and reached the intervention, while there should be other parents who are still at the early phase of the service pathway. Thus, these parents could represent service users who had reached the extreme end of the service. The Hong Kong sample should be considered as having reasonable generalisation for the population in Hong Kong, since they were drawn from the general system for ASC. However, the centres involved in the investigation of service provision only accepted children aged three to six in mainland, and children aged two to six in Hong Kong. Thus, it may be possible that older children with ASC in those regions had different experience or have undergone different pathways.

Another limitation of the service provision was that it based on semi-structured interviews, which had limitations when accessing more in-depth information. Further research for the measurement development of service evaluation should employ multiple interviews and longer-term observation of families.

One limitation of the validation study was that the sample was drawn from one district in Beijing city. Due to Beijing's special political and economic status[378], it is considered as not a national representative region for mainland China. Parents in Beijing are considered to have a higher socioeconomic status as they are likely to be better-educated and more up to date with knowledge and new technology[378]**.** Previous research had suggested the inconsistent effect of socioeconomic status towards the risk of having ASC in the West[474-477]. More recent large population-based studies suggested that lower socioeconomic status predicted a higher risk of ASC[474] whereas previous studies suggested the opposite[475, 478]. Thus, caution needs to be employed when applying the results reported in this study to a national level.

Another weakness of the studies on the M-CAST was that there was no prospective data collection of a clinical sample. Due to the relatively limited study period and the lack of resources in clinical settings, it was not possible to recruit children with ASC prospectively for this thesis. The autistic cases in the pilot and validation studies were recruited from existing records. As expected children with an existing diagnosis of ASC scored significantly higher on the M-CAST than children who were given an ASC diagnosis after further assessment. It is possible that parents whose children had been diagnosed prior to this study had more knowledge of autistic behaviours than the parents whose children had not been diagnosed before. The former have already been through the phase of seeking information from first awareness to diagnosis, and they may be familiar with some diagnostic instruments after the diagnostic process. Thus, because of their experience, they may have a better understanding of what the items on the M-CAST were looking for than the latter.

In the validation, all ADOS and ADI-R assessments were conducted by a single examiner within a relatively short period of time. Due to the limitation of resources, interrater reliability could not be conducted. However, the researcher was a reliable examiner with technical support from senior examiners in Cambridge during the assessment phase. The final diagnosis was made according to the consensus diagnosis between examiners and experienced child psychiatrists. Thus, it is unlikely this could have introduced bias and influenced the results. Future research should ensure that consensus coding meetings for equality control of the assessment reliability will be conducted throughout the assessment phase.

The sample of the psychometric properties study was a combination of clinical sample and general population. Although, there were studies using such combined sample for factor analysis in China[479] and the West[433], this approach needs to be further investigated in turns of its representativeness of the Chinese population.

14.3 Implications for study design and instrument development

Since there was no systematic network for tracking on the healthcare or education pathway of children with ASC, a top-down method was adopted. The questionnaire used for mapping service provision in China was developed on a sample of 69 parents and 34 parents in Hong Kong. It contains 50 questions. In the future, a combined version should be developed that can be applicable to different regions in China. A relatively shorter version of this questionnaire with self-completion answers can be developed for large population-based survey on service evaluation. Without face-to-face interview, research time and resources can be saved and more data from the general population can be collected.

In the pilot study, the item endorsements in eight items showed no differences between children with ASC and typically developing children. This indicated that these items might not distinguish well and need refinement. Since some of the wording of these items were similar, it might be valuable to consider dropping or combining a few of these items, and then validating the new version of the M-CAST.

The sample of the validation study was relatively small and the participants were only in mainstream schools. As mentioned before, in mainland China, children with mental disorders were suggested to have been turned away from mainstream schools for a long time. Most children with ASC were found in special intervention centres for ASC or special education schools. While the CAST was developed in the UK population in which children with special conditions are integrated in mainstream schools. Thus, it would be valuable to apply the M-CAST in both mainstream and special schools and centres in mainland China in order to get a more representative population sample.

The test-retest reliability of the M-CAST had a period of two to four months between the completions of two CASTs. Further examination on the reliability should have shorter time lag and ensure that the same parent/caregiver completes the two CASTs. In addition, the reliability was tested in a sample consisting of a larger proportion of high score

children on the M-CAST. It might be valuable to further examine the reliability in a more representative sample of the general population to gain additional evidence.

The interrater reliability of the M-CAST needs to be explored. During the test-retest reliability study, the scores on the M-CAST completed by fathers were found significantly different from those completed by mothers for the same child. This suggested potential different perceptions on the child's behaviours between father and mother. Since these findings were drawn from a small sample of 34 children, it will be helpful to further explore this difference and the interrater reliability in a larger sample.

The comparison between the M-CAST and the CABS was conducted in the assessment sample of the validation study. The same was relatively small and not representative for the general population. It would be helpful to apply the M-CAST to a larger population. If similar result is found, it might be valuable to consider replacing the CABS with the M-CAST in further epidemiological research.

The exploratory of the psychometric properties of the M-CAST suggested that three items did not load saliently on any of the identified two factors. There might be three factors, but the third factor was excluded because only two items saliently loaded on it. It is possible that, if new items focusing on the third factor are added, all items can saliently load on one of the factors. In addition, different analytical approaches might be adopted for future factor analysis such as conducting the principle component analysis in STATA first and then the IRT in MPlus. In order to examine the stability of the latent traits measured by the CAST in different cultures to ensure the utility of CAST is across-culturally stable, it will be helpful to conduct multi-group factor analysis to samples from both UK and China and make comparison. This approach could help to understand the nature and presentation of the latent traits of ASC which has taken the cultural influence into account.

14.4 Recommendations

14.4.1 Population Screening

The M-CAST cannot be recommended as a whole population screening instrument for ASC in China in its current format. The current version generates a large proportion of false positives. If applied to whole regional population directly, a large amount of resource will be required for assessing all children who actually do not have ASC. This could also possibly cause unnecessary anxiety for their families. However, it can be considered as a promising screening instrument for ASC after revision due to the fact that, unlike studies in the West, epidemiological studies in mainland China under proper administration can achieve very high response rates at a relatively low cost.

14.4.2 Use in primary care, clinical and educational settings

Since this was the first study on the M-CAST, the utility of the M-CAST in other settings requires further investigation. Therefore, recommendations cannot yet be made for its use in other settings. However, learning from the experience on the UK CAST, it might be helpful to consider recommending the M-CAST in certain contexts in the future after adequate validation and proper understanding of these contexts.

The primary care system in mainland China has undergone great reforms and changes since the late 1990s and early 2000s. In 2003, the government established a rural Cooperative Medical Scheme to protect people from catastrophic losses[480]. In urban areas, the government aimed to assign primary care to community health centres and hospitals for inpatient care[481]. As a result, family medicine, which can be considered as equivalent to the General Practice in the West, will become the major provider of primary healthcare in urban areas[482]. The new reform of the health system in China was announced in 2006, which addressed the leading role of family physicians in community health centres for primary care[482]. The establishment of universal coverage of primary care for both rural and urban areas by 2020 within mainland China has been set up as a target by the government[483]. It is possible that, when the new primary care system is established, the

validation of the M-CAST can be conducted in primary care settings. However, before this, it needs revision in order to improve its performance in a low prevalence setting.

After full validation, it is possible for the M-CAST to be used in clinics or special centres for assessment purposes with other assessments. In order to apply the M-CAST to schools, a teacher's version should be developed and validated. The applicable age range of the M-CAST is from 4 to 11 years. So far, there has been no evidence that the M-CAST can be applied to children outside this age range.

14.4.3 Research context

The M-CAST demonstrated acceptable validity and reliability as a screening instrument for ASC within the Chinese population. It can be recommended for epidemiological research on ASC in China. For example, it could be used in a large population-based study to estimate the prevalence of the whole autism spectrum. It can also be used as an instrument to detect social and communication difficulties in the general population. It has potential to be used in studies that focus on the comparison between children with ASC and their siblings in normal development, which might help with further aetiological or genetic studies. It can also be used in studies focusing on the comparison of autistic features between the Western and Chinese populations.

14.5 Ongoing research with the M-CAST

The work described in this thesis has provided the groundwork for a large epidemiological study. After revision, the M-CAST is going to be used as a screening instrument in a large population-based prevalence study in mainland China, the Social and Communication Research and Epidemiological study in China (China SCORE). The M-CAST will be distributed to children who are in school years 1 to 4 (aged 6-11) in six cities selected from six provinces in mainland China. In order to capture all children in this age range, mainstream schools, special education settings and intervention centres will be covered as many as possible in the six cities. Due to limited resources, not all children participated in screening will be invited to further diagnostic phrase. Two cities with preferable representativeness as well as available resources will be selected. A

proportion of children in those two selected cities will receive a diagnostic assessment using the ADOS and the ADI-R. This will provide the distribution of the M-CAST score in the whole regional population in mainland China. The utility of the M-CAST will be re-evaluated in this large epidemiological study. Within this study, the validity, reliability, as well as the psychometric properties of the M-CAST will be further investigated. In addition, children who already have a diagnosis of ASC will be tracked through the health system in the studied cities. With the existing records in the health system and a previous national survey of disability, the number of existing cases and new identified cases in children aged 6-11 in the general population can be identified. With the geographical records from National Bureau of Statistics, this study will provide a prevalence estimate of ASC within the primary school aged population in mainland China. A research protocol is provided in Appendix 14.1. At the same time, a pilot and validation study of the M-CAST will be conducted in Hong Kong using similar methodology described in this thesis. Following the validation, a prevalence study will be conducted in Hong Kong using similar methodology as the China SCORE study to generate the prevalence of ASC in Hong Kong.

14.6 Further development of the M-CAST

There has been no screening instrument available for ASC in primary school aged children in China before the M-CAST. Further investigation is required to improve the M-CAST, possibly through the following research listed in Box 14.2.

Box 14.2 Further research on the M-CAST

- Investigate the utility of the M-CAST in distinguishing children with ADHD, learning difficulty or language delay.
- Investigate the perception of items on the M-CAST among Chinese parents.
- Examine cultural influences (such as stigma, eye contact, language delay) more extensively and revise the M-CAST accordingly.
- Add pre-screening questions regarding parental concern with the child's development to test the utility within children whose parents have concerns.
- Remove items that have similar wordings or do not differentiate well.
- Add new items on Attention to Details or on repetitive, restricted and stereotyped behaviours, interests and activities.
- Investigate scoring of the M-CAST by comparing current additive scoring with weighted scoring based on the latent autistic traits identified in IRT.
- Re-examine the psychometric properties of revised M-CAST in a large and more representative population.
- Evaluate the interrater reliability of the M-CAST.
- Compare the M-CAST with other currently used screening instruments in mainland China such as the ABC.
- Develop a teacher's version of the M-CAST.

14.7 Contribution of this thesis

This thesis presents evidence on the epidemiology of ASC in China. Existing knowledge in developed countries on ASC was summarised including the condition, international diagnostic criteria, recent prevalence studies, available screening and standardised diagnostic instruments as well as the importance of prevention and intervention. Detailed systematic reviews illustrated the availability of service provision, prevalence estimates of ASC, as well as currently-used screening and diagnostic instruments in mainland China. This thesis has contributed new evidence to service provision of ASC in mainland China and Hong Kong. It developed a Mandarin version of an English screening instrument and adopted standardised diagnostic instrument to autism research in China. The suitability of the M-CAST as a screening instrument in the Chinese population was investigated. The standardised diagnostic instruments on ASC, the ADOS and the ADI-R, were applied to the Chinese general population for the first time. The M-CAST can be recommended as a screening instrument for ASC in large epidemiological studies in mainland China after revision. This is a starting point in developing autism research in mainland China, and there is much to be done through further epidemiological research and long-term follow-up to achieve better utility of the M-CAST.

14.8 The future of service provision in China

Service provision for children with ASC has not been unified or systematically implemented in mainland China. Current provision involved various systems including healthcare, education, and intervention. So far, there has been little cooperation and interaction between those systems, thus the network for ASC in mainland China has not been well-developed. Several areas for potential service development drawn from studies in this thesis are listed in Box 14.3.

Box 14.3 Future directions for service provision for ASC in China

- Conduct surveys to investigate the knowledge and awareness of ASC and explore stigma in the general population.
- Improve medical education of ASC in general medical training, especially among child psychiatrists and paediatricians.
- Conduct workshops on ASC for practice physicians both in hospitals and community health centres.
- Provide workshops and study materials on ASC to teachers both in mainstream schools and special schools.
- Develop and validate intervention programmes for their adaptation in Chinese population.
- Study the structure of in house training and professional development of current successful intervention centres to develop learning materials for other centres.
- Provide more support to both state-run and private intervention centres.
- Establish standardised and systematic regulation on the operation of intervention centres.
- Establish network of service provision between various systems for ASC.
- Develop clear pathway guidelines from diagnosis to intervention.
- Develop a special education strategy for children with ASC who are older than six.
- Improve the education inclusion for children with ASC.
- Apply refined screening and diagnostic instruments to primary care system for screening and to hospitals for diagnosis.

14.9 The future of research on ASC in China

The research described in this thesis is a starting point to introduce advanced screening and diagnostic instruments for ASC to China, especially mainland China. The adoption of standardised instruments can help to improve the comparability of case identification between Western and Chinese populations. After the identification of autistic cases, further research can be conducted in various areas related to ASC. Through the introduction of advanced research methodology from the West, the research capacity of ASC in China can be gradually built up. This needs to include the following listed in Box 14.4.

Box 14.4 Future directions for autism research in China

- Introduce well-developed culturally appropriate screening instruments from the West for different age groups and subtypes of ASC.
- Further development of the adoption of the ADOS and the ADI-R.
- Build up well-trained examiner teams of the ADOS and the ADI-R.
- Establish the diagnosis of other subtypes within the autism spectrum such as Asperger Syndrome and PDD-NOS and also take the DSM-V revisions into account.
- Establish a database for autism surveillance and research.
- Set up cohort studies to monitor the prevalence of ASC for public health education and evaluation.
- Conduct case-control studies to investigate the natural history and aetiology of ASC.
- Conduct comparison research between Western and Chinese populations to test aetiological hypothesis.
- Develop and validate culturally adapted intervention programmes.

14.10 Conclusions

The system of healthcare and education service provision for ASC in mainland China has not been established. Service provision in Hong Kong is better developed than mainland China, but still needs improvement. The M-CAST has demonstrated good validity as a screening instrument for ASC, and showed better utility than the CABS, a currently used screening instrument in mainland China, although the positive predictive value is relatively poor. It has demonstrated good test-retest reliability and appropriate psychometric properties for screening, and shown to be a promising candidate for population-based epidemiological research. Recommendations for further research on the M-CAST and service provision are made. After revision and further validation, the M-CAST could be recommended for use in settings other than research such as hospitals, primary care, and mainstream and special education settings. This thesis provides the underpinning for the first large epidemiological study of ASC across China including Hong Kong.

References

1. WHO. *The ICD-10 Classification of Mental and Behavioural Disorder: Diagnosis Criteria for Research.* Geneva: WHO; 1993.

2. Williams JG, Higgins JP, Brayne CE. Systematic review of prevalence studies of autism spectrum disorders. *Arch Dis Child.* 2006;91(1):8-15.

3. Wing L. Language, social, and cognitive impairments in autism and severe mental retardation. *J Autism Dev Disord.* 1981;11(1):31-44.

4. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders.(DSM-IV) (4th ed.).* Washington DC: APA: American Psychiatric Association; 1994.

5. Newschaffer CJ, Croen LA, Daniels J, et al. The epidemiology of autism spectrum disorders. *Annu Rev Public Health.* 2007;28:235-258.

6. Wilson J, Jungner G. *The Principles and Practice of Screening for Disease.* Geneva: WHO; 1968.

7. Porta M. *A dictionary of epidemiology*: A handbook sponsored by the I.E.A.Oxford Press.; 2008.

8. Webb P. *Essential Epidemiology: An introduction for students and health professionals*: Cambridge University Press; 2005.

9. Kanner L, Eiisenberg L. Early infantile autism, 1943-1955. *Psychiatr Res Rep.Am Psychiatr Assoc.* 1957(7):55-65.

10. Croen LA, Grether JK, Hoogstrate J, Selvin S. The changing prevalence of autism in California. *J Autism Dev Disord.* 2002;32(3):207-215.

11. Blaxill MF. What's going on? The question of time trends in autism. *Public Health Reports.* 2004;119(6):536-551.

12. Asperger H. Autistic psychopathy in childhood (1944)-translated and annotated by U. Frith. in: Frith U, editor. *Autism Asperger Syndrome.* 1991:p.37-p.92.

13. Williams J. *Screening for autism spectrum disorders*, University of Cambridge; 2003.

14. Rutter M. Incidence of autism spectrum disorders: changes over time and their meaning. *Acta Paediatr.* 2005;94(1):2-15.

15. Baron-Cohen S, Wheelwright S, Robinson J, Woodbury-Smith M. The Adult Asperger Assessment (AAA): a diagnostic method. *J Autism Dev Disord.* 2005;35(6):807-819.

16. Boyd BA, Baranek GT, Sideris J, et al. Sensory features and repetitive behaviors in children with autism and developmental delays. *Autism Res.* 2010;3(2):78-87.

17. Wing L, Gould J. Severe impairments of social interaction and associated abnormalities in children: epidemiology and classification. *J Autism Dev Disord.* 1979;9(1):11-29.

18. American Psychiatric Association. *Diagnostic and statistical manual of mental disorders. 3rd ed.rev*. Washington: American Psychiatric Association; 1980.

19. Ghaziuddin M. Should the DSM V drop Asperger syndrome? *J Autism Dev Disord.* 2010;40(9):1146-1148.

20. Matson JL, Hattier MA, Williams LW. How Does Relaxing the Algorithm for Autism Affect DSM-V Prevalence Rates? *J Autism Dev Disord.* 2012.

21. Kanner L. Early infantile autism revisited. *Psychiatry Dig.* 1968;29(2):17-28.

22. Rutter M. Autistic children: infancy to adulthood. *Semin Psychiatry.* 1970;2(4).

23. American Psychiatric Association. *Diagnostic and Statistical Manual of mental disorders. 3rd ed., rev.(DSM-III-R)*. Washington DC.; 1987.

24. American Psychiatric Association. *Diagnostic and statistical manual of mental disorders, DSM-IV-TR*. Washington DC: American Psychiatric Association; 2000.

25. American psychiatric Association. Proposed revision of DSM-V: Autism Spectrum Disorder. http://www.dsm5.org/ProposedRevision/Pages/proposedrevision.aspx?rid=94.

26. Johnson CP, Myers SM. Identification and evaluation of children with autism spectrum disorders. *Pediatrics.* 2007;120(5):1183-1215.

27. Lord C, Rutter M, Le Couteur A. Autism Diagnostic Interview-Revised: a revised version of a diagnostic interview for caregivers of individuals with possible pervasive developmental disorders. *J Autism Dev Disord.* 1994;24(5):659-685.

28. Charman T. Autism Spectrum Disorders. *Elseiver Ltd.Psychiatry.* 2008.

29. Allison C, Baron-Cohen S, Wheelwright S, et al. The Q-CHAT (Quantitative CHecklist for Autism in Toddlers): a normally distributed quantitative measure of autistic traits at 18-24 months of age: preliminary report. *J Autism Dev Disord.* 2008;38(8).

30. Mundy P, Crowson M. Joint attention and early social communication: implications for research on intervention with autism. *J Autism Dev Disord.* 1997;27(6):653-676.

31. Wetherby AM, Watt N, Morgan L, Shumway S. Social communication profiles of children with autism spectrum disorders late in the second year of life. *J Autism Dev Disord.* 2007;37(5):960-975.

32. Leekam SR, Lopez B, Moore C. Attention and joint attention in preschool children with autism. *Dev.Psychol.* 2000;36(2):261-273.

33. Kjellmer L, Hedvall A, Fernell E, Gillberg C, Norrelgen F. Language and communication skills in preschool children with autism spectrum disorders: Contribution of cognition, severity of autism symptoms, and adaptive functioning to the variability. *Res Dev Disabil.* 2012;33(1):172-180.

34. Charman T, Drew A, Baird C, Baird G. Measuring early language development in preschool children with autism spectrum disorder using the MacArthur Communicative Development Inventory (Infant Form). *J Child Lang.* 2003;30(1):213-236.

35. McConachie H, Le CA, Honey E. Can a diagnosis of Asperger syndrome be made in very young children with suspected autism spectrum disorder? *J Autism Dev Disord.* 2005;35(2):167-176.

36. Lord C, Rutter M, Goode S, et al. Autism diagnostic observation schedule: a standardized observation of communicative and social behavior. *J Autism Dev Disord.* 1989;19(2):185-212.

37. Honey E, Leekam S, Turner M, McConachie H. Repetitive behaviour and play in typically developing children and children with autism spectrum disorders. *J Autism Dev Disord.* 2007;37(6).

38. Volkmar F, Chawarska K, Klin A. Autism in infancy and early childhood. *Annu Rev Psychol.* 2005;56.

39. Wing L, Gould J, Gillberg C. Autism spectrum disorders in the DSM-V: better or worse than the DSM-IV? *Res Dev Disabil.* 2012;32(2):768-773.

40. Imran N, Chaudry MR, Azeem MW, Bhatti MR, Choudhary ZI, Cheema MA. A survey of Autism knowledge and attitudes among the healthcare professionals in Lahore, Pakistan. *BMC Pediatr.* 2011;11:107.

41. Ospina MB, Krebs SJ, Clark B, et al. Behavioural and developmental interventions for autism spectrum disorder: a clinical systematic review. *PLoS One*. 2008;3(11):e3755.

42. Blenner S, Reddy A, Augustyn M. Diagnosis and management of autism in childhood. *BMJ*. 2011;343:d6238.

43. Ozonoff S, Heung K, Byrd R, Hansen R, Hertz-Picciotto I. The onset of autism: patterns of symptom emergence in the first years of life. *Autism Res.* 2008;1(6):320-328.

44. Kalb LG, Law JK, Landa R, Law PA. Onset patterns prior to 36 months in autism spectrum disorders. *J Autism Dev Disord.* 2010;40(11):1389-1402.

45. Siperstein R, Volkmar F. Brief report: parental reporting of regression in children with pervasive developmental disorders. *J Autism Dev Disord.* 2004;34(6):731-734.

46. Kleinman JM, Ventola PE, Pandey J, et al. Diagnostic stability in very young children with autism spectrum disorders. *J Autism Dev Disord.* 2008;38(4):606-615.

47. Manning SE, Davin CA, Barfield WD, et al. Early diagnoses of autism spectrum disorders in Massachusetts birth cohorts, 2001-2005. *Pediatrics.* 2011;127(6):1043-1051.

48. Baird G, Charman T, Cox A, et al. Current topic: Screening and surveillance for autism and pervasive developmental disorders. *Arch Dis Child.* 2001;84(6):468-475.

49. Bryson SE, Rogers SJ, Fombonne E. Autism spectrum disorders: early detection, intervention, education, and psychopharmacological management. *Can J Psychiatry.* 2003;48(8):506-516.

50. Baron-Cohen S, Allen J, Gillberg C. Can autism be detected at 18 months? The needle, the haystack, and the CHAT. *Br J Psychiatry.* 1992;161:839-843.

51. Baron-Cohen S, Cox A, Baird G, et al. Psychological markers in the detection of autism in infancy in a large population. *Br J Psychiatry.* 1996;168(2):158-163.

52. National Screening Committee. National Screening Committee policy-autism screening-current consultation. 2011/12/04/.

53. Ouellette-Kuntz HM, Coo H, Lam M, et al. Age at diagnosis of autism spectrum disorders in four regions of Canada. *Can.J Public Health.* 2009;100(4):268-273.

54. O'Toole BI. Screening for low prevalence disorders. *Aust N Z.J Psychiatry.* 2000;34 Suppl:S39-S46.

55. Zager D. *Autism Spectrum Disorders: Identification, Education, and Treatment 3rd ed*. London: LEA; 2011.

56. Greenhalgh T. How to read a paper. Papers that report diagnostic or screening tests. *BMJ.* 1997;315(7107):540-543.

57. Read C, Lachs S, Feinstein R. Use of methodological standard in diagnostic test research: getting better but still not good. *JAMA.* 1995(274):645-651.

58. Sackett D, Haynes B, Guyatt G, Tugwell P. *Clinical epidemiology: a basic science for clinical medicine*. Boston/Toronto/London: Little Brown and Company; 1991.

59. Sahyoun C, Soulieres I, Belliveau J, Mottron L, Mody M. Cognitive differences in pictorial reasoning between high-functioning autism and Asperger's syndrome. 2009(1573-3432 (Electronic)):1014-1023.

60. Noterdaeme M, Wriedt E, Hohne C. Asperger's syndrome and high-functioning autism: language, motor and cognitive profiles. *Eur Child Adolesc Psychiatry.* 2010;19(6):475-481.

61. Mordre M, Groholt B, Knudsen AK, Sponheim E, Mykletun A, Myhre AM. Is long-term prognosis for pervasive developmental disorder not otherwise specified different from prognosis for autistic disorder? Findings from a 30-year follow-up study. *J Autism Dev Disord.* 2012;42(6):920-928.

62. Hagberg KW, Jick H. Autism in the UK for birth cohorts 1988-2001. *Epidemiology.* 1983;21(3):426-427.

63. Chahrour M, Zoghbi HY. The story of Rett syndrome: from clinic to neurobiology. *Neuron.* 2007;56(3):422-437.

64. Naidu S, Johnston MV. Neurodevelopmental disorders: Clinical criteria for Rett syndrome. *Nat Rev Neurol.* 2011;7(6):312-314.

65. Ogier M, Katz DM. Breathing dysfunction in Rett syndrome: understanding epigenetic regulation of the respiratory network. *Respir Physiol Neurobiol.* 2008;164(1-2):55-63.

66. Le-Couteur A. National autism plan for children (NAPC): Plan for the identification, assessment, diagnosis and access to early interventions for pre-

school and primary school aged children with autism spectrum disorders (ASD). *The National Autistic Society.* 2003.

67. Dover CJ, Le CA. How to diagnose autism. *Arch Dis Child.* 2007;92(6):540-545.

68. Health Do. *Framework for Assessment of Children in Need and their Families.* UK:DH 2000.

69. Wing L, Yeates SR, Brierley LM, Gould J. The prevalence of early childhood autism: comparison of administrative and epidemiological studies. *Psychol.Med.* 1976;6(1):89-100.

70. Baron-Cohen S, Scott FJ, Allison C, et al. Prevalence of autism-spectrum conditions: UK school-based population study. *Br J Psychiatry.* 2009;194(6):500-509.

71. Centres of Disease Control and Prevention. Prevalence of autism spectrum disorders--Autism and Developmental Disabilities Monitoring Network, 14 sites, United States, 2008. *MMWR Surveill Summ.* 2012;61(3):1-19.

72. Sun X, Allison C. A review of the prevalence of Autism Spectrum Disorder in Asia. *Res Autism Spectr Disord.* 2009;4(2):156-167.

73. Dales L, Hammer SJ, Smith NJ. Time trends in autism and in MMR immunization coverage in California. *JAMA.* 2001;285(9):1183-1185.

74. Waterhouse L. Autism overflows: increasing prevalence and proliferating theories. *Neuropsychol Rev.* 2008;18(4).

75. Tao KT. Infantile autism in China. *J Autism Dev Disord.* 1987;17(2):289-296.

76. The Chinese Autism Society. *Ten years' quest of autism in China*. Beijing: Rehabilitation Association of Autistic Children in Beijing; 2003.

77. Shen YC. *Psychiatry*. Beijing: People's Medical Publishing House; 2001.

78. Zhang MY, Yan HQ. Community rehabilitation, and prevention and treatment work for psychoses in Shanghai. *Shanghai Arch Psychiatry.* 1990;2(114):8-10.

79. Li YH, Yao XW, Zhang MY. Investigation and suggestion on community rehabilitation facilities for psychotic patients in Shanghai. *Shanghai Arch Psychiatry.* 2005;17(35):7-8.

80. Ministry of Health, Ministry of Public Security, Ministry of Civil Affairs, China Disabled Persons Federation. *First National Mental Health Plan (2002-2012)* 2002.

81. Park L, Xiao Z, Worth J, Park MJ. Mental health care in China: Recent changes and future challenges. *Harvard Health Policy Review.* 2005;6(2):35-45.

82. China Disabled Persons C, State of People's Republic of C. *12th Development Programme for China Disabled Persons* 2011.

83. Baron-Cohen S, Wheelwright S, Cox A, et al. Early identification of autism by the Checklist for Autism in Toddlers (CHAT). *J R Soc Med.* 2000;93(10):521-525.

84. Lord C, Spence S. Autism spectrum disorders: phenotype and diagnosis. *Moldin SO, Rubenstein JLRUnderstanding Autism: From Basic Neuroscience to Treatment.* 2006:1-23.

85. Fenske EC, Zalenski S, Krantz PJ, McClannahan LE. Age at Intervention and Treatment Outcome for Autistic-Children in A Comprehensive Intervention Program. *Ana Interv Dev Disabils.* 1985;5(1-2):49-58.

86. Harris SL, Handleman JS. Age and IQ at intake as predictors of placement for young children with autism: a four- to six-year follow-up. *J Autism Dev Disord.* 2000;30(2):137-142.

87. Levy SE, Mandell DS, Schultz RT. Autism. *Lancet.* 2009;374(9701):1627-1638.

88. Dawson G. Early behavioral intervention, brain plasticity, and the prevention of autism spectrum disorder. *Dev Psychopathol.* 2008;20(3):775-803.

89. McEachin JJ, Smith T, Lovaas OI. Long-term outcome for children with autism who received early intensive behavioral treatment. *Am J Ment Retard.* 1993;97(4):359-372.

90. Sheinkopf SJ, Siegel B. Home-based behavioral treatment of young children with autism. *J Autism Dev Disord.* 1998;28(1):15-23.

91. Birnbrauer JS, Leach DJ. The Murdoch Early Intervention Program after 2 years. *Behavior Change.* 1993;10:63-74.

92. Cohen H, merine-Dickens M, Smith T. Early intensive behavioral treatment: replication of the UCLA model in a community setting. *J Dev Behav Pediatr.* 2006;27(2 Suppl):S145-S155.

93. Harris SL, Handleman JS, Gordon R, Kristoff B, Fuentes F. Changes in Cognitive and Language Functioning of Preschool-Children with Autism. *J Autism Dev Disord.* 1991;21(3):281-290.

94. Howard JS, Sparkman CR, Cohen HG, Green G, Stanislaw H. A comparison of intensive behavior analytic and eclectic treatments for young children with autism. *Res Dev Disabil.* 2005;26(4):359-383.

95. Lovaas OI. Behavioral Treatment and Normal Educational and Intellectual-Functioning in Young Autistic-Children. *J Consult Clin Psychol.* 1987;55(1):3-9.

96. Rogers SJ. Empirically supported comprehensive treatments for young children with autism. *J Clin Child Psychol.* 1998;27(2):168-179.

97. Sallows GO, Graupner TD. Intensive behavioral treatment for children with autism: Four-year outcome and predictors. *Am J Ment Retard.* 2005;110(6):417-438.

98. Howlin P, Gordon RK, Pasco G, Wade A, Charman T. The effectiveness of Picture Exchange Communication System (PECS) training for teachers of children with autism: a pragmatic, group randomised controlled trial. *J Child Psychol Psychiatry.* 2007;48(5):473-481.

99. Yoder P, Stone WL. A randomized comparison of the effect of two prelinguistic communication interventions on the acquisition of spoken communication in preschoolers, with ASD. *J Speech Lang Hear Res.* 2006;49(4):698-711.

100. Yoder P, Stone WL. Randomized comparison of two communication interventions for preschoolers with autism spectrum disorders. *J Consult Clin Psychol.* 2006;74(3):426-435.

101. Aldred C, Green J, Adams C. A new social communication intervention for children with autism: pilot randomised controlled treatment study suggesting effectiveness. *J Child Psychol Psychiatry.* 2004;45(8):1420-1430.

102. Drew A, Baird G, Baron-Cohen S, et al. A pilot randomised control trial of a parent training intervention for pre-school children with autism. Preliminary findings and methodological challenges. *Eur Child Adolesc Psychiatry.* 2002;11(6).

103. Siller M, Sigman M. The behaviors of parents of children with autism predict the subsequent development of their children's communication. *J Autism Dev Disord* 2002;32(2):77-89.

104. Green J, Charman T, McConachie H, et al. Parent-mediated communication-focused treatment in children with autism (PACT): a randomised controlled trial. *Lancet.* 2010;375(9732):2152-2160.

105. Smith T, Groen AD, Wynn JW. Randomized trial of intensive early intervention for children with pervasive developmental disorder (vol 105, pg 269, 2000). *Am J Ment Retard.* 2000;105(6):508-508.

106. Virues-Ortega J. Applied behavior analytic intervention for autism in early childhood: Meta-analysis, meta-regression and dose-response meta-analysis of multiple outcomes. *Clinl Psychol Rev.* 2010;30(4):387-399.

107. Dawson G, Rogers S, Munson J, et al. Randomized, controlled trial of an intervention for toddlers with autism: the Early Start Denver Model. *Pediatrics.* 2010;125(1):e17-e23.

108. Mawle E, Griffiths P. Screening for autism in pre-school children in primary care: systematic review of English Language tools. *Int J Nurs Stud.* 2006;43(5):623-636.

109. Midence K, O'Neill M. The experience of parents in the diagnosis of autism: A pilot study. *Autism.* 1999;3(3):273-285.

110. Calzada LR, Pistrang N, Mandy WPL. High-Functioning Autism and Asperger's Disorder: Utility and Meaning for Families. *J Autism Dev Disord.* 2012;42(2):230-243.

111. Zaidman-Zait A, Mirenda P, Zumbo BD, et al. Factor analysis of the Parenting Stress Index-Short Form with parents of young children with autism spectrum disorders. *Autism Res.* 2011;4(5):336-346.

112. Schieve LA, Blumberg SJ, Rice C, Visser SN, Boyle C. The relationship between autism and parenting stress. *Pediatrics.* 2007;119 Suppl 1:S114-S121.

113. Knapp M, Romeo R, Beecham J. Economic cost of autism in the UK. *Autism.* 2009;13(3):317-336.

114. Bitterman A, Daley TC, Misra S, Carlson E, Markowitz J. A national sample of preschoolers with autism spectrum disorders: Special education services and parent satisfaction. *J Autism Dev Disord.* 2008;38(8):1509-1517.

115. Chambers JG, Shkolnik J, Perez M. Total expenditures for students with disabilities, 1999-2000: Spending variation by disability. *Special education expenditure project.pp1-16.* 2003.

116. Jarbrink K, Fombonne E, Knapp M. Measuring the parental, service and cost impacts of children with autistic spectrum disorder: a pilot study. *J Autism Dev Disord.* 2003;33(4):395-402.

117. Constantino JN, Zhang Y, Frazier T, Abbacchi AM, Law P. Sibling recurrence and the genetic epidemiology of autism. *Am J Psychiatry.* 2010;167(11):1349-1356.

118. O'Roak BJ, State MW. Autism genetics: strategies, challenges, and opportunities. *Autism Res.* 2008;1(1).

119. Ozonoff S, Young GS, Carter A, et al. Recurrence risk for autism spectrum disorders: a Baby Siblings Research Consortium study. *Pediatrics.* 2010;128(3):e488-495.

120. Bolton P, Macdonald H, Pickles A, et al. A case-control family history study of autism. *J Child Psychol Psychiatry.* 1994;35(5):877-900.

121. Scott FJ, Baron-Cohen S, Bolton P, Brayne C. The CAST (Childhood Asperger Syndrome Test): preliminary development of a UK screen for mainstream primary-school-age children. *Autism.* 2002;6(1):9-31.

122. Close HA, Lee LC, Kaufmann CN, Zimmerman AW. Co-occurring Conditions and Change in Diagnosis in Autism Spectrum Disorders. *Pediatrics.* 2012.

123. Gadow KD, Guttmann-Steinmetz S, Rieffe C, DeVincent CJ. Depression Symptoms in Boys with Autism Spectrum Disorder and Comparison Samples. *J Autism Dev Disord.* 2011.

124. National Research Council. *Educating children with autism. Committee on educational intervention for children with autism. Commission on behavioural and social science and education* 2001.

125. Fombonne E. Epidemiology of pervasive developmental disorders. *Pediatrics in Review.* 2009;65(6):591-598.

126. Ozonoff S, Goodlin-Jones BL, Solomon M. Evidence-based assessment of autism spectrum disorders in children and adolescents. *J Clin Child Adolesc.Psychol.* 2005;34(3):523-540.

127. Wiggins LD, Baio J, Rice C. Examination of the time between first evaluation and first autism spectrum diagnosis in a population-based sample. *J Dev Behav Pediatr.* 2006;27(2 Suppl):S79-S87.

128. Howlin P, Asgharian A. The diagnosis of autism and Asperger syndrome: findings from a survey of 770 families. *Dev Med Child Neurol.* 1999;41(12).

129. Sivberg B. Parents' detection of early signs in their children having an autistic spectrum disorder. *J Pediatr Nurs.* 2003;18(6):433-439.

130. Norris M, Lecavalier L. Screening accuracy of Level 2 autism spectrum disorder rating scales. A review of selected instruments. *Autism.* 2010;14(4):263-284.

131. Vostanis P, Smith B, Chung MC, Corbett J. Early detection of childhood autism: a review of screening instruments and rating scales. *Child Care Health Dev.* 1994;20(3):165-177.

132. Glascoe FP. Screening for developmental and behavioral problems. *Ment Retard Dev Disabil Res Rev.* 2005;11(3):173-179.

133. Campbell JM. Diagnostic assessment of Asperger's disorder: a review of five third-party rating scales. *J Autism Dev Disord.* 2005;35(1):25-35.

134. Stoesz BM, Montgomery JM, Smart SL, Hellsten LA. [image omitted] Review of five instruments for the assessment of Asperger's Disorder in adults. *Clin Neuropsychol.* 2011;25(3):376-401.

135. Schopler E, Reichler RJ, DeVellis RF, Daly K. Toward objective classification of childhood autism: Childhood Autism Rating Scale (CARS). *J Autism Dev Disord.* 1980;10(1):91-103.

136. Krug DA, Arick J, Almond P. Behaviour checklist for identifying severely handicapped individuals with high levels of autistic behaviour. *J Child Psychol Psychiatry.* 1980;21(3):221-229.

137. Gilliam JE. *Gilliam Autism Rating Scale: Examiner's manual. Autism,TX:Pro-Ed*; 1995.

138. Ehlers S, Gillberg C, Wing L. A screening questionnaire for Asperger syndrome and other high-functioning autism spectrum disorders in school age children. *J Autism Dev Disord.* 1999;29(2):129-141.

139. Berument SK, Rutter M, Lord C, Pickles A, Bailey A. Autism screening questionnaire: diagnostic validity. *Br J Psychiatry.* 1999;175.

140. Constantino JN, Przybeck T, Friesen D, Todd RD. Reciprocal social behavior in children with and without pervasive developmental disorders. *J Dev Behav Pediatr.* 2000;21(1):2-11.

141. Rellini E, Tortolani D, Trillo S, Carbone S, Montecchi F. Childhood Autism Rating Scale (CARS) and Autism Behavior Checklist (ABC) correspondence and

conflicts with DSM-IV criteria in diagnosis of autism. *J Autism Dev Disord.* 2004;34(6):703-708.

142. Chlebowski C, Green JA, Barton ML, Fein D. Using the childhood autism rating scale to diagnose autism spectrum disorders. *J Autism Dev Disord.* 2010;40(7):787-799.

143. Volkmar FR, Cicchetti DV, Dykens E, Sparrow SS, Leckman JF, Cohen DJ. An evaluation of the Autism Behavior Checklist. *J Autism Dev Disord.* 1988;18(1):81-97.

144. Wadden NP, Bryson SE, Rodger RS. A closer look at the Autism Behavior Checklist: discriminant validity and factor structure. *J Autism Dev Disord.* 1991;21(4):529-541.

145. Nordin V, Gillberg C. Autism spectrum disorders in children with physical or mental disability or both. II: Screening aspects. *Dev Med Child Neurol.* 1996;38(4):314-324.

146. South M, Williams BJ, McMahon WM, et al. Utility of the Gilliam Autism Rating Scale in research and clinical populations. *J Autism Dev Disord.* 2002;32(6):593-599.

147. Lecavalier L. An evaluation of the Gilliam Autism Rating Scale. *J Autism Dev Disord.* 2005;35(6):795-805.

148. Sikora DM, Hall TA, Hartley SL, Gerrard-Morris AE, Cagle S. Does parent report of behavior differ across ADOS-G classifications: analysis of scores from the CBCL and GARS. *J Autism Dev Disord.* 2008;38(3):440-448.

149. Posserud MB, Lundervold AJ, Gillberg C. Validation of the autism spectrum screening questionnaire in a total population sample. *J Autism Dev Disord.* 2009;39(1):126-134.

150. Kaufman J, Birmaher B, Brent D, et al. Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-

PL): initial reliability and validity data. *J Am Acad Child Adolesc Psychiatry.* 1997;36(7):980-988.

151. Mattila ML, Jussila K, Kuusikko S, et al. When does the Autism Spectrum Screening Questionnaire (ASSQ) predict autism spectrum disorders in primary school-aged children? *Eur Child Adolesc Psychiatry.* 2009;18(8):499-509.

152. Eaves LC, Wingert HD, Ho HH, Mickelson EC. Screening for autism spectrum disorders with the social communication questionnaire. *J Dev Behav Pediatr.* 2006;27(2):S95-S103.

153. Chandler S, Charman T, Baird G, et al. Validation of the social communication questionnaire in a population cohort of children with autism spectrum disorders. *J Am Acad Child Adolesc Psychiatry.* 2007;46(10):1324-1332.

154. Charman T, Baird G, Simonoff E, et al. Efficacy of three screening instruments in the identification of autistic-spectrum disorders. *Br J Psychiatry.* 2007;191:554-559.

155. Johnson S, Hollis C, Hennessy E, Kochhar P, Wolke D, Marlow N. Screening for autism in preterm children: diagnostic utility of the Social Communication Questionnaire. *Arch Dis Child.* 2011;96(1):73-77.

156. Schanding GT, Jr., Nowell KP, Goin-Kochel RP. Utility of the Social Communication Questionnaire-Current and Social Responsiveness Scale as Teacher-Report Screening Tools for Autism Spectrum Disorders. *J Autism Dev Disord.* 2011.

157. Constantino JN, Lavesser PD, Zhang Y, Abbacchi AM, Gray T, Todd RD. Rapid quantitative assessment of autistic social impairment by classroom teachers. *J Am AcadChild Adolesc Psychiatry.* 2007;46(12):1668-1676.

158. Aldridge FJ, Gibbs VM, Schmidhofer K, Williams M. Investigating the clinical usefulness of the Social Responsiveness Scale (SRS) in a tertiary level, autism spectrum disorder specific assessment clinic. *J Autism Dev Disord.* 2011;42(2):294-300.

159. Williams J, Scott F, Stott C, et al. The CAST (Childhood Asperger Syndrome Test): test accuracy. *Autism.* 2005;9(1):45-68.

160. Mayes SD, Calhoun SL, Murray MJ, et al. Comparison of Scores on the Checklist for Autism Spectrum Disorder, Childhood Autism Rating Scale, and Gilliam Asperger's Disorder Scale for Children with Low Functioning Autism, High Functioning Autism, Asperger's Disorder, ADHD, and Typical Development. *J Autism Dev Disord.* 2009.

161. Perry A, Condillac RA, Freeman NL, Dunn-Geier J, Belair J. Multi-site study of the Childhood Autism Rating Scale (CARS) in five clinical groups of young children. *J Autism Dev Disord.* 2005;35(5):625-634.

162. Creak EM, Englewood C. Infantile autism. NJ: Prentice-Hall; 1964.

163. Rutter M. Diagnosis and definition of childhood autism. *J Autism Child Schizophr.* 1978;8(2).

164. Ritvo ER, Freeman BJ. National Society of Autistic Children definition of autism. *J Autism Dev Disord.* 1978;8:162-167.

165. Schopler E, Reichler J, Renner B. *The Childhood Autism Rating Scale (CARS).* Los Angeles: Western Psychological Service; 1988.

166. Sponheim E. Changing criteria of autistic disorders: a comparison of the ICD-10 research criteria and DSM-IV with DSM-III-R, CARS, and ABC. *J Autism Dev Disord.* 1996;26(5):513-525.

167. Miranda-Linne FM, Melin L. A factor analytic study of the Autism Behavior Checklist. *J Autism Dev Disord.* 2002;32(3):181-188.

168. Kanner L. Autism disturbances of affective contact [reprinted from Nervous Child 1943;2;217-50]. *Acta Paedopsychiatrica.* 1968;35.

169. Lovaas OI, Freitag G, Gold VJ, Kassorla IC. Recording apparatus and procedure for observation of behaviors of children in a free play setting. *J Exper Child Psychol.* 1965;2:108-120.

170. Rimland B. The differentiation of childhood psychoses: an analysis of checklists for 2,218 psychotic children. *J Autism Child Schizophr.* 1971;1(2):161-174.

171. Rutternberg BA, Kalish BI, Wenar C, Wolf EG. *Behavioral rating instrument for autistic and other atypical children.* Philadelphia; 1977.

172. Clancy H, Dugdale A, Rendle-Short J. The diagnosis of infantile autism. *Dev Med Child Neurol.* 1969;11(4):432-442.

173. Lotter V. Factors related to outcome in autistic children. *J Autism Child Schizophr.* 1974;4(3):263-277.

174. Schreck KA, Mulick JA. Parental report of sleep problems in children with autism. *J Autism Dev Disord.* 2000;30(2):127-135.

175. Lukens CT, Linscheid TR. Development and validation of an inventory to assess mealtime behavior problems in children with autism. *J Autism Dev Disord.* 2008;38(2):342-352.

176. Ehlers S, Gillberg C. The epidemiology of Asperger syndrome. A total population study. *J Child Psychol Psychiatry.* 1993;34(8):1327-1350.

177. Kopp S, Gillberg C. The Autism Spectrum Screening Questionnaire (ASSQ)-Revised Extended Version (ASSQ-REV): an instrument for better capturing the autism phenotype in girls? A preliminary study involving 191 clinical cases and community controls. *Res Dev Disabil.* 2011;32(6):2875-2888.

178. Posserud MB, Lundervold AJ, Gillberg C. Autistic features in a total population of 7-9-year-old children assessed by the ASSQ (Autism Spectrum Screening Questionnaire). *J Child Psychol Psychiatry.* 2006;47(2):167-175.

179. Mattila ML, Kielinen M, Jussila K, et al. An epidemiological and diagnostic study of Asperger syndrome according to four sets of diagnostic criteria. *J Am Acad Child Adolesc Psychiatry.* 2007;46(5):636-646.

180. Rutter M, LeCouteur A, Lord C. *Autism Diagnostic Interview-Revised Manual.* Los Angeles: CA: Western Psychological Services; 2003.

181. Constantino JN, Gruber CP. *Social Responsiveness Scale (SRS)*. Los Angeles, CA.: Western Psychological Services.; 2005.

182. Constantino JN, Davis SA, Todd RD, et al. Validation of a brief quantitative measure of autistic traits: comparison of the social responsiveness scale with the autism diagnostic interview-revised. *J Autism Dev Disord.* 2003;33(4):427-433.

183. Murray MJ, Mayes SD, Smith LA. Brief report: excellent agreement between two brief autism scales (Checklist for Autism Spectrum Disorder and Social Responsiveness Scale) completed independently by parents and the Autism Diagnostic Interview-Revised. *J Autism Dev Disord.* 2011;41(11):1586-1590.

184. Scott FJ, Baron-Cohen S, Bolton P, Brayne C. Brief report: prevalence of autism spectrum conditions in children aged 5-11 years in Cambridgeshire, UK. *Autism.* 2002;6(3):231-237.

185. O'Brien G, Pearson J, Berney T, Barnard L. Measuring behaviour in developmental disability: a review of existing schedules. *Dev Med Child Neurol Suppl.* 2001;87:1-72.

186. Lord C, Risi S, Lambrecht L, et al. The autism diagnostic observation schedule-generic: a standard measure of social and communication deficits associated with the spectrum of autism. *J Autism DevDisord.* 2000;30(3):205-223.

187. Le-Couteur A, Rutter M, Lord C, et al. Autism diagnostic interview: a standardized investigator-based instrument. *J Autism Dev Disord.* 1989;19(3):363-387.

188. Bolte S, Poustka F, Constantino JN. Assessing autistic traits: cross-cultural validation of the social responsiveness scale (SRS). *Autism Res.* 2008;1(6):354-363.

189. Lee H, Marvin AR, Watson T, et al. Accuracy of phenotyping of autistic children based on Internet implemented parent report. *Am J Med Genet B Neuropsychiatr Genet.* 2010;153B(6):1119-1126.

190. Papanikolaou K, Paliokosta E, Houliaras G, et al. Using the Autism Diagnostic Interview-Revised and the Autism Diagnostic Observation Schedule-Generic for the diagnosis of autism spectrum disorders in a Greek sample with a wide range of intellectual abilities. *J Autism Dev Disord.* 2009;39(3):414-420.

191. Ward-King J, Cohen IL, Penning H, Holden JJ. Brief report: telephone administration of the autism diagnostic interview--revised: reliability and suitability for use in research. *J Autism Dev Disord.*;40(10):1285-1290.

192. Lord C, Rutter M, DiLavore P, Risi S. *Autism Diagnostic Observation Schedule (ADOS)*. Los Angeles, CA: Western Psychological Services; 2001.

193. Klein-Tasman BP, Risi S, Lord CE. Effect of language and task demands on the diagnostic effectiveness of the autism diagnostic observation schedule: the impact of module choice. *J Autism Dev Disord.* 2007;37(7):1224-1234.

194. DiLavore PC, Lord C, Rutter M. The pre-linguistic autism diagnostic observation schedule. *J Autism Dev Disord.* 1995;25(4):355-379.

195. Berument SK, Starr E, Pickles A, et al. Pre-linguistic Autism Diagnostic Observation Schedule adapted for older individuals with severe to profound mental retardation: a pilot study. *J Autism Dev Disord.* 2005;35(6):821-829.

196. Leyfer OT, Tager-Flusberg H, Dowd M, Tomblin JB, Folstein SE. Overlap between autism and specific language impairment: comparison of Autism Diagnostic Interview and Autism Diagnostic Observation Schedule scores. *Autism Res.* 2008;1(5):284-296.

197. Luyster R, Gotham K, Guthrie W, et al. The Autism Diagnostic Observation Schedule-toddler module: a new module of a standardized diagnostic measure for autism spectrum disorders. *J Autism Dev Disord.* 2009;39(9).

198. Gray KM, Tonge BJ, Sweeney DJ. Using the Autism Diagnostic Interview-Revised and the Autism Diagnostic Observation Schedule with young children with developmental delay: evaluating diagnostic validity. *J Autism Dev Disord.* 2008;38(4):657-667.

199. Cicchetti DV, Lord C, Koenig K, Klin A, Volkmar FR. Reliability of the ADI-R: multiple examiners evaluate a single case. *J Autism Dev Disord.* 2008;38(4):764-770.

200. Moss J, Magiati I, Charman T, Howlin P. Stability of the autism diagnostic interview-revised from pre-school to elementary school age in children with autism spectrum disorders. *J Autism Dev Disord.* 2008;38(6).

201. Lord C, Pickles A, McLennan J, et al. Diagnosing autism: analyses of data from the Autism Diagnostic Interview. *J Autism Dev Disord.* 1997;27(5):501-517.

202. McLennan JD, Lord C, Schopler E. Sex differences in higher functioning people with autism. *J Autism Dev Disord.* 1993;23(2):217-227.

203. Risi S, Lord C, Gotham K, et al. Combining information from multiple sources in the diagnosis of autism spectrum disorders. *J Am Acad Child Adolesc Psychiatry.* 2006;45(9):1094-1103.

204. Cox A, Klein K, Charman T, et al. Autism spectrum disorders at 20 and 42 months of age: stability of clinical and ADI-R diagnosis. *J Child Psychol Psychiatry.* 1999;40(5).

205. Gilchrist A, Green J, Cox A, Burton D, Rutter M, Le Couteur A. Development and current functioning in adolescents with Asperger syndrome: a comparative study. *J Child Psychol Psychiatry.* 2001;42(2):227-240.

206. Elsabbagh M, Divan G, Koh YJ, et al. Global prevalence of autism and other pervasive developmental disorders. *Autism Res.* 2012;5(3):160-179.

207. Fombonne E. Epidemiology of autistic disorder and other pervasive developmental disorders. *J Clin Psychiatry.* 2005;66 Suppl 10.

208. Tanoue Y, Oda S, Asano F, Kawashima K. Epidemiology of infantile autism in southern Ibaraki, Japan: differences in prevalence in birth cohorts. *J Autism Dev Disord.* 1988;18(2):155-166.

209. Kim YS, Leventhal BL, Koh YJ, et al. Prevalence of autism spectrum disorders in a total population sample. *Am J Psychiatry.* 2011;168(9):904-912.

210. Catherine R. Prevalence of autism spectrum disorders--autism and developmental disabilities monitoring network, six sites, United States, 2000. *MMWR Surveill Summ.* 2007;56(1).

211. Gillberg C, Wing L. Autism: not an extremely rare disorder. *Acta Psychiatr Scand.* 1999;99(6).

212. Gillberg C, Steffenburg S, Schaumann H. Is autism more common now than ten years ago? *Br J Psychiatry.* 1991;158:403-409.

213. Treffert DA. Epidemiology of infantile autism. *Arch Gen Psychiatry.* 1970;22(5):431-438.

214. Bertrand J, Mars A, Boyle C, Bove F, Yeargin-Allsopp M, Decoufle P. Prevalence of autism in a United States population: the Brick Township, New Jersey, investigation. *Pediatrics.* 2001;108(5).

215. Tanino S. The prevalence of autistic children and suspected autistic childrne in Toyama Prefercture. *Child Psychiatry.* 1971;12(150):8.

216. Matsuishi T, Shiotsuki Y, Yoshimura K, Shoji H, Imuta F, Yamashita F. High prevalence of infantile autism in Kurume City, Japan. *J Child Neurol.* 1987;2(4):268-271.

217. Kawamura Y, Takahashi O, Ishii T. Revaluating the incidence of pervasive developmental disorders: impact of elevated rates of detection through implementation of an integrated system of screening in Toyota, Japan. *Psychiatry Clin Neurosci.* 2008;62(2).

218. Lotter V. Epidemiology of autism conditions in young children. *Soc Psychiatry.* 1966;1:124-135.

219. Ritvo ER, Freeman BJ, Pingree C, et al. The UCLA-University of Utah epidemiologic survey of autism: prevalence. *Am J Psychiatry.* 1989;146(2):194-199.

220. Webb EV, Lobo S, Hervas A, Scourfield J, Fraser WI. The changing prevalence of autistic disorder in a Welsh health district. *Dev Med Child Neurol.* 1997;39(3).

221. Taylor B, Miller E, Farrington CP, et al. Autism and measles, mumps, and rubella vaccine: no epidemiological evidence for a causal association. *Lancet.* 1999;353(9169).

222. Powell JE, Edwards A, Edwards M, Pandit BS, Sungum-Paliwal SR, Whitehouse W. Changes in the incidence of childhood autism and other autistic spectrum disorders in preschool children from two areas of the West Midlands, UK. *Dev Med Child Neurol.* 2000;42(9).

223. Baird G, Charman T, Baron-Cohen S, et al. A screening instrument for autism at 18 months of age: a 6-year follow-up study. *J Am Acad Child Adolesc Psychiatry.* 2000;39(6).

224. Fombonne E, Simmons H, Ford T, Meltzer H, Goodman R. Prevalence of pervasive developmental disorders in the British nationwide survey of child mental health. *J Am Acad Child Adolesc Psychiatry.* 2001;40(7).

225. Chakrabarti S, Fombonne E. Pervasive developmental disorders in preschool children. *JAMA.* 2001;285(24).

226. Croen LA, Grether JK, Selvin S. Descriptive epidemiology of autism in a California population: who is at risk? *J Autism Dev Disord.* 2002;32(3):217-224.

227. Yeargin-Allsopp M, Rice C, Karapurkar T, Doernberg N, Boyle C, Murphy C. Prevalence of autism in a US metropolitan area. *JAMA.* 2003;289(1).

228. Lingam R, Simmons A, Andrews N, Miller E, Stowe J, Taylor B. Prevalence of autism and parentally reported triggers in a north east London population. *Arch Dis Child.* 2003;88(8).

229. Tebruegge M, Nandini V, Ritchie J. Does routine child health surveillance contribute to the early detection of children with pervasive developmental disorders? An epidemiological study in Kent, U.K. *BMC Pediatrics.* 2004;4:4.

230. Chakrabarti S, Fombonne E. Pervasive developmental disorders in preschool children: confirmation of high prevalence. *Am J Psychiatry.* 2005;162(6).

231. Harrison MJ, O'Hare AE, Campbell H, Adamson A, McNeillage J. Prevalence of autistic spectrum disorders in Lothian, Scotland: an estimate using the "capture-recapture" technique. *Arch Dis Child.* 2006;91(1).

232. Baird G, Simonoff E, Pickles A, et al. Prevalence of disorders of the autism spectrum in a population cohort of children in South Thames: the Special Needs and Autism Project (SNAP). *Lancet.* 2006;368(9531):210-215.

233. Williams E, Thomas K, Sidebotham H, Emond A. Prevalence and characteristics of autistic spectrum disorders in the ALSPAC cohort. *Dev Med Child Neurol.* 2008;50(9).

234. Nicholas JS, Charles JM, Carpenter LA, King LB, Jenner W, Spratt EG. Prevalence and characteristics of children with autism-spectrum disorders. *Ann Epidemiol.* 2008;18(2):130-136.

235. Yamazaki K, Yamashita I, Suwa N, Kunoda T, Iwabuchi J, Imamura S. Survey on the morbidity rate of "autistic children" in the Hokkaido district. *Child Psychiatry.* 1971;12(141):9.

236. Haga H, Miyamoto H. A survey on the actual state of so-called autistic children in Kyoto prefecture. *Child Psychiatry.* 1971;12(160):7.

237. Nakai K. A survey pf so-called autistic children in Cifu prefecture. *Child Psychiatry.* 1971;12(262):6.

238. Hoshino Y, Kumashiro H, Yashima Y, Tachibana R, Watanabe M. The epidemiological study of autism in Fukushima-ken. *Folia Psychiatr Neurol Jpn.* 1982;36(2):115-124.

239. Ishii T, Takahashi O. The epidemiology of autistic children in Toyota. *Child Adolesc Psychiatry.* 1983;24(311):21.

240. Sugiyama T, Abe T. The prevalence of autism in Nagoya, Japan: a total population study. *J Autism Dev Disord.* 1989;19(1).

241. Ohtaki E, Kawano Y, Urabe F, et al. The prevalence of Rett syndrome and infantile autism in Chikugo District, the southwestern area of Fukuoka prefecture, Japan. *J Autism Dev Disord.* 1992;22(3):452-454.

242. Honda H, Shimizu Y, Misumi K, Niimi M, Ohashi Y. Cumulative incidence and prevalence of childhood autism in children in Japan. *Br J Psychiatry.* 1996;169(2):228-235.

243. Honda H, Shimizu Y, Imai M, Nitto Y. Cumulative incidence of childhood autism: a total population study of better accuracy and precision. *Dev Med Child Neurol.* 2005;47(1):10-18.

244. Lazoff T, Zhong L, Piperni T, Fombonne E. Prevalence of pervasive developmental disorders among children at the English Montreal School Board. *Can J Psychiatry.* 2010;55(11):715-720.

245. Fombonne E. Estimated prevalence of autism spectrum conditions in Cambridgeshire is over 1%. *Evid Based Ment Health.* 2010;13(1):32.

246. Fombonne E. Epidemiological surveys of autism and other pervasive developmental disorders: an update. *J Autism Dev Disord.* 2003;33(4).

247. Newschaffer CJ. Investigating diagnostic substitution and autism prevalence trends. *Pediatrics.* 2006;117(4):1436-1437.

248. Posserud M, Lundervold AJ, Lie SA, Gillberg C. The prevalence of autism spectrum disorders: impact of diagnostic instrument and non-response bias. *Soc Psychiatry Psychiatr Epidemiol.* 2010;45(3):319-327.

249. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ.* 2003;327(7414):557-560.

250. Zhang F, Sui Q, Wang J. The latest investigation of autism epidemic of children aged from 1 to 6 years old in Wuxi city. *Chinese women child healthcare.* 2008;23(3878-3879.).

251. Zhang L, Wong MH. Environmental mercury contamination in China: sources and impacts. *Environ Int.* 2007;33(1).

252. Chien IC, Lin CH, Chou YJ, Chou P. Prevalence and incidence of autism spectrum disorders among national health insurance enrollers in Taiwan from 1996 to 2005. *J Child Neurol.* 2011;26(7):830-834.

253. Li N, Chen G, Song X, Du W, Zheng X. Prevalence of autism-caused disability among Chinese children: A national population-based survey. *Epilepsy & behavior : E&B.* 2011;22(4):786-789.

254. Chang HL, Juang YY, Wang WT, Huang CI, Chen CY, Hwang YS. Screening for autism spectrum disorder in adult psychiatric outpatients in a clinic in Taiwan. *Gen Hosp Psychiatry.* 2003;25(4).

255. Wong VC, Hui SL. Epidemiological Study of Autism Spectrum Disorder in China. *J Child Neurol* 2008;23(1):67-72.

256. Wang X, Yang W, Jin Y, et al. Prevalence of autism spectrum disorders in preschool children of Guangzhou kindergartens. *Chinese Ment Health J.* 2011;25(6):401-408.

257. Wang W, Xiao G, Xie Y, Ouyang X. Autism survey for 2 to 6 years old children in Meizhou. *China J Health Psychol.* 2009;1(8):91-92.

258. Zhang J, Xu C, Zhang J. Survey of Autism among Preschool Children in Wuhan. *China Maternal and Child Health.* 2005;20:2395-2396.

259. Wang W, Zai L, Zhen Lea. An epidemiological investigation on autistic disorder in Changzhou Province. *J Clin Psychiatric Med.* 2002;12(3):148-149.

260. Yang S, Hu Y, Han Y. Prevalence Investigation of Autism in Children. *J Clin Paediatric.* 2007;22(24).

261. Chen Y, Huang H, Zhao Y, et al. Epidemiological survey on Autism Spectrum Disorders in 2 to 6 years old children in Ranghulu District in Daqing City. *China J Child Health Care.* 2010;18(4):331-333.

262. Yu C, Xia W, Sun A, et al. Survey on autistic spectrum disorders in 2 to 6 years old children in Harbin city. *China J Child Health Care.* 2010;18(10):750-753.

263. Nylander L, Gillberg C. Screening for autism spectrum disorders in adult psychiatric out-patients: a preliminary report. *Acta Psychiatr Scand.* 2001;103(6):428-434.

264. Chinese Society of Psychiatry. *Chinese Classification of Mental Disorders. 2nd edition revised. (CCMD-2-R)*; 1993.

265. Liu J, Yang X, Jia M, et al. Epidemiological survey of the Pervasive Developmental Disorder of 2-6 years old children in Beijing. *Chinese Ment Health J.* 2007;2(3):290-293.

266. Luo W, Li L, Chen R. Epidemiological investigation on autistic disorder in Fujian Province. *Shanghai Arch Psychiatry.* 2000;12(1):3-5.

267. Ren L, Duan Z, Xu J. An analysis on positive rate of autism among preschool children in Tongling city. *Chinese J Child Healthcare*. 2002;11(2):105-107.

268. Wang W, Huo L, Zhen L. An epidemiological investigation on autistic disorder in Jiangsu Province. *Behav Med Sci China.* 2003;12(2).

269. Guo R. Epidemiological investigation analysis of 5000 Chinese between 0 and 6 years old with childhood autism in Tianjin city. *Chinese J Clin Rehab.* 2004;8(6).

270. Guo C. Epidemiology investigation of 2-6 years old children with mental disabilities in Dingxi county. *China J Rehab Theory Practice.* 2004;10(2).

271. Zhang X, Ji CY. Autism and mental retardation of young children in China. *Biomedical and Environmental Sciences.* 2005;18(5):334-340.

272. Liu QJ, Ma F, Li D, et al. Detection of chromosome aberrations in Chinese children with autism using G-banding and BAC FISH. *Zhonghua Yi Xue Yi Chuan Xue Za Zhi.* 2005;22(3).

273. Zhang G, Huang X, Yang H, Lu Y. Epidemiological investigation of Childhood Autism in Yunyan district of Guiyang city. *J Guiyang Med college.* 2009;34(4).

274. Li A, Zhang X, Lv C, Zhu Y, Li Y, Liu Y. Analysis of behavioural characteristics of children with autism aged 1.5-3 years old. *Child Mental Health J.* 2010;24(3):215-218.

275. Wu X, Lu Y, Wang Y, et al. Investigation of childhood autism status in Lianyungang city. *J Modern Med Hygiene.* 2010;26(24):3724-3726.

276. Liang M, Chen Q, Liu C, Gu Z, Mai M, Jiang Y. Analysis of screening for autism in preschool children in Maoming. *Jf China Maternal Child Health Care.* 2011;26:1164-1165.

277. Higgins J, Green S. Cochrane Handbook for Systematic Reviews of Interventions. 2011/03//.

278. Groen WB, Swinkels SH, van der Gaag RJ, Buitelaar JK. Finding effective screening instruments for autism using bayes theorem. *Arch.Pediatr.Adolesc.Med.* 2007;161(4):415-416.

279. Oosterling IJ, Swinkels SH, van der Gaag RJ, Visser JC, Dietz C, Buitelaar JK. Comparative analysis of three screening instruments for autism spectrum disorder in toddlers at high risk. *J Autism Dev Disord.* 2009;39(6).

280. Grimes DA, Schulz KF. Uses and abuses of screening tests. *Lancet.* 2002;359(9309):881-884.

281. Yang XL, Huang LQ, Jia MX, Chen S. Validation study of Autism Behavior Checklist. *Chinese J Ment Health.* 1993;7(6):279-280.

282. Wang Y, Wang G, Wang Y. Analysis of childhood autism by using Clancy Autism Behavior Scale and Autism Behavior Checklist. *J Shandong University (Health Science).* 2003;41(2):213-214.

283. Wang Y, Wang Y, Shen Y. Investigation of intelligence and behavior impairment in autistic children. *Chinese J Child Health Care.* 2003;11(2):133-134.

284. Lu J, Yang Z. Neuroodevelopment anormalities assessment in autistic children. *Chinese J Modern Med.* 2004;14(12):42-48.

285. Li J, Zhong J, Cai L, Chen Y, Zhou M. Comparison of clinical application of three autism rating scale. *China J Contemporary Paediatrics.* 2005;7(1):59-62.

286. Yin Q, Chen J, Luo X, Li X. Reliability and validity of Childhood Autism Rating Scale and Autism Behaviour Checklist. *International Medicine and Hygiene Guideline Newspaper.* 2011;17(12):1470-1475.

287. Zhang Q. The evaluation of diagnosis of Childhood Autism by DSM-IV and Clancy Autism Behavvior Scale. *J Med Theory Practice.* 2006;19(5):586-587.

288. Zhang N, Tan H, Xiao H, Zhang J, Zhang S. A comparison study of three early screening instruments of autism for preschool children. *Chinese J Clin Paediatrics.* 2011;29(7):656-660.

289. Gong Y, Liu J, Li C, Jia M, Song W, Guo Y. Reliability and validity of the Chinese version of the Modified Checklist for Autism in Toddlers. *Chinese J Ment Health.* 2011;25(6):409-414.

290. Guo YQ, Tang Y, Rice C, Lee LC, Wang YF, Cubells JF. Validation of the Autism Spectrum Screening Questionnaire, Mandarin Chinese Version (CH-ASSQ) in Beijing, China. *Autism.* 2011;15(6):713-727.

291. Song Y, Fang J, Sun L. A new, high precision behavior-based questionnaire for screening and pre-diagnosing autism in children: implication for clinical applications and large population investigation. *J Psychol Sci.* 2009;32(6):1504-1507.

292. Yang W, Shao Z, Gan W, Shen W, Tang L, Wang Y. Modification and clinical application of Childhood Autism Screening Checklist. *Chinese J Child Health Care.* 2010;18(12):954-956.

293. Li J, Zhong J, Cai L, Chen Y, Zhou M. An investigation of clinical application of Childhood Autism Rating Scale. *Chinese J Child Health Care.* 2005;13(3):267-268.

294. Tao K-t. *Child Psychiatry*. Nanjing: Jiangsu Science and technology press; 1999.

295. Chinese Society of P. *Chinese Classification of Mental Disorders, 3rd edition (CCMD-3)*; 2001.

296. Yama B, Freeman T, Graves E, Yuan S, Karen CM. Examination of the Properties of the Modified Checklist for Autism in Toddlers (M-CHAT) in a Population Sample. *J Autism Dev Disord.* 2012.

297. Dumont-Mathieu T, Fein D. Screening for autism in young children: The Modified Checklist for Autism in Toddlers (M-CHAT) and other measures. *Ment Retard Dev Disabil Res Rev.* 2005;11(3):253-262.

298. Wong V, Hui LH, Lee WC, et al. A modified screening tool for autism (Checklist for Autism in Toddlers [CHAT-23]) for Chinese children. *Pediatrics.* 2004;114(2):e166-e176.

299. Zhang F, Liu Y, Xie Y, et al. An investigation of awareness of childhood autism in Wuxi city. *Jiangsu Med J.* 2011;37(14):1704-1705.

300. Yong R. Current research in the area of Autism and Savant Syndrome. *Int Educ J.* 2001;2(4):329-333.

301. Ke X, Luo S, Tao K-t. A study of Clancy Behavior Scale on Childhood Autism. *Acta Academic Medicine Jiangxi.* 2002;142(6):136-137.

302. Chen Y, Chen Z, Hu R. Clinical application of Clancy Autism Behavior Scale. *Guangdong Med J.* 2007;28(3):376-377.

303. Aman MG, Singh NN, Stewart AW, Field CJ. The aberrant behavior checklist: a behavior rating scale for the assessment of treatment effects. *Am J Ment Defic.* 1985;89(5):485-491.

304. Guo Y, Liu J. Reliability and diagnostic validity study on Autism Diagnostic Interview-Revised. *Chinese J Psychiatry.* 2002(35):42-45.

305. Fombonne E. Diagnostic assessment in a sample of autistic and developmentally impaired adolescents. *J Autism Dev Disord.* 1992;22(4):563-581.

306. Yirmiya N, Sigman M, Freeman BJ. Comparison between diagnostic instruments for identifying high-functioning children with autism. *J Autism Dev Disord.* 1994;24(3):281-291.

307. Liu J, Guo WY, Guo Y, Yang X, Jia M. The developmental of a screening checklist of childhood autism. *Chinese J Ment Health.* 2004;18(6):400-404.

308. Guo Y, Yang X. Introduction and clinical application of Autism Diagnostic Interview. *J Foreign Psychiatry.* 1998;25(3):174-177.

309. Tan Za, K.X, Lu R. A comparison study of three diagnostic criteria on Autism. *Chinese J Psychiatry.* 1998;31:175-177.

310. Guo L, Wan Y, Shan Y. A clinical study of the 3rd edition of Chinese classification of mental disorders for childhood autism. *Chinese J Psychiatry.* 2002;35(3):162-165.

311. Liu J, Jia M. A comparative study of Diagnostic Criteria of CCMD-3 and DSM-IV on Childhood Autism. *Chinese J Medical Health.* 2006;20(9):568-571.

312. Zhang D, Mou J, Cheng JQ, Griffiths SM. Public health services in Shenzhen: a case study. *Public Health.*125(1):15-19.

313. Fernandes FD, Miilher LP. [Relations between the Autistic Behavior Checklist (ABC) and the functional communicative profile]. *Pro.Fono.* 2008;20(2):111-116.

314. Le Roux J. Effective educators are culturally competent communicators. *Int Educ.* 2002;13(1):37-48.

315. McLennan JD, Huculak S, Sheehan D. Brief report: pilot investigation of service receipt by young children with autistic spectrum disorders. *J Autism Dev Disord.* 2008;38(6):1192-1196.

316. McConachie H, Robinson G. What services do young children with autism spectrum disorder receive? *Child Care Health Dev.* 2006;32(5):553-557.

317. Excellence. NIoHaC. NICE guideline for autism: recignition, referral and diagnosis of people on the autism spectrum. http://guidance.nice.org.uk/CG128.

318. Volkmar F, Cook EH, Jr., Pomeroy J, Realmuto G, Tanguay P. Practice parameters for the assessment and treatment of children, adolescents, and adults with autism and other pervasive developmental disorders. American Academy of Child and Adolescent Psychiatry Working Group on Quality Issues. *J Am Acad Child Adolesc Psychiatry.* 1999;38(12 Suppl):32S-54S.

319. Filipek PA, Accardo PJ, Baranek GT, et al. The screening and diagnosis of autistic spectrum disorders. *J Autism Dev Disord.* 1999;29(6):439-484.

320. Jones G. Department for Education and Skills/Department of Health Good Practice Guidance on the education of children with autistic spectrum disorder. *Child Care Health Dev.* 2006;32(5):543-552.

321. White SW, Scahill L, Klin A, Koenig K, Volkmar FR. Educational placements and service use patterns of individuals with autism spectrum disorders. *J Autism Dev Disord.* 2007;37(8):1403-1412.

322. Ruble LA, Heflinger CA, Renfrew JW, Saunders RC. Access and service use by children with autism spectrum disorders in Medicaid Managed Care. *J Autism Dev Disord.* 2005;35(1):3-13.

323. Rahbar MH, Ibrahim K, Assassi P. Knowledge and attitude of general practitioners regarding autism in Karachi, Pakistan. *J Autism Dev Disord.* 2011;41(4):465-474.

324. Golnik A, Ireland M, Borowsky IW. Medical homes for children with autism: a physician survey. *Pediatrics.* 2009;123(3):966-971.

325. McCabe H. The beginnings of inclusion in the People's Republic of China. *Res Prac Pers SeveDisabil.* 2003;28(1):16-22.

326. National People's Congress. *Zhonghua renmin gongheguo yiwu jiaoyu fa [The compulsory education act of the People's Republic of China]*. Beijing: Law Publisher Edition.; 1986.

327. National People's Congress. *Zhonghua renmin gongheguo canji ren baozhang fa [Law of the People's Republic of China on the protection of persons with disabilities]*. Beijing: Law Publishers Edition; 1990.

328. State Council. *Canji ren jiaoyu tiaoli. [Regulations on the education of persons with disabilities]*. Beijing: Law Publishers Edition.; 1994.

329. McCabe H. Two decades of serving children with autism in the People's Republic of China: achievements and challenges of a state-run mental health centre. *Disability & Society.* 2008;23(3):271-282.

330. Huang YZ. The paradoxical transition in China's health system. *Harvard Health Policy Review.* 2002;3(No.1 Spring):1-4.

331. Ming X, Hashim A, Fleishman S, West T, Chen X. Parent initiated evaluation is prevalent in autism spectrum disorders. *J soc commu child rehab.* 2007:158.

332. Xiong X. An investigation of current situation in educational support and healthcare service for autistic children. *J outside school educ China.* 2010;08:37-39.

333. Guo D. An investigation of social support system for autistic children in Jiangxi province. *J Yichun College.* 2012;33:66-70.

334. Tao R, Liang H, Li D, et al. An investigation of current situation of autistic children and parents in Hubei province. *J educ res exper.* 2011;2:93-96.

335. Wu H. The current situation and reform strategy for rehabilitation in autistic children. *J Changsha Soc Work College.* 2011;18(2):41-42.

336. Chen L. The hope and difficulties for parents with autistic children. *J educ res.* 2011;10:131-134.

337. Gao J. The investigation of current situation of autistic children in primary school. *Journal of Education.* 2005;2:56-57.

338. McCabe H. The Importance of Parent-to-Parent Support among Families of Children with Autism in the People's Republic of China. *Int J Disabily Dev Educ.* 2008;55(4):303-314.

339. McCabe H. Autism and Family in the People's Republic of China: Learning from Parents' Perspectives. *Res Prac Pers SeverDisabil.* 2008;33(1-2):37-47.

340. McCabe H. Employment Experiences, Perspectives, and Wishes of Mothers of Children with Autism in the People's Republic of China. *J Appl Res Intellect Disabil.* 2010;23(2):122-131.

341. Xiong N, Yang L, Yu Y, et al. Investigation of raising burden of children with autism, physical disability and mental disability in China. *Res Dev Disabil.* 2011;32(1):306-311.

342. Granpeesheh D, Tarbox J, Dixon DR. Applied behavior analytic interventions for children with autism: a description and review of treatment research. *Ann Clin Psychiatry.* 2009;21(3):162-173.

343. Gutstein SE, Burgess AF, Montfort K. Evaluation of the relationship development intervention program. *Autism.* 2007;11(5):397-411.

344. Wieder S, Greenspan SI. Climbing the symbolic ladder in the DIR model through floor time/interactive play. *Autism.* 2003;7(4):425-435.

345. Tsang SK, Shek DT, Lam LL, Tang FL, Cheung PM. Brief report: application of the TEACCH program on Chinese pre-school children with autism--Does culture make a difference? *J Autism Dev Disord.* 2007;37(2):390-396.

346. Flippin M, Reszka S, Watson LR. Effectiveness of the Picture Exchange Communication System (PECS) on communication and speech for children with autism spectrum disorders: a meta-analysis. *Am J Speech Lang Pathol.* 2010;19(2):178-195.

347. Yuan Q, Wu ZF, Wang RC, Deng JJ, Zhou HL, Lang JY. [Observation on the therapeutic effect of acupuncture treatment of autism children]. *Zhen Ci Yan Jiu.* 2009;34(3).

348. Deng M, Poon-McBrayer KF, Farnsworth EB. The development of special education in China - A sociocultural review. *Remedial and Special Education.* 2001;22(5):288-298.

349. McCabe H. Children with autism in the People's Republic of China: Parents' perspectives of early educational experiences; 2002.

350. American Academy of Paediatrics. American Academy of Pediatrics: The pediatrician's role in the diagnosis and management of autistic spectrum disorder in children. *Pediatrics.* 2001;107(5):1221-1226.

351. Chen K, Zheng X, Second national sample survey of disability o. *Data Analysis of the Second China National Sample Survey on Disability*. Beijing: Huaxia Press; 2008.

352. Liu Y, Wen J. The investigation of the current situation on the education of autistic children in rural areas in Jiangxi Province. *Agricultural Archaeology.* 2006;6:32-33.

353. Chen X, Chen Ya. *The Status Analysis and Strategies Study of Children with Disability in China*. Beijing: Huaixa; 2008.

354. Lu C, Zhang X, Liu H. The investigation of current situation on hospital referral and rehabilitaion of autistic children in Tianjin city. *Chinese J Rehab Med.* 2008;23(4):79-80.

355. Cooper S, O'Carroll J, Jenkin A, Badger B. Collaborative practices in unscheduled emergency care: role and impact of the emergency care practitioner--quantitative findings. *Emer Med.* 2007;24(9):630-633.

356. Cooper S, Endacott R. Generic qualitative research: a design for qualitative research in emergency care? *Emer Med.* 2007;24(12):816-819.

357. Robertson L, Richards R, Egan R, Szymlek-Gay EA. Promotion and support of physical activity among cancer survivors: a service provider perspective. *Psychooncology.* 2012.

358. Russell G, Kelly S, Golding J. A qualitative analysis of lay beliefs about the aetiology and prevalence of autistic spectrum disorders. *Child Care Health Dev.* 2010;36(3):431-436.

359. Cheng L, Ge Q, Sun B, Yu P, Ke X, Lu Z. Polyacrylamide gel-based microarray: a novel method applied to the association Study between the polymorphisms of BDNF gene and autism. *J Biomed Nanotechnol.* 2009;5(5):542-550.

360. Cheng L, Ge Q, Xiao P, et al. Association study between BDNF gene polymorphisms and autism by three-dimensional gel-based microarray. *Int J Mol Sci.* 2009;10(6):2487-2500.

361. Jiao Y, Chen R, Ke X, Chu K, Lu Z, Herskovits EH. Predictive models of autism spectrum disorder based on brain regional cortical thickness. *Neuroimage.* 2010;50(2):589-599.

362. Chinese Society of P. *Chinese Classification of Mental Disorders (CCMD), 2nd edition*; 1984.

363. Tao. The problems of diagnosis and classification of infantile autism. *J Chinese Neuropsychiatry.* 1982;2:104.

364. Wang L, Jia M, Yue W, et al. Association of the ENGRAILED 2 (EN2) gene with autism in Chinese Han population. *Am J Med Genet B Neuropsychiatr Genet.* 2008;147B(4):434-438.

365. Wu S, Jia M, Ruan Y, et al. Positive association of the oxytocin receptor gene (OXTR) with autism in the Chinese Han population. *Biol Psychiatry.* 2005;58(1):74-77.

366. Zhang X, Lv CC, Tian J, et al. Prenatal and perinatal risk factors for autism in China. *J Autism Dev Disord.* 2010;40(11):1311-1321.

367. Hilton JC, Seal BC. Brief report: comparative ABA and DIR trials in twin brothers with autism. *J Autism Dev Disord.* 2007;37(6):1197-1201.

368. Panerai S, Ferrante L, Caputo V. The TEACCH strategy in mentally retarded children with autism: a multidimensional assessment. Pilot study. Treatment and

Education of Autistic and Communication Handicapped children. *J Autism Dev Disord.* 1997;27(3):345-347.

369. Fung CW, Wong V. Program for Chinese children with developmental disabilities--the Hong Kong model. *Brain Dev.* 2005;27(2):141-147.

370. Wong VC, Hui SL. Brief report: emerging services for children with autism spectrum disorders in Hong Kong (1960-2004). *J Autism Dev Disord.* 2008;38(2):383-389.

371. Mandell DS, Morales KH, Xie M, Lawer LJ, Stahmer AC, Marcus SC. Age of diagnosis among Medicaid-enrolled children with autism, 2001-2004. *Psychiatric Ser.* 2010;61(8):822-829.

372. Mak WW, Kwok YT. Internalization of stigma for parents of children with autism spectrum disorder in Hong Kong. *Soc Sci Med.* 2010;70(12):2045-2051.

373. Ling CYM, Mak WWS, Cheng JNS. Attribution Model of Stigma towards Children with Autism in Hong Kong. *J Appl Res Intellect Disabil.* 2010;23(3):237-249.

374. Strauss A, Corbin J. *Basics of qualitative research: Techniques and procedures for developing grounded theory (2nd ed)*. CA: Thousand Oaks, CA: Sage.; 1998.

375. Sun X, Allison C, Auyeung B, Matthews F, Baron-Cohen S, Brayne C. Service Provision for Autism in Mainland China: A Service Providers' Perspective (In press). *Res Dev Disabil.* 2012.

376. Furaker C, Hellstrom-Muhli U, Walldal E. Quality of care in relation to a critical pathway from the staff's perspective. *J Nurs Manag.* 2004;12(5):309-316.

377. Jun GT, Ward J, Morris Z, Clarkson J. Health care process modelling: which method when? *Int J Qual Health Care.* 2009;21(3):214-224.

378. National Bureau of Statistics of China. The national statistics on population. 2011.

379. People's Republic of Ninth National People's Congress. *Population and Family Planning Law of the People's Republic of China*; 2002.

380. Mak WWS, Cheung RYM. Affiliate Stigma Among Caregivers of People with Intellectual Disability or Mental Illness. *J Appl Res Intellect Disabil.* 2008;21(6):532-545.

381. Lauber C, Roessler W. Stigma towards people with mental illness in developing countries in Asia. *Int Rev Psychiatry.* 2007;19(2):157-178.

382. Pugliesi KL. Deviation in emotion and the labeling of mental illness. *Deviant Behavior.* 1987;8:79-102.

383. Daley TC, Sigman MD. Diagnostic conceptualization of autism among Indian psychiatrists, psychologists, and pediatricians. *J Autism Dev Disord.* 2002;32(1):13-23.

384. Sleebom-Faulkner M. Just One Child: Science and Policy in Deng's China. *Biosocieties.*6(4):495-500.

385. Chen B. A little emperor. One-child family. *Integration.* 1994(39):27.

386. Health and Welfare Bureau. *Report by the Working Group on Service for Autistic Persons*. Hong Kong: Hong Kong: Health and Welfare Bureau, Government of Hong Kong.; 1994.

387. Shek DT, Tsang SK, Lam LL, Tang FL, Cheung PM. Psychometric properties of the Chinese version of the Psycho-educational Profile-Revised (CPEP-R). *J Autism Dev Disord.* 2005;35(1):37-44.

388. C.W.Fund, V.Wong, S.L.H.Hui. Autism spectrum disorders in Hong Kong. *Brain Dev.* 2002;24(5):330.

389. Wong V, Chan CW, Mak R, et al. Child neurology and developmental paediatrics in Hong Kong - The Hong Kong Society of Child Neurology & Developmental Paediatrics. *Brain Dev.* 1996;18(3):245-245.

390. Abstracts of Satellite Symposium of the Joint Congress of ICNA & AOCNA 2002, Symposium on Child Neurology 2002 Autism/Neuromuscular Disorders. Hong Kong, 18-19 September 2002. *Brain Dev.* 2002;24(5):316-339.

391. Singh S. Review of epidata entry and analysis freewares. *Indian J Community Med.* 2009;34(1):76-77.

392. Epidata association. Epidata. 2012.

393. Raven JC, Court JH, Raven J. *Raven manual: Coloured progressive matrices.* Oxford, UK: Oxford Psychologists Press; 1995.

394. Raven JC. *Standard progressive matrices: Sets A,B,C, D, and E.* London: Lewis, H.K.; 1938.

395. Dan L. *Chinese Raven Test*: East China Normal University Press; 1989.

396. *Microsoft Excel 2003* [computer program]. Version; 2003.

397. *Stata Corporation. Stata Statistical Software: Release 10.0. College Station* [computer program]. Version; 2007.

398. Eriksson M, Westerlund M. [Screening for low-prevalence conditions is problematic. Examples from the Gothenburg autism study]. *Lakartidningen.* 2011;108(8):384-385.

399. Lundberg I, Damstrom TK, Hallstrom T, Forsell Y. Determinants of non-participation, and the effects of non-participation on potential cause-effect relationships, in the PART study on mental disorders. *Soc Psychiatry Psychiatr Epidemiol.* 2005;40(6):475-483.

400. Croen LA, Braunschweig D, Haapanen L, et al. Maternal mid-pregnancy autoantibodies to fetal brain protein: the early markers for autism study. *Biol Psychiatry.* 2008;64(7).

401. Alonzo TA, Brinton JT, Ringham BM, Glueck DH. Bias in estimating accuracy of a binary screening test with differential disease verification. *Stat.Med.* 2011;30(15):1852-1864.

402. Begg CB, Greenes RA. Assessment of diagnostic tests when disease verification is subject to selection bias. *Biometrics.* 1983;39(1):207-215.

403. Cohen J. A coefficient of agreement for nominal scales. *Educ Psychol Measu.* 1960;20:37-46.

404. Pereira A, Riesgo RS, Wagner MB. Childhood autism: translation and validation of the Childhood Autism Rating Scale for use in Brazil. *J Pediatr.(Rio J).* 2008;84(6):487-494.

405. Yen M, Lo LH. Examining test-retest reliability: an intra-class correlation approach. *Nurs Res.* 2002;51(1):59-62.

406. Gilliamm JE. *Gilliam Asperger's Disorder Scale: Examiner's manual*: Austin; 2003.

407. Goodman R, Minne C. Questionnaire screening for comorbid pervasive developmental disorders in congenitally blind children: a pilot study. *J Autism Dev Disord.* 1995;25(2):195-203.

408. Gau SSF, Lee CM, Lai MC, et al. Psychometric properties of the Chinese version of the Social Communication Questionnaire. *Res Autism Spectr Disord.* 2011;5(2):809-818.

409. Bolte S, Crecelius K, Poustka F. The Questionnaire on Behaviour and Social Communication (VSK): An autism screening instrument for research and practice. *Diagnostica.* 2000;46(3):149-155.

410. Pine E, Luby J, Abbacchi A, Constantino JN. Quantitative assessment of autistic symptomatology in preschoolers. *Autism.* 2006;10(4):344-352.

411. Williams J, Allison C, Scott F, et al. The Childhood Asperger Syndrome Test (CAST): test-retest reliability. *Autism.* 2006;10(4):415-427.

412. Allison C, Williams J, Scott F, et al. The Childhood Asperger Syndrome Test (CAST): test-retest reliability in a high scoring sample. *Autism.* 2007;11(2):177-190.

413. Cohen J. Weighted kappa: nominal scale agreement with provision for scaled disagreement or partial credit. *Psychol.Bull.* 1968;70(4):213-220.

414. Altman D. *Practical Statistics for Medical Research. 1st edn*. London: Chapman & Hall.; 1991.

415. Landis JR, Koch GG. The measurement of observer agreement for categorical data. *Biometrics.* 1977;33(1):159-174.

416. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet.* 1986;1(8476):307-310.

417. Allison C. *The quantitative checklist for autism in toddlers (Q-CHAT).* Cambridge, UK, University of Cambridge; 2009.

418. Barnett AG, van der Pols JC, Dobson AJ. Regression to the mean: what it is and how to deal with it. *Int J Epidemiol.* 2005;34(1):215-220.

419. Wallis KE, Pinto-Martin J. The challenge of screening for autism spectrum disorder in a culturally diverse society. *Acta Paediatrica.* 2008;97(5):539-540.

420. Corsello C, Hus V, Pickles A, et al. Between a ROC and a hard place: decision making and making decisions about using the SCQ. *J Child Psychol Psychiatry.* 2007;48(9):932-940.

421. Auyeung B, Wheelwright S, Allison C, Atkinson M, Samarawickrema N, Baron-Cohen S. The children's Empathy Quotient and Systemizing Quotient: sex differences in typical development and in autism spectrum conditions. *J Autism Dev Disord.* 2009;39(11):1509-1521.

422. Williams JG, Allison C, Scott FJ, et al. The Childhood Autism Spectrum Test (CAST): sex differences. *J Autism Dev Disord.* 2008;38(9):1731-1739.

423. Newschaffer CJ, Curran LK. Autism: an emerging public health problem. *Public Health Rep.* 2003;118(5).

424. Magyar CI, Pandolfi V. Factor structure evaluation of the childhood autism rating scale. *J Autism Dev Disord.* 2007;37(9):1787-1794.

425. Mandy WP, Skuse DH. Research review: What is the association between the social-communication element of autism and repetitive interests, behaviours and activities? *J Child Psychol Psychiatry.* 2008;49(8):795-808.

426. Constantino JN, Todd RD. Autistic traits in the general population: a twin study. *Arch Gen Psychiatry.* 2003;60(5):524-530.

427. Spiker D, Lotspeich LJ, Dimiceli S, Myers RM, Risch N. Behavioral phenotypic variation in autism multiplex families: evidence for a continuous severity gradient. *Am J Med Genet.* 2002;114(2):129-136.

428. Kuenssberg R, McKenzie K, Jones J. The association between the social and communication elements of autism, and repetitive/restrictive behaviours and activities: a review of the literature. *Res Dev Disabil.* 2011;32(6):2183-2192.

429. Happe F, Ronald A. The 'fractionable autism triad': a review of evidence from behavioural, genetic, cognitive and neural research. *Neuropsychol Rev.* 2008;18(4):287-304.

430. Bolte S, Westerwald E, Holtmann M, Freitag C, Poustka F. Autistic traits and autism spectrum disorders: the clinical validity of two measures presuming a continuum of social communication skills. *J Autism Dev Disord.* 2011;41(1):66-72.

431. Constantino JN, Gruber CP, Davis S, Hayes S, Passanante N, Przybeck T. The factor structure of autistic traits. *J Child Psychol.Psychiatry.* 2004;45(4):719-726.

432. Lecavalier L, Aman MG, Scahill L, et al. Validity of the autism diagnostic interview-revised. *Am J Ment Retard.* 2006;111(3):199-215.

433. Van Lang ND, Boomsma A, Sytema S, et al. Structural equation analysis of a hypothesised symptom model in the autism spectrum. *J Child Psychol Psychiatry.* 2006;47(1):37-44.

434. Georgiades S, Szatmari P, Zwaigenbaum L, et al. Structure of the autism symptom phenotype: A proposed multidimensional model. *J Am Acad Child Adolesc Psychiatry.* 2007;46(2):188-196.

435. Snow AV, Lecavalier L, Houts C. The structure of the Autism Diagnostic Interview-Revised: diagnostic and phenotypic implications. *J Child Psychol Psychiatry.* 2009;50(6):734-742.

436. Frazier TW, Youngstrom EA, Kubu CS, Sinclair L, Rezai A. Exploratory and confirmatory factor analysis of the autism diagnostic interview-revised. *J Autism Dev Disord.* 2008;38(3):474-480.

437. Kamp-Becker I, Ghahreman M, Smidt J, Remschmidt H. Dimensional structure of the autism phenotype: relations between early development and current presentation. *J Autism Dev Disord.* 2009;39(4):557-571.

438. Steer CD, Golding J, Bolton PF. Traits contributing to the autistic spectrum. *PLoS One.* 2010;5(9):e12633.

439. Posserud B, Lundervold AJ, Steijnen MC, Verhoeven S, Stormark KM, Gillberg C. Factor analysis of the Autism Spectrum Screening Questionnaire. *Autism.* 2008;12(1):99-112.

440. Stewart ME, Austin EJ. The structure of the Autism-Spectrum Quotient (AQ): Evidence from a student sample in Scotland (vol 47, pg 224, 2009). *Pers Individ Dif.* 2010;48(1):88-88.

441. Hoekstra RA, Bartels M, Cath DC, Boomsma DI. Factor structure, reliability and criterion validity of the Autism-Spectrum Quotient (AQ): a study in Dutch population and patient groups. *J Autism Dev Disord.* 2008;38(8):1555-1566.

442. Auyeung B, Baron-Cohen S, Wheelwright S, Allison C. The Autism Spectrum Quotient: Children's Version (AQ-Child). *J Autism Dev Disord.* 2008;38(7):1230-1240.

443. Kanne SM, Wang J, Christ SE. The Subthreshold Autism Trait Questionnaire (SATQ): Development of a Brief Self-Report Measure of Subthreshold Autism Traits. *J Autism Dev Disord.* 2011.

444. Pandolfi V, Magyar CI, Dill CA. Confirmatory factor analysis of the child behavior checklist 1.5-5 in a sample of children with autism spectrum disorders. *J Autism Dev Disord.* 2009;39(7):986-995.

445. Kuenssberg R, McKenzie K. Confirmatory factor analysis of the Adult Asperger Assessment: the association of symptom domains within a clinical population. *Res Dev Disabil.* 2011;32(6):2321-2329.

446. Bartholornew DJ, Steel F, Moustaki I, Galbraith J. *The Analysis and Interpretation of Multivariate Data for Social Scientists*: Chapman & Hall/CRC; 2002.

447. Kline P. *Handbook of Psychometric Testing*. London: Routledge; 2000.

448. Sharp C, Goodyer IM, Croudace TJ. The Short Mood and Feelings Questionnaire (SMFQ): a unidimensional item response theory and categorical data factor analysis of self-report ratings from a community sample of 7-through 11-year-old children. *J Abnorm Child Psychol.* 2006;34(3):379-391.

449. Angold A, Erkanli A, Silberg J, Eaves L, Costello EJ. Depression scale scores in 8-17-year-olds: effects of age and gender. *J Child Psychol Psychiatry.* 2002;43(8):1052-1063.

450. Muthen B. Multiple-Group Structural Modeling with Non-Normal Continuous-Variables. *Br J Math Stat Psychol.* 1989;42:55-62.

451. McDonald RP. *Test theory: A unified treatment*. Mahwah, NJ: LEA; 1999.

452. Muthen LK, Muthen BO. *Mplus Users' guide version 6*; 2010.

453. Khalid MN. An overview of statistical approaches for assessing model fit. *The international journal of educational and psychological assessment.* 2011;8(2):69-87.

454. Bandalos DLB-K, M.R. *Four common misconceptions in exploratory factor analysis In Statistical and methodological myths and urban legends: Doctrine, verity and fable in the organizational and social sciences.* New York: Routledge. ; 2009.

455. Bentler PM, Bonett DG. Significance tests and goodness of fit in the analysis fo covariance structures. *Psychol Bull.* 1980;88(3):588-606.

456. Browne MW, Cudeck R. Alternative Ways of Assessing Model Fit. *Soc Meth Res.* 1992;21(2):230-258.

457. Hu LT, Bentler PM. Cutoff Criteria for Fit Indexes in Covariance Structure Analysis: Conventional Criteria Versus New Alternatives. *Struc Equ Modeling.* 1999;6(1):1-55.

458. Floyd FJ, Widaman KF. Factor analysis in the development and refinement of clinical assessment instruments. *Psychol Assess.* 1995;7(3):286-299.

459. DeCoster J. Overview of Factor Analysis. http://www.stat-help.com/notes.html. Accessed Sixth, August, 2012.

460. Muthen LK, Muthen B. MPlus short courses. 2009; http://www.statmodel.com/download/Topic%202v20%20[Compatibility%20Mode]1.pdf

461. Yu CY, Muthen B. *Evaluation of model fit indices for latent variable models with categorical and continuous outcomes* 2002.

462. Edelen MO, Reeve BB. Applying item response theory (IRT) modeling to questionnaire development, evaluation, and refinement. *Qual Life Res.* 2007;16:5-18.

463. Muthen B, du Toit SHC, Spisic D. Robust inference using weighted least squares and quadratic estimating equations in latent variable modeling with categorical and continuous outcomes; 1997.

464. Flora DB, Curran PJ. An empirical evaluation of alternative methods of estimation for confirmatory factor analysis with ordinal data. *Psychol Meth.* 2004;9(4):466-491.

465. Baker FB. *The basics of item response theory*: ERIC Cleaninghouse on Assessment and Evaluation.; 2001.

466. Cronbach LJ, Shavelson RJ. My Current Thoughts on Coefficient Alpha and Successor Procedures. *Educ Psychol Meas* 2004;64(3):391-418.

467. Bland JM, Altman DG. Statistics notes:Cronbach's alpha. *BMJ.* 1997:314-572.

468. Sun X, Allison C, Auyeung B, Baron-Cohen S, Brayne C. Healthcare and educational provision for autism in mainland China. (In press). *Res Dev Disabil.* 2012.

469. Sevik AE, Kultur EC, Demirel H, et al. Asperger Syndrome with Highly Exceptional Calendar Memory: A Case Report. *Turk Psikiyatri Dergisi.* 2010;21(3):249-255.

470. Conson M, Salzano S, Grossi D. Neuropsychological functioning of an Asperger child with exceptional skill in arranging picture stories. *Neurocase.* 2011;17(4):353-359.

471. James I. Autism and Mathematical Talent. *Mathematical Intelligencer.* 2010;32(1):56-58.

472. Glanzman M. Developing Talents: Careers for Individuals with Asperger Syndrome and High-Functioning Autism, 2nd edition. *J Autism Dev Disord.* 2010;40(2):266-267.

473. Clark A, Harrington R. On diagnosing rare disorders rarely: appropriate use of screening instruments. *J Child Psychol Psychiatry.* 1999;40(2):287-290.

474. Rai D, Lewis G, Lundberg M, et al. Parental socioeconomic status and risk of offspring autism spectrum disorders in a Swedish population-based study. *J Am Acad Child Adolesc Psychiatry.* 2012;51(5):467-476.

475. King MD, Bearman PS. Socioeconomic Status and the Increased Prevalence of Autism in California. *Am Sociol Rev.* 2011;76(2):320-346.

476. Maenner MJ, Arneson CL, Durkin MS. Socioeconomic disparity in the prevalence of autism spectrum disorder in Wisconsin. *WMJ.* 2009;108(5).

477. Larsson HJ, Eaton WW, Madsen KM, et al. Risk factors for autism: perinatal factors, parental psychiatric history, and socioeconomic status. *Am J Epidemiol.* 2005;161(10).

478. Durkin MS, Maenner MJ, Meaney FJ, et al. Socioeconomic inequality in the prevalence of autism spectrum disorder: evidence from a U.S. cross-sectional study. *PLoS One.* 2010;5(7):e11551.

479. Gau SS, Lin CH, Hu FC, et al. Psychometric properties of the Chinese version of the Swanson, Nolan, and Pelham, Version IV Scale-Teacher Form. *J Pediatr Psychol.* 2009;34(8):850-861.

480. Hou T. The Chinese Primary Care System: Its Evolutiion, Challenges and Legal Aspects fo Refom. *CUREJ-College Undergraduate Research Elec.* 2009.

481. Meng Q. Developing and implementing equity-promoting health care policies in China: A case study commissioned by the Health Systems Knowledge Network. 2007.

482. Wang J, Kushner K, Frey JJ, III, Ping DX, Qian N. Primary care reform in the Peoples' Republic of China: implications for training family physicians for the world's largest country. *Fam.Med.* 2007;39(9):639-643.

483. Yip W, Hsiao W. The Chinese Health System at Crossroads. *Health Aff.* 2008;27(2):460-468.

484. Howlin P. Autism and diagnostic substitution. *Dev Med Child Neurol.* 2008;50(5).

485. Waterhouse L, Morris R, Allen D, et al. Diagnosis and classification in autism. *J Autism Dev Disord.* 1996;26(1):59-86.

486. Gillberg C, Coleman M. Autism and medical disorders: a review of the literature. *Dev Med Child Neurol.* 1996;38(3):191-202.

487. Shattuck PT. The contribution of diagnostic substitution to the growing administrative prevalence of autism in US special education. *Pediatrics.* 2006;117(4).

488. Shattuck PT. Diagnostic substitution and changing autism prevalence. *Pediatrics.* 2006;117(4).

489. Rosenberg RE, Daniels AM, Law JK, Law PA, Kaufmann WE. Trends in autism spectrum disorder diagnoses: 1994-2007. *J Autism Dev Disord.* 2009;39(8):1099-1111.

490. Murphy M, Bolton PF, Pickles A, Fombonne E, Piven J, Rutter M. Personality traits of the relatives of autistic probands. *Psychol Med.* 2000;30(6).

491. Bennett T, Szatmari P, Bryson S, et al. Differentiating autism and Asperger syndrome on the basis of language delay or impairment. *J Autism Dev Disord.* 2008;38(4):616-625.

492. Factor DC, Freeman NL, Kardash A. Brief report: a comparison of DSM-III and DSM-III-R criteria for autism. *J Autism Dev Disord.* 1989;19(4):637-640.

493. Glascoe FP. Early detection of developmental and behavioral problems. *Pediatr Rev.* 2000;21(8).

494. Ornitz EM. Childhood autism. A review of the clinical and experimental literature. *Calif Med.* 1973;118(4):21-47.

495. Centre of Disease Control and P. Prevalence of autism spectrum disorders - Autism and Developmental Disabilities Monitoring Network, United States, 2006. *MMWR Surveill Summ.* 2009;58(10).

496. Bernier R, Mao A, Yen J. Psychopathology, families, and culture: autism. *Child Adolesc Psychiatr Clin N Am.* 2010;19(4):855-867.

497. Keen DV, Reid FD, Arnone D. Autism, ethnicity and maternal immigration. *Br J Psychiatry.* 2010;196(4):274-281.

498. Akinsola HA, Fryers T. A comparison of patterns of disability in severely mentally handicapped children of different ethnic origins. *Psychol Med.* 1986;16(1):127-133.

499. Wing L. The definition and prevalence of autism: A review. *Eur Child Adolesc Psychiatry.* 1993;2(1):61-74.

500. Lotter V. Childhood autism in africa. *J Child Psychol Psychiatry.* 1978;19(3):231-244.

501. Mandell DS, Palmer R. Differences among states in the identification of autistic spectrum disorders. *Arch Pediatr Adolesc Med.* 2005;159(3):266-269.

502. Lee LC, Harrington RA, Louie BB, Newschaffer CJ. Children with autism: quality of life and parental concerns. *J Autism Dev Disord.* 2008;38(6).

503. Lung FW, Shu BC, Chiang TL, Lin SJ. Parental concerns based general developmental screening tool and autism risk: the Taiwan National Birth cohort study. *Pediatr Res.* 2010;67(2):226-231.

504. Windham GC, Fessel K, Grether JK. Autism spectrum disorders in relation to parental occupation in technical fields. *Autism Res.* 2009;2(4):183-191.

505. Koyama T, Miyake Y, Kurita H. Parental ages at birth of children with pervasive developmental disorders are higher than those of children in the general population. *Psychiatry Clin Neurosci.* 2007;61(2).

506. Croen LA, Najjar DV, Fireman B, Grether JK. Maternal and paternal age and risk of autism spectrum disorders. *Arch Pediatr Adolesc Med.* 2007;161(4).

507. Gillberg C. Maternal age and infantile autism. *J Autism Dev Disord.* 1980;10(3):293-297.

508. Steinhausen HC, Gobel D, Breinlinger M, Wohlleben B. Maternal age and autistic children. *J Dev Behav Pediatr.* 1984;5(6):343-345.

509. Reichenberg A, Gross R, Sandin S, Susser ES. Advancing paternal and maternal age are both important for autism risk. *Am J Public Health.* 2010;100(5).

510. Grether JK, Anderson MC, Croen LA, Smith D, Windham GC. Risk of autism and increasing maternal and paternal age in a large north American population. *Am J Epidemiol.* 2009;170(9).

511. Ma J, Guo Y, Jia M, Li X, Liu J. The reliability of Chinese version of Aberrant Behavior Checklist. *Chinese Ment Health.* 2011;25(1):14-18.

Appendices

Appendix 1.1 The UK national screening committee criteria

The condition	
1	The condition should be an important health problem
2	The epidemiology and natural history of the condition, including development from latent to declared disease, should be adequately understood and there should be a detectable risk factor, disease marker, latent period or early symptomatic stage.
3	All the cost-effective primary prevention interventions should have been implemented as far as practicable.
4	If the carriers of a mutation are identified as a result of screening the natural history of people with this status should be understood, including the psychological implications.
The test	
1	There should be a simple, safe, precise and validated screening test.
2	The distribution of test values in the target population should be known and a suitable cut-off level defined and agreed.
3	The test should be acceptable to the population.
4	There should be an agreed policy on the further diagnostic investigation of individuals with a positive test result and on the choices available to those individuals.
5	If the test is for mutations the criteria used to select the subset of mutations to be covered by screening, if all possible mutations are not being tested, should be clearly set out.
The treatment	
1	There should be an effective treatment or intervention for patients identified through early detection, with evidence of early treatment leading to better outcomes than late treatment.
2	There should be agreed evidence based policies covering which individuals should be offered treatment and the appropriate treatment to be offered.
3	Clinical management of the condition and patient outcomes should be optimised in all health care providers prior to participation in a screening programme.
The screening programme	
1	There should be evidence from high quality Randomised Controlled Trials that the screening programme is effective in reducing mortality or morbidity. Where screening is aimed solely at providing information to allow the person being screened to make an “informed choice” (eg. Down’s syndrome, cystic fibrosis carrier screening), there must be evidence from high quality trials that the test accurately measures risk. The information that is provided about the test and its outcome must be of value and readily understood by the individual being screened.
2	There should be evidence that the complete screening programme (test, diagnostic procedures, treatment/ intervention) is clinically, socially and ethically acceptable to health professionals and the public.
3	The benefit from the screening programme should outweigh the physical and psychological harm (caused by the test, diagnostic procedures and treatment).
4	The opportunity cost of the screening programme (including testing, diagnosis and treatment,

	administration, training and quality assurance) should be economically balanced in relation to expenditure on medical care as a whole (ie. value for money). Assessment against the criteria should have regard to evidence from cost benefit and/or cost effectiveness analyses and have regard to the effective use of available resource.
5	All other options for managing the condition should have been considered (eg. improving treatment, providing other services), to ensure that no more cost effective intervention could be introduced or current interventions increased within the resources available.
6	There should be a plan for managing and monitoring the screening programme and an agreed set of quality assurance standards.
7	Adequate staffing and facilities for testing, diagnosis, treatment and programme management should be available prior to the commencement of the screening programme.
8	Evidence-based information, explaining the consequences of testing, investigation and treatment, should be made available to potential participants to assist them in making an informed choice.
9	Public pressure for widening the eligibility criteria for reducing the screening interval, and for increasing the sensitivity of the testing process, should be anticipated. Decisions about these parameters should be scientifically justifiable to the public.
10	If screening is for a mutation the programme should be acceptable to people identified as carriers and to other family members.

(Adapted from National Screening Committee website:http://www.screening.nhs.uk/criteria#fileid9287)

Appendix 2.1 Tasks in each ADOS module

Module 1	Module 2	Module 3	Module 4
Preverbal/single words/phrases	Flexible phrase speech	Fluent speech child/adolescent	Fluent speech adolescent/adult
Anticipation of a social routine	Construction task	Construction task	Construction task
Functional and symbolic imitation	Make-believe play	Make-believe play	Current work/school/daily living
	Joint interactive play	Joint interactive play	Socio-emotional questions: Plans and dreams
Free play	Free play	Break	Break
Snack	Snack	Cartoons	Cartoons
Response to name	Response to name	Socio-emotional questions: Emotions	Socio-emotional questions: Emotions
Response to joint attention	Response to joint attention	Socio-emotional questions: Friends/loneliness/marriage	Socio-emotional questions: Friends/loneliness/marriage
Birthday party	Birthday party	Socio-emotional questions: Social difficulties/annoyance	Socio-emotional questions: Social difficulties/annoyance
Bubble play	Bubble play	Creating a story	Creating a story
Anticipation of a routine with objects	Anticipation of a routine with objects	Conversation/reporting a non-routine event	Conversation/reporting a non-routine event
	Demonstration task	Demonstration task	Demonstration task
	Description of picture	Description of picture	Description of picture
	Looking at a book	Telling a story from a book	Telling a story from a book
	Conversation		

(Adapted from the ADOS manual)

Appendix 2.2 Items in the ADOS algorithm for each module and a sample of Module 2 algorithm

Module 1	Module 2	Module 3	Module 4
Algorithm items			
Stereotyped/idiosyncratic words or phrases	Stereotyped/idiosyncratic words or phrases	Stereotyped/idiosyncratic words or phrases	Stereotyped/idiosyncratic words or phrases
Gestures	Descriptive, conventional. Instrumental gestures	Descriptive, conventional. Instrumental gestures	Descriptive, conventional. Instrumental gestures
Unusual eye contact	Unusual eye contact	Unusual eye contact	Unusual eye contact
Facial expression directed to others	Facial expression directed to others	Facial expression directed to others	Facial expression directed to others
Quality of social overtures	Quality of social overtures	Quality of social overtures	Quality of social overtures
Response to joint attention	Amount of reciprocal social communication	Amount of reciprocal social communication	Amount of reciprocal social communication
Shared enjoyment	Quality of social response	Quality of social response	Quality of social response
Use of other's body to communicate	Conversation	Conversation	Conversation
Point	Point to express interest		Emphatic or emotional gestures
Showing	Overall quality of rapport	Overall quality of rapport	Empathy/comments on others
Frequency of vocalization directed to others	Amount of social overtures	Insight	
Spontaneous initiation of joint attention	Spontaneous initiation of joint attention	Report of events	Responsibility
Other items			
Immediate echoing	Immediate echoing	Immediate echoing	Immediate echoing
Speech abnormality	Speech abnormality	Speech abnormality	Speech abnormality
Imagination/functional play	Imagination/functional play	Imagination	Imagination
Mannerisms	Mannerisms	Mannerisms	Mannerisms
Unusual sensory behaviours	Unusual sensory behaviours	Unusual sensory behaviours	Unusual sensory behaviours
Repetitive interests and behaviours	Repetitive interests and behaviours	Excessive, specific interests	Excessive, specific interests
		Rituals and compulsive behaviours	Rituals and compulsive behaviours
Overactivity	Overactivity	Overactivity	Overactivity
Negative behaviours	Negative behaviours	Negative behaviours	Negative behaviours
Anxiety	Anxiety	Anxiety	Anxiety

(Adapted from the ADOS manual)

ADOS MODULE 2

Child ID: _____ Date of Birth: _____

Gender: _____ Date of Evaluation: _____

Examiner: _____ Chronological Age: _____

ADOS Algorithm for DSM-IV/ICD-10 Autism Diagnosis
(Convert scores of 3 on the protocol to 2, and treat all scores other than 0–3 as 0.)

Communication

Amount of Social Overtures/Maintenance of Attention	(A-2)	_____
Stereotyped/Idiosyncratic Use of Words or Phrases	(A-5)	_____
Conversation	(A-6)	_____
Pointing	(A-7)	_____
Descriptive, Conventional, Instrumental, or Informational Gestures	(A-8)	_____
Communication Total		_____

(Autism cut-off = 5; *autism spectrum* cut-off = 3)

Reciprocal Social Interaction

Unusual Eye Contact	(B-1)	_____
Facial Expressions Directed to Others	(B-2)	_____
Spontaneous Initiation of Joint Attention	(B-6)	_____
Quality of Social Overtures	(B-8)	_____
Quality of Social Response	(B-9)	_____
Amount of Reciprocal Social Communication	(B-10)	_____
Overall Quality of Rapport	(B-11)	_____
Social Interaction Total		_____

(Autism cut-off = 6; *autism spectrum* cut-off = 4)

Communication + Social Interaction Total _____

***(Autism* cut-off = 12; *autism spectrum* cut-off = 8)**

Imagination/Creativity

(C-2) _____

Stereotyped Behaviors and Restricted Interests

Unusual Sensory Interest in Play Material/Person	(D-1)	_____
Hand and Finger and Other Complex Mannerisms	(D-2)	_____
Unusually Repetitive Interests or Stereotyped Behaviors	(D-4)	_____
Stereotyped Behaviors and Restricted Interests Total		_____

Diagnosis

ADOS Classification: _____

_____

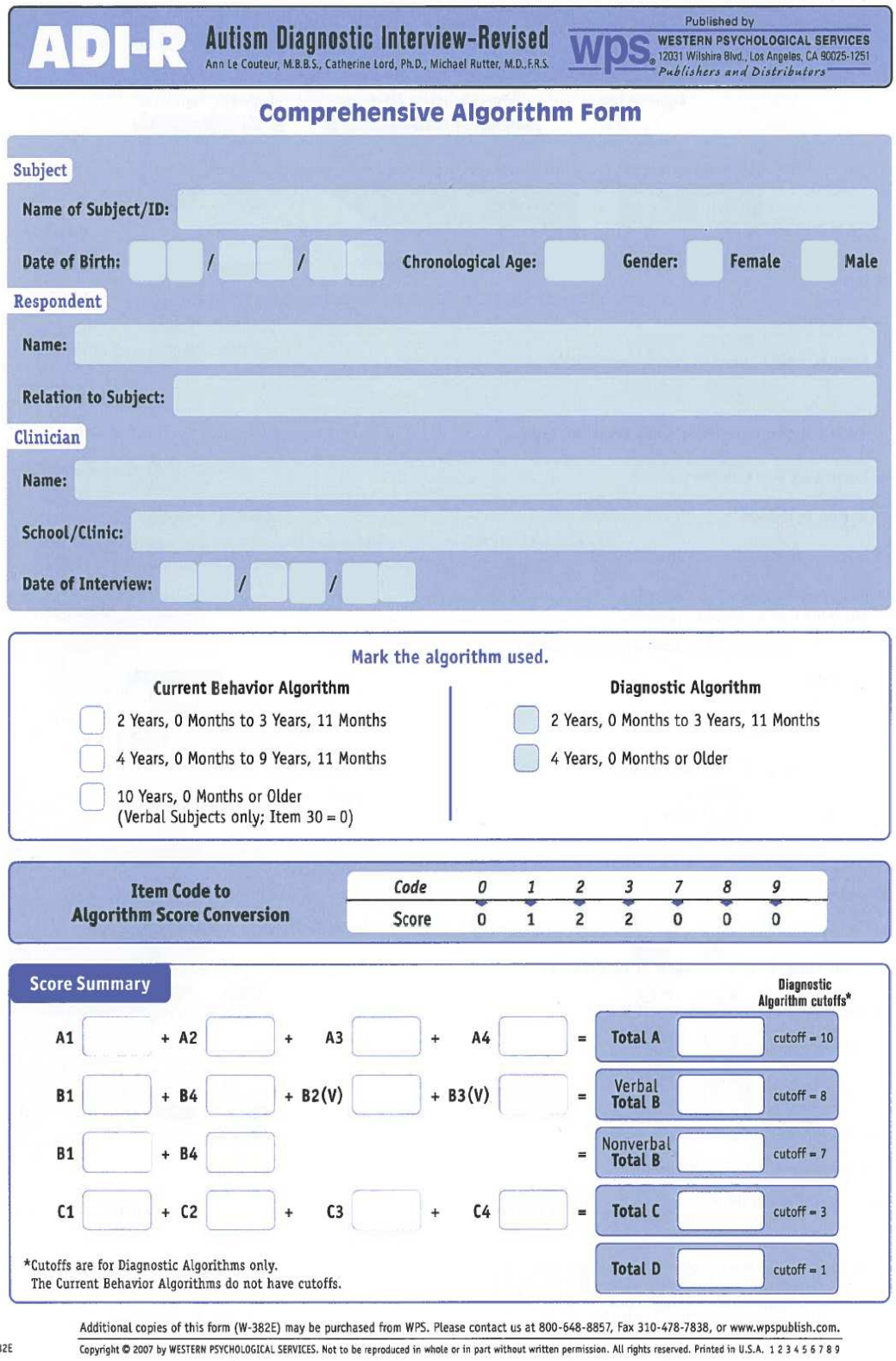
_____

Overall Diagnosis: _____

_____

_____

Appendix 2.3 ADI-R algorithm



ADI-R Autism Diagnostic Interview-Revised
Ann Le Couteur, M.B.B.S., Catherine Lord, Ph.D., Michael Rutter, M.D., F.R.S.

Published by
WPS WESTERN PSYCHOLOGICAL SERVICES
12031 Wilshire Blvd., Los Angeles, CA 90025-1251
Publishers and Distributors

Comprehensive Algorithm Form

Subject

Name of Subject/ID:

Date of Birth: / / Chronological Age: Gender: Female Male

Respondent

Name:

Relation to Subject:

Clinician

Name:

School/Clinic:

Date of Interview: / /

Mark the algorithm used.

Current Behavior Algorithm

- 2 Years, 0 Months to 3 Years, 11 Months
- 4 Years, 0 Months to 9 Years, 11 Months
- 10 Years, 0 Months or Older (Verbal Subjects only; Item 30 = 0)

Diagnostic Algorithm

- 2 Years, 0 Months to 3 Years, 11 Months
- 4 Years, 0 Months or Older

Item Code to Algorithm Score Conversion

Code	0	1	2	3	7	8	9
Score	0	1	2	2	0	0	0

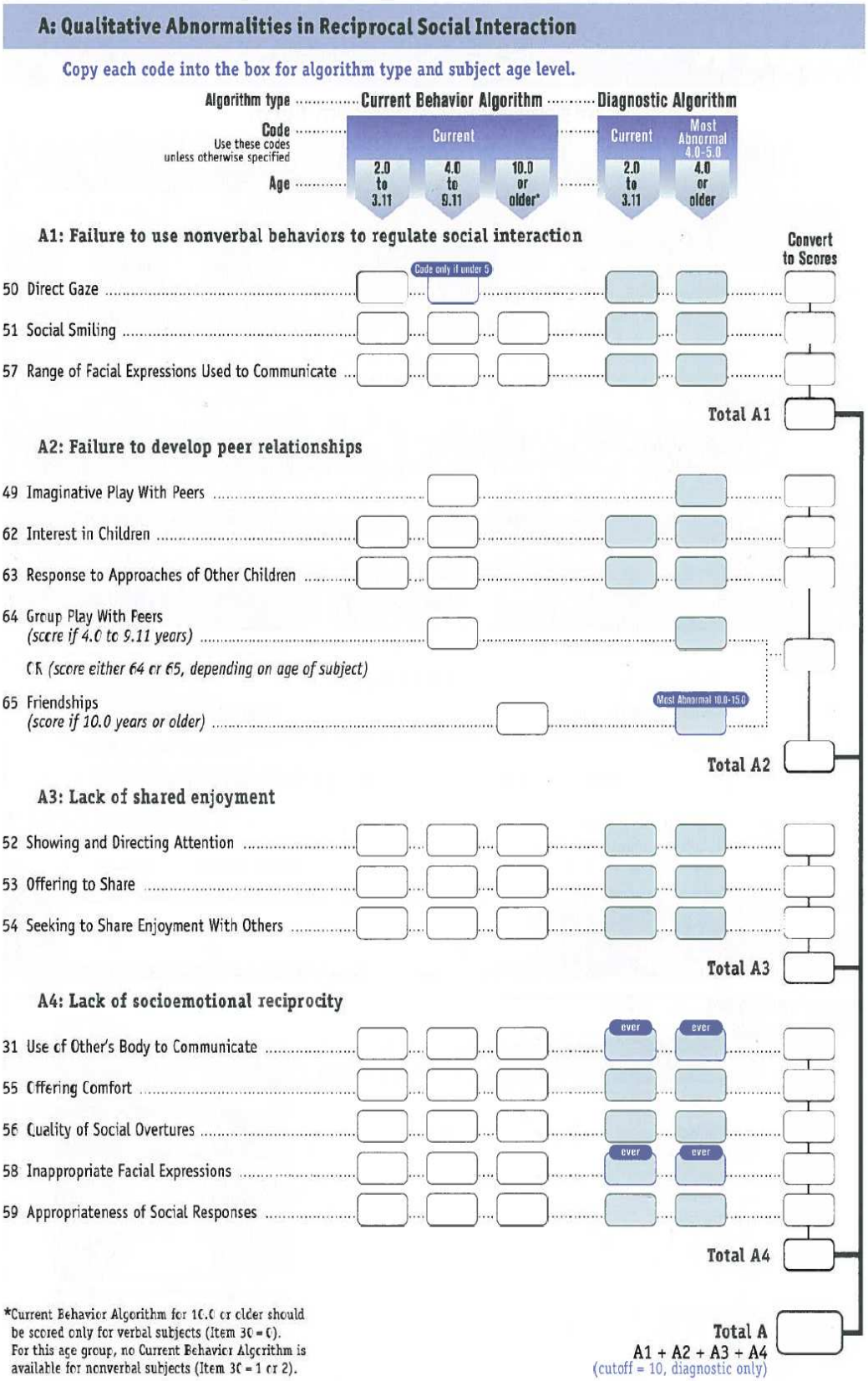
Score Summary

									Diagnostic Algorithm cutoffs*
A1		+ A2		+ A3		+ A4		= Total A	cutoff = 10
B1		+ B4		+ B2(V)		+ B3(V)		= Verbal Total B	cutoff = 8
B1		+ B4						= Nonverbal Total B	cutoff = 7
C1		+ C2		+ C3		+ C4		= Total C	cutoff = 3
								Total D	cutoff = 1

*Cutoffs are for Diagnostic Algorithms only.
The Current Behavior Algorithms do not have cutoffs.

Additional copies of this form (W-382E) may be purchased from WPS. Please contact us at 800-648-8857, Fax 310-478-7838, or www.wpspublish.com.

W-382E


A: Qualitative Abnormalities in Reciprocal Social Interaction
Copy each code into the box for algorithm type and subject age level.
Algorithm type
Current Behavior Algorithm
Diagnostic Algorithm
Code
Use these codes unless otherwise specified
Current
Current
Most Abnormal 4.0-5.0
Age
2.0 to 3.11
4.0 to 9.11
10.0 or older*
2.0 to 3.11
4.0 or older
A1: Failure to use nonverbal behaviors to regulate social interaction
Convert to Scores
Code only if under 5
50 Direct Gaze
51 Social Smiling
57 Range of Facial Expressions Used to Communicate
Total A1
A2: Failure to develop peer relationships
49 Imaginative Play With Peers
62 Interest in Children
63 Response to Approaches of Other Children
64 Group Play With Peers
(score if 4.0 to 9.11 years)
OR (score either 64 or 65, depending on age of subject)
65 Friendships
(score if 10.0 years or older)
Most Abnormal 10.0-15.0
Total A2
A3: Lack of shared enjoyment
52 Showing and Directing Attention
53 Offering to Share
54 Seeking to Share Enjoyment With Others
Total A3
A4: Lack of socioemotional reciprocity
ever
ever
31 Use of Other's Body to Communicate
55 Offering Comfort
56 Quality of Social Overtures
ever
ever
58 Inappropriate Facial Expressions
59 Appropriateness of Social Responses
Total A4
*Current Behavior Algorithm for 10.0 or older should be scored only for verbal subjects (Item 30 = 0). For this age group, no Current Behavior Algorithm is available for nonverbal subjects (Item 30 = 1 or 2).
Total A
A1 + A2 + A3 + A4
(cutoff = 10, diagnostic only)

B: Qualitative Abnormalities in Communication

- Score B1, B4, B2(V), and B3(V) for verbal subjects (Item 30 = 0).
- Score only B1 and B4 for nonverbal subjects (Item 30 = 1 or 2).

Copy each code into the box for algorithm type and subject age level.

B1: Lack of, or delay in, spoken language and failure to compensate through gesture

Convert to Scores

42 Pointing to Express Interest

43 Nodding

44 Head Shaking

45 Conventional/Instrumental Gestures

Total B1

B4: Lack of varied spontaneous make-believe or social imitative play

(B4 is not scored on Current Behavior Algorithm for 10.0 or older.)

47 Spontaneous Imitation of Actions

48 Imaginative Play

61 Imitative Social Play

Total B4

VERBAL SUBJECTS ONLY

B2(V): Relative failure to initiate or sustain conversational interchange

34 Social Verbalization/Chat (ever)

35 Reciprocal Conversation (ever)

Total B2(V)

B3(V): Stereotyped, repetitive, or idiosyncratic speech

33 Stereotyped Utterances and Delayed Echolalia (ever) (ever)

36 Inappropriate Questions or Statements (ever) (ever)

37 Pronominal Reversal (ever) (ever)

38 Neologisms/Idiosyncratic Language (ever) (ever)

Total B3(V)

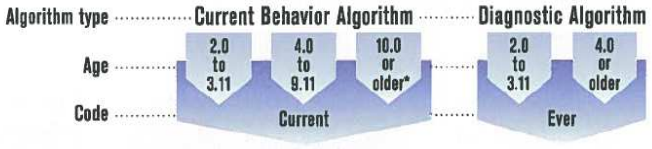
Verbal Subjects — **Total B(V)** B1 + B4 + B2(V) + B3(V) (cutoff = 8, diagnostic only)

Nonverbal Subjects — **Total B(NV)** B1 + B4 (cutoff = 7, diagnostic only)

*Current Behavior Algorithm for 10.0 or older should be scored only for verbal subjects (Item 30 = 0). For this age group, no Current Behavior Algorithm is available for nonverbal subjects (Item 30 = 1 or 2).

C: Restricted, Repetitive, and Stereotyped Patterns of Behavior

Copy each code into the box for algorithm type and subject age level.



C1: Encompassing preoccupation or circumscribed pattern of interest

Convert to Scores

67 Unusual Preoccupations .....

68 Circumscribed Interests *(score if 3 years or older)* .....

Total C1

C2: Apparently compulsive adherence to nonfunctional routines or rituals

39 Verbal Rituals *(score only if Item 30 = 0)* .....

70 Compulsions/Rituals .....

Total C2

C3: Stereotyped and repetitive motor mannerisms

77 Hand and Finger Mannerisms .....

78 Other Complex Mannerisms or Stereotyped Body Movements .....

Record the higher of the two scores

Total C3

C4: Preoccupation with parts of objects or nonfunctional elements of material

69 Repetitive Use of Objects or Interest in Parts of Objects .....

71 Unusual Sensory Interests .....

Record the higher of the two scores

Total C4

*Current Behavior Algorithm for 10.0 or older should be scored only for verbal subjects (Item 30 = 0). For this age group, no Current Behavior Algorithm is available for nonverbal subjects (Item 30 = 1 or 2).

Total C
C1 + C2 + C3 + C4
(cutoff = 3, diagnostic only)

D: Abnormality of Development Evident at or Before 36 Months

Diagnostic Algorithms only.

Code Score

2 Age Parents First Noticed *(if <36 months, score 1)* .....

9 Age of First Single Words *(if >24 months, score 1)* .....

10 Age of First Phrases *(if >33 months, score 1)* .....

86 Age When Abnormality First Evident *(if coded 3 or 4, score 1)* .....

87 Interviewer's Judgment on Age When Abnormalities First Manifest *(if <36 months, score 1)* .....

Total D
(cutoff = 1, diagnostic only)

Appendix 2.4 Possible reasons for prevalence variation in developed countries

1) The broader definition of autism and possible diagnostic substitution[247, 484]

Since the first recognition, the definition of ASC has been changed many times[14]. In the early period of autism research, there was a tendency to focus on the core syndrome of autism which was defined under the Kanner's criteria[485]. However, more children were given an ASC diagnosis after understanding that autism is a biologically determined neurodevelopmental disorder which can present with other medical conditions[486]. For example, it is thought that many children with autsim were previously incorrectly given a diagnosis of mental retardation (MR)[487] or learning disabilities. Since the recognition of ASC, those cases have been re-diagnosed as ASC. Shattuck's study[488] showed, from 1994 to 2003, the prevalence of MR and learning disabilities declined by 2.8 and 8.3 per 10,000, respectively. This study found the high autism prevalence was significantly associated with the declines in the prevalence in MR and learning disabilities. Another study reported similar findings drawn from the analysis based on the US longitudinal online database for individuals with ASC, the Interactive Autism Network (IAN)[489]. In this sample, from 1994 to 2007, the overall proportion for MR/Intellectual Disability (ID) diagnosis decreased from nearly 50% to less than 20%. The authors suggested the children who might be diagnosed as MR/ID or developmental delay in the past might be given an ASC diagnosis instead under current practice. More cases were identified after family studies that discovered many milder autistic features exist in the relatives of individuals with autism. Those people with milder autistic features were considered the so-called "border phenotype" of autism[84, 490]. The recognition of Asperger Syndrome potentially increased the case load as it showed ASC can occur in the presence of normal intelligence[12, 491].

2) Changes in diagnostic criteria

Two international diagnostic criteria for autism are the ICD-10 and DSM-IV. When autism appeared in DSM-III in 1980[18], it was an independent diagnostic term, which was more specific[26]. In 1987, DSM-III-R introduced the Autistic Disorder criteria and introduced new subtype of autism, the PDD-NOS. This change was considered as having potentially encouraged overdiagnosis[492], so in 1994, the DSM-IV[4] aimed to reduce over-inclusion caused by the DSM-III. However, DSM-IV first included Asperger Syndrome into the spectrum. The inclusion of AS into diagnostic criteria

will inevitably lead to more cases in research after that. In 2000, the DSM-IV-TR[24] introduced more specific definition for PDD-NOS than those in the DSM-IV. The new definition of PDD-NOS requires less extreme impairments in social and communication than those with Autistic Disorder.

3) The development in screening and diagnostic instruments[50]

As the broader phenotypes of ASC are more recognised, more screening tests have been developed in order to capture milder autistic conditions. These screening tests aim to target people in different age groups as well as with different conditions within the spectrum[15, 493]. In terms of diagnostic instruments, the combination of the ADOS and the ADI-R has been widely adopted as standardised diagnostic instruments in research settings. More advanced instruments lead to more thorough detection of autistic conditions especially for borderline phenotypes that might have been missed by previous instruments.

4) Change in research methodology[248]

Many prevalence studies of ASC used retrospective research method to track already diagnosed cases through available records in clinical settings[494] or through healthcare systems[242]. This method could cause referral bias to the result. First, as ASC was not well recognised before, the number of people who sought for medical help because of ASC was expected to be less than nowadays. Second, there are many factors that could confound the referral samples. For example, there might be differences in referral patterns, availability of health services, clinical practice, local awareness and so on[125]. There were generally four approaches of case identification in prevalence studies. One approach was purely case finding through records without directly contact with autistic cases. Second approach is prospective screening and further diagnostic assessment within the sample population. Third approach is the combination of the former two which includes the case finding in the records of high risk population such as in special educational settings and clinical records as well as conducting prospective screening in general population. The studies which adopted both screening and diagnostic process for case identification (the capture-recapture methods) appeared to generate higher prevalence estimates than those using passive case finding method[125]. Fourth, a few studies[71, 495] depended on the surveillance of ASC in a defined population to detect new developed autistic cases which brought

more confidence in the reported incidence of ASC. The third and fourth methods developed on the combination of the first and second methods. Thus studies used the latter two methods might report higher prevalence estimates.

5) Geographical differences among targeted population in different studies.

The sample size of target populations has been proposed as a confounding factor in prevalence estimation. Gillberg suggested the higher rates might be found in studies performed on very small populations by chance[211, 212]. She also suggested the effect of migration especially in Europe and Japan would contribute to the increase in prevalence[212]. This cultural influence[496] and ethnicity[497] has been investigated in several studies and possible explanations were proposed including genetic, the maternal viral infections in pregnancy and environmental risk factors[498-500]. There may also be differences in participants between the rural and metropolitan areas due to the accessibility and availability of health services. The diagnosis of ASD in rural areas is usually performed in special centres while in metropolitan cities the diagnosis can be given locally[501]. The socioeconomic status of targeted population may influence the referral of ASC which again might influence the reported prevalence[476]. King's study suggested that income status is associated with a decreased risk of an autism diagnosis[475] and the importance of community wealth declined as the increase of prevalence slowed down because the diagnosis became more common. Liu's study based on California database suggested the social diffusion process contributed to the increased prevalence[274]. Another confounding source in the prevalence estimates might come from the parents, such as the parental concern[502, 503], parental educational background[504] and parental age[505] especially maternal age[506-510].

Appendix 3.1 Descriptive epidemiology of the population studied in reviewed papers

No	Year	First author	Region	City or county	Sample size	Area	Age	Sample selection method	Sample source
1	1987	Tao[75]	Mainland	Nanjing	457,200*	Urban	3-8	Case counting	Clinical patients
2	2000	Luo [266]	Mainland	Fujian Province	10,802	Mixed	2-14	Randomized sampling	Stratified general population
3	2002	Wang [259]	Mainland	Changzhou	3.978	Urban	2-6	Randomized sampling	Kindergarten population
4	2002	Ren [267]	Mainland	Tongling	3,559	Urban	3-5	Whole sample	Stratified general population
5	2003	Wang [268]	Mainland	Changzhou, Yizheng	7,488	Mixed	2-6	Whole sample	Stratified general population
6	2003	Chang [254]	Taiwan	Taiwan	660	Mixed	15-93	Case counting	Clinical patients
7	2004	Guo [269]	Mainland	Tianjin	5,000	Urban	0-6	Whole population	One district population
8	2004	Guo [270]	Mainland	Dingxi	3,776	Rural	2-6	Randomized sampling	Stratified general population
9	2005	Zhang [271]	Mainland	Tianjin	7,416	Urban	2-6	Randomized sampling	Stratified general population
10	2005	Zhang [258]	Mainland	Wu Han	1,305	Urban	3-7	Clustered randomized sampling	Kindergarten population
11	2005	Liu [272]	Mainland	Beijing	21,866	Mixed	2-6	Clustered probability sampling	Stratified general population
12	2007	Yang [260]	Mainland	Zunyi	10,412	Urban	3-12	Randomized sampling	Primary school population
13	2007	Wong [255]	Hong Kong	Hong Kong	4,247,206*	Mixed	0-14	Case counting	Population in health system
14	2008	Zhang [250]	Mainland	Wuxi	8,681	Urban	2-3	Randomized sampling	Stratified general population
15	2008	Zhang [250]	Mainland	Wuxi	12,430	Urban	4-6	Randomized sampling	Stratified general population
16	2009	Zhang [273]	Mainland	Guiyang	5,000	Urban	0-6	Clustered probability sampling	Stratified general population
17	2009	Wang [257]	Mainland	Meizhou	4,156	Urban	2-6	Clustered randomized sampling	Kindergarten population
18	2010	Li [274]	Mainland	Tianjin	8,006	Mixed	1.5-3	Clustered randomized sampling	Stratified general population
19	2010	Wu [275]	Mainland	Lianyungang	8,532	Urban	0-3	Clustered randomized sampling	Stratified general population
20	2010	Yu [262]	Mainland	Harbin	7,059	Mixed	2-6	Clustered probability sampling	Stratified general population
21	2010	Chen [261]	Mainland	Daqing	7,034	Mixed	2-6	Clustered randomized sampling	Stratified general population
22	2011	Wang [256]	Mainland	Guangzhou	7,500	Urban	2-6	Clustered randomized sampling	Kindergarten population
23	2011	Liang [276]	Mainland	Maoming	2,485	Urban	3-6	Clustered randomized sampling	Kindergarten population
24	2011	Li [253]	Mainland	National	616,940	Mixed	0-17	Clustered probability sampling	Stratified general population
25	2011	Chien [252]	Taiwan	Taiwan	372,642*	Mixed	0-17	Case counting	Population in health system

Appendix 3.2 Methodology of Screening for case identification in reviewed studies

No	Year	First author	Sample screened	Screen methods	Screen instruments	Cut-off of screening (range)	Response rate	Screen informants	Further screen (Yes/No)
1	1987	Tao[75]	Clinical services	R	N/A	N/A	N/A	Clinicians	No
2	2000	Luo [266]	General population	QI	ABC	31	100%	Parents & Researchers	No
3	2002	Wang [259]	General population	QI	CABS*	7 (0-14)	98.3%	Clinicians	No
4	2002	Ren [267]	Kindergarten	QI	CABS	14 (0-28)	99.1%	Researchers	No
5	2003	Wang [268]	General population	QI	CABS	7 (0-14)	98.08%	Clinicians	No
6	2003	Chang [254]	Clinical patients	C	ASDASQ	5 (0-9)	100%	Clinicians	No
7	2004	Guo [269]	Whole population	QI	CABS	7 (0-14)	99.1%	Researchers	No
8	2004	Guo [270]	General population	QI	CABS	7 (0-14)	100%	Clinicians	No
9	2005	Zhang [271]	General population	QI	CABS	7 (0-14)	99%	Researchers	Yes- CARS
10	2005	Zhang [258]	Kindergarten	QI	CABS	14 (0-28)	100%	Researchers	No
11	2005	Liu [272]	General population	QI	CABS	7 (0-14)	100%	Researchers	Yes--CARS
12	2007	Yang [260]	General population	QI	ABC	31	100%	Researchers	No
13	2007	Wong [255]	Clinical services	R	N/A	N/A	N/A	Clinicians	No
14	2008	Zhang [250]	General population	QI	CHAT (2-3 yrs)	CHAT: N/A	100%	Clinicians	No
15	2008	Zhang [250]	General population	QI	CABS (4-6 yrs)	CABS: 14 (0-28)	100%	Clinicians	No
16	2009	Zhang [273]	General population	QI	CABS	7 (0-14)	99.98%	Clinicians	No
17	2009	Wang [257]	Kindergarten	QI	CABS	14 (0-28)	100%	Researchers	No
18	2010	Li [274]	General population	QI	CHAT	Failed 2 domains	92.99%	Clinicians	Yes-ABC
19	2010	Wu [275]	General population	QI	CHAT	N/A	100%	Researchers	No
20	2010	Yu [262]	General population	Q	CABS	7 (0-14)	89.7%	Parents	Yes-ABC
21	2010	Chen [261]	General population	Q	CABS	7 (0-14)	98.78%	Parents	Yes-ABC
22	2011	Wang [256]	Kindergarten	QI	CABS	14 (0-28)	87.8%	Clinicians & researchers	No
23	2011	Liang [276]	Kindergarten	QI	CABS	14 (0-28)	100%	Researchers	No
24	2011	Li [253]	General population	QI	ABC	N/A	N/A	Clinicians	No
25	2011	Chien [252]	Taiwan	R	N/A	N/A	N/A	Clinicians	No

Screen methods: R=Records; QI= Questionnaire based interview; C= Clinical referral; Q=Questionnaire distribution. ABC: Autism Behaviour Checklist; CABS: Clancy Autism Behavioural Scale; ASDASQ: Autism Spectrum Disorder in Adults Screening Questionnaire; CHAT= Checklist for Autism in Toddlers; CARS: Childhood Autism Rating Scale. *CABS has two scales: one is 1or 2 for each item and the other is 0,1or 2.

Appendix 3.3 Methodology of diagnostic assessment for case confirmation in reviewed studies

No	Year	First author	P/R	Assessment tool	Diagnostic criteria	IQ or other tests	Assessment informants	Clinical judgement	Assessment Agreement
1	1987	Tao[75]	R	N/A	Rutter	N/A	Clinicians	Yes	N/A
2	2000	Luo [266]	P	N/A	CCMD-2-R, DSM-III-R	N/A	Researchers	Yes	0.6-1.0
3	2002	Wang [259]	P	CARS	CCMD-2-R	Gaseel, PEP	Clinicians	Yes	0.81-0.90
4	2002	Ren [267]	P	N/A	N/A	N/A	N/A	No	N/A
5	2003	Wang [268]	P	CARS	CCMD-2-R	Gaseel, PEP	Clinicians	Yes	N/A
6	2003	Chang [254]	P	N/A	DSM-IV	N/A	Clinicians	Yes	N/A
7	2004	Guo [269]	P	CARS	CCMD-2-R	PEP	Researchers	Yes	≥0.95
8	2004	Guo [270]	P	CARS	DSM-IV	PEP	Clinicians	Yes	0.998
9	2005	Zhang [271]	P	CARS	DSM-IV	DDST, Gaseel	Clinicians	Yes	≥0.95
10	2005	Zhang [258]	P	N/A	N/A	N/A	N/A	No	N/A
11	2005	Liu [272]	P	CARS	DSM-IV	N/A	Clinicians	Yes	1.0
12	2007	Yang [260]	P	N/A	DSM-IV	N/A	Researchers	Yes	N/A
13	2007	Wong [255]	R	CARS, ADI-R	DSM-IV	N/A	Clinicians	Yes	N/A
14	2008	Zhang [250]	P	CARS	DSM-IV	DDST	Clinicians	Yes	≥0.95
15	2008	Zhang [250]	P	CARS	DSM-IV	DDST	Clinicians	Yes	≥0.95
16	2009	Zhang [273]	P	CARS	CCMD-2-R	Gaseel, PEP	Clinicians	Yes	0.81-0.90
17	2009	Wang [257]	P	N/A	N/A	N/A	N/A	No	N/A
18	2010	Li [274]	P	CARS	DSM-IV	N/A	Clinicians	Yes	0.98
19	2010	Wu [275]	P	CARS	DSM-IV	DDST	Clinicians	Yes	≥0.95
20	2010	Yu [262]	P	N/A	DSM-IV	N/A	Clinicians	Yes	N/A
21	2010	Chen [261]	P	CARS	DSM-IV	N/A	Clinicians	Yes	≥0.98
22	2011	Wang [256]	P	N/A	DSM-IV	N/A	Clinicians	Yes	N/A
23	2011	Liang [276]	P	N/A	DSM-IV, ICD-10	N/A	Clinicians	Yes	N/A
24	2011	Li [253]	P	N/A	ICD-10	N/A	Clinicians	Yes	N/A
25	2011	Chien [252]	R	N/A	ICD-9	N/A	Clinician	Yes	N/A

DDST: Denver Developmental Screening Test; Gesell: Gesell Developmental Scale; P/R: Prospective/Retrospective.

Appendix 3.4 Diagnostic criteria for Childhood Autism in CCMD-2-R

(1) The onset is generally by three years old.
(2) Impairment in social interaction by at least two of the following symptoms:
    a) Extremely lonely, obvious lack of social emotional reactions, does not have normal communication of emotion with others (including parents);
    b) Cannot use eye gaze, facial expression, gestures or hand gestures to communicate;
    c) Cannot establish relationship with peers;
    d) Lack of interests in group games, cannot have fun or emotional resonance through group activities;
    e) Does not seek for help or comfort when has illness or difficulties; Does not offer support or comfort to others when others encounter problems.
(3) Language impairments by at least two of the following symptoms:
    a) Language delay or cannot vocalize, such as cannot mimic others words , but may show attempts to use gestures or other formats to substitute verbal communication;
    b) Stereotyped and repetitive words which are unrelated to the current environment or ongoing activities;
    c) Oddness in the intonation, speed, rhythm or tone of speech;
    d) Obvious impairments in understanding;
    e) Normal development of language before two years old, but delayed development of language after two, or even cannot speak.
(4) Peculiar interests or activities by at least two of the following symptoms:
    a) Stereotyped or circumscribed interests (for example preoccupations with date, advertisements, weather reports etc.);
    b) Special attachment to specific objectives;
    c) Specific compulsions and rituals;
    d) Stereotyped and repetitive movements or gestures;
    e) Specific interests in parts of object that is clearly separate from that which is ordinarily accepted (such as smell, feel of the surface, certain noise etc.);
    f) Resistance to any changes in personal life environment.
(5) Exclude the following diagnoses: Childhood Schizophrenia, Asperger Syndrome, Heller Syndrome, and Rett’s Syndrome.

Appendix 3.5 Prevalence estimates in reviewed studies

No	Year	First author	Screen positives	Final No of cases	Childhood autism		Other ASC		All ASC	
					Prevalence/SE (per 10,000)	Gender ratio (Male : Female)	Prevalence/SE (per 10,000)	Gender ratio (Male : Female)	Prevalence/SE (per 10,000)	Gender ratio (Male : Female)
1	1987	Tao[75]	-	10	0.32 (0.08)	6.5:1	-	-	-	-
2	2000	Luo [266]	39	3	2.8 (1.60)	4.1:1	-	-	-	-
3	2002	Wang [259]	N/A	7	17.9 (211.94)	2.5:1	-	-	-	-
4	2002	Ren [267]	89	N/A	250 (2.31)	8:9	-	-	-	-
5	2003	Wang [268]	16	9	12.3 (4.05)	2:1	-	-	-	-
6	2003	Chang [254]	N/A	4	-	-	-	-	60 (30.06)	N/A
7	2004	Guo [269]	5	5	10 (4.47)	All male	-	-	-	-
8	2004	Guo [270]	18	3	7.97 (4.59)	N/A	-	-	-	-
9	2005	Zhang [271]	16	8	11 (3.85)	7:1	-	-	-	-
10	2005	Zhang [258]	26	N/A	19.9 (2.47)	2.71:1	-	-	-	-
11	2005	Liu [272]	54	16	13.4 (2.47)	N/A	1.92 (0.94)	N/A	15.3 (2.64)	1.29:1
12	2007	Yang [260]	24	6	5.6 (2.32)	5:1	-	-	-	-
13	2007	Wong [255]	N/A	682	-	-	-	-	16.1 (0.19)	6.58:1
14	2008	Zhang [250]	31	14	16.1 (4.3) (2-3 yrs)	3.2:1	-	-	-	-
15	2008	Zhang [250]		11	8.85 (2.7) (4-6 yrs)		-	-	-	-
16	2009	Zhang [273]	5	5	10 (4.47)	4:1	-	-	-	-
17	2009	Wang [257]	81	N/A	19.5 (6.84)	2.68:1	-	-	-	-
18	2010	Li [274]	432	21	26.2 (5.71)	4.25:1	-	-	-	-
19	2010	Wu [275]	7	N/A	8.2 (3.10)	3.5:1	-	-	-	-
20	2010	Yu [262]	115	16	21.2 (5.47)	N/A	1.42 (1.42)	N/A	22.7 (5.66)	7:1
21	2010	Chen [261]	44	17	14.2 (4.49)	N/A	9.95 (3.76)	N/A	24.2 (5.86)	3.25:1
22	2011	Wang [256]	746	46	29.5 (6.26)	2.6:1	45.9 (7.81)	27:1	75.4 (9.99)	6.6:1
23	2011	Liang [276]	35	35	14.1 (7.53)	6:1	-	-	-	-
24	2011	Li [253]	N/A	77,301	2.38 (0.20)	2.46:1	-	-	-	-
25	2011	Chien [252]	N/A	N/A	-	-	-	-	28.7 (0.88)	N/A

Appendix 4.1 Diagnostic criteria for Childhood Autism in CCMD-3

(I) Definition: Childhood Autism is one of the pervasive developmental disorders, more common in boys with early childhood onset. Individuals with Childhood Autism have impairments in social communication, circumscribed interests and stereotyped behaviours. Approximately three quarters of affected children have obvious mental retardation, and some children show special talents although their intelligence are generally below the average.

(II) Diagnostic criteria:

At least seven items in the following three categories, of which at least two items in category 1, and at least one item each in category 2 and 3.

1. Impairments in social interaction, at least two items:
   1) Lack of interests in group games, alone, cannot have fun or emotional resonance through group activities;
   2) Lack of communication technique, failure to develop peer relationships, such as only communicate by dragging, pushing or hugging peers;
   3) Self-entertained, lack of interaction with others in surroundings, lack of social observation and emotional reciprocity (including no appropriate reaction to the existence of parents);
   4) Marked impairments in the use of eye-to-eye gaze, facial expression, body posture, and gestures to regulate social interaction;
   5) Failure to play social games or imitative games (such as cannot play with figures for a familiar family event);
   6) When discomfort or unhappy, does not seek for sympathy or comfort, and does not show sympathy or offer to comfort to others when others are discomfort or unhappy.
2. Impairments in verbal communication, mainly in the functional usage of language:
   1) Delay in spoken language or cannot use language to express him/herself, does not use gestures, or imitate other people for communication either;
   2) Marked impairments in language understanding, usually cannot understand instructions or orders, failure to show needs or difficulties, seldom ask questions and lack of response to what the others say;
   3) Refuse to change repetitive and stereotyped movements or gestures, otherwise he/she will be irritated and restless;
   4) Persistent preoccupation with parts of objects such as a piece of paper, a smooth piece of cloth, wheels of toy cars and so on, usually shows great satisfaction from these parts of objects;
   5) Compulsive adherence to specific, non-functional routines or rituals.

(III) Criteria for severity: impairments in social interaction.

(IV) Onset: generally before three years old.

(V) Exclusion criteria: exclude the following diagnoses including Asperger Syndrome, Heller Syndrome, Rett's Syndrome, Specific receptive language impairments, and Childhood Schizophrenia.

Appendix 4.2 Studies on screening instruments that did not meet the inclusion criteria

Tool	Year	Author	Case No	Cases age (mean age)	Sample source	Control No	Control age	Cut-off point for suspicion	Cut-off for diagnosis	Validity	Reliability Kappa	Reference standard
CABS	2002	Ke[301]	52	2-14 (6.1)	Clinical	48 (N)	3-11 (5.9)	14	14	13/14 items had significant value of diagnosis	--	ICD-10
CABS	2007	Chen[302]	32	1.3-9 (3.72)	Clinical	30 (OC) 28 (N)	2-14 (4.44) 2-12.5 (4.69)	14	14	Significantly distinguish cases and controls	--	ICD-10
ABC	2011	Ma[511]	206	1.5-14 (4.5)	Clinical	0	--	--	--	--	--	DSM-IV

Appendix 4.3 Limitations of reviewed studies on instruments for autism in China

In reviewed studies, the information related to subject selection and diagnostic procedures was generally missing. This lack of useful research techniques would make it difficult to replicate the research or compare the results with other studies.

In terms of sampling method, the samples in reviewed studies were mostly drawn from clinical patients who already had an autism diagnosis before the validation took place (17, 89.5%). Two study selected children with other subtypes of ASC as cases while other studies only selected children with Childhood Autism[265, 290]. Only two studies identified cases prospectively within the general population[275, 292].

After the diagnosis, cases were examined by clinicians using screening instruments. Then the performance of the screening instruments was examined by calculating the agreements between screening results and the existing diagnosis. The clinicians in research were generally not blind to the diagnostic status of the participants. This could bias the results of the screening validity and reliability or comparison of diagnosis.

Six studies investigated the utility of instruments in children with Childhood Autism without comparable controls. Those studies which had a control group did not provide information on whether the controls were drawn from the same population as the cases. Therefore, it is possible that the results were confounded by other variables other than the autistic condition.

The screening instruments used in mainland China often had two cut-offs. The lower cut-off is for screening and the higher cut-off is for diagnosis. The individuals who scored above the lower cut-off were considered a potential case of autism and who scored above the higher cut-off were given an autism diagnosis. The cut-off for the same screening instrument varied among reviewed studies which made it difficult to compare the results.

The analytical methods on the validity and reliability of instruments varied among studies. There were four analytical approaches adopted in reviewed studies: 1) simple

percentage: examine the performance of an instrument by calculating the percentage of cases the instrument identified within the number of cases that had an existing diagnosis to generate the agreement between screening instruments with the reference diagnostic criteria; 2) Cohen's Kappa agreement test: a statistical measure of interrater agreement for qualitative items. It investigates the extent to which there is agreement other than that expected by chance expressed as a ratio to the maximum possible agreement[413]; 3) validity: using sensitivity and specificity.; 4) statistic test to investigate whether the instruments can distinguish children with autism from children without autism, such as the Chi-square test. Some studies reported really high sensitivity and specificity such as in the first validation study of the ABC (sensitivity=100%, specificity=100%)[281]. However, the samples of those studies were very severe autistic cases and typically developing children. Those samples were not representative for the children on the whole autism spectrum in the general population. The details of analytic methodology were generally lacking in the method section of reviewed papers. The type of analysis could only be learned from the presentation of results. Without such information, it is difficult to verify or compare the results of these studies.

Appendix 7.1 Questionnaire for service provision mapping in mainland China

Questionnaire for interview with parents for mapping healthcare pathway of autism in China

Part 1: General information of the child

1. Sex
2. Age: specific to month
3. Birth order
4. Relationship with the child: parent or grandparent or nursemaid
5. Who raised the child and how he or she was brought up? Grandparents or parents? Spoiled or not?

Part 2: Description of first notice of the abnormality of the child

6. Who first notice that there might be something wrong with your child and in what settings?
7. How old was the child when the first notice and suspicion happened?
8. What were the most obvious characteristics of your child which made you become suspicious at that time?
9. What was the other characteristics and general condition of your child when you first noticed?
10. How did the family members response to the first suspicion?
11. What happened after the first suspicion? Go to hospital or stay at home or search on the internet?

Part 3: Description of finding the right hospitals and get diagnosis until the parent accepted the diagnosis.

12. If went to a hospital, how did you choose the hospital? What kind of hospital and what department was first referred to?
13. How old was the child when you first taken him or her to check for the suspicion?

Part 4: Description of the diagnostic process:

14. Book an appointment or not?
15. What kind of questionnaire the doctor used? Name of the questionnaire. Clinician-completed or parent-completed? What was the score at that time?
16. What kind of observation the doctor used?
17. What was the first diagnosis?
18. What were the recommendations for treatment by the doctor after the diagnosis?
19. How long in total including the completion of questionnaire and the observation.
20. What the other check-up or examination after the diagnosis?
21. How much did the referral to hospital cost?
22. If stay at home, what you did to help the child during that time and how did you come to the next stage: go to hospital and so on.
23. What happened after getting the first diagnosis? Go to training centre? Go to another hospital? Stay at home with denial?

Part 5: Description of finding the training centres

24. If went to a training centre, how did you find out and chose the training centre?
25. How old was the child when he or she first got training of any kind?
26. How old was the child when he or she got training according to ABA theory? How long did your child wait to get in the centre?

Part 6: Description of all the courses the child has taken in the centres

27. What kind of method used in this centre?
28. Which class did you think was most effective?
29. How long was the child in each centre?
30. What did you think was the biggest and least improvement of your child after training in this centre?
31. What do you think should be improved first in the future?
32. What triggered you to give up one centre and go to another one? How did you find the other one?
33. How much did each training cost?

Part 7: Description of family burden for autism

34. How much was the average expense for supporting one child with autism?
35. Who supported the child and how?
36. Average income of both parents
37. What do you think of the degree of burden for the family because of child's condition?

Part 8: Description of local policy for autism

38. Where do you come from?
39. Are there any policy related to autism in your region? Have you heard of that or seek help to local authority?
40. If there is, what is the policy? How much is the subsidy? The requirements of getting the subsidy?
41. Is there any policy for having another child? If there is, what are those requirements?
42. If there is no policy, what effort have you made or you know somebody else made to create such policy? What was the government response to that?
43. Does your child have a disability certificate? How to get one in your region? If not, do you want one in the future?
44. What do you think is the biggest barrier for establish and implementation of the policy?

Part 9: Description of the suspicious causes of autism

45. What do you suspect the most for the cause of autism according to your experience?
46. Why did you think of that?

Part 10: General information of parents

47. Age of both parents when mother gave birth.
48. Education background of parents
49. Occupation of parents
50. Stability of work and life

Appendix 7.2 Description of local policies for autism in mainland China

In this sample, the children were from 19 regions within mainland China.

1. Beijing city

Twenty-one children were from Beijing, the capital of China. The parents reported that it was not easy to get the disability certificate even if their child was eligible under the criteria. The authorities involved for applying for this certificate are BCDPF, the local community, hospitals authorized to make an autism diagnosis. It was reported that the clerks in the local community were not familiar with autism and thus it took a long time for parents to find out where to apply. The hospitals that are authorized by the local community only provide evaluation once a week. After the child has a disability certificate, £50 per month is paid annually to the parents if they provide receipts for the training. Sometimes the money would go to the training centres directly as the tuition fee. However, there is a requirement that a child living in one district cannot go to a training centre in another district.

2. Dongbei region (including three provinces)

Six children were from Dongbei region which includes three provinces in the far north of China. Only one of them heard of the local policy for autism. A limited number of families can get subsidy from the government and autism was not included in the medical insurance. There were private training centres (called development centres) for children in Dongbei and also branch centres of institutes in Beijing, such as the Star Rain training centre. The Star Rain training centre provides courses in Dongbei once a year to train parents using the ABA. The development centres evaluate children abilities of cognition, language and sensory integration. They provide training using ABA and sensory integration.

3. Shangdong province

Seven children were from Shandong province. There are doctors in the Qingdao Child hospital who are specialised in autism. There is no subsidy for children with autism in Shandong, but the local community provide gifts to children who have a disability certificate during the Spring festival. If the parents of a child with autism want to have another child, there are several requirements: (1) the child has a existing diagnosis of

autism; (2) the mother must be older than 32 years old; (3) the child must score less than 60 in the IQ test which is conducted by local evaluation group from the Family Planning committee in Shandong province.

4. Shanxi province

Four children were from Shanxi province. If the child is 2 to 6 years old with a disability certificate and the family's economic status is below the baseline living level, then the government provides a single payment of 10000RMB (£1000) to the family. All the local training centres are free to children with autism. However, there is a limited number of families who can get the subsidy every year and the parents expressed that they were not satisfied with the quality of training provided by local training centres.

5. Fujian Province

Five children were from Fujian province. Three of the parents mentioned the policy for autism in Xiamen city. The document for the application for a disability certificate is the diagnosis from the local well-known professionals of autism. When the application is accepted, the local government provides an evaluation of the child. The evaluation is conducted twice a year on fixed days. If the child is a legal resident in Xiamen, the cost is 500RMB (£50). If the child is not, the cost is 900RMB (£90). Once the child gets the disability certificate, the family will receive 1200RMB (£120) per month from the government. If the parents want another child, they just need to provide evidence of the diagnosis of autism or mental disability from well-known professionals.

6. Zhejiang province

Four children were from Zhejiang province. One parent reported that if the child does not speak after the third birthday and the parents want a second child, they can apply for an evaluation of their child by the professionals from the government (including an IQ test and EEG).

7. Guangdong province

One parent reported that in Shenzhen city in Guangzhou province, the policy is more flexible and the government provides more subsidy than Xiamen city.

8. Sichuan province

Two children were from Sichuan province. Both parents had not heard of any local policy for autism, but one reported that if the parent wanted a second child, a disability certificate is required.

9. Other regions

The rest of the parents in this sample had not heard of any local policy for autism in their regions. Thus, according to this opportunistic sample, local policies for autism vary within mainland China and policy in one region is usually not applicable to other regions.

Appendix 8.1 Questionnaire for service provision mapping in Hong Kong

Questionnaire for interview with parents for mapping healthcare pathway of autism in China---Hong Kong

Part 1: General information of the child

1. Sex
2. Age: specific to month
3. Birth order
4. Relationship with the child: parent or grandparent or nursemaid
5. Who raised the child and how he or she was brought up? Grandparents or parents? Spoiled or not?

Part 2: Description of first notice of the abnormality of the child

6. Who first notice that there might be something wrong with your child and in what settings?
7. How old was the child when the first notice and suspicion happened?
8. What were the most obvious characteristics of your child which made you become suspicious at that time?
9. What was the other characteristics and general condition of your child when you first noticed?
10. How did the family members response to the first suspicion?
11. What happened after the first suspicion? Go to hospital or stay at home or search on the internet?

Part 3: Description of finding the right hospitals and get diagnosis until the parent accepted the diagnosis.

12. If went to a hospital, how did you choose the hospital? What kind of hospital and what department was first referred to?
13. How old was the child when you first taken him or her to check for the suspicion?

Part 4: Description of the diagnostic process:

14. Book an appointment or not?
15. What kind of questionnaire the doctor used? Name of the questionnaire. Clinician-completed or parent-completed? What was the score at that time?
16. What kind of observation the doctor used?
17. What was the first diagnosis?
18. What were the recommendations for treatment by the doctor after the diagnosis?
19. How long in total including the completion of questionnaire and the observation.
20. What the other check-up or examination after the diagnosis?
21. How much did the referral to hospital cost?
22. If stay at home, what you did to help the child during that time and how did you come to the next stage: go to hospital and so on.
23. What happened after getting the first diagnosis? Go to training centre? Go to another hospital? Stay at home with denial?

Part 5: Description of finding the training centres

24. If went to a training centre, how did you find out and chose the training centre?
25. How old was the child when he or she first got training of any kind?
26. How old was the child when he or she got training according to ABA theory? How long did your child wait to get in the centre?

Part 6: Description of all the courses the child has taken in the centres

27. What kind of method used in this centre?
28. Which class did you think was most effective?
29. How long was the child in each centre?
30. What did you think was the biggest and least improvement of your child after training in this centre?
31. What do you think should be improved first in the future?
32. What triggered you to give up one centre and go to another one? How did you find the other one?
33. How much did each training cost?

Part 7: Description of family burden for autism

34. How much was the average expense for supporting one child with autism?
35. Who supported the child and how?
36. Average income of both parents
37. What do you think of the degree of burden for the family because of child's condition?

Part 8: Description of local policy for autism

38. Where do you come from?
39. Are there any policy related to autism in your region? Have you heard of that or seek help to local authority?
40. If there is, what is the policy? How much is the subsidy? The requirements of getting the subsidy?
41. Is there any policy for having another child? If there is, what are those requirements?
42. If there is no policy, what effort have you made or you know somebody else made to create such policy? What was the government response to that?
43. Does your child have a disability certificate? How to get one in your region? If not, do you want one in the future?
44. What do you think is the biggest barrier for establish and implementation of the policy?

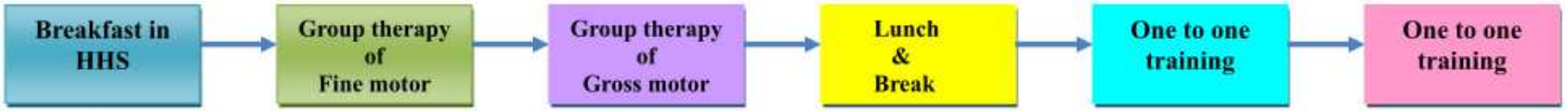
Part 9: Description of the suspicious causes of autism

45. What do you suspect the most for the cause of autism according to your experience?
46. Why did you think of that?

Part 10: General information of parents

47. Age of both parents when mother gave birth.
48. Education background of parents
49. Occupation of parents
50. Stability of work and life

Appendix 8.2 HHS daily schedule for children with ASC in Hong Kong



Appendix 9.1 The Childhood Autism Spectrum Test (CAST)

The Childhood Autism Spectrum Test (CAST)

Child's Name: ..... Age: ..... Sex: Male / Female

Birth Order: ..... Twin or Single Birth: .....

Parent/Guardian: .....

Parent(s) occupation: .....

Age parent(s) left full-time education: .....

Address: .....
.....
.....

Tel.No: ..... School: .....

Please read the following questions carefully, and circle the appropriate answer. All responses are confidential.

1. Does s/he join in playing games with other children easily?	Yes	No
2. Does s/he come up to you spontaneously for a chat?	Yes	No
3. Was s/he speaking by 2 years old?	Yes	No
4. Does s/he enjoy sports?	Yes	No
5. Is it important to him/her to fit in with the peer group?	Yes	No
6. Does s/he appear to notice unusual details that others miss?	Yes	No
7. Does s/he tend to take things literally?	Yes	No
8. When s/he was 3 years old, did s/he spend a lot of time pretending (e.g., play-acting being a superhero, or holding teddy's tea parties)?	Yes	No
9. Does s/he like to do things over and over again, in the same way all the time?	Yes	No
10. Does s/he find it easy to interact with other children?	Yes	No
11. Can s/he keep a two-way conversation going?	Yes	No

12. Can s/he read appropriately for his/her age?	Yes	No
13. Does s/he mostly have the same interests as his/her peers?	Yes	No
14. Does s/he have an interest which takes up so much time that s/he does little else?	Yes	No
15. Does s/he have friends, rather than just acquaintances?	Yes	No
16. Does s/he often bring you things s/he is interested in to show you?	Yes	No
17. Does s/he enjoy joking around?	Yes	No
18. Does s/he have difficulty understanding the rules for polite behaviour?	Yes	No
19. Does s/he appear to have an unusual memory for details?	Yes	No
20. Is his/her voice unusual (e.g., overly adult, flat, or very monotonous)?	Yes	No
21. Are people important to him/her?	Yes	No
22. Can s/he dress him/herself?	Yes	No
23. Is s/he good at turn-taking in conversation?	Yes	No
24. Does s/he play imaginatively with other children, and engage in role-play?	Yes	No
25. Does s/he often do or say things that are tactless or socially inappropriate?	Yes	No
26. Can s/he count to 50 without leaving out any numbers?	Yes	No
27. Does s/he make normal eye-contact?	Yes	No
28. Does s/he have any unusual and repetitive movements?	Yes	No
29. Is his/her social behaviour very one-sided and always on his/her own terms?	Yes	No
30. Does s/he sometimes say "you" or "s/he" when s/he means "I"?	Yes	No

31. Does s/he prefer imaginative activities such as play-acting or story-telling, rather than numbers or lists of facts?	Yes	No
32. Does s/he sometimes lose the listener because of not explaining what s/he is talking about?	Yes	No
33. Can s/he ride a bicycle (even if with stabilisers)?	Yes	No
34. Does s/he try to impose routines on him/herself, or on others, in such a way that it causes problems?	Yes	No
35. Does s/he care how s/he is perceived by the rest of the group?	Yes	No
36. Does s/he often turn conversations to his/her favourite subject rather than following what the other person wants to talk about?	Yes	No
37. Does s/he have odd or unusual phrases?	Yes	No

SPECIAL NEEDS SECTION
Please complete as appropriate

38. Have teachers/health visitors ever expressed any concerns about his/her development?	Yes	No

If Yes, please specify.....

39. Has s/he ever been diagnosed with any of the following?:

Language delay	Yes	No
Hyperactivity/Attention Deficit Disorder (ADHD)	Yes	No
Hearing or visual difficulties	Yes	No
Autism Spectrum Condition, incl. Asperger's Syndrome	Yes	No
A physical disability	Yes	No
Other (please specify)	Yes	No

Appendix 9.2 The Mandarin Childhood Autism Spectrum Test
Information sheet:

北京市学龄儿童社会交往和交流能力调查

给家长的一封信

家长同志您好！

我们盛情邀请您和您的孩子来参加中英合作项目——北京市学龄儿童社会交往和交流能力的调查。此项目是由北京大学第一医院和英国剑桥大学合作开展，以了解北京市 5 到 11 岁儿童的社会交往和交流能力。

每一个孩子都有其独特的与人相处的方式。 有的孩子活泼好动，有的孩子文静内敛。 他们的性格也许是内向的，也许是外向的。社会交往和交流能力对于孩子非常重要，这些能力会影响到他们将来的学习和事业发展。

我们需要您协助我们填写问卷。在填写问卷时，请您逐项填写，填完之后请签名，并检查有无漏填或错填。最后，请让孩子将问卷带回学校交给班主任老师。

问卷回收以后, 我们将邀请部分家长和孩子参加进一步面对面的评估，以更加全面地了解孩子的社会交往和交流能力。 评估包括与家长的谈话和与孩子的游戏互动。

本调查自愿参加。您和您的孩子所提供的信息都是保密的，任何个人的资料都不会对外泄露。参加本调查决不表明您的孩子存在任何问题，我们仅仅是为了保证项目的科学性和准确性。

本次研究已经由北京大学第一医院的伦理委员会审查通过。

如果您有什么问题，请随时联系。

项目负责人：孙翔

邮箱： annie19870701@126.com 电话：010-83575971

非常感谢您的参与和支持！

北京大学第一医院儿科、预防保健科

《学龄儿童社会交往和交流能力研究》课题组

2010-12-10

Main questionnaire:

学校：_____ 年级：_____班级：_____学号：_____

北京市学龄儿童社会交往和交流能力调查问卷

学生姓名：	出生日期： 年 月 日	性别：□男 □女
出生地：	有无其他兄妹：□无 □有（如“有”，请说明 ）	
填表人和孩子的关系：□父亲；□母亲；□其他		
父亲的职业：	父亲的学历：□初中及以下；□高中；□大学；□研究生	
母亲的职业：	母亲的学历：□初中及以下；□高中；□大学；□研究生	
第一联系人：	联系人电话：	

指导语：为了了解孩子的社会交往能力，提高全面素质，请您仔细阅读以下的问题，并用“√”标出您认为符合您孩子情况的合适答案。为了能够全面的了解孩子的情况，请您一定不要错填，漏填。请您放心您所提供的所有信息和回答都将是保密的，我们对您的真诚合作表示衷心的感谢！

1. 他／她容易加入和其他孩子一起玩游戏吗？	① 是	② 否
2. 他／她会不会主动找你聊天？	① 是	② 否
3. 他／她在两岁以前就开始说话吗？（比如他/她会主动叫妈妈，会说“我要…”）	① 是	② 否
4. 他／她喜欢运动吗？	① 是	② 否
5. 他／她喜欢（或想要）和同龄的小孩混在一起吗？	① 是	② 否
6. 他／她会注意到别人忽略的不寻常的细节吗？(比如第一次到别人家，会记住墙上的画或者桌子上的摆设等常人不会注意的事或物)	① 是	② 否
7. 他／她倾向于按照字面意思来理解事情吗？（例如：大人为了制止孩子再说，就说“你再说话试试看”，而孩子理解为“再说一次”）	① 是	② 否
8. 他／她三岁时，他／她是否会用很多时间来玩角色扮演游戏？（比如假装自己是孙悟空，或过家家等）	① 是	② 否
9. 他／她喜欢一再重复使用相同的方式做一件事吗？（比如他/她每天必须用同样的方式穿衣服，或者走固定的路线，或者吃固定的食物)	① 是	② 否
10. 他／她和别的孩子互动容易吗？（比如他/她能够很开心和轻松地和其他孩子一起玩而不是更喜欢自己玩吗？）	① 是	② 否
11. 他／她可以和别人维持一来一往的对话吗？	① 是	② 否
12. 他／她的阅读能力和他／她的年龄相当吗？	① 是	② 否

学校：_____ 年级：_____班级：_____学号：_____

13. 他 / 她大多数的兴趣爱好和同伴们（例如同学，邻居小孩）相同吗？	① 是	② 否
14. 他 / 她是否花了很多时间专注在某种兴趣上，以至于没有时间做其他事情？(比如说他/她可能专注于某种事物或玩具，如果不加阻拦，每天可能有半天甚至一天的时间都花在这件事上)	① 是	② 否
15. 他 / 她是否有要好的朋友，而不仅仅是认识他们？(比如他们曾经在课余的时间自己组织一起出去玩，看电影或者其他的活动)	① 是	② 否
16. 他 / 她是否经常将他她感兴趣的东西拿给你看？	① 是	② 否
17. 他 / 她喜欢开玩笑吗？	① 是	② 否
18. 他 / 她不太能了解什么是“有礼貌的行为”吗？(“有礼貌的行为”是指常识性的合乎礼仪和社交场合的表示尊敬的态度或行为。比如见到长辈主动打招呼，在公共场合知道不应该大声喧哗等)	① 是	② 否
19. 他 / 她是否对于事物的细节记得异常清楚？(比如说他/她可能对于很久以前仅去过一次的地方记得非常清楚，或者记得去年的今天穿的什么衣服等等)	① 是	② 否
20. 他 / 她说话的声调是不是有点特别？（例如太像大人讲话，或过于平坦，或单调而缺乏抑扬顿挫）	① 是	② 否
21. 别人对于他 / 她来讲重要吗？（别人与他/她的交流对他/她来说重要吗？父母或朋友情绪的变化，他/她是否能主动觉察到呢？）	① 是	② 否
22. 他 / 她会自己穿衣服吗？	① 是	② 否
23. 他 / 她在与别人谈话时，是否能把握轮流对答的时机？	① 是	② 否
24. 他 / 她是不是会和其他孩子一起玩具有想象力的游戏（例如过家家），并且能够融入到角色扮演之中？	① 是	② 否
25. 他 / 她是否会经常没有技巧地说话或做事，或是经常说些社交中不太恰当的话，或做些社交上不合适的行为？	① 是	② 否
26. 他 / 她可不可以从 1 数到 50，并且中间不遗漏数字？	① 是	② 否
27. 他 / 她可不可以和别人进行正常的眼神交流？（“眼神交流”是指不需要语言，仅通过视线接触和眼睛转动来接受外来信息，以及表达自己的兴趣和意愿）	① 是	② 否
28. 他 / 她是否有不寻常的重复动作或举动？（比如不停地旋转身体）	① 是	② 否
29. 他 / 她的社交行为是否总是以自我为中心，而很少顾及到别人？	① 是	② 否
30. 他 / 她是否有时说“你”或“她”、“他”的时候，其实是在指“我”（他 / 她自己）？（比如说他/她说“你要喝水”,实际是想说“我要喝水”）	① 是	② 否
31. 他 / 她是不是更喜欢有想象力的游戏，比如说角色扮演或讲故事，而不太喜欢数字或条例信息？	① 是	② 否

学校：_____ 年级：_____班级：_____学号：_____

32. 他／她是否有时会因为不去解释他究竟在说什么，而让别人不想听他说下去了？ （比如有时别人很难理解或听不明白他/她在讲的事情）	① 是	② 否
33. 他／她会骑自行车吗？（即使是有辅轮的也算）	① 是	② 否
34. 他／她是否会因为要求自己或别人一定要遵循某种“规则”或“固定程序”而造成困扰？	① 是	② 否
35. 他／她是否在意别的小朋友对他／她有什么看法？	① 是	② 否
36. 他／她与别人谈话时，是否经常只说自己感兴趣的话题，而不理会别人想要说什么？	① 是	② 否
37. 他／她是否会使用一些奇怪的或不同寻常的词语或句子？	① 是	② 否

请您针对您孩子的情况填写：

38.是否曾经有老师或者医务人员对于他她的发育表示过担心？ ① 是 ② 否

如果是，请说明是哪一方面：

您认为您的孩子有哪些特殊的才能，或者是其他情况您希望让我们知道的吗？

本问卷调查到此结束，非常感谢您的合作！请在以下空白处写下您的宝贵建议或感想：

Consent form:

北京学龄儿童社会交往和交流能力调查

家长同意书

调查保密性: 本次调查的所有数据和信息都将由调查团队进行保密处理。数据将由专人保管和密码设置。任何有关参加者的个人资料都不会在将来的调查报告中出现。

调查记录: 对于本次调查进行的记录都要经过参加者的知情同意，所有记录都仅以编号进行识别, 不牵扯任何个人信息。

参加者签名: 在同意书的最后,请提供您的签名。

请仔细阅读以上内容, 并在以下相关处打勾√。

1。 我确定已经看完并且了解了本次调查给家长的信。 ☐

2。 我是自愿参加的。 ☐

3。 我同意我和我的孩子一起参加本次关于儿童社会交往和交流能力调查。 ☐

家长姓名: _____ 母亲 ☐ 父亲 ☐ 其他 ☐ 日期: _____ 家长签名: _____

非常感谢您的参与和支持!

如果您有什么问题，请随时联系。

项目负责人：孙翔

邮箱： annie19870701@126.com 电话：010-83575971

北京大学第一医院儿科、预防保健科

《学龄儿童社会交往和交流能力调查》课题组

Appendix 9.3 Possible cultural influence on the interpretation of items on M-CAST

There are likely to be cultural influences that may affect the way in which Chinese parents interpret and answer some items on the M-CAST. For example, the two items on attention to details (Item 6&9). However, in Chinese culture, noticing details or recalling long ago event is considered as something good. It might be possible that parents in Group 2 wanted to show good of their children, so more parents in Group 2 provided an autism positive response on these items than Group 1.

Item 7 (Does s/he tend to take things literally?) on the M-CAST was given the same example as the Taiwanese version of CAST. The example indicated a scenario that sometimes parents wanted the child to stop talking when they were arguing, the parent might say "try to say it again" which actually delivers a message to the child that you need to listen to what I say and stop arguing with me. However, children with autism may take this literally and just repeat what they have already said. However, there may be other reasons for such behaviour in typically developing children in China because most families only have one child following the One-Child Policy[385]. It is possible that the child is spoiled and continues arguing with their parents. And also, it is possible that the autistic cases in Group 1 had severe language delay, so the parents in Group 1 might have given a zero to this item.

The examples given for Item 9 on the M-CAST (Does s/he like to do things over and over again, in the same way all the time?) were insisting on wearing the same clothes every day, or eating the same diet, or following a certain route back home. This item pertains to repetitive and stereotyped behaviours that are typical for children with autism. However, in a Chinese context this item may be misunderstood by parents of typically developing children. In Chinese families, it is the parents that usually determine the daily schedule related to the child. Parents try to adjust their own schedules in order to follow the school regulations, particularly when children are in primary schools. Parents of typically developing children may not be aware of the strong degree of repetition and insistence on sticking to the same routines among children with autism. Therefore it is likely that these parents may give an autism positive response to this item as they did not

realise how much more extreme children with autism are in relation to repetitiveness and routines.

Item 20 (Is his/her voice unusual (e.g., overly adult, flat, or very monotonous?)) was a direct translation from the UK example. Speaking in an overly adult way may be considered as a sign of maturity in Chinese culture. When Chinese parents talk about their child, they very often say that their child sounds like ‘a little adult’, implying that the child is smarter and more sophisticated than other children. However, the item was trying to tap the oddness of speech in terms of voice (e.g. being too loud or monotone) and in content (e.g. speaking in a formal way). Similarly, regarding item 37 (Does s/he have odd or unusual phrases?), Chinese parents may interpret this item as a way of saying that their child has linguistic talents that may lead them to endorse this item with an ASC positive response.

Item 34 (Does s/he try to impose routines on him/herself, or on others, in such a way that it causes problems?) was asking about children with autism imposing their own stereotyped behaviours and activities on other people to an extent that has significantly influenced the lives of the family members. Spoilt children (born under the One-Child Policy) might do things in a single-minded way according to their own needs regardless of other people. This phenomenon was described as the ‘Little Emperor’ in mainland China. It is the children who ‘rule the roost’ especially with the protection and devotion of grandparents around them. Thus, this might lead parents of typically developing children to endorse this item with an ASC positive response.

Appendix 10.1 Results of diagnostic assessments of children in primary schools

No	Age	Previous diagnosis	Diagnosis	ADOS algorithm					ADI-R algorithm					IQ
				A	B	A+B	C	D	A	B1	B2	C	D	
1	6.7	None	Not ASC	0	5	5	0	1	7	6	--	4	0	122
2	6.7	None	Not ASC	1	1	1	1	0	6	5	--	0	0	103
3	8.5	None	Not ASC	0	0	0	1	0	5	5	--	0	0	105
4	6.7	None	Not ASC	1	0	1	0	0	3	10	--	1	0	104
5	8.1	None	ASC	3	4	7	0	0	18	10	--	5	1	118
6	6.5	None	ASC	5	8	13	2	0	10	8	--	3	1	127
7	8.5	None	Not ASC	1	1	2	0	0	14	4	--	6	1	138
8	9.9	None	Not ASC	0	0	0	0	0	10	4	--	0	0	130
9	8.1	None	Not ASC	4	7	11	2	0	2	7	--	0	0	137
10	10.8	None	Not ASC	0	0	0	0	0	6	0	--	0	0	110
11	8.1	None	Not ASC	2	3	5	2	0	1	2	--	3	0	120
12	6.6	None	Not ASC	1	1	2	0	0	3	1	--	3	0	121
13	9.2	None	Not ASC	2	4	6	1	0	6	4	--	1	0	145
14	8.8	None	Not ASC	1	0	1	0	0	0	1	--	0	0	132
15	8.6	None	Not ASC	0	0	0	0	0	0	0	--	0	0	104
16	9.7	None	Not ASC	0	0	0	0	0	0	0	--	1	0	111
17	6.6	None	ASC	2	4	6	1	0	15	15	--	3	1	119
18	7.7	None	Not ASC	0	1	1	0	0	1	1	--	1	0	107
19	8.7	None	Not ASC	0	0	0	0	0	0	0	--	0	0	101
20	6.1	None	Not ASC	1	1	2	1	0	8	9	--	1	1	106
21	9.1	None	Not ASC	0	3	3	1	0	7	1	--	1	0	106
22	10.10	None	Not ASC	0	1	1	0	0	0	2	--	1	1	104
23	6.7	None	Not ASC	0	0	0	0	0	0	0	--	0	3	125
24	6.8	None	Not ASC	0	0	0	0	0	10	5	--	6	0	111
25	6.8	None	Not ASC	0	0	0	0	0	13	4	--	3	0	123
26	8.8	None	Not ASC	2	1	3	2	0	3	1	--	2	0	103
27	8.5	None	Not ASC	0	0	0	0	0	6	4	--	0	0	119
28	10.0	None	Not ASC	0	0	0	0	0	0	0	--	0	0	130
29	7.4	None	Not ASC	0	0	0	0	0	0	2	--	0	0	139
30	7.6	None	Not ASC	2	3	5	2	0	2	1	--	0	0	105
31	8.0	None	Not ASC	1	1	2	1	0	1	0	--	0	0	95
32	8.7	None	ASC	2	8	10	2	0	14	9	--	4	2	117
33	7.3	None	Not ASC	0	0	0	0	0	0	0	--	0	0	121
34	9.6	None	Not ASC	1	0	1	1	0	0	0	--	0	0	125
35	9.9	None	Not ASC	0	0	0	0	0	1	0	--	0	0	81
36	10.4	None	Not ASC	0	0	0	0	0	0	0	--	0	0	112
37	6.6	None	Not ASC	0	0	0	0	0	2	2	--	0	0	105
38	9.10	None	Not ASC	0	0	0	0	0	3	0	--	1	0	130
39	8.6	None	Not ASC	0	0	0	0	0	1	0	--	0	0	128
40	6.11	None	Not ASC	0	1	0	0	0	0	0	--	0	0	119
41	8.3	None	Not ASC	0	0	0	0	0	3	6	--	0	0	119
42	8.6	None	Not ASC	1	4	5	1	0	2	0	--	0	0	117
43	6.7	None	Not ASC	1	1	2	0	0	0	0	--	0	0	120
44	7.11	None	ASC	4	6	10	0	0	11	6	--	2	2	105
45	8.11	None	Not ASC	0	0	0	0	0	0	0	--	0	0	109
46	8.10	None	Not ASC	0	0	0	0	0	2	4	--	0	0	107
47	10.4	None	Not ASC	0	0	0	0	0	5	0	--	0	0	114
48	10.11	None	Not ASC	1	1	2	1	0	3	2	--	0	0	101
49	8.11	None	Not ASC	0	0	0	0	0	0	0	--	0	0	109
50	9.10	None	Not ASC	0	0	0	0	0	1	0	--	0	1	124
51	9.3	None	Not ASC	0	0	0	0	0	3	5	--	1	0	122

No	Age	Previous diagnosis	Diagnosis	ADOS algorithm					ADI-R algorithm					IQ
				A	B	A+B	C	D	A	B1	B2	C	D	
52	8.8	None	Not ASC	0	0	0	0	0	0	0	--	0	0	105
53	8.4	None	Not ASC	1	1	2	0	0	10	4	--	0	0	110
54	9.4	None	Not ASC	0	0	0	0	0	1	2	--	0	0	117
55	8.0	None	Not ASC	0	0	0	0	0	3	0	--	0	0	137
56	9.5	None	Not ASC	0	0	0	0	0	0	0	--	0	0	92
57	6.9	None	Not ASC	0	0	0	0	0	3	0	--	0	0	79
58	8.8	None	Not ASC	0	0	0	0	0	1	1	--	0	0	114
59	9.5	None	Not ASC	0	0	0	0	0	2	0	--	0	0	104
60	7.7	None	Not ASC	1	3	4	1	0	3	0	--	0	0	109
61	10.0	None	Not ASC	0	0	0	0	0	1	1	--	0	0	120
62	9.4	None	Not ASC	0	0	0	0	0	1	0	--	0	0	93
63	8.9	None	Not ASC	0	0	0	0	0	2	0	--	0	0	142
64	8.6	None	Not ASC	0	0	0	0	0	2	1	--	0	0	114
65	7.7	None	Not ASC	0	0	0	0	0	0	0	--	0	0	106
66	9.4	None	Not ASC	0	0	0	0	0	0	0	--	0	1	138
67	7.6	None	ASC	2	5	7	1	0	12	7	--	2	1	114
68	9.6	None	Not ASC	0	0	0	0	0	0	1	--	0	0	131
69	10.4	None	Not ASC	0	0	0	0	0	0	2	--	0	0	98
70	8.7	None	Not ASC	0	0	0	0	0	1	0	--	0	0	120
71	9.11	None	Not ASC	0	0	0	0	0	0	0	--	0	0	106
72	8.6	None	Not ASC	0	0	0	0	0	3	0	--	1	0	112
73	8.10	None	Not ASC	0	3	3	0	0	1	0	--	0	1	85
74	9.11	None	Not ASC	0	0	0	0	0	0	5	--	0	0	117
75	10.4	None	Not ASC	0	0	0	0	0	3	2	--	1	0	87
76	10.3	None	Not ASC	0	0	0	0	0	0	0	--	0	0	105
77	11.5	None	Not ASC	0	0	0	0	0	0	0	--	0	0	85
78	10.1	None	Not ASC	0	0	0	0	0	1	0	--	0	0	124
79	10.2	None	Not ASC	0	0	0	0	0	1	0	--	0	0	104
80	10.2	None	Not ASC	0	0	0	0	0	0	1	--	0	0	117
81	7.0	None	Not ASC	0	0	0	0	0	0	2	--	0	0	126
82	8.8	None	Not ASC	0	0	0	0	0	0	1	--	1	0	114
83	9.0	None	Not ASC	0	0	0	0	0	0	4	--	0	0	126
84	9.3	None	Not ASC	0	0	0	0	0	2	0	--	0	0	113
85	8.9	None	Not ASC	0	0	0	0	0	2	2	--	0	0	107
86	10.0	None	Not ASC	0	0	0	0	0	4	3	--	0	0	84
87	9.3	None	Not ASC	0	0	0	0	0	2	0	--	0	0	117
88	9.4	None	Not ASC	0	0	0	0	0	1	1	--	0	0	122
89	9.11	None	Not ASC	0	0	0	0	0	1	1	--	0	0	108
90	8.11	None	Not ASC	0	0	0	0	0	2	2	--	0	0	139
91	8.9	None	Not ASC	0	0	0	0	0	4	3	--	0	0	135
92	8.0	None	Not ASC	0	0	0	0	0	7	5	--	0	0	143
93	7.2	None	Not ASC	0	0	0	0	0	1	2	--	0	0	114
94	7.8	None	Not ASC	0	0	0	0	0	2	0	--	0	0	106
95	9.4	None	Not ASC	0	0	0	0	0	0	1	--	0	0	96
96	10.0	None	Not ASC	0	0	0	0	0	0	0	--	0	0	120
97	9.1	None	Not ASC	0	0	0	0	0	3	4	--	0	0	94
98	8.9	None	Not ASC	0	0	0	0	0	0	0	--	0	0	135
99	8.6	None	Not ASC	0	0	0	0	0	1	0	--	0	0	112
100	9.3	None	Not ASC	0	0	0	0	0	0	1	--	0	0	111
101	6.8	None	Not ASC	0	0	0	0	0	1	1	--	0	0	114
102	11.2	None	Not ASC	0	0	0	0	0	1	2	--	0	0	127
103	10.5	None	Not ASC	0	0	0	0	0	0	1	--	0	0	114

Appendix 12.1 Clancy Autism Behaviour Scale

Chinese version:

他/她是否有以下的行为特点：

1. 不易与别人混在一起	从不 ☐	偶尔 ☐	经常 ☐
2. 听而不闻，好像是聋子	从不 ☐	偶尔 ☐	经常 ☐
3. 教他学什么，他强烈反抗， 如拒绝模仿，说话或动作	从不 ☐	偶尔 ☐	经常 ☐
4. 不顾危险	从不 ☐	偶尔 ☐	经常 ☐
5. 不能接受日常习惯的变化	从不 ☐	偶尔 ☐	经常 ☐
6. 以手势表达需要	从不 ☐	偶尔 ☐	经常 ☐
7. 莫名其妙的笑	从不 ☐	偶尔 ☐	经常 ☐
8. 不喜欢别人拥抱	从不 ☐	偶尔 ☐	经常 ☐
9. 不停的动，坐不住，活动量大	从不 ☐	偶尔 ☐	经常 ☐
10. 不望对方的脸，避免视线的接触	从不 ☐	偶尔 ☐	经常 ☐
11. 过度偏爱某种物品	从不 ☐	偶尔 ☐	经常 ☐
12. 喜欢旋转的东西	从不 ☐	偶尔 ☐	经常 ☐
13. 反反复复做些怪异的动作或玩耍	从不 ☐	偶尔 ☐	经常 ☐
14. 对周围漠不关心	从不 ☐	偶尔 ☐	经常 ☐

Clancy Autism Behaviour Scale:

English translation from Chinese studies which given the items on the Chinese CABS[282,283]

1. Don't want to play with other children
2. Seldomly responses to other people, seems deaf
3. Strongly resists to learning, usually refuse to imitate, speak or act
4. No fear or regardless of danger
5. Cannot accept changes of daily routines
6. Expresses needs by gestures
7. Smiles for no reasons
8. Does not like to be hugged or held
9. Stays restless, moves consistently and behaves hyperactively
10. Avoids direct looking at others' faces and avoids eye contacts
11. Persists preoccupation with certain objects
12. Likes rolling objects
13. Repetitive actions or play
14. Indifferent with surroundings

Appendix 14.1 Research protocol of China SCORE Study

PROJECT TITLE: SOCIAL AND COMMUNICATION RESEARCH AND EPIDEMIOLOGY (SCORE)

STUDY IN PRIMARY SCHOOL AGE CHILDREN IN MAINLAND CHINA

Cambridge Investigators:

Professor Simon Baron-Cohen (Autism Research Centre University of Cambridge)

Professor Carol Brayne (Institute of Public Health, University of Cambridge)

Dr Carrie Allison (Autism Research Centre, University of Cambridge)

Dr Fiona Matthews (MRC Biostatistics Unit, University of Cambridge)

Dr Bonnie Auyeung (Autism Research Centre, University of Cambridge)

Dr Sophia Xiang Sun (Institute of Public Health & Autism Research Centre, University of Cambridge).

Beijing Investigators:

Professor Zhixiang Zhang (Peking University First Hospital, Peking University)

Pro. Hong You, Rehabilitation Department, China Disabled Persons' Federation

Mr. Jibin Han, Rehabilitation Department, China Disabled Persons' Federation

Summary

To date, there has been almost no prospective epidemiological study of all autism spectrum conditions (ASC) in mainland China. The few available studies focusing on mainland China only reported the prevalence of childhood autism using different methodology to ascertain cases. This makes comparisons of the prevalence of ASC and the extent of the public health impact of ASC in the East and West impossible. No study has examined other diagnostic categories relating to Pervasive Developmental Disorders (PDD), such as Asperger Syndrome (AS) in mainland China.

The proposed research will conduct a multi-stage, multi-source epidemiological study in 6 cities to test the prevalence of ASC and its relationship to normal variation in socio-communicative style. The methodology of this study will be adapted from a previous epidemiological study in Cambridgeshire, UK (known as the Social Communication Research and Epidemiology (SCORE[70]) study) in order to explore and report on the current situation regarding the prevalence of ASC in a Chinese primary school age population.

This study will employ a Mandarin Chinese translation of the Childhood Autism Spectrum Test (M-CAST) in mainland China. This was the screening instrument in the UK SCORE study. The pilot study examined the Chinese translation of CAST in order to adjust it to be culturally acceptable. The validation study assessed the suitability and accuracy of the M-CAST in an unselected Chinese population (aged 6 to 10 years old) to determine whether the existing cut-point (15) is appropriate in Chinese population for epidemiological study of ASC. After the revision of the M-CAST, the main study will conduct a large population screen using the M-CAST in 6 cities in mainland China and further estimate the prevalence of ASC within random selected sample from stratified population from screen. In the prevalence study a proportion of the children within different M-CAST score will be invited for a diagnostic assessment. In parallel, existing cases in the same region will be identified from multiple sources. Together, these data will provide an estimate of the prevalence of ASC in mainland China.

Main Study: Large scale population screen and estimating prevalence of ASC in Mainland China

Stage 1: Large scale population screen

i) Population base

The sample of this study will be 6 cities selected from 6 different provinces within mainland China. The screening sample will be the total population between 6 to 11 years old in selected cities. In China, there are total 34 regions including 23 provinces, 4 municipalities, 5 autonomous regions and 2 special administrative regions. In order to have a representative screening sample, the records about each region in National Bureau of Statistics People's Republic of China will be reviewed to select regions and cities in that region. The following variables will be used to select the regions and cities: economic level, percentage of mobile population of the district, the enrollment of primary schools, the distribution of primary school aged population, enrollment in special education settings, and information about parents such as age, occupation, educational background, social status, annual income of the parents etc. The target population will be total population of 6 selected cities who are 6 to 11 years old.

ii) General approach of screen sampling

In order to cover the whole population in selected cities, two approaches will be taken. The first approach will be though local primary schools for children who are 6 to 11 years old (1-4 grades). The second approach will be through local special education settings such as public special primary schools, public school of disability and public and private training or rehabilitation centres of autism. The process of screen sampling was shown in Figure 1.

iii) Distribution strategy and participant ascertainment in ordinary schools and special settings

All local mainstream schools will be invited to participate in the screening phase. Under the administration of Chinese Disabled Person's Federation, the local district health and

education authorities will be invited to be involved in this study. They will issue official document to encourage the schools or centres to cooperate with the research. Once permission is granted from each school or centre, the questionnaires will be distributed through the administration of each school or centre to class teachers and a member of the research team (Sun) will give a short talk to introduce the study and address questions. Class teachers will be asked to distribute a questionnaire to each child and encourage parents to complete it and return it back to school. Teachers will collect the questionnaires back to return to the research team. This strategy has been used in previous epidemiological studies in mainland China, resulting in participation rates higher than 95%[259, 267-269, 271]. To improve the response, the cover letter to parents will emphasize the importance of returning the questionnaire regardless of whether they think there is problem with their child in terms of social and communication development. With the support of the schools and teachers, it is anticipated that there will be a high response (90-95%) to the screen.

iv) Screening

The Chinese CAST will be sent to parents along with a letter to invite them to take part in the study. The Information Sheet will explain that the study will be examining strengths and weaknesses in social and communication skills, imagination and play, as well as how these skills can influence education. Included in the questionnaire pack will be some additional questions asking about level of parental education and occupation. There will be a consent form that asks parents to indicate whether or not they are willing to be contacted following completion of the questionnaire.

v) Screening for known cases via records of the national survey of disability

In addition to the strategy above, the records from the second national survey for disability in 2006 will help to determine an approximate number of children with an autism diagnosis in the target district. Existing cases of autism in this age group will be identified from local hospital records, locality health authority records as well as the specialist training centres. The CAST will be posted to the parents of cases of autism

identified by tracking from the records who are not current in any ordinary or special educational settings.

A limitation of the UK SCORE study was that no diagnostic validation took place for the existing cases of autism identified through records in the Special Educational Needs (SEN) registration in Cambridgeshire[70]. Therefore, 5% of existing cases found through national survey records and local training centres will be randomly selected and invited to a further assessment to confirm their diagnostic status using the ADOS and ADI-R. Once they agree to participate, a consent form will be given to fill in.

vi) Test-retest reliability

For the current study, a proportion of randomly selected parents (N=200) will be contacted by telephone to be invited to the test-retest study. A second identical CAST will be distributed for the parent to complete within two weeks following completion of the first CAST. Kappa for agreement will be assessed between the test pairs, along with other similar analyses that were conducted in the UK studies.

Stage 2: Estimating prevalence of ASC in mainland China

i) Prevalence study sampling

The sample for further prevalence study will be selected from the screen sample in Stage 1. 2 cities with preferable representativeness as well as available resources will be selected and the population of the two cities will then be stratified according to each age group. The CAST status will be unknown during the sample stratification. The sample for prevalence study for ASC will be randomly selected from the stratified population. For example, the sample size of prevalence sample can be approximately 20,000.

ii) Assessment sampling

According to the distribution of CAST in prevalence sample, the children in this sample will be divided into three groups. The first group will be high score group within which the CAST score will be no less than 15 (≥15). The second group will be the borderline

group with the CAST score ranging from 12 to 14 (12-14). The third group will be low score group with the CAST score no more than 11 (≤11). A new assessment sample will be obtained by randomly selection from the prevalence sample from each score group for a full diagnostic assessment. The proportions within each group will be determined according to the CAST distribution in the prevalence sample which will be unknown until the screen is finished. For example, 20% of high score group, 10% of borderline group and 1% of low score group. If the prevalence sample is 20,000 and the distribution of CAST in validation study was adopted to calculate the expected assessment number, using the proportion rate from the example, we will expect to invite 783 families for further assessments. If 70% of them agree to participate, we will expect 548 assessments. The process of assessment sampling was shown in Figure 2.

iii) Diagnostic assessments

Families will be invited to have a face-to-face assessment. Families will be invited to by telephone on two further occasions if no response is received. After this, it will be assumed that the family do not wish to take part in the further assessment and will not be contacted again. When a family agrees to participate, a consent form will be sent. The consent form will state the purpose of the assessment and explain the procedure. It will be clearly emphasized to parents that participation in the follow-up assessment does not mean there is any problem with their child as a whole range of social communication styles will be under investigation.

Case status will be determined using a standardized diagnostic procedure. The assessment will also include a measure of IQ and adaptive behaviour. The assessment battery will be:

a. Autism diagnostic assessments: Autism Diagnostic Interview-Revised (ADI-R)[27] and Autism Diagnostic Observation Schedule (ADOS)[186]
b. IQ tests: Ravens Progressive Matrices (RPM)[395] .

This study will require a team to conduct the assessments. All interviewers will be fully trained on all assessment tools, and reliability amongst the team will be established prior to the commencement of the assessment phase. A proportion of ADI-R interviews will be tape-recorded and ADOS observations will be video-recorded (with the parental consent)

in order to monitor assessment reliability throughout the assessment phase (in the UK SCORE study, 35% of assessments were taped or video-recorded[70]). Each assessment will take approximately 3 hours to complete. The procedure of prevalence study was shown in Figure 3.

iv) Availability of assessment material

A Chinese version (approved by the publisher) already exists for the ADOS and ADI-R and these will be used in this study. A contract will be signed with the publisher in order to get the official ADOS and ADI-R materials. The RPM already has Chinese versions. The assessments listed above have been shown to be standardized and reliable when used in Western countries. This study will also be an opportunity to assess how these diagnostic instruments perform in a different cultural context.

v) Training strategy for diagnostic assessment

The assessment team will be consisted of 6 researchers of Chinese origin. They will be recruited from Peking University and branches of China Disabled Persons' Federation (CDPF) with a higher than Bachelor's degree in either Medicine, Psychology, Psychiatry, Epidemiology, or Public Health as well as relative experience related to autism. The UK research team will invite a Chinese trainer of the ADOS and ADI-R (Dr Yu-Yu Wu) from Taiwan to train the assessment team in Beijing. Researcher Sun (who is already trained to reliability standards to administer the ADOS and ADI-R) will assist during the training. Reliability will be established through supervision from the UK team and also through Taiwan trainer and colleagues. The Taiwanese team provided the official Chinese translation (approved by the publisher) of the ADOS and ADI-R and have experience of using both instruments in Chinese speaking populations. Interrater reliability on the ADOS and ADI-R will be assessed throughout the study to assure the quality of assessment.

The ADOS and ADI-R training will take 1.5 to 2 months to complete. It will include the following four modules:

First, the pre-course self-learning: using video and tapes from the publisher previous videos of reliable examiners as well as the manual a booklet to get familiar with the administration process.

Second, training courses by Professional Trainer: The ADOS and ADI-R training courses will take two weeks, one week for each course.

Third, assessment practice for obtaining reliability: researchers will be matched in couple and conduct at least 5 ADOS and ADI-R assessments.

Fourth, reliability and agreement evaluation: Evaluation of assessments will take place after the completion of assessment practice. The trainer will supervise and evaluate the performance of researchers and the preferable reliability should be no less than 80%.

Formal training to use the RPM is not required. The assessment team will be trained using a lecture format during half-day workshops to correctly administer these instruments.

vi) After diagnosis

If parents are concerned about their child's development, the research team will recommend that the family seek an assessment at a well-known hospital in the local area. If parents do not have concerns about the child's development but the researchers do, the researchers will discuss the need for a further developmental check with the parents after careful consideration. It is important to highlight that ethically the research team can only make a research diagnosis and not a clinical diagnosis, as they will be acting in their capacity as researchers, and not clinicians.

vii) Predictions

Most Chinese epidemiological studies have reported a very high response rate, ranging from 98.08% to 99.1%[259, 267-269, 271]. The co-investigator partners from Peking University First Hospital and the Chinese Disabled Person's Federation have conducted

epidemiological studies in all over China for many years. During this time they have established a strong network with education and health authorities. This study will therefore benefit from the experience of our co-investigators and improve parental response. It is anticipated that response to the screen will be approximately 90-95%.

viii) Data analysis

Inverse probability weighting methods will be used to weight cases according to non-response at the various stages throughout the study. This will generate empirical weights, defined as the inverse probability of being assessed from a particular score group, reflecting both the sampling and the response rate in each score group[159]. The new identified cases from the screening in mainstream and special schools will be added to the number of existing cases found through the national survey of disability and other health and authority records to generate the total number of autistic children in this district. This number will be divided by the population base of children who are 6 to 10 years old from which the samples have been drawn to generate an estimate of the prevalence of all ASC in this region. Other background variables will be analyzed, such as the social economic status of the parents. All analyses will be carried out using STATA 10.0.

Ethical approval procedure

This research has ethical approval through the Cambridge Psychology Research Ethics Committee, University of Cambridge and the ethics committee of the Peking University First Hospital, Peking University.

Timetable and milestones

Year 1:

2010-2011: Pilot (Item translation) (20 typical children and 20 children with ASC) and Validation study (737 typical children and 50 cases).

Year 2:

12.2012-12.2013: Main Study: Population screen of 6-10 year old children (one to four grade) using the CAST in 6 cities in China. Data entry, analysis and test-retest reliability

of screening. Training examiners for prevalence study. Prevalence and assessment sample selection.

Year 3:

12.2013-12.2014: Further assessment of a proportion of three score groups. Screening existing cases via records from national survey of disability, health professionals. Evaluation of a proportion of existing cases.

Year 4:

12.2014-12.2015: Completion of the assessment. Data analysis. Write up results. Dissemination

Figure 1. Prevalence study screen sampling flowchart

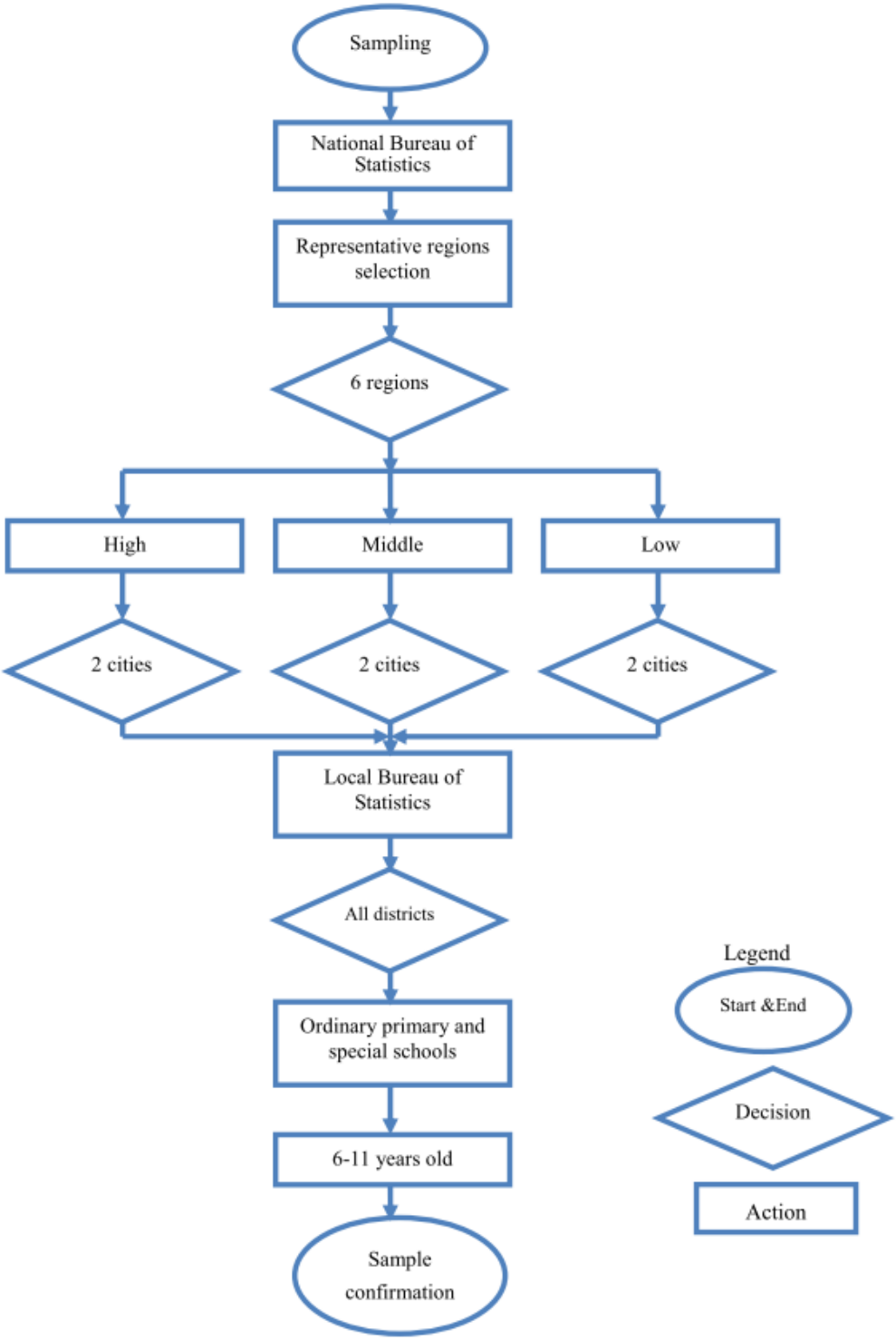


Figure 2. Prevalence study assessment sampling flowchart

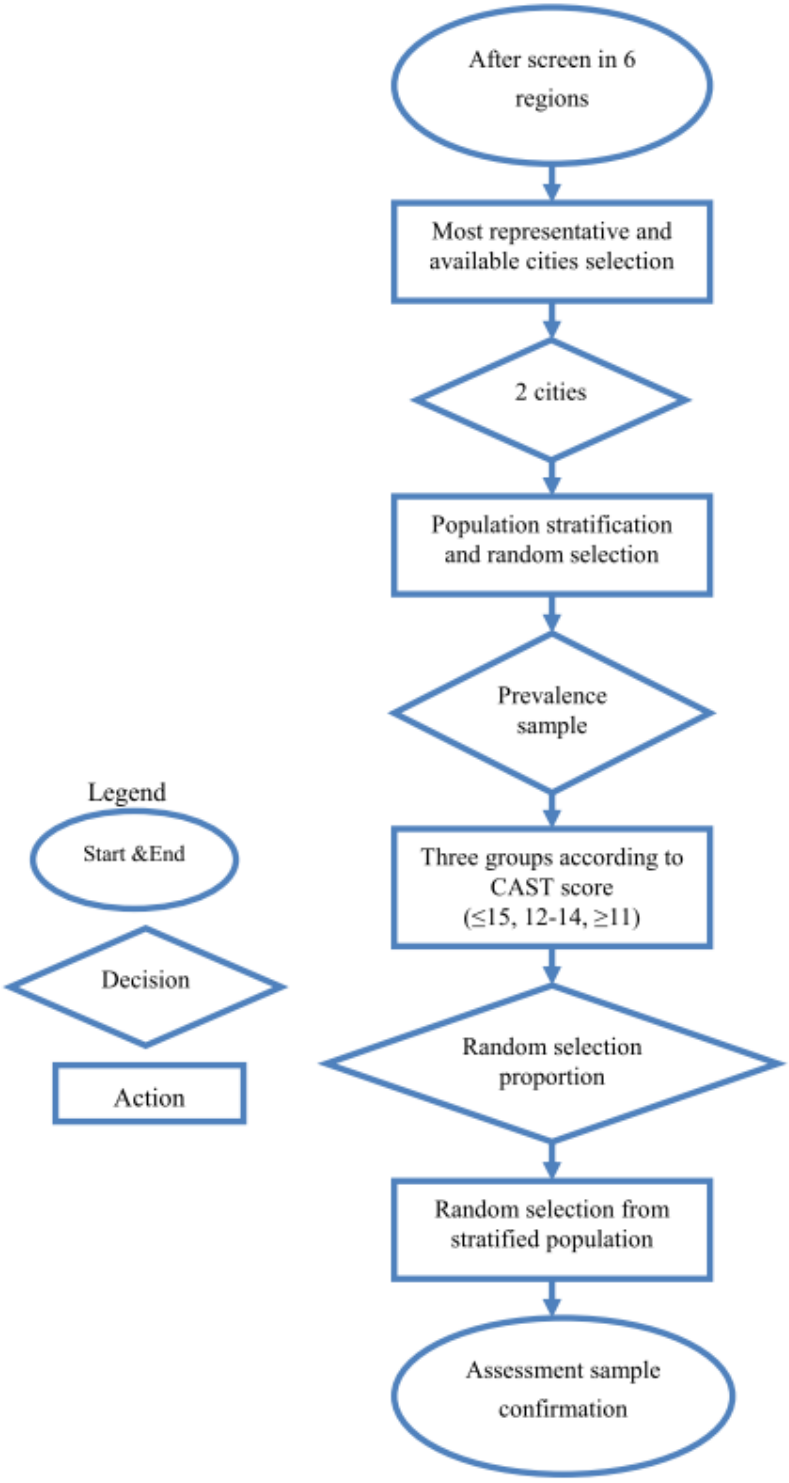
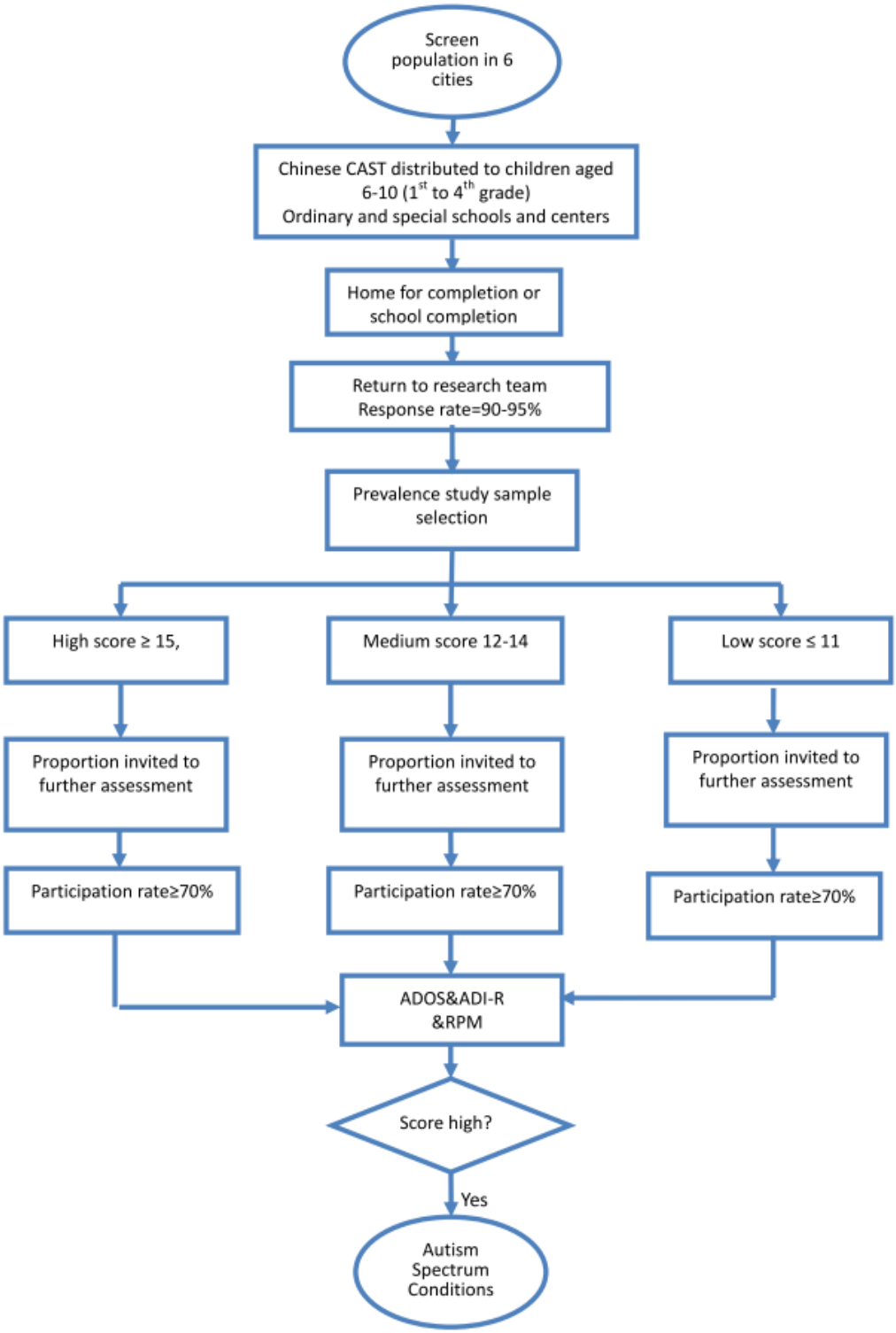


Figure 3. Flow chat of prevalence study.



The Cambridge team

Professor Simon Baron-Cohen is a Fellow at Trinity College, Cambridge and Director of the Autism Research Centre (ARC) in Cambridge University. He worked in the MRC Developmental Psychology Unit (1982-83), the MRC Cognitive Development Unit (1983-85), the MRC Child Psychiatry Unit (1989-1994). His research spans neuroimaging, genetics, hormones, cognition, screening and intervention in relation to children and adults with autism spectrum conditions. He has received awards from the American Psychological Association, the British Association for the Advancement of Science (BA), and the British Psychological Society (BPS) for his research into autism, including the 2006 Presidents' Award for Distinguished Contributions to Psychological Knowledge from the BPS. He is Vice President of the International Society for Autism Research (INSAR). He is a Fellow of the BPS, the British Academy, and the Association for Psychological Science, and co-editor in chief of the new journal *Molecular Autism*. He is Chair of the NICE Guideline Development Group for autism and was appointed to the Dept of Health Autism Strategy Program Board.

Professor Carol Brayne is an epidemiologist and public health physician. She is the Director of Institute of Public Health at Cambridge University. Her programmes include research into dementia, healthy ageing and neuropsychiatric epidemiology. The research is multidisciplinary and the Cambridge team straddles the Department of Public Health and Primary Care and the MRC Biostatistics Unit. It is also part of the Cambridgeshire and Peterborough NIHR CLAHRC. Her main NHS and honorary contract is with Cambridgeshire PCT but she also holds honorary contracts related to her research interest with Cambridgeshire and Peterborough Mental Health Trust, and Addenbrookes Hospital Trust. Her service work includes furthering links between service and academic sectors. She links to the Senior Leadership Team of the Strategic Health Authority and provides regional input in areas of expertise.

Dr Carrie Allison is Research Manager at the Autism Research Centre, Cambridge. She completed her PhD in 2009 at the ARC (Cambridge) in screening toddlers for Autism Spectrum Conditions. Her previous research projects include a prevalence study of

Autism Spectrum Conditions in primary school age children in Cambridgeshire, funded by the Shirley Foundation, and follow-up studies of early screening for autism funded by the Big Lottery and the Cambridgeshire and Peterborough NIHR CLAHRC.

Dr Fiona Matthews is a senior statistician and programme leader at the MRC Biostatistics Unit at the University of Cambridge. Her research includes cognitive modeling in the presence of missing data, healthy active life expectancy, multistate modeling and applied research in aging, cognition, disability, neuropathology and autism. She has been involved in the analysis of the CAST developmental studies since the UK validation study in 2005. She directed the data analysis of UK SCORE data.

Dr Sophia Xiang Sun is PhD student in Institute of Public Health and the Autism Research Centre at Cambridge University. She has an undergraduate and a Masters degree in Surgery in Integrated Western and Chinese Medicine at Hunan University of Traditional Chinese Medicine. She is a medical doctor in mainland China. She completed her MPhil in Public Health in 2009 in Cambridge focusing on the Epidemiology of Autism Spectrum Conditions (ASC).

The Beijing team

Dr Zhixiang Zhang is graduated from the medical school in Shandong University in 1965 and he has been a Paediatrician in Peking University First Hospital since then. He is a professor of Paediatrics Neurology in Peking University First Hospital. He has been the principle investigator in about 30 epidemiological studies in developmental disorder in children in mainland China. His recent international projects including the construction of a Chinese Communication Development Inventory with Hong Kong Research Grants Council, a longitudinal Study of late talkers in Chinese with Hong Kong Research Grants Council and the Timing, Duration, and Severity of Infant Iron Deficiency: Developmental Impacts.

Research Environment

Autism Research Centre (ARC) (www.autismresearchcentre.com) has 6 main research programs focused on autism spectrum conditions (ASC). These are: (1) Perception and Cognition; (2) Neuroscience; (3) Genetics and Proteomics; (4) Hormones; (5) Screening and Diagnosis; and (6) Intervention. The ARC is part of the Clinical School (Department of Psychiatry) at Cambridge University and brings together over 30 active research staff (including doctoral students). It is also part of the NIHR CLAHRC for Mental Health in the NHS Cambridgeshire and Peterborough Foundation Trust. The ARC contributes to the graduate education program in cognitive neuroscience, and serves as advisor to the All Party Parliamentary Group for Autism (APPGA), the National Autistic Society, parent lobbying groups (PACE), and local voluntary services (NAS, Cambridge).

Institute of Public Health (www.iph.cam.ac.uk) was opened as a joint venture between the University, the Medical Research Council (MRC) and the National Health Service (NHS). The aim was for the IPH to become a centre for research and teaching in epidemiology, public health, biostatistics and primary care medicine. The IPH has established a dynamic partnership between the University, the MRC and the regional NHS. Research has spanned many aspects of public health and science, from diagnosing and treating diabetes, studying natural selection and tracking health data across the region. The staff at the IPH also contribute to the education and training of medical students, and of postgraduates who work in the field of public health. The IPH collaborates widely within the Cambridge University Clinical School and with health services in Norfolk, Suffolk and Cambridgeshire and is involved in large-scale studies of disease in the general population. At the Institute, the Department of Public Health and Primary Care is one of the UK's premier university departments in population sciences.

Peking University First Hospital

Peking University First Hospital (http://www.bddyyy.com.cn/english.shtml) is a large comprehensive tertiary hospital integrating medical services with teaching, research and preventive medicine. Founded in 1915, this hospital is the first state-owned hospital and

the first-batch clinical medical school. It was initially the affiliated clinic of Beijing Medical School approved by the Ministry of Education of the Republic of China. For scientific research, the hospital has been among the leading position, and was awarded the 'National Popular Science Education Base'. The Department of Paediatrics has more than 70 years history of treatment and research. It has a solid foundation for research and medical education. It was one of the first groups of institutes which established the doctoral program, the Yangtze River Chair Professor position and the '211 program' national key disciplines by the Ministry of Education in mainland China.

Chinese Disabled Persons' Federation

Established in 1988, the China Disabled Persons' Federation (CDPF) is a unified organization of/for the 83 million persons with various categories of disabilities in China (http://www.cdpf.org.cn/english/home.htm). Headquartered in Beijing, it has a nationwide umbrella network reaching every part of China with about 80 thousand full-time workers. CDPF performs three functions: (1) Representing interests of people with disabilities in China and help protect their legitimate rights; (2) Providing comprehensive and effective services to them; (3) Supervising the affairs relating to people with disabilities in China.

Memoranda of Understanding between Cambridge and Beijing

This research will be conducted based on the collaboration between ARC and IPH in the University of Cambridge and a variety of organization and institutes. Three Memorandum of Understanding (MoU) (drafted by Cambridge University International Office) have been signed by the Autism Research Centre with the following institutes: (1) Peking University First Hospital; (2) Chinese Disabled Person's Federation; (3) Elim Training Centre for Chinese with Autism. Another MoU has been signed by Institute of Public Health with School of Public Health, Peking University. The research was designed by Cambridge team and it will be conducted in mainland China with collaboration with Beijing team. The Chinese Disabled Person's Federation will help the administration of this research. This collaboration is under the umbrella relationship

established by the Vice Chancellor of Cambridge University, Prof Alison Richards, with the Chinese Academy of Sciences.

Collaboration agreement between ARC and CDPF

On June 6th, a delegation from CDPF came to Cambridge and signed an agreement to collaborate on this prevalence project at Trinity College, University of Cambridge. On June 20th, Dr Bonnie Auyeung, a delegation from Autism Research Centre in Cambridge went to China and attended a summit conference of mental health in China which was held by CDPF. This conference was held in Shantou City, Guangdong province. This two way interchange was given publicity in the autism and university sector press in China because of its historic significance.