Autism spectrum disorders in children and young people

recognition, referral and diagnosis

National Collaborating Centre for Women's and Children's Health

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Contents

Contents ii

Guideline development group membership and acknowledgements vi

Guideline development group (GDG) members vi

National Collaborating Centre for Women's and Children's Health (NCC-WCH) staff vi

Acknowledgements vii

Peer reviewers vii

1 Summary of recommendations and care pathway 1

1.1 Introduction 1

1.2 Key priorities for implementation 2

1.3 Recommendations 3

1.3.1 Tables 1–4 14

1.4 Care pathway 17

2 Development of the guideline 22

2.1 Introduction 22

2.1.1 Prevalence of ASD 22

2.1.2 Onset and course of ASD 22

2.1.3 The causes of ASD 23

2.1.4 Why is recognition and diagnosis of ASD important? 24

2.1.5 What does diagnosis bring to the child/young person and family? 24

2.1.6 The national context and previous guidelines 25

2.1.7 Patient-centred care 26

2.2 Aim and scope of the guideline 26

2.3 For whom is this guideline intended? 27

2.4 Other relevant documents 28

2.5 Who has developed the guideline 28

2.6 Guideline development methodology 29

2.6.1 Forming clinical questions and search strategies 29

2.6.2 Reviewing and synthesising the evidence 30

2.6.3 Data extraction and reporting 31

2.6.4 Summary statistics used for diagnostic/predictive accuracy 31

2.6.5 Other summary statistics used 32

2.6.6 Meta-analysis software used 32

2.6.7 Health economics 32

2.6.8 Evidence to recommendations 33

2.7 Specific considerations for this guideline 33

2.8 Schedule for updating the guidance 34

3 Recognition 35

3.1 Introduction 35

3.1.2 Methodological approach 35

3.1.3 Description of included studies 36

3.1.4 Evidence profile 36

3.1.5 Evidence statement 39

3.1.6 Evidence to recommendations 40

3.1.7 Research recommendations 52

3.1.8 Vignettes describing different presentations of ASD in children and young people 52

4 Following referral 55

4.1 Introduction 55

4.2 Screening tools 56

4.2.1 Methodological approach 56

4.2.2 Description of included studies 57
4.2.3 Evidence profiles 57
4.2.4 Evidence statement 60
4.2.5 Evidence to recommendations 60
4.3 Risk factors 62
4.3.1 Methodological approach for population-based risk factors 62
4.3.2 Description of included studies 63
4.3.3 Evidence profiles for autism and ASD 63
4.3.4 Evidence statements 66
4.3.5 Methodological approach for risk/prevalence of ASD in co-existing conditions 66
4.3.6 Description of included studies 67
4.3.7 Evidence profiles 67
4.3.8 Evidence statement 70
4.3.9 Evidence to recommendations 70
4.4 Information from other sources 72
4.4.1 Methodological approach 72
4.4.2 Description of included studies 72
4.4.3 Evidence profile 72
4.4.5 Evidence statement 72
4.4.6 Evidence to recommendations 72
4.4.7 Research recommendations 75
5 Diagnostic assessment 76
5.1 Introduction 76
5.2. Accuracy of assessment tools 77
5.2.1 Methodological approach 77
5.2.2 Description of included studies 78
5.2.3 Evidence profiles 78
5.2.4 Evidence statement 84
5.2.5 Evidence to recommendations 84
5.3 Agreement between ASD specific tools 84
5.3.1 Methodological approach 84
5.3.2 Description of included studies 84
5.3.3 Evidence profiles 84
5.3.4 Evidence statement 84
5.3.5 Evidence to recommendations 84
5.4 Other assessment tools to assist interpretation of the ASD-specific diagnostic tools 85
5.4.1 Methodological approach 85
5.4.2 Description of included studies 85
5.4.3 Evidence profiles 85
5.4.4 Evidence statement 85
5.4.5 Evidence to recommendations 85
5.5 Agreement between single clinician and panel of clinicians to diagnose ASD or autism according to DSM-IV criteria 85
5.5.1 Methodological approach 85
5.5.2 Description of included studies 86
5.5.3 Evidence profile 86
5.5.4 Evidence statement 88
5.5.5 Evidence to recommendations 88
5.6 Stability of ICD-10 and DSM-IV criteria 88
5.6.1 Methodological approach 88
5.6.2 Description of included studies 88
5.6.3 Evidence profiles 88
5.6.4 Evidence statement 91
5.6.5 Evidence to recommendations 91
5.6.6 Research recommendations 99
5.7 Communicating diagnosis to the family 100
5.7.1 Introduction 100

5.7.2 Methodological approach 100
5.7.3 Description of included studies 100
5.7.4 Evidence profile 101
5.7.5 Evidence statements 106
All the evidence was from the UK. All evidence was of low quality. 106
5.7.6 Evidence to recommendations 107
5.8 Actions that should follow assessment for children and young people who are not immediately diagnosed with ASD 109
5.8.1 Introduction 109
5.8.2 Methodological approach 109
5.8.3 Description of included studies 109
5.8.4 Evidence profile 109
5.8.5 Evidence statement 109
5.8.6 Evidence to recommendations 109
6 Differential diagnosis 112
6.1 Introduction 112
6.2 Identifying differential diagnoses 112
6.2.1 Methodological approach 112
6.2.2 Description of included studies 113
6.2.3 Evidence profile - autism 113
6.2.4 Evidence statements –autism 116
6.2.5 Evidence to recommendations 117
6.2.6 Evidence profile - ASD 117
6.2.7 Evidence statement - ASD 121
6.2.8 Evidence to recommendations 123
6.3 Identifying features that differentiate ASD from other conditions 123
6.3.1 Methodological approach 123
6.3.2 Description of included studies 123
6.3.3 Evidence profiles 123
6.3.4 Evidence profiles 124
6.3.5 Evidence to recommendations 125
7 Assessment of co-existing conditions 129
7.1 Introduction 129
7.1.1 Methodological approach 129
7.1.2 Description of included studies 130
7.1.3 Evidence profile for autism 131
7.1.4 Evidence statements for autism 133
7.1.5 Evidence to recommendations 133
7.1.6 Evidence profile for ASD 133
7.1.7 Evidence statements for ASD 135
7.1.8 Evidence to recommendations 135
8 Medical investigations 139
8.1 Introduction 139
8.1.1 Methodological approach to medical investigations 140
8.1.2 Description of included studies 141
8.1.3 Evidence profile – percentage of abnormal results 143
8.1.4 Evidence statement – percentage of abnormal results 147
8.1.5 Evidence to recommendations 148
8.1.6 Evidence profile – percentage of children/young people who had a condition identified or confirmed by biomedical investigation 148
8.1.7 Evidence statement – percentage of children/young people who had a condition identified or confirmed by the biomedical investigation 152
8.1.8 Evidence to recommendations 154
8.1.9 Research recommendations 158
9 Information and support 160
9.1 Introduction 160
9.2 Information during the process of referral, assessment and diagnosis 160

9.2.1 Methodological approach 160
9.2.2 Description of included studies 161
9.2.3 Evidence profile 161
9.2.4 Evidence statement 164
9.2.5 Evidence to recommendations 164
9.3 Support for children, young people, their families and carers 166
9.3.1 Methodological approach 166
9.3.2 Description of included studies 167
9.3.3 Evidence profile 167
9.3.4 Evidence statement 171
9.3.5 Evidence to recommendations 172
10 Service descriptions and resource use 175
10.1 Introduction 175
10.2.1 Service 1: outer city child development centre 177
10.2.2 Service 2: Rural/urban multi disciplinary multiagency team 179
10.2.3 Service 3: rural/ urban service 180
10.2.4 Service 4: specialist hospital-based service 181
10.2.5 Service 5: inner city service 182
10.3 Estimating resource use for an ASD specific assessment 183
10.4 Conclusion 191
11 References, abbreviations and glossary 192
11.1 References 192
11.2 Abbreviations 206
11.3 Glossary 208
Appendix Scope of the guideline 221
Appendix Declarations of interest 228
Appendix Registered stakeholder organisations 231
Appendix Review questions 232
Appendix E Protocols See separate file
Appendix F Search strategies See separate file
Appendix G Excluded studies See separate file
Appendix H Included studies See separate file
Appendix I Diagnostic criteria 235
Appendix J Diagnostic tools 236
Appendix K Differential diagnosis advice for healthcare professionals 238

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1 Summary of recommendations and care pathway

1.1 Introduction

This guideline is concerned with the recognition, referral and diagnosis of an autism spectrum disorder (ASD) in children and young people from birth up to 18 years. When ASD is diagnosed, this can bring a profound sense of relief to some young people, families and carers who may have always known there was something wrong. Diagnosis offers an understanding of why a child or young person is different from their peers, and some relief from what can be an intense sense of isolation from the world experienced by the child, the family and carers. It can also open doors to support and services in education, health services and a route into voluntary organisations and contact with other children and families with similar life experiences. All this can lead to an improvement in the life experience of the child or young person and their families.

The term 'autism spectrum disorders' (ASD) describes the abnormal social interaction and communication behaviours, and the unusual and/or rigid/repetitive behaviours of a group of children, young people and adults.

The core ASD behaviours are typically present in early childhood although features may not always be manifest until the situational demand changes, for example going to nursery or school or (less commonly) transition to secondary school. Autism is strongly associated with a number of co-existing conditions. Recent studies[4] have shown that ~70% of individuals with ASDs also meet diagnostic criteria for at least one other (often unrecognised) psychiatric disorder that is further impairing psychosocial functioning. Intellectual disability (IQ<70) co-occurs in approximately 50% of young people with ASD[5].

Once thought to be an uncommon developmental disorder, more recent studies have reported increased measured prevalence rates such that an autism spectrum disorder is now regarded as occurring in at least 1% of the child population[1-3]. One effect of the rising prevalence has been to increase demand for diagnostic services for children and young people of all ages in the health service.

This guideline aims to improve the experience of children, young people and those who care for them. Currently, levels of understanding of autism amongst healthcare and other relevant professionals and availability of services differ greatly from one area to another. In addition there are reported inequalities of diagnosis such as those with intellectual disability[1]

Health services have a crucial role in recognition and diagnosis of ASD. Coordination between health agencies and with other key services including, education, social services, the voluntary sector, are a crucial element of this work. Multi-agency working should also aim to be a partnership with the child, or young person with ASDs and their family or carers. All this can lead to an improvement in the life experience of the child or young person.

This guideline excludes interventions for ASD but aims to support improved management. When a child or young person presents with a social communication or behavioural concern, the provision of management intervention is based on need. Good management of the impact of an ASD is highly dependent on understanding autism and commonly associated features and accessing appropriate information and services. A timely diagnosis contributes significantly to this process.

1.2 Key priorities for implementation

A local pathway for recognition, referral and diagnostic assessment of possible ASD

There should be a local ASD strategy group with representation from child health and mental health services, education, social care, parent and carer service users and the voluntary sector.

The local ASD strategy group should appoint a lead professional who is responsible for the local ASD pathway for recognition, referral and diagnosis of children and young people. The aims of the group should include:

- improving early recognition of ASD by raising awareness of the signs and symptoms of ASD through training (see tables 1–3)
- making sure the relevant professionals (healthcare, social care and education) are aware of the local ASD pathway and how to access diagnostic services
- supporting the smooth transition to adult services for young people going through the diagnostic pathway.

There should be a multidisciplinary ASD team (the ASD team) which may include a:

- paediatrician
- child and adolescent psychiatrist
- speech and language therapist
- clinical or educational psychologist
- occupational therapist.

Access to the ASD team should be through a single point of entry.

The ASD diagnostic assessment for children and young people

A case coordinator should be appointed from the ASD team for every child or young person who is to have an ASD diagnostic assessment.

Include the following elements in every ASD diagnostic assessment:

- detailed enquiry about parent or carer concerns and if appropriate the child or young person's concerns
- a medical history including prenatal, perinatal and family history and current health
- the child's or young person's experiences of social care and education
- a developmental history focussing on developmental and behavioural features consistent with ICD-10 or DSM-IV criteria (consider using an ASD-specific tool to gather this information)
- assessment through interaction with and observation of the child or young person of their social and communicative skills and behaviours focussing on features consistent with ICD-10 or DSM-IV criteria (consider using an ASD-specific diagnostic tool to gather this information).

Consider the following differential diagnoses for ASD and if an alternative diagnosis is suspected carry out an appropriate assessment, including referral to other appropriate services:

- neurodevelopmental disorders:
  - specific language delay or disorder
  - intellectual disability or global developmental delay
  - developmental coordination disorder (DCD)
- neuropsychiatric disorders:
  - attention deficit hyperactivity disorder (ADHD)
  - mood disorder
  - anxiety disorder
  - attachment disorders
  - oppositional defiant disorder (ODD)
  - conduct disorder
  - obsessive-compulsive disorder (OCD)
- conditions in which there is developmental regression:
  - Rett's syndrome
  - epileptic encephalopathy (EE)
- other conditions:
  - severe hearing impairment
  - severe visual impairment (blind)
  - maltreatment
  - selective mutism.

After the ASD diagnostic assessment

Construct a profile for every child or young person who has had an ASD diagnostic assessment, including their strengths, skills, impairments and needs to create a needs-based management plan. This should cover learning, communication, self-care and other adaptive skills, behaviour and emotional health, taking account of the family context and needs.

Communicating with parents and professionals about the results from the ASD diagnostic assessment

After assessment and diagnosis of ASD, make sure the profile is made available to professionals in education and, and if appropriate, social care, so it can contribute to the child's or young person's individual education plan and other aspects of the needs-based management plan, through for example, a school visit by a member of the ASD team.

1.3 Recommendations

ID	Recommendations	See section
	A local pathway for recognition, referral and diagnostic assessment of possible ASD	
1	There should be a local ASD strategy group with representation from child health and mental health services, education, social care, parent and carer service users and the voluntary sector.	3.1.6
2	The local ASD strategy group should appoint a lead professional who is responsible for the local ASD pathway for recognition, referral and diagnosis of children and young people. The aims of the group should include: • improving early recognition of ASD by raising awareness of the	3.1.6

ID	Recommendations	See section
	signs and symptoms of ASD through training (see tables 1–3) • making sure the relevant professionals (healthcare, social care and education) are aware of the local ASD pathway and how to access diagnostic services • supporting the smooth transition to adult services for young people going through the diagnostic pathway.	
3	There should be a multidisciplinary ASD team (the ASD team) which may include a: • paediatrician • child and adolescent psychiatrist • speech and language therapist • clinical or educational psychologist • occupational therapist.	5.6.5
4	The ASD team should: • provide advice to professionals about referring for ASD assessments • decide on the assessment needs of those referred • be skilled in communicating with children and young people with suspected or known ASD and with their parents and carers • develop the profile (see recommendation 51) and management plan for each child or young person • with parent or carer consent, share information from the ASD diagnostic assessment directly with relevant services, for example a school visit by an ASD team member • give information to families and carers about appropriate services and support (see recommendation 63).	5.6.5
5	Access to the ASD team should be through a single point of entry.	3.1.6
6	The ASD team should either have the skills needed to carry out an ASD diagnostic assessment or have access to professionals that do, for assessing: • children and young people of all ages taking into account the cultural setting or language background **and** • children and young people with co-existing conditions such as deafness, blindness, motor disorders including cerebral palsy, intellectual disability, language disorders or additional mental health disorders.	5.6.5
7	If young people present at the time of transition to adult services, the ASD team should consider carrying out the diagnostic assessment jointly with the adult ASD diagnostic team, regardless of the young persons' intellectual ability.	5.6.5
	Recognising children and young people with possible ASD	
8	Consider the possibility of ASD when there are concerns about development or behaviour, but be aware that there may be other explanations for individual signs and symptoms.	3.1.6

ID	Recommendations	See section
9	Always take parental concerns about behaviour or development seriously, even if these are not shared by others.	3.1.6
10	When considering the possibility of ASD and whether to refer a child or young person to the ASD team, be self-critical about your professional competence and seek advice from a colleague if in doubt about the next step.	3.1.6
11	Use tables 1–3 to help identify the signs and symptoms of possible ASD.	3.1.6
12	Do not rule out ASD because the exact behaviours described in tables 1–3 are not evident. The features described should be used for guidance, but do not include all possible manifestations of ASD.	3.1.6
13	When considering the possibility of ASD, be aware that: • signs and symptoms should be seen in the context of the child's overall development • signs and symptoms will not always have been recognised by parents or by other professionals • when secondary school children present with possible ASD, signs or symptoms may have been masked by the child's coping mechanisms and/or a supportive environment • you should not assume language delay is accounted for because English is not the family's first language because language delay could be a pointer to ASD • ASD may be missed in children with an intellectual disability • the signs and symptoms of ASD may be more subtle in girls • important information about early development may not be readily available for some children and young people in whom ASD is suspected, for example looked after children and those in the criminal justice system.	3.1.6
14	Do not rule out ASD because of any of the following: • a child's or young person's difficulties appear to resolve after a needs-based intervention (such as a supportive structured learning environment) • reported normal or advanced pre-school development • good eye contact, smiling and showing affection to family members.	3.1.6
15	When considering the possibility of ASD, do not rule in or out the possibility of ASD because of a conclusion from a previous diagnostic assessment.	3.1.6
16	When considering the possibility of ASD, ask about the child's use and understanding of their first language.	3.1.6
17	Discuss developmental or behavioural concerns about a child or young person with parents or carers and the young person themselves where appropriate. Discuss sensitively the possible causes, which may include ASD, emphasising that there may be many explanations for the child's or young person's behaviour.	3.1.6
18	Be aware that if parents or carers have not suspected a developmental or behavioural condition, raising the possibility may cause distress, and that:	3.1.6

ID	Recommendations	See section
	• it may take time for them to come to terms with the concern • they may not share the concern to start with.	
19	Take time to listen to parents or carers, and if appropriate the child or young person, to discuss concerns and agree any actions to follow including referral.	3.1.6
	Referring children and young people to the ASD team	
20	Refer children and young people urgently to the ASD team if there is regression of language or social skills together with any signs and symptoms of ASD (see tables 1–3).	3.1.6
21	If you have concerns about development or behaviour but you are not sure whether the signs and/or symptoms suggest ASD, consider consulting a member of the ASD team or referring to another appropriate service. These services can then refer to the ASD team if necessary.	3.1.6
22	Consider referring to the ASD team if you are concerned about possible ASD on the basis of reported or observed signs or symptoms (see tables 1–3). Take account of the following: • the severity and duration of the signs and/or symptoms • the extent to which the signs and/or symptoms are present across different settings (for example, home and school) • the impact of the signs and/or symptoms on the child or young person and on their family • the level of parental or carer concern • the presence of risk factors for ASD (see table 4) • the likelihood of an alternative diagnosis.	3.1.6 4.3.9
23	Be aware that: • ASD-specific screening tools may be useful in gathering information about signs and symptoms of ASD in a structured way but are not essential and should not be used to make or rule out a diagnosis of ASD: a positive score on a screening instrument may support a decision to refer but can also be positive for reasons other than ASD a negative score does not rule out ASD.	4.2.5
24	When referring to the ASD team, provide in a written report all relevant and available information, including: • reported information from parents, carers and professionals about signs and/or symptoms of concern • your own observations of the signs and/or symptoms • antenatal and perinatal history • developmental milestones • known risk factors for ASD (see table 4) • relevant medical history and investigations.	3.1.6 4.3.9

ID	Recommendations	See section
25	Explain to parents what will happen after referral.	3.1.6
26	Watch and wait if you do not think concerns are sufficient to prompt a referral. If you remain concerned about ASD, reconsider your referral decision.	3.1.6
27	If the parents or carers prefer not to be referred to the ASD team, consider a period of watchful waiting. If you remain concerned about ASD, reconsider referral.	3.1.6
28	If a concern about possible ASD has been raised but there are no signs or symptoms or other reasons to suspect ASD, use professional judgment to decide on management.	3.1.6
	After referral to the ASD team	
29	When a child or young person is referred to the ASD team, at least one member of the ASD team should consider without delay whether to proceed to: • an ASD diagnostic assessment **and/or** • an alternative assessment.	4.4.6
30	Carry out an ASD diagnostic assessment without delay if there is regression of language or social skills together with any signs and symptoms of ASD (see tables 1–3).	4.4.6
31	In the absence of regression, decide whether to carry out an ASD diagnostic assessment taking into account the following: • the severity and duration of the signs and/or symptoms • the extent to which the signs and/or symptoms are present across different settings (for example home and school) • the impact of the signs and/or symptoms on the child or young person and on their family or carer • the level of parental or carer concern • the presence of risk factors (see table 4) • the likelihood of an alternative diagnosis.	4.4.6 4.3.9
32	If there is insufficient information to decide whether an ASD diagnostic assessment is needed, consider: • offering the child or young person a consultation with a relevant healthcare professional(s) • gathering necessary information from other healthcare professionals (for example, hearing test results for a pre-school child) • with parental or carer consent, obtaining information from schools or other agencies.	4.4.6
	The ASD diagnostic assessment for children and young people	
33	Once it is decided to carry out an ASD diagnostic assessment, this should start without delay and within 3 months of the initial referral to the ASD team.	4.4.6
34	A case coordinator should be appointed from the ASD team for every child or young person who is to have an ASD diagnostic assessment.	9.3.5
35	The ASD case coordinator should:	9.3.5

ID	Recommendations	See section
	• act as a single point of contact for the parents or carers and for the child or young person undergoing an ASD diagnostic assessment, and for relevant professionals • make sure that parents, carers, children and young people have appropriate information and access to appropriate support during diagnostic assessment • explain to parents and carers the likely time and sequence of assessments.	
36	Include the following elements in every ASD diagnostic assessment: • detailed enquiry about parent or carer concerns and if appropriate the child or young person's concerns • a medical history including prenatal, perinatal and family history and current health • the child's or young person's experiences of social care and education • a developmental history focussing on developmental and behavioural features consistent with ICD-10 or DSM-IV criteria (consider using an ASD-specific tool to gather this information) • assessment through interaction with and observation of the child or young person of their social and communicative skills and behaviours focussing on features consistent with ICD-10 or DSM-IV criteria (consider using an ASD-specific diagnostic tool to gather this information).	5.6.5
37	Carry out a physical examination in: • preschool children • those with intellectual disability or a family history of intellectual disability • those with dysmorphic features • those in whom there is concern regarding physical maltreatment or neglect (see 'When to suspect child maltreatment' [NICE clinical guideline 89]) or self-injurious behaviour/self-harm (see 'Self-harm: the short-term physical and psychological management and secondary prevention of self-harm in primary and secondary care' [NICE clinical guideline 16]) • those with a history suggesting a neurological disorder including suspicion of epilepsy • children or young people in whom you think it appropriate.	5.6.5
38	In the physical examination, look for: • skin stigmata of neurofibromatosis or tuberous sclerosis using a Wood's light • signs of injury, for example self-harm or child maltreatment (see NICE clinical guidelines 16 and 89 respectively).	5.6.5
39	Consider the following differential diagnoses for ASD and if an alternative diagnosis is	6.3.5

ID	Recommendations	See section
	suspected carry out an appropriate assessment, including referral to other appropriate services: • neurodevelopmental disorders: specific language delay or disorder intellectual disability or global developmental delay developmental coordination disorder (DCD) • neuropsychiatric disorders: attention deficit hyperactivity disorder (ADHD) mood disorder anxiety disorder attachment disorders oppositional defiant disorder (ODD) conduct disorder obsessive-compulsive disorder (OCD) • conditions in which there is developmental regression: Rett's syndrome epileptic encephalopathy (EE) • other conditions: severe hearing impairment severe visual impairment (blind) maltreatment selective mutism.	
40	Avoid repeated information gathering and assessments by efficient communication between professionals and agencies.	4.4.6
41	Consider whether specific assessments are necessary to help the interpretation of the ASD history and observations, for example a cognitive or language assessment appropriate to the child or young persons' age and ability.	5.6.5
42	Consider which assessments are required to profile each child's or young person's skills and impairments, for example: • intellectual ability and learning style • academic skills • speech, language and communication • fine and gross motor skills • adaptive behaviour (including self-help skills) • mental and emotional health (including self esteem) • physical health • sensory sensitivities	5.6.5

ID	Recommendations	See section
	• behaviour likely to affect participation.	
43	Use information from all sources, together with clinical judgment, to diagnose ASD based on ICD-10 or DSM-IV criteria.	5.6.5
44	Do not rely on any single ASD-specific diagnostic tool without other sources of information to diagnose ASD.	5.6.5
45	Be aware that in some children and young people there may be uncertainty about the diagnosis of ASD, particularly in those with: • a chronological age of less than 24 months • a mental age of less than 18 months • a lack of available information about their early life (for example some looked-after or adopted children) • a complex comorbid mental health disorder (for example ADHD, conduct disorder, a possible attachment disorder) sensory impairment (for example blindness or deafness), or motor disorder such as cerebral palsy.	5.6.5
46	Consider whether the child or young person may have, or have symptoms of, any of the following coexisting conditions and if suspected, carry out appropriate assessments: • Neuropsychiatric: ADHD anxiety disorders and phobias mood disorders oppositional defiant behaviour tics and Tourette syndrome obsessive compulsive disorder self-injurious behaviour • Neurodevelopmental: global delay or intellectual disability motor coordination academic learning problems, for example literacy and numeracy speech and language disorder • Medical or genetic problems and disorders: epilepsy and epileptic encephalopathy chromosome disorders genetic abnormalities including fragile X tuberous sclerosis Duchenne muscular dystrophy neurofibromatosis • Functional problems:	7.1.8

ID	Recommendations	See section
	eating/feeding urinary continence/eneuresis bowels/encopresis sleep vision and hearing impairment.	
47	Be aware that in children and young people with communication difficulties it may be difficult to recognise functional problems or mental health problems.	5.6.5
	After the ASD diagnostic assessment	
48	If after the ASD diagnostic assessment there is uncertainty about the diagnosis: • consider keeping the child or young person under review • carry out another ASD diagnostic assessment within 6 months • take account of information arising from any needs-based interventions provided in the interim.	5.8.6
49	If during the ASD diagnostic assessment, there were discrepancies between reported signs or symptoms and the findings of the ASD observation in the clinic setting, consider: • gathering additional information from other sources • carrying out further ASD-specific observation(s) in a different setting such as the school or nursery.	5.8.6
50	Consider obtaining a second opinion, including referral to a specialised tertiary ASD team if necessary, if after assessment there is: • continued uncertainty about the diagnosis • disagreement about the diagnosis within the ASD team • disagreement with parents or carers about the diagnosis • a lack of local access to particular skills and competencies required to reach a diagnosis in a child or young person who has a complex comorbidity, such as a severe sensory or motor impairment or mental health problem • a failure to respond as expected to any therapeutic interventions being provided.	5.8.6
51	Construct a profile for every child or young person who has had an ASD diagnostic assessment, including their strengths, skills, impairments and needs to create a needs-based management plan. This should cover learning, communication, self-care and other adaptive skills, behaviour and emotional health, taking account of the family context and needs.	5.6.5
52	Assess the risk of harm to and from the child or young person arising from their condition.	5.6.5
	Medical investigations	
53	Do not routinely perform any medical investigations as part of an ASD diagnostic assessment but consider the following in individual circumstances and based on clinical judgment:	8.1.8

ID	Recommendations	See section
	• electroencephalography (EEG) if there is suspicion of epilepsy (see 'The epilepsies: the diagnosis and management of the epilepsies in adults and children in primary and secondary care' [NICE clinical guideline 20]) • genetic tests, as recommended by your regional genetics centre, when there are specific dysmorphic features and/or evidence of intellectual disability.	
	Communicating with parents, carers and professionals about the results from the ASD diagnostic assessment	
54	After the ASD diagnostic assessment, discuss the findings in person with the parents or carers without delay. Explain the basis of conclusions even if the diagnosis is not yet certain.	5.7.6
55	When discussing the diagnosis with families, carers, children and young people, use generic guidelines for sharing and disclosing diagnosis to children and young people.	5.7.6
56	Discuss with the parents and/or carers how information should be shared with the child or young person. Take into account, for example, their age and ability to understand.	5.7.6
57	Provide information specific to the child or young person based on their profile.	5.7.6
58	When ASD is diagnosed, discuss with parents and/or carers the risk of ASD occurring in siblings and future children.	5.7.6
59	Provide a written report for the child or young person and parents and/or carers explaining the findings of the assessment and the basis for the conclusions drawn.	5.7.6
60	Share information from the diagnostic assessment with the GP and, with parental or carer consent (and if appropriate the consent of the child or young person), key professionals including those in education and social services.	5.7.6
61	Offer a follow-up appointment with an appropriate member of the ASD team within 6 weeks of the assessment for further discussion.	5.7.6
62	After assessment and diagnosis of ASD, make sure the profile is made available to professionals in education and, and if appropriate, social care, so it can contribute to the child's or young person's individual education plan and other aspects of the needs-based management plan, through for example, a school visit by a member of the ASD team.	9.3.5
	Information and support for families and carers	
63	Provide information on support available locally for children and young people with ASD on an individual basis according to the family's needs. This may include: • contact details for: local and national support organisations (who may provide, for example, an opportunity to meet other families with experience of ASD, or information about specific courses for parents and carers and/or young people) advice on available social benefits education and social services • information to help prepare for the future for example, transition to adult services.	9.2.5

1

1.3.1 Tables 1–4

Signs and symptoms of ASD – tables 1–3

These signs and symptoms are a combination of delay in expected features of development and the presence of unusual features. They are not intended to be used in isolation but are intended to alert professionals to think about the possibility of ASD.

Regression in or loss of use of language skills with reduced social interest and play skills and the presence of signs/ symptoms of ASD in the pre-school child requires referral without delay.

Table 1 Preschool children (or equivalent mental age)

Social interaction and communication behaviours

- Delay in language development (babble or words)
- Lack of meeting eye gaze
- Lack of response to name despite normal hearing
- Relative lack of responsive social smiling
- Limited responsiveness to other people's facial expression or feelings
- Rejection of cuddles
- Relative lack of social interest in others
- Lack of joint attention shown by lack of:
  - gaze switching
  - following a point
  - using pointing at or showing objects to share interest
- Lack of gestures and facial expression to communicate (although may place adult's hand on objects)
- Relative lack of sharing enjoyment
- Lack of imitation of others' actions
- Lack of imagination and variety of pretend play
- Lack of initiation of social play with others
- Abnormal-sounding vocalisations
- language present:
  - odd or flat intonation
  - frequent repetition of set words and phrases ('echolalia')
  - reference to self as 'you' or 'she/he' beyond 3 years
- limited and/or infrequent use of language for communication, for example use of single words although can speak in sentences

Unusual and/or rigid/repetitive behaviours

- Unusual repetitive hand, finger and body mannerisms
- Highly repetitive and/or stereotyped play, for example opening and closing doors, spinning
- Over or under reactivity to sensory stimuli, for example textures, sounds, smells
- Extremes of emotional reactivity to change and/or new situations, insistence on things being 'the same'
- Over-focused and/or unusual interests
- Excessive reaction to certain properties of food and/or /extreme food fads
- Unusually negative response to the requests of others (demand avoidant behaviour)

1

Table 2 Primary school children (aged 5–11 years or equivalent mental age)

Social interaction and communication behaviours

- Delay in language development (babble or words)
- Lack of meeting eye gaze
- Lack of response to name despite normal hearing
- Relative lack of responsive social smiling
- Limited or unusual response to other people's facial expression and/or happiness or distress
- Relative lack of social interest in others
- Lack of joint attention shown by lack of:
  - gaze switching
  - following a point
  - using pointing at or showing objects to share interest
- Relative lack of or poorly integrated eye gaze, gestures, facial expressions and body orientation in social communication
- Lack of greeting and farewell behaviours
- Limited or excessive talking, as shown in talking at others rather than a to-and-fro conversation and providing excessive information on topics of own interest
- Frequent repetition of set words and phrases
- Lack of flexible imaginative play and/or creativity although film scenes may be re-enacted
- Relative lack of interest in children of his or her own age
- Lack of ability to share in the play and/or ideas of other children, or inappropriate attempts at joint play that may manifest as aggressive or disruptive behaviour
- Unusually negative response to the requests of others (demand avoidant behaviour)
- Lack of awareness of expected behaviour
- Lack of enjoyment of situations that most children like, for example school trips

Unusual and/or rigid/repetitive behaviours

- Over or under reactivity to sensory stimuli, for example textures, sounds, smells
- Excessive reaction to certain properties of food and/or extreme food fads
- Unusual repetitive hand, finger and body mannerisms
- Over-focused and/or unusual interests
- Strong preferences for familiar routines and things being 'just right'
- Rigid expectation that other children should adhere to rules of play
- Extremes of emotional reactivity excessive for the circumstances, for example in response to change or being hurried

Other factors that may support a concern about ASD

- Unusual profile of skills and/or deficits (for example, social, and/or motor skills poorly developed, while particular areas of knowledge, reading or vocabulary skills are advanced for chronological and/or mental age)

2
3

1

Table 3 Secondary school children (over 11 years or equivalent mental age)
Social interaction and communication behaviours • Long-standing difficulties in social behaviours and social communication • Poorly integrated gestures, facial expressions, body orientation and odd and/or limited eye contact used in social communication • Lack of awareness of personal space, or intolerant of intrusions in own space • Speech peculiarities such as flat or odd tone or pitch • Repetitive speech, use of stereotyped (learnt) phrases • Poor greeting and farewell behaviours • Unable to adapt style of communication to social situations, for example may be overly formal or inappropriately familiar • May take things literally and fail to understand sarcasm or metaphor • Makes comments without awareness of social niceties and/or hierarchies • Lack of understanding of friendship; often an unsuccessful desire to have friends (although may find it easier with adults or younger children) • Social isolation and apparent preference for aloneness • History of a lack of flexible imaginative play • May appear unaware or uninterested in what other young people his or her age are interested in • Social and emotional development more immature than other areas of development, excessive trusting (naivity), lack of common sense, less independent than peers • Problems losing at games, turn taking and understanding 'changing the rules' • Poor response to the requests of others and to the perceived expectations (demand avoidant behaviour) • Lack of awareness of expected behaviour
Unusual and/or rigid/repetitive behaviours • Highly repetitive behaviours and/or rituals that impact negatively on the young person's daily activities • Excessive and unusual reaction to certain sensory stimuli • Excessive reaction to certain properties of food and/or extreme food fads • Unusual repetitive hand, finger and body mannerisms • A strong adherence to rules or fairness that leads to argument • Preference for highly specific interests or hobbies • Disproportionate emotional distress at what seems trivial to others, for example change in routine
Other factors that may support a concern about ASD • Unusual profile of skills and deficits (for example, social and/or motor skills poorly developed, while particular areas of knowledge, reading or vocabulary skills are advanced for chronological and/or mental age)

2
3

Table 4 Risk factors for ASD

- Intellectual disability
- A sibling with ASD
- Birth defects associated with central nervous system malformation and/or dysfunction including cerebral palsy
- Gestational age less than 35 weeks
- Maternal use of sodium valproate in pregnancy
- Neonatal encephalopathy or epileptic encephalopathy including infantile spasms
- Chromosomal disorders such as Down's syndrome
- Genetic disorders such as fragile X
- Duchenne muscular dystrophy
- Neurofibromatosis
- Tuberous sclerosis

1.4 Care pathway

Recognition and referral

Consider the possibility of ASD when there are concerns about development or behaviour, but be aware that there may be other explanations for individual signs and symptoms.

Always take parental concerns about behaviour or development seriously, even if these are not shared by others.

When considering the possibility of ASD and whether to refer a child or young person to the ASD team, be self-critical about your professional competence and seek advice from a colleague if in doubt about the next step.

Use tables 1–3 to help identify the signs and symptoms of possible ASD.

Do not rule out ASD because the exact behaviours described in tables 1–3 are not evident. The features described should be used for guidance, but do not include all possible manifestations of ASD.

When considering the possibility of ASD, be aware that:

- signs and symptoms should be seen in the context of the child's overall development
- signs and symptoms will not always have been recognised by parents or by other professionals
- when secondary school children present with possible ASD, signs or symptoms may have been masked by the child's coping mechanisms and/or a supportive environment
- you should not assume language delay is accounted for because English is not the family's first language because language delay could be a pointer to ASD
- ASD may be missed in children with an intellectual disability
- the signs and symptoms of ASD may be more subtle in girls
- important information about early development may not be readily available for some children and young people in whom ASD is suspected, for example looked after children and those in the criminal justice system

Do not rule out ASD because of any of the following:

- a child's or young person's difficulties appear to resolve after a needs-based intervention (such as a supportive structured learning environment)
- reported normal or advanced pre-school development
- good eye contact, smiling and showing affection to family members.

When considering the possibility of ASD, do not rule in or out the possibility of ASD because of a conclusion from a previous diagnostic assessment.

When considering the possibility of ASD, ask about the child's use and understanding of their first language

Discuss developmental or behavioural concerns about a child or young person with parents or carers and the young person themselves where appropriate. Discuss sensitively the possible causes, which may include ASD, emphasising that there may be many explanations for the child's or young person's behaviour.

Be aware that if parents or carers have not suspected a developmental or behavioural condition, raising the possibility may cause distress, and that:

- it may take time for them to come to terms with the concern
- they may not share the concern to start with.

Take time to listen to parents or carers, and if appropriate the child or young person, to discuss concerns and agree any actions to follow including referral.

Be aware that:

- ASD-specific screening tools may be useful in gathering information about signs and symptoms of ASD in a structured way but are not essential and should not be used to make or rule out a diagnosis of ASD:
  - a positive score on a screening instrument may support a decision to refer but can also be positive for reasons other than ASD
  - a negative score does not rule out ASD

If you have concerns about development or behaviour but you are not sure whether the signs and/or symptoms suggest ASD, consider consulting a member of the ASD team or referring to another appropriate service. These services can then refer to the ASD team if necessary.

Explain to parents what will happen after referral.

Refer children and young people urgently to the ASD team if there is regression of language or social skills together with any signs and symptoms of ASD (see tables 1–3).

Consider referring to the ASD team if you are concerned about possible ASD on the basis of reported or observed signs or symptoms (see tables 1–3). Take account of the following:

- the severity and duration of the signs and/or symptoms
- the extent to which the signs and/or symptoms are present across different settings (for example, home and school)
- the impact of the signs and/or symptoms on the child or young person and on their family
- the level of parental or carer concern
- the presence of risk factors for ASD (see table 4)
- the likelihood of an alternative diagnosis.

Explain to parents what will happen after referral.

When referring to the ASD team, provide in a written report all relevant and available information, including:

- reported information from parents, carers and professionals about signs and/or symptoms of concern
- your own observations of the signs and/or symptoms
- antenatal and perinatal history
- developmental milestones
- known risk factors for ASD (see table 4)

Watch and wait if you do not think concerns are sufficient to prompt a referral. If you remain concerned about ASD, reconsider your referral decision.

If the parents or carers prefer not to be referred to the ASD team, consider a period of watchful waiting. If you remain concerned about ASD, reconsider referral

Continued concern about possible ASD?

Yes

No

If a concern about possible ASD has been raised but there are no signs or symptoms or other reasons to suspect ASD, use professional judgment to decide on management.

Exit ASD pathway

General

There should be a local ASD strategy group with representation from child health and mental health services, education, social care, parent and carer service users and the voluntary sector.

The local ASD strategy group should appoint a lead professional who is responsible for the local ASD pathway for recognition, referral and diagnosis of children and young people. The aims of the group should include:

- improving early recognition of ASD by raising awareness of the signs and symptoms of ASD through training (see tables 1–3)
- making sure the relevant professionals (healthcare, social care and education) are aware of the local ASD pathway and how to access diagnostic services.
- supporting the smooth transition to adult services for young people going through the diagnostic pathway.

There should be a multidisciplinary ASD team (the ASD team) which may include a:

- paediatrician
- child and adolescent psychiatrist
- speech and language therapist
- clinical or educational psychologist
- occupational therapist.

The ASD team should:

- provide advice to professionals about referring for ASD assessments
- decide on the assessment needs of those referred
- be skilled in communicating with children and young people with suspected or known ASD and with their parents and carers
- develop the profile (see recommendation 51) and management plan for each child or young person
- with parent or carer consent, share information from the ASD diagnostic assessment directly with relevant services, for example a school visit by an ASD team member
- give information to families and carers about appropriate services and support (see recommendation 63)

Access to the ASD team should be through a single point of entry.

The ASD team should either have the skills needed to carry out an ASD diagnostic assessment or have access to professionals that do, for assessing:

- children and young people of all ages taking into account the cultural setting or language background and
- children and young people with co-existing conditions such as deafness, blindness, motor disorders including cerebral palsy, intellectual disability, language disorders or additional mental health disorders.

If young people present at the time of transition to adult services, the ASD team should consider carrying out the diagnostic assessment jointly with the adult ASD diagnostic team, regardless of the young persons' intellectual ability.

1

Following a referral

When a child or young person is referred to the ASD team, at least one member of the ASD team should consider without delay whether to proceed to:

- an ASD diagnostic assessment **and/or**
- an alternative assessment.

Carry out an ASD diagnostic assessment without delay if there is regression of language or social skills together with any signs and symptoms of ASD (see tables 1–3).

In the absence of regression, decide whether to carry out an ASD diagnostic assessment taking into account the following:

- the severity and duration of the signs and/or symptoms
- the extent to which the signs and/or symptoms are present across different settings (for example home and school)
- the impact of the signs and/or symptoms on the child or young person and on their family or carer
- the level of parental or carer concern
- the presence of risk factors (see table 4)
- the likelihood of an alternative diagnosis.

If there is insufficient information to decide whether an ASD diagnostic assessment is needed, consider:

- offering the child or young person a consultation with a relevant healthcare professional(s)
- gathering necessary information from other health care professionals (for example, hearing test results for a pre-school child)
- with parental or carer consent, obtaining information from schools or other agencies.

Avoid repeated information gathering and assessments by efficient communication between professionals and agencies.

Be aware that:

- ASD-specific screening tools may be useful in gathering information about signs and symptoms of ASD in a structured way but are not essential and should not be used to make or rule out a diagnosis of ASD:
  - a positive score on a screening instrument may support a decision to refer but can also be positive for reasons other than ASD
  - a negative score does not rule out ASD

Refer for another assessment

Continued concern about ASD?

Yes

No

Exit ASD pathway

Refer for ASD specific assessment

Once it is decided to carry out an ASD diagnostic assessment, this should start without delay and within 3 months of the initial referral to the ASD team.

A case coordinator should be appointed from the ASD team for every child or young person who is to have an ASD diagnostic assessment.

The ASD case coordinator should:

- act as a single point of contact for the parents or carers and for the child or young person undergoing an ASD diagnostic assessment, and for relevant professionals
- make sure that parents, carers, children and young people have appropriate information and access to appropriate support during diagnostic assessment
- explain to parents and carers the likely time and sequence of assessments.

The ASD specific diagnostic assessment

Include the following elements in every ASD diagnostic assessment:

- detailed enquiry about parent or carer concerns and if appropriate the child or young person's concerns
- a medical history including prenatal, perinatal and family history and current health
- the child's or young person's experiences of social care and education
- a developmental history focussing on developmental and behavioural features consistent with ICD-10 or DSM-IV criteria (consider using an ASD-specific tool to gather this information)
- assessment through interaction with and observation of the child or young person of their social and communicative skills and behaviours focussing on features consistent with ICD-10 or DSM-IV criteria (consider using an ASD-specific diagnostic tool to gather this information).

Carry out a physical examination in:

- preschool children
- those with intellectual disability or a family history of intellectual disability
- those with dysmorphic features
- those in whom there is concern regarding physical maltreatment or neglect (see 'When to suspect child maltreatment' [NICE clinical guideline 89]) or self-injurious behaviour/self-harm (see 'Self-harm: the short-term physical and psychological management and secondary prevention of self-harm in primary and secondary care' [NICE clinical guideline 16])
- those with a history suggesting a neurological disorder including suspicion of epilepsy
- children or young people in whom you think it appropriate.

In the physical examination, look for:

- skin stigmata of neurofibromatosis or tuberous sclerosis using a Wood's light
- signs of injury, for example self-harm or child maltreatment (see NICE clinical guidelines 16 and 89 respectively).

Consider the following differential diagnoses for ASD and if an alternative diagnosis is suspected carry out an appropriate assessment, including referral to other appropriate services:

- neurodevelopmental disorders:
  - specific language delay or disorder
  - intellectual disability or global developmental delay
  - developmental coordination disorder (DCD)
- neuropsychiatric disorders:
  - attention deficit hyperactivity disorder (ADHD)
  - mood disorder
  - anxiety disorder
  - attachment disorders
  - oppositional defiant disorder (ODD)
  - conduct disorder
  - obsessive-compulsive disorder (OCD)
- conditions in which there is developmental regression:
  - Rett's syndrome
  - epileptic encephalopathy (EE)
- other conditions:
  - severe hearing impairment
  - severe visual impairment (blind)
  - maltreatment
  - selective mutism.

Consider whether specific assessments are necessary to help the interpretation of the ASD history and observations, for example a cognitive or language assessment appropriate to the child or young persons' age and ability.

Consider which assessments are required to profile each child's or young person's skills and impairments, for example:

- intellectual ability and learning style
- academic skills
- speech language and communication
- fine and gross motor skills
- adaptive behaviour (including self-help skills)
- mental and emotional health (including self esteem)
- physical health
- sensory sensitivities
- behaviour likely to affect participation.

Consider whether the child or young person may have, or have symptoms of, any of the following coexisting conditions and if suspected, carry out appropriate assessments:

- Neuropsychiatric:
  - ADHD
  - anxiety disorders and phobias
  - mood disorders
  - oppositional defiant behaviour
  - tics and Tourette syndrome
  - obsessive compulsive disorder
  - self-injurious behaviour
- Neurodevelopmental:
  - global delay or intellectual disability
  - motor coordination
  - academic learning problems, for example literacy and numeracy
  - speech and language disorder
- Medical or genetic problems and disorders:
  - epilepsy and epileptic encephalopathy
  - chromosome disorders
  - genetic abnormalities including fragile X
  - tuberous sclerosis
  - Duchenne muscular dystrophy
  - neurofibromatosis
- Functional problems:
  - eating/feeding
  - urinary continence/eneuresis
  - bowels/encopresis
  - sleep
  - vision and hearing impairment.

Be aware that in children and young people with communication difficulties it may be difficult to recognise functional problems or mental health problems.

Be aware that in some children and young people there may be uncertainty about the diagnosis of ASD, particularly in those with:

- a chronological age of less than 24 months
- a mental age of less than 18 months
- a lack of available information about their early life (for example some looked-after or adopted children)
- a complex comorbid mental health disorder (for example ADHD, conduct disorder, a possible attachment disorder) sensory impairment (for example blindness or deafness), or motor disorder such as cerebral palsy.

Medical investigation

Do not routinely perform any medical investigations as part of an ASD diagnostic assessment but consider the following in individual circumstances and based on clinical judgment:

- electroencephalography (EEG) if there is suspicion of epilepsy (see 'The epilepsies: the diagnosis and management of the epilepsies in adults and children in primary and secondary care' [NICE clinical guideline 20])
- genetic tests, as recommended by your regional genetics centre, when there are specific dysmorphic features and/or evidence of intellectual disability.

From: Actions if there is continued uncertainty about the diagnosis of ASD

Following the ASD specific diagnostic assessment

Construct a profile for every child or young person who has had an ASD diagnostic assessment, including their strengths, skills, impairments and needs to create a needs-based management plan. This should cover learning, communication, self-care and other adaptive skills, behaviour and emotional health taking, account of the family context and needs.

Assess the risk of harm to and from the child or young person arising from their condition.

After the ASD diagnostic assessment, discuss the findings in person with the parents or carers without delay. Explain the basis of conclusions even if the diagnosis is not yet certain.

When discussing the diagnosis with families, carers, children and young people, use generic guidelines for sharing and disclosing diagnosis to children and young people.

Discuss with the parents and/or carers how information should be shared with the child or young person. Take into account, for example, their age and ability to understand.

Provide information specific to the child or young person based on their profile.

Share information from the diagnostic assessment with the GP and, with parental or carer consent (and if appropriate the consent of the child or young person), key professionals including those in education and social services.

Making a diagnosis

Use information from all sources, together with clinical judgment, to diagnose ASD based on ICD-10 or DSM-IV criteria.

Do not rely on any single ASD-specific diagnostic tool without other sources of information to diagnose ASD.

Not ASD

Exit ASD pathway

ASD

Information and support

Provide a written report for the child or young person and parents and/or carers explaining the findings of the assessment and the basis for the conclusions drawn.

After assessment and diagnosis of ASD, make sure the profile is made available to professionals in education and, and if appropriate, social care, so it can contribute to the child's or young person's individual education plan and other aspects of the needs-based management plan, through for example, a school visit by a member of the ASD team.

Offer a follow-up appointment with an appropriate member of the ASD team within 6 weeks of the assessment for further discussion.

When ASD is diagnosed, discuss with parents and/or carers the risk of ASD occurring in siblings and future children.

Provide information on support available locally for children and young people with ASD on an individual basis according to the family's needs. This may include:

- contact details for:
  - local and national support organisations (who may provide, for example, an opportunity to meet other families with experience of ASD, or information about specific courses for parents and carers and/or young people)
  - advice on available social benefits
  - education and social services
- information to help prepare for the future for example, transition to adult services.

Unsure

Actions if there is continued uncertainty about the diagnosis of ASD

If after the ASD diagnostic assessment there is uncertainty about the diagnosis:

- consider keeping the child or young person under review
- carry out another ASD diagnostic assessment within 6 months
- take account of information arising from any needs-based interventions provided in the interim.

If during the ASD diagnostic assessment, there were discrepancies between reported signs or symptoms and the findings of the ASD observation in the clinic setting, consider:

- gathering additional information from other sources
- carrying out further ASD-specific observation(s) in a different setting such as the school or nursery.

Consider obtaining a second opinion, including referral to a specialised tertiary ASD team if necessary, if after assessment there is:

- continued uncertainty about the diagnosis
- disagreement about the diagnosis within the ASD team
- disagreement with parents or carers about the diagnosis
- a lack of local access to particular skills and competencies required to reach a diagnosis in a child or young person who has a complex comorbidity, such as a severe sensory or motor impairment or mental health problem
- a failure to respond as expected to any therapeutic interventions being provided.

Go back to ASD specific assessment

2 Development of the guideline

2.1 Introduction

This guideline is concerned with the recognition, referral and diagnosis of ASD in children and young people. When ASD is diagnosed, this can bring a profound sense of relief to some young people, families and carers who may have always known there was something wrong. Diagnosis offers an understanding of why a child or young person is different from their peers, reducing what can be an intense sense of isolation from the world experienced by the child, the family and carers. It can also open doors to support and services in education, health services and a route into voluntary organisations and contact with other children and families with similar life experiences. All this can lead to an improvement in the life experience of the child or young person and their families.

The term 'autism spectrum disorders' (ASD) describes the behavioural characteristics of a group of children, young people and adults with qualitative abnormalities in reciprocal social interaction and in patterns of communication, and by a restricted, stereotyped and repetitive repertoire of interests and activities. These qualitative abnormalities are a pervasive feature of the individual's functioning across a range of situations although they may vary in level of severity. They co-occur with other conditions and behaviours causing variable impact to the individual across time and context and have an adverse impact on adaptive function.

The term 'autism spectrum disorders' (ASD) is used throughout this guideline instead of the term 'Pervasive developmental disorder' (PDD), the term used in both the International Classification of Diseases (ICD-10)[6] and the Diagnostic and Statistical Manual (DSM-IV)[7]. The terms PDD and ASD are regarded as conveying the same meaning. Autism is the prototypical disorder in the autism spectrum. It is a lifelong disorder that usually has a profound impact on the child, young person and their families.

2.1.1 Prevalence of ASD

Once thought to be an uncommon developmental disorder, more recent studies have reported increased measured prevalence rates such that an autism spectrum disorder is now regarded as occurring in at least 1% of the child population[1-3]. The factors affecting the rising prevalence are unknown but include changing diagnostic criteria[8], ascertainment methods, dependence on existing registers, a staging approach to screening and diagnostic assessment as well as diagnostic substitution[9;10]. One effect of the rising prevalence has been to increase demand for diagnostic services for children and young people of all ages. This has considerable training and service resource implications for the NHS.

2.1.2 Onset and course of ASD

The core ASD behaviours are typically present in early childhood although features may not always be manifest until the situational demand changes, for example going to nursery or school or (less commonly) transition to secondary school. Regression and/or stasis of language and social behaviour is reported in between one fifth and one third of children, usually but not exclusively in the second year of life, for reasons that are unknown. Other behavioural features of ASD may be manifest in different ways at different ages and in any individual can change over time and vary with maturity,

environmental requirements and co-existing conditions even if the core impairments remain.

2.1.3 The causes of ASD

ASD is a neurodevelopmental and biologically based disorder although the mechanism of causation is unknown. Underlying medical causes are reportedly found in less than 10% of children with ASD[11]. There is no specific diagnostic test for ASD. Diagnosis is made on the basis of the presence of characteristic behaviours. There is a substantial genetic basis with strong heritability[12;13]. At least 60 different metabolic, neurological disorders and complex chromosome abnormalities have been reported as associated with ASD. Potential candidate genes are emerging from the advances in molecular genetic techniques but current thinking is of a genetically heterogenous disorder producing phenotypic heterogeneity (differing physical and behavioural characteristics)[14]. For families with a child with a diagnosis of ASD the likelihood of having another child with ASD is greatly increased, making awareness of this an important part of the diagnostic process. A number of medical conditions are associated with increased risk of ASD. Autism is strongly associated with a number of co-existing conditions which have an impact on the well being of the child, young person and family. Recent studies[4] have shown that ~70% of individuals with ASDs also meet diagnostic criteria for at least one other (often unrecognised) psychiatric disorder that is further impairing psychosocial functioning. Intellectual disability (IQ<70) co-occurs in approximately 50% of young people with ASD[5].

Manifestations of ASD are due to both an absence and/or delay of usual development and the presence of unusual features of development affecting behaviours in the following areas:

- Social and communicative reciprocity – in both initiation and responsiveness to interpersonal verbal and non-verbal communication and social interaction.
- The ability to infer what another person is experiencing or thinking.
- Creative imaginative play and thinking.
- Cognitive and behavioural flexibility
- The range and intensity of interests and activities.
- Sensory interests and sensitivities
- Emotional reactions to the environment
- Self absorption in repetitive behaviours and stereotyped mannerisms
- Motor co-ordination competences

Diagnosis is the decision making process that determines if an individual has a disorder or not. "Disorder" is not an exact term, but it is used here (as in ICD-10) to imply the existence of a clinically recognisable set of symptoms or behaviours associated with distress and with interference with personal functions [6].

Once thought of as a categorical disorder, so that an individual either definitely did or did not have autism, the concept of continuously distributed traits with no clear diagnostic boundary is a challenge to deciding the 'threshold' for a definite disorder and hence the diagnosis of an ASD. Strengths and weaknesses in the core behaviours outlined above of social communication skills and rigidity of thinking are now thought to be distributed throughout the general population as traits[15] and found in approximately 5% of the population[16]. Such traits are found more commonly in the families of those with autism[17]and are referred to as the 'broader autism phenotype'.

The Criteria for the diagnosis of a disorder in the autism spectrum (ASD/PDD) which are used in this guideline are those defined in both the International Classification of Diseases (ICD-10) and the Diagnostic and Statistical Manual (DSM-IV). (see appendix I). Subtypes of PDD/ASD described in ICD-10 and DSM-IV ASD include, atypical autism,

Aspergers syndrome, disintegrative disorder and 'other' (ICD-10); Aspergers Disorder and PDD –not otherwise specified (DSM-IV) as well as Rett's syndrome. Both the ICD-10 and DSM-IV are currently undergoing revision. In this guideline the term 'Autism' is used to refer to the subtype 'childhood autism ' in ICD-10 and 'autistic disorder' in DSM-IV. We are using the term autism spectrum disorders (ASDs) to include all autistic conditions where the 'disorder' criteria are met and thus a 'diagnosis ' is made. The word spectrum implies a range of behaviours manifest in various combinations and levels of severity. Sometimes an individual may have qualitatively similar traits to those of ASD but be below threshold or 'subthreshold' for a diagnosis of ASD. In such cases, the individual and/or family may find the information about a spectrum helpful and support similar to that provided for ASD to be helpful.

2.1.4 Why is recognition and diagnosis of ASD important?

Autism impacts significantly upon both the child or young person and their family members. While it is important to recognise that some people with ASD will have highly productive and fruitful lives, for others with more severe ASD, particularly with associated co-existing conditions, autism is a lifelong significantly impairing disorder with profound effects not only for the individual but on family members who may require assistance from health, education and support services for a long time. Current UK costs of supporting people with ASD and the opportunity costs of lost productivity are estimated at £28 billion per year[18]

Smith et al[19] found that mothers of adolescents and adults with autism experience high levels of distress. Good management of the impact of an ASD is highly dependent on understanding autism and commonly associated features and accessing appropriate information and services. An appropriate and timely diagnosis contributes significantly to this process. Levels of understanding of autism amongst healthcare and other relevant professionals and availability of services currently differ greatly from one local area to another and there are reported inequalities of diagnosis in subgroups such as those with intellectual disability[1]

2.1.5 What does diagnosis bring to the child/young person and family?

Diagnosis can provide parents/carers with a framework for understanding their child and make decisions about which interventions or management strategies to try. Particular examples of how a diagnosis can enable the child, young person and family are shown below. The quotations below from the National Autism Plan for Children, 2003 and the National Autistic Society highlight the parental viewpoint.

Access to information, services and support

Once ASD is diagnosed, parents can more easily access local and national support groups and services where these are available:

> *'Ignorance isn't bliss. You need help as early as possible'*

> *'I now understand how special and unique he is, more so than before'*

> *'Glad I know what he's got now so I can help him'*

> *'Some health specialists may be reluctant and say 'we don't like to label children'. Well, we don't like to label them as parents either, but we have to. Getting that label is the first step to getting some help and you want to know what it is you are dealing with – you just want to know'*

Emotional benefits

Parents realise they are not to blame for their children's autism.

> '*Until we had the diagnosis, we were labelled as neurotic, dysfunctional and unable to cope.'*

Appropriate educational support

Before diagnosis, children and young people may be labelled as 'naughty', may be under-achieving, misunderstood and unsupported, anxious and distressed about attending school or excluded from school

'*It is of no benefit to be within the education system without a diagnosis'*

'From the parents' perspective, the intense distress associated with the diagnosis of autism/ASD cannot be taken away. At least the experience can be assisted by a system that works effectively to answer their questions and provide them with the support they need'

Recognising co-existing conditions

'Because he has other conditions, they couldn't see the wood for the trees. Everyone was reluctant to double-diagnosis and give him another label.'

2.1.6 The national context and previous guidelines

The health service has a crucial role in recognition and diagnosis of ASD. Primary, secondary and tertiary health services are involved in ASD throughout the person's life both directly and through coordination with other key services, education, social services, the voluntary sector, work, leisure, housing, transport, in fact every area of life. Multi-agency working should aim to be a partnership with the child/young person with ASDs and their family. Currently, most diagnosis of ASD takes place within the district health services although initial recognition may be by parents/carers, teachers, health visitors or other members of the primary health care team. Districts have different referral policies although in general, young children will be referred to paediatricians at a child development centre or directly to speech and language therapy services, and older children to paediatricians or Child and Adolescent Mental Health services (CAMHS).

Parents, through the National Autistic Society, say that they want clear referral pathways, health professionals that are well trained and knowledgeable about ASD and for health professionals to work together and with education and social services to enable the child to gain access to appropriate intervention and education and the family access to support. The parental experience is of disbelief of their concerns, difficulty in getting a referral, and often a struggle to get a diagnosis. Their experience is that they have to repeat their story many times to different professionals and assessments are not coordinated.

While clinical guidance on ASD exists; practice parameter from the USA[20], national plans from the UK (National Autism Plan for Children)[21] and guidelines from Scotland (Assessment, Diagnosis and Clinical Interventions for Children and Young People with Autism Spectrum Disorders)[22] and New Zealand (Autism Spectrum Disorders guideline)[23] there remains postcode variation in access to diagnosis in the UK.

The changing picture of presentation of ASD presents challenges for diagnosis. Since NAP-C, there has been an increase in the number of district teams who have a formal ASD assessment protocol, 54% in 2007 compared with 32% in 2001, 93% (compared with 48% in 2001) are using a multidisciplinary/multiagency team approach and 57% have joint clinics with child mental health services (compared 34% in 2001)[24]. However the current estimated prevalence rates of ASD have major resource implications and place a considerable strain on local diagnostic services. Only 49% were able to complete the diagnostic assessment within 30 weeks in 2007.

In 2009 the Autism Bill was passed becoming the Autism Act which puts a duty on the Secretary of State to develop a strategy for adults with autism and lays a legal obligation on local authorities through statutory guidance (still under consultation) to plan (through appointing a lead professional) and provide services for recognition (through awareness training), diagnosis and provision of services from transition to meet the needs of adults with autism regardless of their level of intellectual ability or disability.

There is a stated desire on the part of health professionals involved with children and young people for clear evidence based guidance on the diagnostic process for ASD, guidance on what co-existing conditions should be assessed and which medical investigations should and should not be carried out routinely. Services for children and young people have been critically reviewed by the Kennedy report (Getting it right for Children 2010). Achieving Equity and Excellence for Children and Young People outlines the Government proposals for the NHS as applied to children. This promotes shared decision making between families, young people and professionals and an 'outcomes framework' for services that emphasises enhanced quality of life, ensuring a positive experience of health care, recovery from acute episodes of illness and a safe environment for treatment and care. The latter point is emphasised in the Children's National Service Framework, Chapter 5 of the Hospital Standards[25] 'Care will be provided in an appropriate environment that is safe and well suited to the age and development of the child or young person'. This is a particularly important aspect of health care for those with ASDs of all ages and abilities.

2.1.7 Patient-centred care

Treatment and care should take into account the needs and preferences of children, young people and those who care for them. Children and Young People with Autism Spectrum Disorders (ASDs), and their family/carers should have the opportunity to make informed decisions about their care and treatment, in partnership with their healthcare professionals. If children and young people do not have the capacity to make decisions, healthcare professionals should follow the Department of Health's advice on consent (available from www.dh.gov.uk/consent) and the code of practice that accompanies the Mental Capacity Act (summary available from www.publicguardian.gov.uk). In Wales, healthcare professionals should follow advice on consent from the Welsh Assembly Government (available from www.wales.nhs.uk/consent).

If the child or young person is under 16, healthcare professionals should follow the guidelines in 'Seeking consent: working with children' (available from www.dh.gov.uk/consent).

Good communication between healthcare professionals and children and young people is essential. It should be supported by written information, ideally evidence based, and tailored to the needs of the child or young person. Information and support, treatment and care should be available according to need, culturally appropriate, accessible to people with additional needs such as physical, sensory or intellectual disabilities, and to people who do not speak or read English. Families and carers should also be given the information and support they need.

Care of young people in transition between paediatric and adult services should be planned and managed according to the best practice guidance described in 'Transition: getting it right for young people' (available from www.dh.gov.uk).Adult and paediatric healthcare teams should work jointly to provide assessment and services to young people in transition with ASD.

2.2 Aim and scope of the guideline

This clinical guideline concerns the recognition, referral and diagnosis of autism spectrum disorders (ASD) in children and young people from birth up to 18 years (until their 19th birthday).

The guideline has been developed with the aim of providing guidance in the following areas.

- Signs and symptoms (features of ASD) that should prompt professionals working with children and/or parents or carers to consider ASD in a child or young person, including signs and symptoms that should trigger referral for specialist assessment.

- Information requirements from other agencies.
- The components of diagnostic assessment after referral, including:
    - methods of assessing ASD
    - diagnostic thresholds for ASD
    - assessment of the most common coexisting conditions and differential diagnoses, including other developmental disorders, speech and language disorders, intellectual disabilities, and mental health problems
    - clinical evidence for and cost effectiveness of (which test should be done on whom and for what purpose):
        - biomedical investigations (including sequencing and number of tests)
        - genetic assessments (such as karyotype, fragile x, comparative genomic hybridization [CGH] array)
        - neuroimaging (computed tomography [CT], magnetic resonance imaging [MRI], single photon emission computed tomography [SPECT], positron emission tomography [PET])
        - electroencephalograms [EEGs]
        - metabolic tests.
- The information and day-to-day support (such as a telephone helpline) appropriate for children, young people and parents/carers during the process of referral, assessment and diagnosis of ASD.
- Ineffective diagnostic interventions and approaches.

The following areas are specifically excluded from the guideline.

- Population screening or surveillance.
- The basic components of any routine paediatric or mental health assessment not specific to ASD.
- The role and competencies of different professions in the recognition and diagnosis of ASD.
- Specific models for running a diagnostic service.
- Interventions and ongoing management of ASD, including specific therapeutic interventions during diagnosis.
- Reassessment and review of diagnosis.

Further information about the areas that are covered by the guideline is available in the scope of the guideline (reproduced in Appendix A).

2.3 For whom is this guideline intended?

This guideline is of relevance to those who work in or use the National Health Service (NHS) in England, Wales and Northern Ireland, in particular:

- professionals working with children and young people and/or families and carers in health, education or social services.
- those responsible for commissioning and planning healthcare services, including commissioners, Health Commission Wales commissioners, and public health and trust managers

- children and young people, and their families/carers, going through the referral and diagnosis process for ASD.

A version of this guideline for children and young people, their families/carers and the public is available from the NICE website (www.nice.org.uk/xxx) or from NICE publications on 0845 003 7783 (quote reference number xxx). [This paragraph will be completed in the final guideline]

2.4 Other relevant documents

This guideline is intended to complement other existing and proposed works of relevance, including the following guidance published by NICE.

- 'Attention deficit hyperactivity disorder', NICE clinical guideline 72
- 'Depression in children and young people', NICE clinical guideline 28
- 'Epilepsy', NICE clinical guideline 20
- 'Self harm', NICE clinical guideline 16
- 'When to suspect maltreatment', NICE clinical guideline 89

2.5 Who has developed the guideline

The guideline was developed by a multi-professional and lay GDG convened by the National Collaborating Centre for Women's and Children's Health (NCC-WCH). Membership included:

- two psychologists
- two psychiatrists
- three paediatricians
- a health visitor
- a GP
- a speech and language therapist
- an education professional
- two parent/carer members.

NCC-WCH staff provided methodological support for the guideline development process, undertook systematic searches, retrieved and appraised the evidence, developed health economic models, and wrote successive drafts of the guideline.

Three external advisors were appointed to the GDG to advise on methodology, medical investigations and genetic testing.

All GDG members' and external advisers' potential and actual conflicts of interest were recorded on declaration forms provided by NICE (summarised in Appendix B). None of the interests declared by GDG members constituted a material conflict of interest that would influence recommendations developed by the GDG.

Organisations with interests in the recognition, referral and diagnosis of ASD in children and young people were encouraged to register as stakeholders for the guideline. Registered stakeholders were consulted throughout the guideline development process. The types of organisations eligible to register as stakeholders included:

- national patient and carer organisations that directly or indirectly represent interests of children and young people with ASD and their families/carers.

- national organisations that represent healthcare professionals who provide services children and young people with ASD and their families/carers.
- companies that manufacture preparations and/or products used in the management of ASD
- providers and commissioners of health services in England, Wales and Northern Ireland
- statutory organisations such as the Department of Health and the Welsh Assembly Government
- research organisations that have undertaken nationally recognised research in relation to the topics covered in the guideline.

A list of registered stakeholder organisations for this guideline is presented on the NICE website (and in Appendix C to be added at publication).

2.6 Guideline development methodology

This guidance was commissioned by NICE and developed in accordance with the guideline development process outlined in the NICE *Guidelines Manual (2009)* (see www.nice.org.uk/guidelinesmanual). The general approach is outlined below.

Table 2.1 Stages in the NICE guideline development process

Stage
Scoping the guideline (determining what the guideline would and would not cover)
Preparing the work plan (agreeing timelines, milestones, guideline development group constitution, etc)
Forming and running the guideline development group
Developing review questions
Identifying evidence
Reviewing and synthesising evidence
Incorporating health economics
Making group decisions and reaching consensus
Linking guidance to other NICE guidance
Creating guideline recommendations
Writing the guideline
Stakeholder consultation on the draft guideline
Finalising and publishing the guideline (including pre-publication check)
Declaration of interests

In accordance with NICE's Equality Scheme, ethnic and cultural considerations and factors relating to disabilities have been considered by the GDG throughout the development process and specifically addressed in individual recommendations where relevant. Further information is available from: www.nice.org.uk/aboutnice/howwework/NICEEqualityScheme.jsp.

2.6.1 Forming clinical questions and search strategies

The GDG formulated clinical questions (see Appendix D) from the scope and prepared a protocol for each review question (see Appendix E). These formed the starting point for the subsequent evidence reviews. The GDG were supported in the development of the clinical question and protocols by the NCC –WCH technical team.

Published evidence was identified by systematic searches of the databases (shown below) for the evidence. Reviews of the evidence published between 1990 to Oct 11th 2010 were undertaken by the NCC-WCH technical team. A search strategy designed to

cover all conditions of the Autism Spectrum Disorder was developed in the Medline database before being translated for use in the remaining databases, including Embase, the Cochrane Library Database, PsycInfo and Cinahl. Three educational databases were subsequently searched including ERIC, the British Educational Index and the Australian Educational Index.

Search strategies combined a combination of MESH headings and keyword searches including abbreviations. Searches were restricted to human studies and English language only; publications in languages other than English were not appraised. Methodological filters were not applied. The strategy was to undertake a broad search to identify all the evidence relating to autism spectrum disorders, rather than individual searches for every clinical question. The results were then sifted into individual questions as outlined below.

There was no systematic attempt to search grey literature (conferences, abstracts, theses and unpublished trials). Hand searching of journals not indexed on the database was not undertaken. Reference lists of included studies or reviews for additional references were not checked. Full details of the systematic searches, including the sources searched and the search strategies are presented in Appendix F. Although the condition-based search strategy generated a very large set of records, the Information Scientists considered this was the best method of developing a comprehensive and sensitive strategy in this subject area.

The results of the searches were incorporated into four reference manager databases alphabetised according to author (A-D, E-K, L-R and S-Z). In total there were 47,255 references. Each of these databases were then de-duplicated and weeding performed to remove references unlikely to contain research data including book reviews, book chapters, and letters. Records not related to the subject area were also screened out at this stage, leaving a total database of 20,633 citations.

Two researchers then conducted a more stringent weeding excluding citations which that were not relevant to this guideline (citations dealing with vaccinations, treatments or management of ASD) resulting in 5,173 in the database. These citations were screened and allocated to one of the ten clinical questions and the researchers dealing with each question ordered citations for inclusion or exclusion. This resulted in 1,215 citations being considered and 899 being ordered for the 10 clinical questions

The electronic searches were re-run in June 2010 and in Oct 2010 and another 5,154 references for weeding were identified. After following the stages outlined above, a total of 48 extra papers were ordered. The final cut off date for searches was 11th October 2010.

A total of 925 articles were examined in full text and of these 185 papers are included in the guideline.

2.6.2 Reviewing and synthesising the evidence

Evidence relating to clinical effectiveness was reviewed and synthesised according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach (see http://www.gradeworkinggroup.org/index.htm). Evidence profiles were used to summarise the quality of the evidence and the outcome data for each important clinical outcome The initial quality of evidence was rated according to study design[26;27] (see table 2.2) as advised by NICE during the review process.

Table 2.2 Initial study quality ratings

Quality	Design
High	RCT
Low	Controlled observational studies
Very low	Uncontrolled observational studies

When using data from the cases in a case control study the study was classified as 'uncontrolled observational study' rather than 'controlled observational study'.

Checklist were used to quality rate the studies as follows;

- QUADAS[28] checklist was used for diagnostic accuracy or predictive accuracy studies
- CASP checklist for cohort (http://www.phru.nhs.uk/Pages/PHD/resources.htm) (items 3, 4, 5, 6 and 7) was used for epidemiological /descriptive studies
- NICE checklist for qualitative studies (http://www.nice.org.uk/niceMedia/pdf/GuidelinesManualAppendixH.pdf) was used for qualitative studies.

One exception to this was the assessment of uncontrolled observational studies which were all graded as very low quality and were not subjected to any quality analysis in accordance with the GRADE profile manual at the time of reviewing. Once study quality was determined the studies were then downgraded according to the following factors: limitations, indirectness, inconsistency and imprecision. In each case, one failed item was assigned to represent some limitations of study quality, and 2 items serious limitations of quality

2.6.3 Data extraction and reporting

Quantitative studies

Clinical evidence for individual studies was extracted into evidence tables (see Appendix H) and, where possible, quantitative synthesis (meta-analysis) was carried out. Results from each study are presented in GRADE evidence profiles.

The supporting evidence statements report the outcomes from each evidence profile that meet the GDG agreed levels of accuracy (see section 3.6.4) or prevalence. For reviews of prevalence data, findings were discussed with the GDG and subsequently only those variables (based on evidence and consensus) are reported in the evidence statements.

Qualitative studies

Evidence of the views of children, young people or parents/ carers' experience from individual studies was extracted into evidence tables (see Appendix H) and summarised in modified GRADE evidence profiles. In order to best reflect children and parents' opinions, as well as to avoid the risk of information loss/distortion, themes are reported in the modified GRADE evidence profiles instead of outcomes. These themes are supported by individual verbatim quotations from the included studies. The supporting evidence statements report on the outcomes from each evidence profile.

2.6.4 Summary statistics used for diagnostic/predictive accuracy

The GDG determined that sensitivity and specificity would be more useful to the users of this guideline than other summary statistics for diagnostic/predictive accuracy that could be calculated (predictive values and/or likelihood ratios). These were calculated using a 'two by two' table as below (see Table 2.3).

Table 2.3 '2 × 2' table for calculation of diagnostic accuracy parameters

	Reference standard positive	Reference standard negative	Total
Test positive	a (true positive)	b (false positive)	a+b
Test negative	c (false negative)	d (true negative)	c+d
Total	a+c	b+d	a+b+c+d = N (total number of tests in study)

Sensitivity = a/(a+c), specificity = d/(b+d),

When describing the sensitivity and specificity of the different instruments, the GDG defined a point estimate of 0.8 with a lower 95% confidence interval above 0.7 as an

acceptable threshold for accuracy. A random-effects model was used to calculate heterogeneity across studies as this should be reported in results of test accuracy[29].

2.6.5 Other summary statistics used

Agreement

Agreement between diagnostic tools and methods are presented as kappa scores, which may be interpreted as follows[30]

<0.00	Poor
0.00-0.20	Slight
0.21-0.40	Fair
0.41-0.60	Moderate

Prevalence/Incidence/proportional data

Proportions of the population (percentage with 95% confidence intervals) are presented to illustrate the stability of diagnosis (percentage retaining their diagnosis over time); differential diagnosis (percentage presenting with suspected ASD who are diagnosed with a different condition); and co-existing diagnosis (percentage of the ASD population with the co-existing condition in question).

These are given as pooled percentages with 95% confidence intervals where possible. When there are mitigating factors precluding the pooling of data, results were presented in ranges and an explanation given in the translation for that question. Again, a random-effects model was used to pool data as this has been shown to take account of over-dispersion (where the variability in observed data is greater than that expected) where there is heterogeneity[31]. For the purpose of meta-analysis, StatsDirect first transforms proportions into a quantity (the Freeman-Tukey variant of the arcsine square root transformed proportion – [32] suitable for the usual fixed and random effects summaries [33]. The pooled proportion is calculated as the back-transform of the weighted mean of the transformed proportions, using inverse arcsine variance weights for the fixed effects model and DerSimonian-Laird (1986) weights for the random effects model.

2.6.6 Meta-analysis software used

Meta-Disc software (version 1.4) (http://www.hrc.es/investigacion/metadisc_en.htm)

StatsDirect (Version 2.7.8) (http://www.statsdirect.com/).

2.6.7 Health economics

An economic evaluation aims to integrate data on benefits (ideally in terms of quality adjusted life years (QALYs), harms and cost of alternative options. For a lifelong condition of social communication such as ASD, relevant outcomes for economic evaluation of the diagnostic process are very hard to identify and even more difficult to quantify (see chapter 10 for a more detailed explanation). For this reason it was anticipated that the health economic analysis for this guideline would be very limited. A health economic plan was agreed which included an economic analysis of specific diagnostic strategies and biomedical tests if robust evidence of diagnostic accuracy could be identified.

Descriptions of resource use were gathered from five different ASD diagnostic services around the country of resource use in services that the GDG believed were examples of good current practice, that is, which adhered to many of the important principles highlighted in this guideline; multidisciplinarity, a dedicated ASD team and clear ASD diagnostic pathway, good communication and support for children and families during diagnosis. These were written up as service descriptions.

Finally, every 'Evidence to Recommendation' translation includes the GDG's considerations of the resource use, cost and benefits of specific recommendations. These considerations are not supported by externally verifiable evidence of cost-

effectiveness but represent the GDG's views and show how they weighed up the likely costs and benefits for the decisions they made that had an impact on resource use. The purpose of this is to increase the transparency for the GDG's recommendations where no evidence could be identified.

2.6.8 Evidence to recommendations

For each clinical question, recommendations are derived using, and linked explicitly to, the evidence that supported them. In the first instance, informal consensus methods are used by the GDG to agree clinical and, where appropriate, cost effective evidence statements.

Statements summarising the GDG's interpretation of the clinical and economic evidence and any extrapolation (including economic modelling) from the evidence used to form recommendations were also prepared to ensure transparency in the decision making process.

In areas where no substantial evidence was identified, the GDG considered other evidence-based guidelines and consensus statements and then used with collective experience to identify good practice. The GDG also identified areas where evidence to answer their clinical questions was lacking completely and used this information to draft recommendations for future research. The GDG did not undertaken formal consensus methods, but, in the face of poor evidence or absence of evidence, reached a consensus through discussion during face to face GDG meetings and in subsequent email correspondence. Bias was minimised by ensuring that all voices in the GDG were heard and contributions listened to. Agreement on recommendations was reached by all the GDG members and not a majority.

The GDG selected the key priorities for implementation by consensus at a GDG meeting based on the following criteria outlined in the NICE Guidelines Manual 200934

• have high impact on patients' outcomes that are important to patients, • have a high impact on reducing variation in care and outcomes
• lead to a more efficient use of NHS resources
• promote patient choice and equality

The GDG gave high priority to recommendation that when implemented would mean patients reach critical points in the care pathway more quickly.

The GDG formed key research recommendations to address gaps in the evidence.

2.6.9 Stakeholder involvement in the guideline development process

Registered stakeholder organisations were invited to comment on the draft scope of the guideline and on the draft guideline. Stakeholder organisations were also invited to undertake a pre-publication check of the final guideline to identify factual inaccuracies. The GDG carefully considered and responded to all comments received from stakeholder organisations. The comments and responses, which were reviewed independently for NICE by a Guidelines Review Panel, are published on the NICE website.

2.7 Specific considerations for this guideline

For this guideline, the following main outcomes were identified:

- Signs and symptoms of ASD
- Specificity and sensitivity of ASD specific screening and diagnostic tools
- Yield of medical and genetic tests
- Differential diagnoses
- Co-existing conditions

- Children and young people's views and the views of their parents and carers of the process of referral, assessment and diagnosis, and their support and information needs

2.8 Schedule for updating the guidance

Clinical guidelines commissioned by NICE are published with a review date 3 years from date of publication. Reviewing may begin earlier than 3 years if significant evidence that affects guideline recommendations is identified sooner.

3 Recognition

3.1 Introduction

Prompt recognition of possible ASD enables the child and family to start their journey on the pathway to diagnosis. Signs and symptoms of possible ASD will be seen by parents, carers and professionals in education, health and social services, most of who will not be experts in ASD. Some signs and symptoms suggestive of ASD may also present in children who are typically-developing or children who go on to receive another non-ASD diagnosis[35;36]. We have given consideration to the signs and symptoms that should prompt a parent or professional (for example, health, social care or educational) to consider ASD in any setting and have looked at how inequalities can be evened out by taking cultural norms and disabilities into account. This chapter also considers inequalities in recognising the signs and symptoms of ASD. This chapter includes recommendations about when a health care professional should refer for further assessment including guidance on decision making for referral for assessment, and what information should be included in the referral.

Clinical Question

(a) What are the signs and symptoms that should prompt a health care or other professional in any context to think of ASD,

(b) When should a child or young person be referred for diagnostic assessment?

3.1.2 Methodological approach

To inform the search terms, a list of signs and symptoms were compiled based on GDG consensus. The GDG considered previously published guidelines (SIGN 2007, New Zealand 2008 and NAP-C 2002) and the DSM-IV or ICD-10 diagnostic criteria. All the signs and symptoms in this list were searched for and quality appraised in the systematic review.

Symptoms and signs of ASD were identified in four groups of children and young people: pre-school (0-5yrs), primary school (6-11yrs) and secondary school children (12-19yrs) and children and young people with an intellectual disability (all ages). This approach takes account of the fact that signs and symptoms of ASD vary and manifest differently according to age, developmental maturation and cognitive ability.

The GDG considered the sensitivity and specificity of each sign and symptom in assessing diagnostic accuracy as these were the measures most commonly reported in the literature. If these were not reported in relevant publications the reviewers calculated them. The GDG considered that the sensitivity and specificity should be at least 80% with the lower 95% confidence interval estimate above 70%[37].

After an initial search of 25,787 articles in the overall search, 237 were selected on title and abstract and the papers requested for full review. Nine studies were eligible for inclusion based on the following criteria:

Population: Children or young people with DSM-IV or ICD-10 diagnosed ASD (all PDD excluding Retts).

Index test: A sign or symptom of ASD

Comparison: Typically developing children and young people and children with an intellectual disability but no ASD

Outcomes: The sensitivity and specificity of symptoms and signs to detect ASD (or data allowing this calculation).

A list of the 228 excluded studies and the reasons for exclusion is found in Appendix G– Tables of excluded studies).

3.1.3 Description of included studies

Nine studies with 490 participants, in total were included in the review. These studies were carried out in the USA[38-44] and the UK[45;46]. All were controlled observational studies with case-control design and were graded as low quality. Seven of the studies included children of preschool age [38;40;41;43-46], one of primary school age[42] and none were of solely secondary school children. One study included both primary and secondary school age children[39].

One study[43] reported on intellectual disability indicating that over 53% of the sample had IQ score (full scale) below 70. Only two studies [41 38] reported mean IQ scores but the proportion of children with intellectual disability was not reported. Two studies[39;42] excluded children with IQ ≤ 70. Intellectual ability was not reported in the remaining studies.

One study[47] reported intellectual disability but only indicated that the IQ of samples ranged from 25 to 87. Only two studies[48;49] reported mean IQ scores but the proportion of children with intellectual disability was not reported. Five studies[50-56] included children with intellectual disability but didn't report its prevalence. Four studies[57-60] reported the proportion of children with intellectual disability but no separate outcomes were provided for each IQ group. Three studies[61-64] only recruited children with intellectual disability. Intellectual ability was not reported in the remaining studies.

One study[39] used a screening instrument called the Repetitive Behavior Interview to collect data on signs and symptoms, while another[42] used the Playground Observation Checklist.

Further details regarding individual studies are presented within the evidence tables (see Appendix H – tables of included studies).

3.1.4 Evidence profile

The evidence in Table 3.1 is arranged by age group and then by sign or symptom. The evidence statement that comes after the GRADE evidence profile table summarises the reviewed evidence in terms of what a specific sign or symptom in isolation tells an observer about the chance of a child with that sign or symptom having ASD.

1 **Table 3.1 Accuracy of signs and symptoms to predict ASD**

Diagnostic tool	Quality assessment						Summary of findings			
							Number		Diagnostic accuracy	
	Studies	Design	Limitations	Inconsistency	Indirectness	Quality	ASD	Controls	Sensitivity (95% CI)	Specificity (95% CI)
PRE-SCHOOL CHILDREN (0 – 5 YEARS)										
Failure to perform protodeclarative pointing, gaze monitoring and pretend play[45]	1	Con obs	Some	NA	None	Very low	10	23	100 (100, 100)	100 (100, 100)
Failure to perform protodeclarative pointing or protodeclarative pointing and pretend play[45]	1	Con obs	Some	NA	None	Very low	10	23	100 (100, 100)	70 (51, 88)
No pretend play[46]	1	Con obs	Some	NA	None	Very low	10	19	90 (71, 100)	63 (41, 85)
No functional play[46]	1	Con obs	Some	NA	None	Very low	10	19	40 (10, 70)	84 (68, 100)
No facial concern in response to others distress[46]	1	Con obs	Some	NA	None	Very low	10	19	100 (100, 100)	68 (48, 89)
No attention to distress[41]	1	Con obs	Some	NA	None	Very low	72	39	21 (11, 30)	100 (100, 100)
Atypical use of object[40]	1	Con obs	Some	NA	None	Very low	9	47	78 (51, 100)	77 (64, 88)
Lack of orienting to name[43;44]	2	Con obs	Some	NA	None	Very low	25	76	64 (43, 92)	88 (79, 84)
PRIMARY SCHOOL CHILDREN (6 - 11 YEARS)										
No social play[42]	1	Con obs	Serious	NA	None	Very low	20	37	90 (77, 100)	100 (100, 100)
Social isolation[42]	1	Con obs	Serious	NA	None	Very low	20	37	80 (62, 98)	100 (100, 100)
No respect for personal boundaries[42]	1	Con obs	Serious	NA	None	Very low	20	37	50 (28, 72)	100 (100, 100)
Socially inappropriate behaviour[42]	1	Con obs	Serious	NA	None	Very low	20	37	40 (19, 61)	100 (100, 100)
Unable to follow rules of a game[42]	1	Con obs	Serious	NA	None	Very low	20	37	100 (100, 100)	41 (25, 46)
Doesn't respond to winning/losing a game[42]	1	Con obs	Serious	NA	None	Very low	20	37	100 (100, 100)	46 (30, 62)

Doesn't initiate communication with peers[42]	1	Con obs	Serious	NA	None	Very low	20	37	80 (62, 98)	100 (100, 100)
Doesn't sustain conversation with peers[42]	1	Con obs	Serious	NA	None	Very low	20	37	100 (100, 100)	100 (100, 100)
Gross motor inco-ordination[42]	1	Con obs	Serious	NA	None	Very low	20	37	65 (44, 86)	100 (100, 100)
No functional use of playground equipment[42]	1	Con obs	Serious	NA	None	Very low	20	37	50 (28, 72)	68 (52, 83)
SECONDARY SCHOOL CHILDREN (12 – 19 YEARS)										
No studies identified for this age-group										
MIXED AGE GROUPS (PRIMARY AND SECONDARY SCHOOL CHILDREN										
Repetitive talk about 1 topic[39]	1	Con obs	Some	NA	None	Very low	40	21	83 (71, 94)	86 (71, 100)
Difficulty trying new activities[39]	1	Con obs	Some	NA	None	Very low	40	21	78 (65, 90)	95 (86, 100)
Abnormally obsessional interest[39]	1	Con obs	Some	NA	None	Very low	40	21	70 (56, 84)	100 (100, 100)
Watches same video constantly[39]	1	Con obs	Some	NA	None	Very low	40	21	65 (50, 80)	86 (71, 100)
Insistence on certain routines / rituals[39]	1	Con obs	Some	NA	None	Very low	40	21	53 (37, 68)	95 (86, 100)
Lining objects in rows / patterns[39]	1	Con obs	Some	NA	None	Very low	40	21	50 (35, 56)	90 (78, 100)
Spinning / banging / twiddling[39]	1	Con obs	Some	NA	None	Very low	40	21	48 (32, 63)	95 (86, 100)
Pacing / stereotyped walking[39]	1	Con obs	Some	NA	None	Very low	40	21	60 (45, 75)	100 (100, 100)
Compulsion (contamination / order)[39]	1	Con obs	Some	NA	None	Very low	40	21	50 (35, 56)	86 (71, 100)
Hand / finger mannerisms[39]	1	Con obs	Some	NA	None	Very low	40	21	48 (32, 63)	95 (86, 100)
Vocal / motor tics[39]	1	Con obs	Some	NA	None	Very low	40	21	45 (30, 60)	95 (86, 100)
Sucking objects (eg shirts, pencils)[39]	1	Con obs	Some	NA	None	Very low	40	21	48 (32, 63)	81 (65, 98)
Rocking/ spinning[39]	1	Con obs	Some	NA	None	Very low	40	21	45 (30, 60)	100 (100, 100)
Self-injurious behaviour[39]	1	Con obs	Some	NA	None	Very low	40	21	42 (27, 58)	95 (86, 100)
INTELLECTUAL DISABILITY										
No studies identified for this group										

3.1.5 Evidence statement

Sensitivity and specificity of signs and symptoms

Pre-school (≤5 years)

Of all the sign and/or symptoms examined for this age group, only the combination of 'protodeclarative pointing, gaze monitoring, pretend play' met the pre-defined levels of diagnostic accuracy. The evidence was of very low quality.

Primary school (6 – 11 years)

Of all the sign and/or symptoms examined for this age group, only 'no social play' and 'doesn't sustain conversation with others' met the pre-defined levels of diagnostic accuracy. The evidence was of very low quality.

Children and adolescents aged 12 – 19 years

No studies were identified for signs and symptoms in this age group

ASD children and adolescents in school (primary or secondary school)

Of all the sign and/or symptoms examined for this age group, only 'Repetitive talk about one topic' met the pre-defined levels of diagnostic accuracy. The evidence was of very low quality.

Children and young people with an intellectual disability

No studies were identified for this group

3.1.6 Evidence to recommendations

Relative value placed on the outcomes considered	When concerns first arise about a child or young person's behaviour or development, one consideration is the possibility that the child may have ASD. The child or young person may first be seen by one of a range of health care and other professionals with varied expertise in the recognition of ASD. They might be first seen by a health visitor or general practitioner. The priority is to avoid the risk of failing to recognise children and young people who do actually have ASD. This would result in delayed diagnosis. For this reason, the GDG therefore agreed the referral threshold for deciding whether a particular sign or symptoms or combination symptoms reported in the literature should be low at this early point in the pathway. On the other hand, the decision to refer a child to an ASD Team should not be made without careful consideration because otherwise the service would be quickly overwhelmed. A pragmatic decision was made when reviewing the evidence regarding the accuracy of individual or combined signs and symptoms to consider only the evidence where the test accuracy fulfilled the following criteria: a sensitivity and specificity of 80% with a lower 95% confidence interval threshold of no less than 70%.
Trade-off between clinical benefits and harms	Any child presenting with parental concerns regarding development or behaviour requires careful evaluation by a health care professional. In some children and young people, there may be no real grounds for concern and parental reassurance may be appropriate and helpful. Where there are grounds for concern, a clinical evaluation will be necessary. A decision must be made as to who should best undertake that evaluation. In many children seen in primary care, referral to a child development centre or speech and language therapy or child and adolescent mental health services (CAMHS) may be considered appropriate. In some children and young people, developmental or behavioural disorders might suggest ASD. In cases where a health care professional has real concern about the possibility of ASD, direct referral to the ASD team could expedite assessment. The evidence examined did not directly address possible clinical benefits or harm associated with the recognition of possible ASD and the decision to refer to an ASD team. The GDG considered that there were benefits for children and young people in establishing the nature of any developmental or behavioural disorder including ASD. Many families and carers find the eventual diagnosis of ASD helpful, and early recognition can avoid delayed diagnosis. For some families the GDG were aware that referral for an ASD evaluation might be distressing or even unacceptable to them. For that reason, the GDG emphasised the importance of careful discussion and involvement of the parents and carers in the process while keeping the child and young persons' interests central to the decision making process. Even in children and young people who do not have ASD, an evaluation of their condition will be necessary. In those referred to the ASD Team who turn out not to have ASD, they will be directed to other appropriate pathways. The GDG recognised that a decision to refer to the ASD Team might carry with it a risk of possible subsequent incorrect diagnosis ASD. This could have negative consequences for the children, young people and their families. It was therefore important that this guideline should provide

	recommendations to establish a final accurate diagnosis. Overall, however, this potential harm was considered by the GDG to be outweighed by the benefits of recognition.
Trade-off between net health benefits and resource use	No evidence was identified that addressed the question of the impact of recognition of signs and symptoms on the numbers of children and young people referred for assessment, or on subsequent health or welfare outcomes. The GDG consensus was that the use of a table of signs and symptoms and information on what should prompt a health care professional to refer for further assessment may increase the numbers being referred, but that the guideline would improve recognition of children who required some kind of assessment for a communication or developmental need, regardless of whether they were eventually diagnosed with ASD or another condition. If, further on in their assessment, it was decided that the child did not have ASD but another differential diagnosis, the initial referral could still lead to earlier identification of the child's other developmental or communication needs which would be a cost effective use of resources. The list of signs and symptoms may reassure parents and carers that ASD is unlikely and reduce unnecessary consultations. The GDG consensus was that, if referrals increased, there had to be in place an efficient process of decision making by the ASD Team that is quick, simple and effective at identifying children who should proceed to an ASD-specific Diagnostic Assessment since this is the high cost part of the pathway. This means it is important that the ASD team's decision about who should go on to the assessment is accurate. Otherwise it could lead to increased waiting times and cost. The additional benefit of correctly identifying and referring on children with ASD needs to be weighed up against the added cost to the NHS and stress to the family of over assessing children who do not have the condition. There was no data to help the GDG in making its considerations, but the GDG consensus was that the benefits would outweigh the costs.
Quality of evidence	The GDG acknowledged that the evidence for this clinical question was of very low quality. The results for the eight included studies was the identification of only three individual signs (and of these, only one in any specific age group], and only one combination of signs in preschool children that met the criteria for accuracy set by the GDG. Although these signs broadly reflected the GDG's clinical experience, they captured only a very small number of the signs and symptoms recognised by health care professionals as being useful for identifying children who have ASD at different ages. The GDG's recommendations regarding when it was appropriate to refer to an ASD Team were therefore based on GDG consensus. No studies exist that are designed to compare the effectiveness of decision rules for referral.
Other considerations	The published evidence was generally unsupportive in compiling a clinical helpful list of signs and symptoms being of very low quality, and addressing a limited number of signs and symptoms in evidence some of which were impractical to be identified by non experts. The identified evidence only supported 'protodeclarative pointing, gaze monitoring, pretend play as an accurate combinations of signs, and this was in the preschool group only. However the population of this study was less than 2 years old so it is unclear how generalisable this evidence

	is to older pre-school children. For primary age children only the individual signs 'no social play' and 'doesn't sustain conversation with others' met the pre-defined levels of diagnostic accuracy. There were no accurate signs or symptoms in older children identified in the evidence. The GDG recognised that a health care professional, other professional or parent will always consider the child or young person as a whole, that is, look for combinations of signs and symptoms to identify patterns of behaviour or development. Health care professionals take into account a range of other factors when deciding whether to refer a child for further assessment such as the setting in which a child is observed, the number of symptoms that are observed, the severity and duration of impact, the duration of concern, and the signs and symptoms along with risk factors and other information. The GDG have therefore produced a list intended to be used to help the concerned professional or parent give a global view of behaviour in social communication and restricted repetitive interests and behaviours that are the features of ASD. The GDG is aware that it is not possible to list all the possible permutations of signs and symptoms in a table so health care professionals should not rule out ASD if these signs and symptoms are not observed. The signs and symptoms in this guideline are a combination of signs where there is identified evidence and other signs where there was no identified evidence but are included based on the consensus agreement of the GDG. The GDG also translated some of the more obscure signs in the evidence into terms which could be readily understood by the non-expert. The GDG considered these signs and symptoms to be clinically relevant and easily observable or easily elicited by professionals working with children. The items chosen reflect the core deficits in ASD of 'social communication and interaction', and 'fixated interests and unusual behaviours.' Although the features listed in the signs and symptoms tables (tables 3.2 to 3.4) are consistent with ASD, the GDG recognised that these features were variable from one individual to the next. It was important that health care professionals should not dismiss the possibility of ASD simply because certain features were absent, or, following a needs based intervention, the difficulties appear to resolve. Some children and young people would have good eye contact, smiling and showing affection to family members. School-age children with ASD might have normal or even advanced pre-school development. The signs and symptoms presented are divided into three age and developmental groups; under 5 years, 5-11 years and over 11 years corresponding with pre-school, primary school and secondary school age. This reflects the recognition that signs and symptoms will differ by chronological and developmental ages. The signs and symptoms should therefore be placed in the context of the child or young person's overall development. It was the experience of members of the GDG that children with ASD may have significant developmental delays that have not been previously recognised either by parents or previously involved health care professionals. The GDG considered whether there were any potential inequality issues in the signs and symptoms of ASD that might affect recognition and hence access to the referral pathway. The GDG consensus was that health care and other professionals may

	have difficulties interpreting behaviour that is different from the norm in children and young people from cultural contexts outside the UK. In this context the GDG recognised the need for the health care professional to be self critical about any lack of knowledge about a culture they were not familiar with. This includes certain child rearing practices, interpretation of how children play with adults and each other, and the expectations of families about child development. In addition language delay associated with ASD may also be wrongly attributed to difficulties in learning a second or third language. The GDG view is that it is important to consider whether the child is behaving in a way that is different from that which would be expected in their own culture, or whether they had problems understanding language in their mother tongue to minimise the risk of overlooking signs of ASD. For this reason it is always important to take parental concerns seriously in this context even if they are not shared by others. The GDG acknowledged that ASD is under diagnosed in children and young people with intellectual disability as the signs and symptoms of ASD may be masked. The signs and symptoms need to be considered from the perspective of the intellectual age of the child, rather than their biological age. The GDG consensus opinion is that some health care professionals may fail to consider ASD because of an existing intellectual disability diagnosis. Furthermore, some health care professionals undervalue the importance of a diagnosis of ASD where there are significant other intellectual difficulties, as a diagnosis of ASD can be seen as an extra burden on the family caring for a child who already has profound difficulties. Consequently, they may wait until the child is older to seek further assessment, or not seek it at all. The GDG view is that diagnosis of ASD in children and young people with intellectual disability is important in providing the right kind of help and support to the child and to the parents/ carers. The GDG recognised that children from very deprived backgrounds who have experienced considerable psycho-social disadvantage with multiple carers pose a particular challenge. Some of the signs and symptoms of ASD have considerable overlap with attachment disorders, a diagnosis that is made more frequently in 'looked after' children. The disorders are not mutually exclusive. There is also anecdotal evidence that presentation of signs and symptoms may be more variable in 'looked after' children and that recognition of the signs of ASD may be delayed as a consequence of this and the challenge of providing consistent care to this group of vulnerable children. Young people in the Criminal Justice System are an additional group where the history of signs and symptoms of ASD may not be readily available. Based on clinical experience the GDG recognised that compared with boys, girls with ASD who had with good verbal skills more often presented with subtle features. They were concerned that the diagnosis might more easily be missed in such cases and so a specific recommendation was made advising health care professionals to be aware of this phenomenon. The GDG agreed that the recognition of ASD could be difficult in young people presenting at secondary school age. Earlier in the child's life symptoms may be masked through coping strategies they employed. The GDG considered that four factors commonly prompted initial referral at secondary school age. First, social difficulties when differences in the young person's social behaviour compared with their peers became more obvious with the increasingly complex social demands of adolescence, and with the increasing demands of independence and intimacy. Second, academic difficulties, in which the young person may be unable to achieve expectations for which there is no obvious explanation, and their

response to increasing educational demands gives rise to concern. Third, a situation in which young people previously thought to have another condition, now with changing behavioural and emotional characteristics, experience a change in their symptoms and it then becomes apparent that the underlying diagnosis was one of ASD. Finally, a situation where previously accepted explanations for the young person's dysfunctional behaviour – family or community environment, cultural or demographic fractures - are no longer considered plausible, and the diagnosis of ASD therefore becomes apparent.

Finally, the GDG agreed that a previous assessment resulting in a negative diagnosis should not rule out the possibility of ASD.

The GDG acknowledged that the skills required to recognise signs and symptoms of ASD and to consider these signs in the context of, developmental and chronological age, coexisting conditions, culture and family context and transition between age groups is potentially very difficult. The GDG recommend that all health care and other professionals consider their own personal and professional competence and seek advice from an appropriate colleague if in doubt about how to proceed.

Concerns about ASD should be discussed with the parents/ carers and the child or young person themselves, including discussion of the possible causes of ASD, emphasising that there may be many explanations for the perceived behaviour.

When to refer to an ASD Team

The existence of a local ASD Team is central to this guideline. The role of the ASD Team is discussed in Chapter 5 on Diagnostic Assessment.

The GDG consensus was that the possibility of ASD should always be considered when there were concerns about development or behaviour. It was very important to take parental concerns about development or behaviour seriously, even if those concerns were not shared by others. If specific concern about ASD was raised by anybody who was in direct contact with the child, some form of action would always be necessary. The GDG believed that whenever a parent or carer was concerned about the child or a young person's development behaviour this was an issue that deserved careful attention, whatever the final conclusion might be.

The GDG noted that discussion about such parental concerns required a high level of professional skill. Sometimes the first concerns might be raised by someone other than parents, for example healthcare professional. In that situation, the GDG emphasised the need for care and sensitivity when raising the concern with an unsuspecting young person, parent or carer. The suggestion that a diagnosis of ASD was possible might cause great distress. Time was often required to come to terms with these matters. The initial response to suggested diagnosis of ASD might be one of disbelief. The GDG agreed that it was very important to allow those affected the time and opportunity to come to terms with the possibility of ASD, and that a sensitive approach would have long term benefits.

The GDG recognised that the decision on whether to refer a child for further assessment does not follow a simple algorithm with clearly defined thresholds. In addition to parents and carers, a wide range of people have contact with the children and young people. These include primary health care professionals such as Health Visitors and General Practitioners, nursery nurses, teachers, social workers, secondary and tertiary healthcare professionals. Children might be seen in Child Development Centres or again the Child and Adolescent Mental Health

Services (CAMHS). The level of expertise and training among these many individuals regarding development and behaviour and specifically ASD clearly varies greatly across these individuals.

The GDG recognised the complexity of determining whether particular signs and symptoms pointed to a diagnosis of ASD specifically whether they might be explained in other ways. The GDG concluded that professionals should use judgement in each individual case about whether to refer a child or young person to the ASD Team or to an alternative care pathway according to the local referral pathway. The GDG provided recommendations regarding factors that should be considered in deciding whether or not referral to the ASD Team was appropriate. The GDG also provided descriptive vignettes to illustrate the range of features that should prompt a clinician to refer. These are presented at the end of the signs and symptoms tables.

The GDG consensus was that children with regression of language or social skills and without loss of motor skills should be referred without delay to the ASD Team. There was a high likelihood of ASD with this presentation.

If a health care professional had concerns regarding development or behaviour but did not think the symptoms and/or symptoms were suggestive of ASD, they should consider referring to another appropriate service. They should be aware that if following that referral concerns about ASD arose subsequent referral to the ASD Team could then be arranged. In the event that they had just minor concerns they should consider regular review. A decision to refer to an ASD team should be considered if the healthcare professional was concerned about possible ASD on the basis of a signs or symptoms, but it was important for them to take into account the severity, duration, pervasiveness and impact of the signs and symptoms. They should pay special attention to the level of parental concern about the child or young person. They should take into account the presence of any known risk factors for ASD – for example, the presence of an intellectual disability, a sibling with ASD, or history of extreme prematurity. The GDG recognised the importance of the parents/carers readiness for and acceptance of the need for referral to an ASD Team.

The GDG considered that it was important to have in place and effective process for referral to the ASD Team. Recommendations were made on how to refer. It was important that the parents/carers and where appropriate a young person should be in agreement. In the event that they were not yet ready to accept the need for referral it was recommended that the child or young person should be monitored regularly and the plan to refer kept under review. The person referring should provide a written report containing relevant information. This would reduce the risk of delaying the assessment and avoid the need for repetitious seeking of information following the referral.

The local ASD pathway

The GDG consensus is that in order for health care professionals to be clear about when to refer a child or young person and who to refer to, there should be a local ASD pathway for the recognition of possible ASD, and for referral, diagnosis and assessment of ASD. A clinical pathway that describes the components of an effective diagnostic service, based on multiprofessional working is an identified outcome in the scope of this guideline. The local pathway should be specific to ASD and should be widely disseminated amongst health care and other professionals. There should be an identified ASD team with named individuals to which professionals can refer to from any NHS service (for example, primary

	care, other community assessment services, hospital specialties). The function and the composition of the ASD team are addressed in chapter 5 on Diagnostic Assessment. **The ASD strategy group** The GDG considered that improving the efficiency and cost-effectiveness of recognition and referral for an ASD assessment also requires a wider, strategic approach to be in place at a local level. The GDG agreed that a local ASD Strategy Group should be in place with the responsibility of developing the local ASD pathway, , ensuring that it is widely understood and followed, to lead training in recognising ASD and to enhance the ethos of multiprofessional working. This was an identified priority of scope of this guideline. The strategy group should be made up of named representatives from child health, mental health services, education, social care, patent/ carer/ service users and the voluntary sector (including where appropriate the criminal justice system).
Recommendations	1. There should be a local ASD strategy group with representation from child health and mental health services, education, social care, parent and carer service users and the voluntary sector. 2. The local ASD strategy group should appoint a lead professional who is responsible for the local ASD pathway for recognition, referral and diagnosis of children and young people. The aims of the group should include: • improving early recognition of ASD by raising awareness of the signs and symptoms of ASD through training (see tables 1–3) • making sure the relevant professionals (healthcare, social care and education) are aware of the local ASD pathway and how to access diagnostic services • supporting the smooth transition to adult services for young people going through the diagnostic pathway. 5. Access to the ASD team should be through a single point of entry. 8. Consider the possibility of ASD when there are concerns about development or behaviour, but be aware that there may be other explanations for individual signs and symptoms. 9. Always take parental concerns about behaviour or development seriously, even if these are not shared by others. 10. When considering the possibility of ASD and whether to refer a child or young person to the ASD team, be self-critical about your professional competence and seek advice from a colleague if in doubt about the next step. 11. Use tables 1–3 to help identify the signs and symptoms of possible ASD. 12. Do not rule out ASD because the exact behaviours described in tables 1–3 are not evident. The features described should be used for guidance, but do not include all possible manifestations of ASD. 13. When considering the possibility of ASD, be aware that: • signs and symptoms should be seen in the context of the child's overall development • signs and symptoms will not always have been

recognised by parents or by other professionals

- when secondary school children present with possible ASD, signs or symptoms may have been masked by the child's coping mechanisms and/or a supportive environment
- you should not assume language delay is accounted for because English is not the family's first language because language delay could be a pointer to ASD
- ASD may be missed in children with an intellectual disability
- the signs and symptoms of ASD may be more subtle in girls
- important information about early development may not be readily available for some children and young people in whom ASD is suspected, for example looked after children and those in the criminal justice system.

14. Do not rule out ASD because of any of the following:

- a child's or young person's difficulties appear to resolve after a needs-based intervention (such as a supportive structured learning environment)
- reported normal or advanced pre-school development
- good eye contact, smiling and showing affection to family members.

15. When considering the possibility of ASD, do not rule in or out the possibility of ASD because of a conclusion from a previous diagnostic assessment.

16. When considering the possibility of ASD, ask about the child's use and understanding of their first language.

17. Discuss developmental or behavioural concerns about a child or young person with parents or carers and the young person themselves where appropriate. Discuss sensitively the possible causes, which may include ASD, emphasising that there may be many explanations for the child's or young person's behaviour.

18. Be aware that if parents or carers have not suspected a developmental or behavioural condition, raising the possibility may cause distress, and that:

- it may take time for them to come to terms with the concern
- they may not share the concern to start with.

19. Take time to listen to parents or carers, and if appropriate the child or young person, to discuss concerns and agree any actions to follow including referral.

20. Refer children and young people urgently to the ASD team if there is regression of language or social skills together with any signs and symptoms of ASD (see tables 1–3).

21. If you have concerns about development or behaviour but you are not sure whether the signs and/or symptoms suggest ASD, consider

	consulting a member of the ASD team or referring to another appropriate service. These services can then refer to the ASD team if necessary. 22. Consider referring to the ASD team if you are concerned about possible ASD on the basis of reported or observed signs or symptoms (see tables 1–3). Take account of the following: • the severity and duration of the signs and/or symptoms • the extent to which the signs and/or symptoms are present across different settings (for example, home and school) • the impact of the signs and/or symptoms on the child or young person and on their family • the level of parental or carer concern • the presence of risk factors for ASD (see table 4) • the likelihood of an alternative diagnosis. 24. When referring to the ASD team, provide in a written report all relevant and available information, including: • reported information from parents, carers and professionals about signs and/or symptoms of concern • your own observations of the signs and/or symptoms • antenatal and perinatal history • developmental milestones • known risk factors for ASD (see table 4) • relevant medical history and investigations. 25. Explain to parents what will happen after referral. 26. Watch and wait if you do not think concerns are sufficient to prompt a referral. If you remain concerned about ASD, reconsider your referral decision. 27. If the parents or carers prefer not to be referred to the ASD team, consider a period of watchful waiting. If you remain concerned about ASD, reconsider referral. 28. If a concern about possible ASD has been raised but there are no signs or symptoms or other reasons to suspect ASD, use professional judgment to decide on management.

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Signs and symptoms of ASD

These signs and symptoms are a combination of delay in expected features of development and the presence of unusual features. They are not intended to be used in isolation but are intended to alert professionals to think about the possibility of ASD.

Regression in or loss of use of language skills with reduced social interest and play skills and the presence of signs/ symptoms of ASD in the pre-school child requires referral without delay.

Table 1Preschool children (or equivalent mental age)

Social interaction and communication behaviours

- Delay in language development (babble or words)
- Lack of meeting eye gaze
- Lack of response to name despite normal hearing
- Relative lack of responsive social smiling
- Limited responsiveness to other people's facial expression or feelings
- Rejection of cuddles
- Relative lack of social interest in others
- Lack of joint attention shown by lack of:
  - gaze switching
  - following a point
  - using pointing at or showing objects to share interest
- Lack of gestures and facial expression to communicate (although may place adult's hand on objects)
- Relative lack of sharing enjoyment
- Lack of imitation of others' actions
- Lack of imagination and variety of pretend play
- Lack of initiation of social play with others
- Abnormal-sounding vocalisations
- language present:
  - odd or flat intonation
  - frequent repetition of set words and phrases ('echolalia')
  - reference to self as 'you' or 'she/he' beyond 3 years
- limited and/or infrequent use of language for communication, for example use of single words although can speak in sentences

Unusual and/or rigid/repetitive behaviours

- Unusual repetitive hand, finger and body mannerisms
- Highly repetitive and/or stereotyped play, for example opening and closing doors, spinning
- Over or under reactivity to sensory stimuli, for example textures, sounds, smells
- Extremes of emotional reactivity to change and/or new situations, insistence on things being 'the same'
- Over-focused and/or unusual interests
- Excessive reaction to certain properties of food and/or /extreme food fads
- Unusually negative response to the requests of others (demand avoidant behaviour)

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Table 2 Primary school children (aged 5–11 years or equivalent mental age)

Social interaction and communication behaviours

- Delay in language development (babble or words)
- Lack of meeting eye gaze
- Lack of response to name despite normal hearing
- Relative lack of responsive social smiling
- Limited or unusual response to other people's facial expression and/or happiness or distress
- Relative lack of social interest in others
- Lack of joint attention shown by lack of:
  - gaze switching
  - following a point
  - using pointing at or showing objects to share interest
- Relative lack of or poorly integrated eye gaze, gestures, facial expressions and body orientation in social communication
- Lack of greeting and farewell behaviours
- Limited or excessive talking, as shown in talking at others rather than a to-and-fro conversation and providing excessive information on topics of own interest
- Frequent repetition of set words and phrases
- Lack of flexible imaginative play and/or creativity although film scenes may be re-enacted
- Relative lack of interest in children of his or her own age
- Lack of ability to share in the play and/or ideas of other children, or inappropriate attempts at joint play that may manifest as aggressive or disruptive behaviour
- Unusually negative response to the requests of others (demand avoidant behaviour)
- Lack of awareness of expected behaviour
- Lack of enjoyment of situations that most children like, for example school trips

Unusual and/or rigid/repetitive behaviours

- Over or under reactivity to sensory stimuli, for example textures, sounds, smells
- Excessive reaction to certain properties of food and/or extreme food fads
- Unusual repetitive hand, finger and body mannerisms
- Over-focused and/or unusual interests
- Strong preferences for familiar routines and things being 'just right'
- Rigid expectation that other children should adhere to rules of play
- Extremes of emotional reactivity excessive for the circumstances, for example in response to change or being hurried

Other factors that may support a concern about ASD

- Unusual profile of skills and/or deficits (for example, social, and/or motor skills poorly developed, while particular areas of knowledge, reading or vocabulary skills are advanced for chronological and/or mental age)

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Table 3 Secondary school children (over 11 years or equivalent mental age)
Social interaction and communication behaviours • Long-standing difficulties in social behaviours and social communication • Poorly integrated gestures, facial expressions, body orientation and odd and/or limited eye contact used in social communication • Lack of awareness of personal space, or intolerant of intrusions in own space • Speech peculiarities such as flat or odd tone or pitch • Repetitive speech, use of stereotyped (learnt) phrases • Poor greeting and farewell behaviours • Unable to adapt style of communication to social situations, for example may be overly formal or inappropriately familiar • May take things literally and fail to understand sarcasm or metaphor • Makes comments without awareness of social niceties and/or hierarchies • Lack of understanding of friendship; often an unsuccessful desire to have friends (although may find it easier with adults or younger children) • Social isolation and apparent preference for aloneness • History of a lack of flexible imaginative play • May appear unaware or uninterested in what other young people his or her age are interested in • Social and emotional development more immature than other areas of development, excessive trusting (naivity), lack of common sense, less independent than peers • Problems losing at games, turn taking and understanding 'changing the rules' • Poor response to the requests of others and to the perceived expectations (demand avoidant behaviour) • Lack of awareness of expected behaviour
Unusual and/or rigid/repetitive behaviours • Highly repetitive behaviours and/or rituals that impact negatively on the young person's daily activities • Excessive and unusual reaction to certain sensory stimuli • Excessive reaction to certain properties of food and/or extreme food fads • Unusual repetitive hand, finger and body mannerisms • A strong adherence to rules or fairness that leads to argument • Preference for highly specific interests or hobbies • Disproportionate emotional distress at what seems trivial to others, for example change in routine
Other factors that may support a concern about ASD • Unusual profile of skills and deficits (for example, social and/or motor skills poorly developed, while particular areas of knowledge, reading or vocabulary skills are advanced for chronological and/or mental age)

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3.1.7 Research recommendations

PICO research question	What is the effectiveness and cost effectiveness of training professionals in early recognition and identification of children and young people with ASD?
Why this is needed	
Importance to 'patients' or the population	Earlier (and quicker) recognition would probably be more acceptable to children and young people and their parents and families. It could also reduce distress (although parents who have not recognised the problems themselves may find a diagnosis distressing). We do not have information on whether earlier identification reduces morbidity or improves outcomes (on the basis that supports and interventions are put in place earlier). We have limited information on effectiveness of training.
Relevance to NICE guidance	The GDG view is that this is a high priority research area
Relevance to the NHS	Cost of training. If training improved earlier recognition and referral then the flow of work though the ASD would change. This would not necessarily increase overall in volume but might have an impact on the age at which children are seen. It might lead to a reduction in number of contacts over a child/young person's life, reducing the overall cost of care. This may offset the upfront cost of training. .
National priorities	The GDG were unaware of a policy specific document relating to training of staff for ASD.
Current evidence base	Only one Dutch study was identified in the guideline development process. It was a robust randomised controlled study and demonstrated that training led to earlier referral and age of diagnosis. Such effects might be very country/service specific so a UK replication in the NHS of such an approach would be warranted.
Equality	If training improved earlier recognition and referral uniformly then it might increase access and acceptability to disadvantaged groups (EAL, those with sensory impairments, intellectual disability, girls in whom recognition can be later. Currently ASD under-recognised when parents are of lower educational level-might help to redress the balance.
Feasibility	It would take 3-5 years I suspect to run a suitable study to assess is training reduced age of referral/diagnosis. Moderate ot high costs but not inconceivable. No ethical issues were identified.
Other comments	None

3.1.8 Vignettes describing different presentations of ASD in children and young people

Presentation of challenging behaviour

Child A: aged 7 years. Presented because of challenging behaviour in school—very non compliant; hitting staff and pupils. Early language delay, now fluent sentences; moderately impaired intellectual ability with above average reading skills; marked failure to develop any peer relationships and lacks peer interest; stereotyped and repetitive use of language, repeats videos/DVDs, very limited initiation of social communication, a restricted pattern of interests, currently an over focus on DVDs; stereotyped repetitive motor mannerisms; seeks to feel people's clothes. Does use eye gaze, facial expression and gesture but infrequent initiator of communication. Shows some appropriate response to other people's emotions but also often odd response e.g. smiles if distress shown; unconcerned to modulate behaviour according to the social context; some fixed routines, for example reading through all the notices at the swimming pool every time.

Presentation with academic difficulties

Child B: aged 7 years. School concerned which prompted referral because the child not able to focus on class instruction and tasks, not attaining despite above average IQ and language, particular problems with writing, very frustrated if makes mistakes, not interested in making friends, 'in own world'. Parents report frustration if things 'not right', insistence on perfectionism and routine; focus of interest on second world war—last of several intense interests; talks at people about this and does not tolerate interruption; not responsive to name called; seldom chats; responds without looking at people; spends 1-2 hours daily in own world re-enacting fantasy with actions; warm relationship with parents; kind to sibling but is anxious that the sibling does not break rules.

Presentation with school refusal and anxiety

Child C: male aged 10 years and of above average intellectual ability. Presented because of school refusal, anxiety and aggression: general anxiety, separation anxiety, specific phobias, sleep problems with elaborate routine; aggressive outbursts, particularly directed towards mother and siblings, which occurred in the mornings before school and at times when required to do something he did not want to do, or was anxious about doing. Preschool concerns (not resulting in referral): fear of the vacuum cleaner & hand-dryer; obsessed with buses and trains; extreme food limitation-lumps and texture sensitive; limited chat; literal understanding; uses stereotyped phrases; play inflexible; limited eye contact; lack of interest in others; complex flapping arms when excited; period of selective mutism. Now distressed with change of routine; fear of catching germs; excessive concern about own health; avoiding school if another child in class taken ill; asking reassurance-seeking questions such as 'am I alright mum?' lacking confidence to communicate verbally with strangers; controlling in home environment; extremely low self-esteem.

Presentation in Pre-school years

Child D: male, pre-school age. Presented following joint concerns from parents and from nursery. No concerns in first year of life and he achieved all the usual physical milestones. Parents became concerned when his development appeared to plateau in the second year. He was a passive child who accepted the structure of family life and would occupy himself watching videos. Lack of speech was noted at nursery and he was referred to speech and language therapy. He only had a few words that he used to label things but rarely used words to gain any social interest or joint attention. Nursery also noticed other difficulties such as preferring to play on his own terms and particularly involving his own interests (guns). He was always good at puzzles. He could not function if there was any change in routine or if another child tried to become involved in his play. Noisy situations and children coming too near would cause a behavioural outburst. This had an impact on his peer relationships. As Child D's language developed he built up a sophisticated vocabulary about his own interests which was used repetitively and he often learned phrases from TV programmes which were used out of context and often with an American accent.

Presentation with physical symptoms and friendship problems

Child E: female aged 13 years. Well above average IQ, all early milestones age appropriate but in retrospect, always problems with social interaction with peers, liking for routines, tendency to literal understanding of what people say and do, naïve and immature compared with peers. Need for some extra support for learning recognised and well supported in primary school, but since secondary transfer began to complain more frequently of headaches and stomach aches, and does not wish to go to school. Never any behavioural difficulties but long-standing concerns about friendship difficulties with peers. In school, Child E frequently fails to understand task instructions but does not ask for help; does not wish to draw attention to herself. Aware she is different and wants to be like everyone else. Gifted musician, but tends to talk in too much detail about specific composers or compositions. Does not know what to do in social situations; often thinks

peers are teasing her; thinks she herself is stupid. Homework assignments often late and often not quite what was asked for. At home, increasingly self isolating. Parents now concerned she is depressed.

4 Following referral

4.1 Introduction

This chapter describes the stage following referral of a child or young person with signs and symptoms suggestive of autism spectrum disorder. At this phase of the clinical pathway, a decision has to be made on what type of further assessment is required. The ASD team that has received the referral for further assessment usually requires more information to determine what type of assessment should be initiated. This is important as there are a number of other conditions that can present with similar signs and symptoms. This chapter considers the information that could assist decision making.

In current practice, screening instruments are used when a concern is first raised about ASD to determine the likelihood that a child or young person will go on to receive a diagnosis of ASD. Information from other sources about the child or young person is also gathered but it is often not clear to parents and carers what the information is for and how it should be used to determine the next steps in the diagnostic process.

The first section in this chapter considers with the use of screening instruments to aid decision-making about whether a child requires an ASD specific diagnostic assessment. .

The second section looks at risk factors for two specific groups: the general population and children with identified coexisting conditions. ASD may have as a higher than usual prevalence in some conditions and if so, it would be important to identify these conditions as risk factors for ASD.

The final section considers information from other sources such as schools and other agencies that may help to make the decision whether to proceed to an ASD specific assessment.

The GDG was aware from the outset that it was unlikely that there would be any evidence on what type of information from other sources should be gathered, but, since this is an important and potentially costly part of the ASD pathway, with widespread differences in current practice, the GDG included this issue in the guideline. This chapter also includes recommendations on when to proceed to an ASD specific diagnostic assessment.

Clinical Questions

In children with suspected ASD (based on signs and symptoms) what information assists in the decision to refer for a formal ASD diagnostic assessment?

a) Are there screening instruments that are effective in assessing the need for specialist ASD assessment?

b) What information about the child and family increases the likelihood of a diagnosis of ASD and would assist in the decision to refer for a formal ASD diagnostic assessment?

- part 1. General risk factors
- part 2. Risk of ASD in co-existing conditions

c) Information from other sources as contextual information: information about how the child functions in different environments such as school and home; social care reports (i.e. 'Looked After' children); other agencies

4.2 Screening tools

4.2.1 Methodological approach

The evidence considers whether screening is useful in identifying which children and young people with a higher risk of ASD are more likely to receive a diagnosis of ASD.

Questionnaires designed to be completed by non experts were included in the review as these instruments can be used by anyone in the team receiving the referral to support the decision whether to proceed to an ASD specific diagnostic assessment. Observation-based instruments, such as Screening Tool for Autism in Two-year-olds (STAT), were not included as they require more time and professional expertise to complete and to interpret the results.

The diagnostic accuracy of specific screening instruments was identified for four specific sub groups: pre-school (0-5yrs), primary school (6-11yrs) and secondary school children (12-19yrs) and children and young people with an intellectual disability (all ages).

The acceptable threshold for screening test accuracy was defined in terms of predictive accuracy for a later diagnosis of ASD. The GDG agreed a point estimate cut off of 80% and lower confidence interval estimate above 70% for sensitivity and/or specificity for screening tools when used at two stages of the ASD pathway: at the initial referral stage, and when used to help the ASD team decide whether to proceed to an ASD specific assessment.

After an initial search of 25,787 articles in the overall search, 176 papers were assessed in full text and from these, 9 studies were eligible for inclusion based on the following criteria

Population: Children or adolescents under 19 years identified as being at risk for ASD by either:

- having signs or symptoms suggestive of an ASD and/or
- having been identified as at risk of ASD using another structured assessment such as Checklist for Autism in Toddlers – Modified (M-CHAT; and/or
- are a high risk population (eg with Fragile X, have a sibling with an ASD)

Index test: Screening instruments that can be used to assess the risk of ASD

Reference test: Diagnosis of ASD made according to DSM-IV or ICD-10 criteria.

Outcomes: Sensitivity and specificity to predict a later diagnosis of ASD.

A full list of the 167 excluded studies and the reason for exclusion is available (see Appendix G – tables of excluded studies).

4.2.2 Description of included studies

In total, 9 studies were included in this review. These studies were carried in Australia[65;66], Canada[67;68], Sweden[69;70] the UK[71] and the USA[72;73].

Five of the studies included children of preschool age[66-68;72;73] and one of primary school age[72]. No study dealt exclusively with children of secondary school age. Three studies included mixed pre-school and primary school age children[65;69;71] and two study included all age groups[70;72]. All studies were uncontrolled observational in design and were graded very low quality. One study[66] reported on intellectual disability indicating that the IQ level of over 69% of the sample were below age equivalent 21 months. Only one study[72] reported mean IQ scores but the proportion of children with intellectual disability was not reported. Three studies reported the proportion of children with intellectual disability, but no separate outcome data for each IQ group were provided. Intellectual ability was not reported in the remaining studies. Five studies examined the Social Communication Questionnaire (SCQ) [65;67;68;72;73], two the Checklist for Autism in Toddlers – Modified (M-CHAT) [67;73], two the Autism Behavior Checklist (ABC)[70;71] and one each the Developmental Behaviour Checklist – Autism – Early Screen (DBC-ES)[66] and the Autism Spectrum Screening Questionnaire (ASSQ)[69].

Further details regarding individual studies are presented within the evidence tables (see Appendix H – tables of included studies).

4.2.3 Evidence profiles

This section reports the evidence on accuracy of each screening instrument in predicting later diagnosis of ASD. The evidence is first presented for children of all age groups and then in subgroups by age group and by intellectual disability. Table 4.1 below presents the evidence on the predictive accuracy of each screening instrument.

The quality assessment does not report the individual studies' limitations, inconsistencies or indirectness because all studies are uncontrolled observational studies (see the methodology section in chapter 2 for a full explanation).

Table 4.1 Predictive accuracy of screening instruments

Diagnostic tool	Quality assessment						Summary of findings			
							Number		Diagnostic accuracy	
	Studies	Design	Limitations	Inconsistency	Indirectness	Quality	ASD	Non ASD	Sensitivity (95% CI)	Specificity (95% CI)
ALL STUDIES										
SCQ (≥15)[65;67;68;72;73]	5	Uncon obs	NA	NA	NA	Very low	590	365	71 (67, 75)	62 (57, 67)
M-CHAT (≥2 of 6)[67;73]	2	Uncon obs	NA	NA	NA	Very low	95	43	74 (64, 82)	42 (27, 58)
ABC-Teacher (≥67)[70;71]	2	Uncon obs	NA	NA	NA	Very low	11	103	46 (17, 77)	96 (90, 99)
ASSQ (Teacher, ≥22)[69]	1	Uncon obs	NA	NA	NA	Very low	21	88	71 (52, 91)	91 (85, 97)
ASSQ (Parent, ≥19)[69]	1	Uncon obs	NA	NA	NA	Very low	21	88	62(41, 83)	90 (83, 96)
DBC-ES (cut-off: 11)[66]	1	Uncon obs	NA	NA	NA	Very low	142	65	83 (76, 89)	48 (35, 60)
PRE-SCHOOL CHILDREN (≤ 5 YEARS)										
SCQ (cut-off: 15)[67;72;73]	3	Uncon obs	NA	NA	NA	Very low	232	127	69 (63-75)	61 (52-69)
M-CHAT (≥2 of 6)[67;73]	2	Uncon obs	NA	NA	NA	Very low	143	117	74 (64, 82)	57 (41, 72)
ASSQ	No study met the inclusion criteria for this review									
DBC-ES (cut-off: 11)[66]	1	Uncon obs	NA	NA	NA	Very low	142	65	83 (77-89)	48 (36-60)
PRIMARY SCHOOL CHILDREN (6 - 11 YEARS)										
SCQ (cut-off: 15)[68;72]	2	Uncon obs	NA	NA	NA	Very low	200	166	69 (62-75)	62 (54-70)
M-CHAT	No study met the inclusion criteria for this review									
ASSQ	No study met the inclusion criteria for this review									
DBC-ES	No study met the inclusion criteria for this review									
SECONDARY SCHOOL CHILDREN (≥12 YEARS)										
SCQ (cut-off: 15)	No study met the inclusion criteria for this review									
M-CHAT	No study met the inclusion criteria for this review									
ASSQ	No study met the inclusion criteria for this review									
DBC-ES	No study met the inclusion criteria for this review									

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CHILDREN WITH INTELLECTUAL DISABILITY										
SCQ (cut-off: 15)[72]	1	Uncon obs	Some	None	Some	Very low	205	52	80 (75, 86)	69 (57, 82)
M-CHAT	No study met the inclusion criteria for this review									
ASSQ	No study met the inclusion criteria for this review									
DBC-ES	No study met the inclusion criteria for this review									

4.2.4 Evidence statement

Sensitivity and specificity of screening instruments

Only studies examining the SCQ, M-CHAT, ABC, ASSQ and DBC-ES met the inclusion criteria for this review. No evidence was identified for other screening instruments, such as ATAC, BISCUIT, BITSEA, CAST, CCC, CHECKLIST, CSI-4, ECI-4, ESAT, ESCS, GADS, ITC, KADI, MCDI, PCQ, PDD-MRS, PDDRS, PDDST, RBS, SSI, SDQ, SRS, STAT, YACHT-18.

All studies

No screening instruments met the pre-defined acceptable levels for predictive accuracy. The evidence was of very low quality

Pre-school children (≤5 years)

None of the screening instruments examined for this age group met the pre-defined levels of diagnostic accuracy. The evidence was of very low quality.

Primary school children (6 – 11 years)

None of the screening instruments examined for this age group met the pre-defined levels of diagnostic accuracy. The evidence was of very low quality.

Secondary school children (12 – 19 years)

No studies were identified for signs and symptoms in this age group

Children with intellectual disability

None of the screening instruments examined for this age group met the pre-defined levels of diagnostic accuracy. The evidence was of very low quality.

4.2.5 Evidence to recommendations

Relative value placed on the outcomes considered	The GDG set an arbitrary but low threshold for the predictive accuracy of screening instruments: 80% sensitivity and specificity with a lower 95% confidence interval threshold of 70% The GDG considered that an instrument that wrongly identified 20% of children and young people with or without the condition would still be useful if it increased the number of children correctly identified as requiring further assessment.
Trade-off between clinical benefits and harms	The benefit of a sufficiently accurate screening tool is that it may improve the early recognition of children requiring further assessment. It could also increase the confidence of health care and other professionals in the appropriateness of their referrals and provide reassurance to children, young people and their carers either that a referral is warranted or that they should lower their concern that a child or young person has ASD. The harm of using a screening tool is that it might reduce professional confidence in decision making based on other important factors and might increase the likelihood that it would be used instead of professional judgement rather than an aid to it. It might also, if incorrectly used, lead to an increased number of unnecessary referrals and perhaps of diagnostic assessments. Overall, the GDG opinion was that, if accurate, a screening instrument could be an aid to decision-making by non experts and could improve the quality of professionals' face-to-face time with children, young people and parents during clinical review. However, none of the instruments met the predefined level of accuracy specified by the GDG for identifying children with ASD or with autism.
Trade-off between net health benefits and resource use	The systematic review did not identify any studies that considered the costs and benefits of using these instruments in primary care for the purpose of deciding who to refer on for further assessment. Therefore there is no

	evidence that a screening tool would either increase or decrease the amount of face to face time required to decide whether to refer child for further assessment. As a data gathering tool only, (without calculating scores) the use of screening tools could increase the amount of clinic time required for each child (including the time to interpret and communicate the results of these instruments) or decrease the amount of time (by focussing structured discussion of signs and symptoms. On the benefit side, useful information gathered using a screening tool could reduce the number of unnecessary referrals for an ASD-specific Diagnostic Assessment which is the costliest part of the ASD pathway. The information gathered from these instruments could also reduce the amount of information gathering required by the ASD team when making the decision whether to proceed to an ASD-specific Diagnostic Assessment. The GDG view was that ASD specific screening tools are not essential but may be useful in gathering information about signs and symptoms. A positive score on a screening instrument may support a decision to refer but factors other than the use of a screening tool would be very important determining whether to proceed to a full ASD assessment. It was the GDG view that screening instruments require a level of competence that would require training and experience which many health care and other professionals would not have. Achieving this level of competency would require additional resources, both in start up costs of training, and time to analyse the results whether completed by parents/carers or professionals. Some of the screening tools are covered by patent. Specific instruments are under copyrighted and the developers may charge for their use (the GDG note, for example, that the SCQ is approximately £1.50 per questionnaire). In departments that do not routinely use this or other screening tools for ASD there may be additional costs.
Quality of evidence	The studies that have looked at these tools have evaluated how well they map onto eventual diagnosis for ASD or autism. Evidence was not identified that considered the effectiveness of using screening tools for referral. The role of screening tools at this stage of the pathway is not adequately understood. The studies considered the use of screening instruments in populations of children and young people where signs and symptoms of ASD had been recognised, and where the population was therefore defined as being 'at risk' of ASD. The GDG considered that the small group of studies that met the inclusion criteria addressed only a limited proportion of the instruments currently in use. The evidence base for these instruments was limited to just one study for each of the instruments in the review except for the SCQ (five studies) and M-CHAT (2 studies). The studies reported the sensitivity and specificity of these questionnaires as 'tests' for ASD. At the pre-defined threshold for accuracy agreed by the GDG before seeing the data, none of the studies reported adequate levels of accuracy for the screening questionnaires in identifying children with and without ASD. All were considered to be of "very low quality". When analysed by age, none of the questionnaires were accurate at both correctly identifying children and young people diagnosed and not diagnosed with ASD in any of the age groups. The GDG considered that the evidence base regarding screening instruments was therefore limited in its scope and the available evidence

	was of very low quality, The reported accuracy in the available studies indicated that this was unsatisfactory for screening purposes. Therefore the GDG did not recommend any specific instrument as a secondary screening tool for use, on its own, in identifying children who should be referred for an ASD specific assessment.
Other considerations	The GDG concluded that it could not recommend the use of any particular screening instrument to identify children or young people who should or should not be referred to an ASD Team. The GDG did accept that a screening instrument might be useful as a means of gathering information on signs and symptoms in a structured way. The primary care clinician might find this useful. However, if a screening instrument was employed to gather information the associated score results should not be relied on to decide on referral - the low specificity and sensitivity with these instruments might result in both unnecessary referrals and failure to refer when appropriate. The clinician should rely on clinical judgement. If a screening tool has been used in primary care, that information should accompany any referral as it includes useful information for the ASD Team.
Recommendations	23. Be aware that: • ASD-specific screening tools may be useful in gathering information about signs and symptoms of ASD in a structured way but are not essential and should not be used to make or rule out a diagnosis of ASD: a positive score on a screening instrument may support a decision to refer but can also be positive for reasons other than ASD a negative score does not rule out ASD.

4.3 Risk factors

4.3.1 Methodological approach for population-based risk factors

This section considers the evidence for specific risk factors in ASD and whether these risk factors are of practical use in decision-making about who to refer, and whether to proceed to assessment. The evidence is reviewed in two parts. The first review considers risk factors for autism or ASD in the general population from controlled observation studies which have adjusted for confounding variables. The second review considers the risk of ASD in children and young people who already have an identified condition that can coexist with ASD.

The evidence for the first general population review is reported as the increased risk of ASD in the general population where there are specific factors. These factors are grouped into pregnancy-related factors, familial or parental factors, perinatal or neonatal factors and environmental factors. The evidence for the second review reports the prevalence of the condition in children and young people with ASD compared with the prevalence of that condition in a non ASD population.

Subgroup analysis by ASD and autism was carried out because it was expected that some co-existing conditions would be more strongly associated with autism than with ASD.

Outcomes are presented in a table of statistically and clinically significant risk factors along with a GRADE assessment of the quality of the evidence available. An odds ratio or relative risk is statistically significant if both the point estimate and lower 95% confidence interval are greater than 1. The GDG agreed a higher threshold for clinical significance (minimally important difference) of 1.25 as the point estimate and lower 95% confidence interval.

Adjusted odds ratios were extracted and pooled where there were sufficient data to do so. While it is possible in some circumstances to pool relative risk (RR) data with odds ratios, it was agreed by the GDG *a priori* not do so but to present the results side by side if available. Where it was not possible to pool studies (for example if studies used different references against which the OR's for other categories were calculated) we have reported these separately with an explanation in the footnote.

After an initial search of 25,787 articles in the overall search, 40 papers were assessed in full text and from these, 18 studies were eligible for inclusion based on the following criteria:

Population: Children/young people diagnosed under 19 years with ASD

Reference population: Children without ASD

Outcomes: Risk factors presented as odds ratios or relative risks after adjustment for possible confounding variables

A list of the 22 excluded studies and the reason for exclusion is available (see Appendix G – tables of excluded studies).

We have analysed and presented the data for risk factors for autism and ASD in separate evidence profile (section 4.3.3) with a combined supporting evidence statement (section 4.3.4). We have separated the data for autism from ASD as it the studies were expected to report on risk factors for either autism or ASD and so it would not be appropriate to pool across these categories.

4.3.2 Description of included studies

In total, 18 studies were included in the review. All of the studies were controlled observational in design and were graded as low. The studies were carried out in Australia[74-76], Denmark[77-80], Sweden[81;82] and the USA[83-91].

Two of the studies included children of preschool age[89 76], one of primary school age[86], and one of secondary school age[88]. Ten studies included mixed pre-school and primary school age children [78-85;87;91] and two study included all age groups[74;90].Two studies included adults: the range of age for one study[77] is 1-24 years with a mean 7.7 years; while the range for another study[75] is 5 to 20 y, with mean age unknown.

Only three studies[83;86;89] reported the proportion of children with intellectual disability, but no separate outcome data for each IQ group level were provided. Intellectual ability was not reported in the remaining studies. Further details regarding individual studies are presented within the evidence tables (see Appendix H – tables of included studies).

4.3.3 Evidence profiles for autism and ASD

This section reports the evidence on accuracy of risk factors in predicting later diagnosis of ASD. The data are presented for all studies with no sub-group analysis.

Table 4.2 and Table 4.3 present the evidence on the adjusted relative risk or odds ratio for risk factors for autism and ASD respectively.

1 **Table 4.2 Adjusted relative risk or odds ratio for risk factors for autism**

Factors	Quality assessment						Summary of findings		
	Studies	Design	Limitations	Inconsistency	Indirectness	Quality	ASD	NON-ASD	Adj OR/RR (95%CI)
FAMILIAR OR PARENTAL FACTORS									
Maternal age > 40 years[87]	1	Con obs	None	NA	None	Low	12159	4935776	adj OR 1.51 (1.35, 1.70)
Mother's race (black)[83;89]	2	Con obs	None	NA	None	Low	4957	3498470	adj OR 1.67 (1.48, 1.85)
Paternal age > 40 years[87]	1	Con obs	None	NA	None	Low	12159	4935776	adj OR 1.36 (1.26, 1.47)
PERINATAL OR NEONATAL FACTORS									
Birthweight < 2500 g[76;79]	2	Con obs	None	NA	None	Low	655	90358	adj OR 2.15 (1.47, 3.15)
Prematurity (< 37 weeks)[76]	1	Con obs	None	NA	None	Low	182	85628	adj OR 2.3 (1.5, 3.7)
Admission to neonatal intensive care unit[79]	1	Con obs	None	NA	None	Low	461	461	adj OR 1.8 (1.3, 2.7)
Male gender[76;83;89]	3	Con obs	None	NA	None	Low	5439	3584098	adj OR 4.28 (4.02, 4.57)
Serum bilirubin test undertaken[80]	1	Con obs	None	NA	None	Low	461	461	adj OR 3.7 (1.3, 10.5)
Hypertonic/hyper-reflexive/jittery[80]	1	Con obs	None	NA	None	Low	461	461	adj OR 6.7 (1.5, 29.7)
PREGNANCY-RELATED FACTORS									
No studies found for this analysis									
ENVIRONMENTAL FACTORS									
No studies found for this analysis									

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3 **Table 4.3 Adjusted relative risk or odds ratio for risk factors for ASD**

Factors	Quality assessment						Summary of findings		
	Studies	Design	Limitations	Inconsistency	Indirectness	Quality	ASD	NON-ASD	Adj OR/RR (95%CI)
FAMILIAR OR PARENTAL FACTORS									
Sibling history of autism[78]	1	Con obs	None	NA	None	Low	818	942836	adj RR 22.27 (13.09, 37.90)
Sibling history of ASD[78]	1	Con obs	None	NA	None	Low	818	942836	adj RR 13.40 (6.93, 25.92)
Parental history of schizophrenia-like psychosis[77]	1	Con obs	None	NA	None	Low	698	17450	adj RR 3.44 (1.48, 7.95)
Parental affective disorder[77]	1	Con obs	None	NA	None	Low	698	17450	adj RR 2.91 (1.65, 5.14)

Parental history of other psychiatric diagnosis [77]	1	Con obs	None	NA	None	Low	698	17450	adj RR 2.85 (2.20, 3.69)
Paternal age between 40 and 49 years[88]	1	Con obs	None	NA	None	Low	110	132161	adj OR 5.75 (2.65, 12.46) a
Paternal age between 31 and 39 years[81]	1	Con obs	None	NA	None	Low	1227	30693	adj OR 1.7 (1.3, 2.1) b
Paternal age between 36 and 40 years[81]	1	Con obs	None	NA	None	Low	1227	30693	adj OR 1.8 (1.4, 2.4) b
Paternal age between 41 and 50 years[81]	1	Con obs	None	NA	None	Low	1227	30693	adj OR 1.9 (1.4, 2.5) b
Paternal age ≥ 50 years[81b]	1	Con obs	None	NA	None	Low	1227	30693	adj OR 2.7 (1.3, 2.2) b
Maternal history of neurotic/personality disorders [81]	1	Con obs	None	NA	None	Low	1227	30693	adj OR 1.7 (1.3, 2.2)
Parental psychiatric diagnosis[81]	1	Con obs	None	NA	None	Low	1227	30693	adj OR 1.7 (1.5, 2.0)
PERINATAL OR NEONATAL FACTORS									
Multiple birth defects[74;91]	2	Con obs	None	NA	None	Low	882	2548	adj OR 2.73 (1.37, 5.42)
Prematurity (< 28 weeks)[86]	1	Con obs	None	NA	None	Low	1251	253347	Adj OR 2.5 (1.6, 3.9)
Prematurity (< 35 weeks)[77]	1	Con obs	None	NA	None	Low	595	14875	adj OR 2.45 (1.55 , 3.86)
Multiple birth defects[74;91]	2	Con obs	None	NA	None	Low	882	6380	adj OR 2.78 (1.57 , 5.42)
Male gender[86]	1	Con obs	None	NA	None	Low	1251	253347	adj OR 4.2 (3.7, 4.9)
PREGNANCY-RELATED FACTORS									
Threatened abortion < 20 weeks[75]	1	Con obs	None	NA	None	Low	465	1313	adj OR 2.09 (1.32, 3.32)
Elective caesarean[75]	1	Con obs	None	NA	None	Low	465	1313	adj OR 1.83 (1.32, 2.54)
ENVIRONMENTAL FACTORS									
Residing in capital city[78]	1	Con obs	None	NA	None	Low	818	942836	adj RR 2.05 (1.67, 2.51)
Residing in capital city suburb[78]	1	Con obs	None	NA	None	Low	818	942836	adj RR 1.67 (1.35, 2.06)

4.3.4 Evidence statements

Low quality evidence demonstrated the following risk factors for autism or ASD to be clinically and statistically important:

- sibling history of autism
- sibling history of another ASD
- parental history of schizophrenia-like psychosis
- parental history of affective disorder
- parental history of another psychiatric disorder
- paternal age between 40 and 49 years
- paternal age > 40 years
- maternal age > 40 years
- birthweight < 2500 g
- prematurity < 35 weeks
- admission to a neonatal intensive care unit
- presence of birth defects
- presence of multiple birth defects
- male gender
- threatened abortion at less than 20 weeks
- residing in a capital city
- residing in suburb of a capital city

4.3.5 Methodological approach for risk/prevalence of ASD in co-existing conditions

The purpose of the review was to determine what information regarding the medical history would help determine if there was an increased the likelihood of ASD and would assist in the decision to refer for an ASD assessment. The evidence was examined by comparing the prevalence of ASD in specific conditions with the prevalence of ASD in the general population. The review adopted general population prevalence rates agreed with the GDG for ASD[1] in order to create unadjusted odds ratios for ASD in these conditions.

The GDG pre-selected the following conditions as likely to have a higher than normal prevalence of ASD's and these conditions were included in the review.

- Intellectual disability,
- Fragile X
- Tuberous sclerosis
- Neonatal encephalopathy / Epileptic encephalopathy (including Infantile Spasms)
- Cerebral palsy,
- Down syndrome
- Duchenne muscular dystrophy
- Neurofibromatosis
- Fetal alcohol syndrome

Sub group analysis by ASD and autism was carried out because it was expected that some co-existing conditions would be more strongly associated with autism than with ASD. However, prevalence of autism in a condition is not reported if data are available

for ASD as two values for the relative risk of AS in a condition would not be helpful in decision-making.

As in the previous section, the GDG agreed a higher threshold for clinical significance (minimally important difference) of 1.25 as the point estimate and lower 95% confidence interval. Quality was assessed by study and any limitations of the evidence were noted. Outcomes are presented alongside a GRADE assessment of the quality of the evidence available. Further details regarding individual studies are presented within the evidence tables (Appendix H).

The title and abstract (if available) of all 25,787 papers identified by the search strategies were screened for this question. 89 articles were reviewed in full text, of these 28 studies (from 31 papers) were eligible for inclusion based on the following criteria:

Population: Cases: Children or young people under 19 years who have one of the following co-existing conditions

- Intellectual disability,
- Fragile X
- Tuberous sclerosis
- Neonatal encephalopathy / Epileptic encephalopathy (including Infantile Spasms)
- Cerebral palsy,
- Down syndrome
- Duchenne muscular dystrophy
- Neurofibromatosis
- Fetal alcohol syndrome

Outcomes: Prevalence rates and relative risk of ASD diagnosed according to DSM-IV or ICD-10

A list of the 58 excluded studies and the reasons for exclusion is found in Appendix G – Tables of excluded studies).

4.3.6 Description of included studies

The 29 studies were carried out in Australia[92], Canada[93;94], Iceland[53-55], Italy[95], the Netherlands[57;60;60], the UK[51;52;63;64;96;97 63;64] the USA[47;48;50;56;58;61;98-102], Sweden[62], and Turkey[59]. Three studies have multi-national samples, two studies[49;103] in both Australia and the USA and the third[104] from the Netherlands and the USA. All were uncontrolled observational and were graded as very low. One study[53-55] was reported in three articles; a second study[63;64] was reported in two articles; and a third study [63;64] was reported in two articles.

Three [51;58;98] of the studies included children of preschool age and one[60] of secondary school age. No study dealt exclusively with children of secondary school age. Two studies[48;100] included mixed pre-school and primary school age children; two [92;93] studies included mixed primary and secondary school age; and seven [52;57;59;63;64;97;101] studies included all age groups. Ten[47;49;53-56;61;62;99;104] studies included adults (age>19 year). Age was not reported for the remaining studies.

Further details regarding individual studies are presented within the evidence tables (see Appendix H – tables of included studies).

4.3.7 Evidence profiles

Table 4.4 reports prevalence and unadjusted relative risks for the existing conditions pre-selected by the GDG as being commonly associated with autism and Table 4.5 reports on children with ASD.

Table 4.4: Prevalence and relative risk of Autism in co-existing conditions

Co-existing conditions	Quality assessment						Summary of findings			
	Studies	Design	Limitations	Inconsistency	Indirectness	Quality	Autism	Non-autism	Prevalence (Range, %)	Unadj RR (Range)
RISK/PREVALENCE OF AUTISM IN CO-EXISTING CONDITIONS										
Intellectual disability[94]	1	Uncon obs	NA	NA	NA	Very low	43	111	28	99
Fragile X[102]	1	Uncon obs	NA	NA	NA	Very low	4	13	24	79
Tuberous sclerosis[95]	1	Uncon obs	NA	NA	NA	Very low	7	7	50	256
Neonatal encephalopathy / Epileptic encephalopathy / Infantile Spasms	No studies were identified for this disease.									
Cerebral palsy	No studies were identified for this disease.									
Down syndrome	No studies were identified for this disease.									
Muscular dystrophy[103]	1	Uncon obs	NA	NA	NA	Very low	2	22	8	23
Neurofibromatosis	No studies were identified for this disease.									
Fetal alcohol syndrome	No studies were identified for this disease.									

1 **Table 4.5: Prevalence and relative risk of ASD in co-existing conditions**

2

Co-existing conditions	Quality assessment						Summary of findings			
	Studies	Design	Limitations	Inconsistency	Indirectness	Quality	ASD	Non-ASDs	Prevalence (Range, %)	Unadj RR (Range)
RISK/PREVALENCE OF ASD IN CO-EXISTING CONDITIONS										
Intellectual disability[57;60;60;63;64]	4	Uncon obs	NA	NA	NA	Very low	493	3139	8 - 17	7 - 17
Fragile X[47-49,100]	4	Uncon obs	NA	NA	NA	Very low	95	129	30 - 60	37 - 130
Tuberous sclerosis[51;52;58;96]	4	Uncon obs	NA	NA	NA	Very low	72	66	36 – 79	48 – 322
Neonatal encephalopathy / Epileptic encephalopathy / Infantile Spasms[53-55;92]	2	Uncon obs	NA	NA	NA	Low	25	346	4 – 14	4 – 14
Cerebral palsy[59]	1	Uncon obs	NA	NA	NA	Very low	19	107	15 - 15	15 - 15
Down syndrome[50;61;97;98;101]	5	Uncon obs	NA	NA	NA	Very low	91	829	6 - 15	5 - 15
Muscular dystrophy[62;99;104]	3	Uncon obs	NA	NA	NA	Very low	38	528	3 –37	3 - 50
Neurofibromatosis[56]	1	Uncon obs	NA	NA	NA	Very low	3	71	4 - 4	4 - 4
Fetal alcohol syndrome [93]	1	Uncon obs	NA	NA	NA	Very low	6	617	1 - 1	1 - 1

4.3.8 Evidence statement

ASD or autism is observed more frequently in children with the following co-existing conditions than in the general population:

- Intellectual disability
- Fragile X
- Tuberous sclerosis
- Neonatal encephalopathy/epileptic/encephalopathy/infantile spasms
- Cerebral palsy
- Down syndrome
- Muscular dystrophy
- Neurofibromatosis

The quality of the evidence was very low in all studies.

4.3.9 Evidence to recommendations

Relative value placed on the outcomes considered	The *a priori* decision rule agreed by the GDG was an odds ratio or relative risk above 1.25 signified an important risk factor for ASD. This threshold was applied to the evidence for risk factors in the general population and in children with coexisting condition. In the absence of any other guidance for what the threshold for a clinically important risk factor for ASD should be, the GDG agreed to use of 1.25 as a threshold. This is the advice offered in the GRADE manual which recommends decision-makers should consider a minimally important difference of 1.25 in the absence of a more clinically relevant decision rule. Although this guidance is meant for intervention studies, the GDG adopted this decision rule for risk factors.
Trade-off between clinical benefits and harms	The GDG agreed that the clinical benefit of identifying risk factors was that it allowed health care professionals to make better judgements about their level of concern about a child or young person with signs and symptoms of ASD and the need for an ASD specific assessment. The GDG did not identify any harms in identifying risk factors in children with signs and symptoms of ASD.
Trade-off between net health benefits and resource use	As with all information gathering, the trade off is between the time taken to collect accurate information about a child and young person and the value of that information in making good decisions about how to proceed towards a diagnosis. The GDG agreed that the risk factors had to be of practical use in NHS settings and should not require that a great deal of background information would have to be obtained that parents and carers or young people would not themselves be aware of. The evidence did not identify important differences in risk factors for the general population and ADS when ASD and autism were considered separately. The evidence for ASD in coexisting conditions did not identify differences in risks when ASD and autism were considered separately. The GDG view is that the final list is a cost-effective trade off between the need to obtain information that is practical, and the value of that information in predicting children and young people with ASD.
Quality of evidence	The initial protocol for the evidence search stipulated that the population should be all children, since risk factors should be considered alongside signs and symptoms in all children, by any professional, at any time. For this population, the adjusted odds ratio was reported by the authors. A second search was undertaken because the GDG wished to look for

	evidence for other diseases as risk factors. The justification for this is that there are conditions that, although rare in the general population (and therefore not identified in the initial search) have a very strong association with ASD in children and young people. The quality of the evidence was very low, meaning that the GDG did not feel able to rely on this evidence to make its recommendations.
Other considerations	The evidence identified specific risk factors, some of which were considered to be clinically relevant by the GDG some of which were not. The decision rule used by the GDG for deciding which risk factors was clinically relevant was whether the risk factor was sufficiently uncommon in all children to be of practical use in clinical decision-making. It was the GDG's considered view that the presence of clinically important risk factors should act to increase professionals' vigilance and readiness to refer if signs and symptoms suggestive of ASD were present, No risk factor in isolation would necessitate referral to an ASD Team or to the performance of an ASD-specific Diagnostic Assessment. It would not be appropriate for all of professional considering possible ASD to enquire about all of the risk factors specifically, but there should be an awareness of their importance and they should be systematically considered as part of an ASD-specific Diagnostic Assessment. The GDG recognised that there was some uncertainty regarding the certain "risk factors". The GDG acknowledged the evidence of a link between site of residence and increased prevalence rates for ASD but thought that this could be partially explained by proximity to specialist diagnostic and treatment centres, therefore site of residence was not included in the final list of risk factors The GDG considered that although male gender was a strong and well known risk factor it was important to recognise that ASD does occur in girls and there was anecdotal evidence that ASD may be under-recognised in girls of normal IQ. Although psychotropic drugs as a category was not identified in any of the literature, it was the GDG's opinion that sodium valproate in pregnancy is a concern as a risk factor for ASD. It was noted by the GDG that ASD can co occur with a number of chromosomal abnormalities (see chapter 8 on Medical investigations). A search for evidence was undertaken for Down's syndrome but others were so uncommon that they would not have been identified in the search. Although it was identified in the systematic review, the GDG did not consider that it was clinically plausible for maternal psoriasis to be considered a useful risk factor for ASD.
Recommendations	22. Consider referring to the ASD team if you are concerned about possible ASD on the basis of reported or observed signs or symptoms (see tables 1–3). Take account of the following: • the presence of risk factors for ASD (see table 4) 31. In the absence of regression, decide whether to carry out an ASD diagnostic assessment taking into account the following: • the presence of risk factors (see table 4)

1

Table 4 Risk factors for ASD
• Intellectual disability • A sibling with ASD • Birth defects associated with central nervous system malformation and/or dysfunction including cerebral palsy • Gestational age less than 35 weeks • Maternal use of sodium valproate in pregnancy • Neonatal encephalopathy or epileptic encephalopathy including infantile spasms • Chromosomal disorders such as Down's syndrome • Genetic disorders such as fragile X • Duchenne muscular dystrophy • Neurofibromatosis • Tuberous sclerosis

4.4 Information from other sources

4.4.1 Methodological approach

It was expected that no studies would be available since no empirical research evidence could address this type of question. A clinical trial, observational study or qualitative study would not be helpful since no specific intervention can be definitively linked to an ASD specific outcome. Therefore the GDG decided to use consensus methodology to answer this question. No evidence was reviewed for this question.

4.4.2 Description of included studies

No systematic search of the evidence was undertaken

4.4.3 Evidence profile

No systematic search of the evidence was undertaken

4.4.5 Evidence statement

No systematic search of the evidence was undertaken

4.4.6 Evidence to recommendations

Relative value placed on the outcomes considered	The GDG did not anticipate that there would be any published evidence that addressed this issue and therefore did not explicitly define specific outcomes for this question.
Trade-off between clinical benefits and harms	Given the lack of any published evidence to support the recommendations on what information should be gathered by whom and how, the GDG discussed in detail the purpose and value of gaining additional information following referral to the ASD Team. It was the GDG's view that, since ASD can affect a child or young person's function across varied settings it was important to have available adequate information about from different contexts. Disorders other than ASD can present with similar signs and symptoms, and so the availability of such information at this stage would be helpful in determining which children and young people referred to the ASD Team should proceed to an ASD-specific Diagnostic Assessment. Information could usefully be obtained from pre-school and school placements and from other professionals involved with the child especially if it likely that particular assessments may already have been undertaken - for example a speech and language or educational

	assessment. The GDG did not consider that there would be harm to the child or the family in gathering this information. The GDG believe gathering such information would, in conjunction with other information increase the proportion of children who are referred appropriately for an ASD-specific Diagnostic Assessment and so would reduce waiting times for those who are in need of this assessment.
Trade-off between net health benefits and resource use	The GDG considered whether gathering information would represent a net cost to the NHS. No evidence was identified that could support these deliberations although it was recognised that obtaining information from a variety of sources uses up professional and administrative time. The clinical experience of the GDG of current NHS practice is that information gathering is often poorly managed, takes too long to coordinate and increases waiting times for children, young people and their families. It is the GDG's considered opinion that a coordinated system for collecting the information and reports from all agencies who have had recent contact with the child, young person and their carers should make an important contribution to speeding up decision-making, reducing waiting times, avoiding unnecessary referrals, and therefore lead to an improvement the welfare of children waiting for assessment. The GDG members were aware of very good practice around the country where such a process of coordination is already in place where health care professionals have the appropriate information at their disposal at the point of deciding the best pathway for a child or young person through further assessment. Such a coordinated approach to information gathering should, in the GDG's view, be integral to the recognition, referral and diagnosis of ASD in any service in the NHS, however it is configured.
Quality of evidence	No evidence was identified for this question, in particular no evidence for the best way to collect information from schools although the GDG is aware that different services use different semi-structured tools.
Other considerations	The GDG consensus view it that, on receipt of a referral of a child with signs or symptoms of ASD, a decision needs to be made whether to proceed with a full ASD assessment or whether another type of assessment is required. The GDG consensus was that this decision can be made by the ASD Team in a referral meeting or by an individual member of the ASD Team if this speeds up the process (for a description of the role of the ASD team, see the evidence to recommendations section in chapter 5 on Diagnostic assessment). Once the decision has been made, the consensus was that the diagnostic assessment be arranged without delay and should start within 3 months of the initial referral to the ASD team. The GDG consensus was that the same considerations would be necessary to decide whether to proceed to an ASD specific assessment as were necessary to decide whether to refer a child to the ASD team, that is a review of the range of signs of symptoms, their severity, pervasiveness, impact and context. These considerations would be taken by people with more expertise and usually with more information than non experts deciding whether to refer, but the considerations are the same and are discussed in more detail in the previous chapter. The GDG considered that in addition to the information supplied by the referring HCP, additional information would usually be required in order to decide whether to proceed to an ASD-specific Diagnostic Assessment. This would include the results of any previous undertaken assessments - for example Speech and Language, hearing, or educational assessments. School reports could also be of value. Home of school video recordings, where available and considered relevant and useful by the parent/carer or professional may be

	helpful. An efficient process for collecting and reviewing such information would be important in avoiding delay and avoiding repetitious requesting of information at different points through the ASD pathway. The GDG considered that the ASD Team would need to decide following receipt of a referral whether an initial face-to-face meeting was required to decide whether an ASD-specific Diagnostic Assessment or perhaps an alternative type of assessment was needed. The GDG did not wish to be prescriptive about this, as it would depend on many factors, including the information already available about the child or young person, and also the level of expertise of the individual making the referral. Only in cases with signs and symptoms of ASD where regression of language or social skills were present did the GDG consider that the child or young person should always proceed to an ASD assessment without waiting to gather further information. Regression in preschool children is very strongly associated with ASD. Only the presence of other clinical manifestations suggesting an alternative medical disorder would require a different assessment pathway. In that case conditions such as a brain tumour or a neurodevelopmental regression disorder would need consideration. Parental / carer consent should be sought in gathering information from other sources outside the health service to enhance parental support and retain transparency in the process. The referral teams should not delay putting into place appropriate support while gathering information if it thought to be necessary based on the information already available to the team since support should be based on the needs of the child or young person once they are known and not the final diagnosis.
Recommendations	29. When a child or young person is referred to the ASD team, at least one member of the ASD team should consider without delay whether to proceed to: • an ASD diagnostic assessment **and/or** • an alternative assessment. 30. Carry out an ASD diagnostic assessment without delay if there is regression of language or social skills together with any signs and symptoms of ASD (see tables 1–3). 31. In the absence of regression, decide whether to carry out an ASD diagnostic assessment taking into account the following: • the severity and duration of the signs and/or symptoms • the extent to which the signs and/or symptoms are present across different settings (for example home and school) • the impact of the signs and/or symptoms on the child or young person and on their family or carer • the level of parental or carer concern • the presence of risk factors (see table 4) • the likelihood of an alternative diagnosis. 32. If there is insufficient information to decide whether an ASD diagnostic assessment is needed, consider: • offering the child or young person a consultation with a relevant healthcare professional(s) • gathering necessary information from other healthcare

	professionals (for example, hearing test results for a pre-school child) • with parental or carer consent, obtaining information from schools or other agencies. 33. Once it is decided to carry out an ASD diagnostic assessment, this should start without delay and within 3 months of the initial referral to the ASD team. 40. Avoid repeated information gathering and assessments by efficient communication between professionals and agencies.

1

2 ### 4.4.7 Research recommendations

PICO research question	What are the effectiveness and cost effectiveness of gathering information in schools or nurseries on children referred to the ASD team to improve diagnostic certainty?
Why is this needed	
Importance to 'patients' or the population	The GDG considered that gathering information in schools and nurseries could improve the timing, effectiveness and quality of the diagnostic assessment, and the accuracy of diagnosis.
Relevance to NICE guidance	The GDG view is that this is a high priority research area.
Relevance to the NHS	The increased time spent by teachers could be offset by improved multiagency cooperation and sharing of information.
National priorities	This is not a national priority area in ASD, but the GDG did acknowledge that the "Equality and Excellence" white paper focuses on working across agencies.
Current evidence base	There is some evidence about screeners for use in school but little systematic research comparing routine use of school/preschool information before or subsequent to diagnostic assessment and the contribution of such information or the best tool in difficult to diagnose cases.
Equality	No equality issues were identified for this question
Feasibility	The GDG considered a study could be done in a 2 year time frame and at moderate cost only and would be fairly straightforward to undertaken. They did not identify any specific ethical or technical issues.
Other comments	None

3

5 Diagnostic assessment

5.1 Introduction

The purpose of a diagnostic assessment is to establish whether or not the developmental and behavioural concerns about the child or young person can be attributed to ASD or an alternative diagnosis. It is also intended to provide a "profile" of the child or young person's strengths and weaknesses to identify their developmental, health, behavioural and learning needs. Such a profile can inform their future management plan.

This chapter considers all aspects of the ASD specific Diagnostic Assessment. It provides recommendations on the core elements of the ASD-specific Diagnostic Assessment; the information that should be gathered to develop a profile of the child or young person and any specific assessments including a physical examination. It also covers the criteria for making a diagnosis of ASD, risk assessment, and what to do when there is continued diagnostic uncertainty. Finally, it considers how professionals should communicate with the child or young person and their parents and carers about the diagnosis, as well as with other professionals

The first five sections look at the evidence relating to the ASD specific diagnostic assessment tools and the information required to interpret the findings of an ASD specific diagnostic tool and arrive at a diagnosis. These sections cover the accuracy of diagnostic tools compared with ICD-10/DSM-IV, the accuracy of other assessment tools to assist interpretation of the ASD-specific diagnostic tools, agreement between the specific ASD tools, agreement between single clinician and panel of clinicians to diagnose ASD or autism according to DSM-IV criteria, and the stability of ICD-10 and DSM-IV criteria

The next sections consider how the diagnosis should be communicated and the last part of the chapter considers the actions that should be taken when there is continued diagnostic uncertainty and when to refer for another opinion.

For some children the completion of a diagnostic assessment will result in a finding that confirms that they do not have ASD. These children leave the ASD specific pathway but will almost always require further assessment and management. However this is beyond the scope of this guideline.

Clinical Questions

What should be the components of the diagnostic assessment? When should they be undertaken, in what subgroups and in what order?

- Assessment tools specific to ASD: e.g. Autism Diagnostic Interview (ADI), Developmental, Dimensional and Diagnostic Interview (3di), Diagnostic Interview for Social and Communication Disorders (DISCO), Autism Diagnostic Observation Schedule (ADOS), Gilliam Autism Rating Scale
- Other assessment tools that help the interpretation of the specific ASD tools and ratings scales (e.g. ADI, 3di, DISCO, ADOS, Gilliam Autism

Rating Scale): an assessment of intellectual ability; an assessment of receptive and expressive language etc.

How should information be integrated to arrive at diagnosis?

- Is the diagnostic assessment more accurate and reliable when performed by a multidisciplinary team or a single practitioner?
- What is the stability of an ASD diagnosis over time?
- What is the agreement of an ASD diagnosis across different diagnostic tools?

How should the findings of the diagnostic assessment be communicated to children and young people, and their families/carers?

What actions should follow assessment for children and young people who are not immediately diagnosed with ASD?

5.2. Accuracy of assessment tools

5.2.1 Methodological approach

ASD specific assessment tools are defined here as semi-structured interview or observational schedules developed for use as diagnostic instruments to be used by professionals.

Accuracy is reported in four groups of children and young people: pre-school 0-5yrs), primary school (6-11yrs) and secondary school children (12-19yrs) and children and young people with an intellectual disability (all ages).

The data on accuracy of each diagnostic tools for autism and ASD were analysed and presented in separate evidence profiles and evidence statements (section 5.2.1) as one of the tools (ADI-R) was designed to differentiate between autism and no autism, while the other tools examined differentiate between autism, ASDs and no ASDs. Recently the ADI-R has been used to differentiate ASD but this is still been examined.

As for signs and symptoms and screening for ASD, the GDG considered a point estimate greater than 80% with the lower confidence interval estimate above 70% for sensitivity and/or specificity as acceptable in terms of predictive accuracy for diagnosis of ASD. Meta-analyses were performed where two or more studies reported on the same combination of diagnostic tool and reference standard. A list of diagnostic tools was drawn up by the GDG to be searched for in the literature. Added to this list during guideline development were other diagnostic tools which were identified in the literature search. These tools were known to some members of the GDG but are not in routine clinical practice in the NHS. A full list of diagnostic tools is given below and details of the tools are outlined in Appendix J.

The data obtained from included studies are presented, along with a GRADE assessment of the quality of the evidence. Sub group analysis was also undertaken based on the following where the data were available:

- Intellectual disability
- Pre-school (<5 years) only
- Primary school (5 – 11 years) only
- Secondary school (≥12 years) only

The title and abstract (if available) of all 25,787 papers identified by the search strategies were screened for this question. A total of 95 papers were reviewed in full-text and of these 11 studies were eligible for inclusion based on the following criteria.

Population:

Children and young people under 19 years identified as having signs or symptoms suggestive of an ASD; and/or

who have failed a surveillance tool such as M-CHAT; and/or

are an 'at risk' population (eg with Fragile X, having a sibling with an ASD).

Index test:

Autism Diagnostic Interview-Revised (ADI-R)

Developmental, Dimensional and Diagnostic interview (3di)

Diagnostic Interview for Social and Communication Disorders (DISCO)

Childhood Autism Rating Scale (CARS)

Gilliam Autism Rating Scale (GARS)

Autism Diagnostic Observation Schedule (ADOS)

Development And Well-Being Assessment (DAWBA)

Parent Interview for Autism (PIA)

Combinations of the above.

Reference test:

DSM-IV or ICD-10 diagnosis of ASD

Outcomes:

Sensitivity and specificity of individual or combinations of diagnostic tools to predict ASD.

After further scrutiny the GDG decided that because the studies examining the accuracy of the CARS used a variety of administration procedures (direct observation, parent interview) and used different procedures to code data from the assessment, it was not possible to combine studies. For this reason CARS has been excluded from the review.

A list of the 84 excluded studies and the reasons for exclusion is found in Appendix G (Tables of excluded studies).

5.2.2 Description of included studies

The ADI-R was examined in 10 studies[47;72;105-112], the ADOS in 9 studies[47;72;105;106;108-112], the 3di in a single study[113] and the GARS in a single study[109]. All were uncontrolled observational studies and so were graded as very low quality. No study examining the DISCO met the pre-stipulated inclusion criteria. One study examined a combination of the ADI-R and the ADOS[72]. The studies were carried out in Australia[106], Greece[110], the Netherlands[105], the UK[113] and the USA[47;72;107-109;111;112].

One study[106] reported on intellectual disability indicating that over 90% of the sample had delayed language and over 80% were developmentally delayed (both defined as 6 months behind calendar age norms). Only three studies[72;106;110] reported mean IQ scores but the proportion of children with intellectual disability was not reported. Only one sub-group analysis by age group for Pre-school (< 5 years)' was possible. Data for School age children (5-11 years) and Adolescents (>12 years) were not available.

Further details regarding individual studies are presented within the evidence tables (see Appendix H – tables of included studies).

5.2.3 Evidence profiles

The evidence is presented below in two GRADE profiles reporting the diagnostic accuracy (sensitivity and specificity) of diagnostic tools compared to recognised

diagnostic criteria and the quality of the evidence. Table 5.1 represents the accuracy for diagnosing autism and Table 5.2 the accuracy in diagnosing ASD.

Table 5.1 Accuracy of diagnostic tools in diagnosing autism compared to DSM-IV or ICD-10 criteria

Diagnostic tool	Quality assessment						Summary of findings			
							Number		Diagnostic accuracy	
	Studies	Design	Limitations	Inconsistency	Indirectness	Quality	Cases	Controls	Sensitivity(%) (95% CI)	Specificity(%) (95% CI)
ACCURACY IN DIAGNOSING AUTISM										
ALL STUDIES										
ADI-R[47;72;105-112]	10	Uncon obs	NA	NA	NA	Very low	716	871	84 (81, 86)	67 (64, 71)
3di	No study met the inclusion criteria for this review									
GARS	No study met the inclusion criteria for this review									
DAWBA	No study met the inclusion criteria for this review									
PIA	No study met the inclusion criteria for this review									
DISCO	No study met the inclusion criteria for this review									
ADOS[47;72;105;106;108-112]	9	Uncon obs	NA	NA	NA	Very low	716	871	91 (89, 94)	75 (72, 80)
ADI-R + ADOS[72]	1	Uncon obs	NA	NA	NA	Very low	274	297	85 (81, 89)	87 (83, 91)
SUBGROUP ANALYSIS – CHILDREN WITH INTELLECTUAL DISABILITY										
ADI-R[106]	1	Uncon obs	NA	NA	NA	Very low	120	89	77 (68, 84)	70 (59, 79)
3di	No study met the inclusion criteria for this review									
GARS	No study met the inclusion criteria for this review									
DAWBA	No study met the inclusion criteria for this review									
PIA	No study met the inclusion criteria for this review									
DISCO	No study met the inclusion criteria for this review									
ADOS[106]	1	Uncon obs	NA	NA	NA	Very low	120	89	85 (77, 91)	89 (80, 95)
ADI-R + ADOS[72]	1	Uncon obs	NA	NA	NA	Very low	274	297	85 (81, 89)	87 (83, 91)
SUBGROUP ANALYSIS – PRE-SCHOOL CHILDREN (≤ 5 YEARS)										
ADI-R[106-108;111;112]	5	Uncon obs	NA	NA	NA	Low	290	308	80 (75, 84)	77 (72, 82)
3di	No study met the inclusion criteria for this review									
GARS	No study met the inclusion criteria for this review									
DAWBA	No study met the inclusion criteria for this review									
PIA	No study met the inclusion criteria for this review									
DISCO	No study met the inclusion criteria for this review									
ADOS[106;108;111;112]	4	Uncon obs	NA	NA	NA	Low	290	308	89 (84, 93)	76 (70, 82)

ADI-R + ADOS[72]	1	Uncon obs	NA	NA	NA	Very low	274	297	85 (81, 89)	87 (83, 91)
SUBGROUP ANALYSIS – PRIMARY SCHOOL CHILDREN (6-- 11 YEARS)										
No study met the inclusion criteria for this review										
SUBGROUP ANALYSIS – SECONDARY SCHOOL CHILDREN (≥12 YEARS)										
No study met the inclusion criteria for this review										

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Table 5.2 Accuracy of diagnostic tools in diagnosing ASD compared to DSM-IV or ICD-10 criteria

Diagnostic tool	Quality assessment						Summary of findings			
							Number		Diagnostic accuracy	
	Studies	Design	Limitations	Inconsistency	Indirectness	Quality	Cases	Controls	Sensitivity% (95%CI)	Specificity% (95%CI)
ACCURACY IN DIAGNOSING ASD										
ALL STUDIES										
ADI-R[47;72;105;106;108-112]	9	Uncon obs	NA	NA	NA	Very low	1009	471	78 (77, 82)	71 (66, 75)
3di[113]	1	Uncon obs	NA	NA	NA	Very low	27	33	100 (100, 100)	94 (86, 100)
GARS[109]	1	Uncon obs	NA	NA	NA	Very low	56	19	39 (27, 52)	Not calculable
DAWBA	No study met the inclusion criteria for this review									
PIA	No study met the inclusion criteria for this review									
DISCO	No study met the inclusion criteria for this review									
ADOS[47;72;105;106;108-112]	9	Uncon obs	NA	NA	NA	Very low	1009	471	87 (85, 89)	73 (69, 76)
ADI-R + ADOS[72]	1	Uncon obs	NA	NA	NA	Very low	274	297	83 (79, 87)	86 (81, 92)
SUBGROUP ANALYSIS – CHILDREN WITH INTELLECTUAL DISABILITY										
ADI-R[106]	1	Uncon obs	NA	NA	NA	Very low	143	66	73 (65, 80)	77 (65, 87)
3di	No study met the inclusion criteria for this review									
GARS	No study met the inclusion criteria for this review									
DAWBA	No study met the inclusion criteria for this review									
PIA	No study met the inclusion criteria for this review									
DISCO	No study met the inclusion criteria for this review									
ADOS[106]	1	Uncon obs	NA	NA	NA	Very low	143	66	76 (68, 83)	94 (85, 98)
ADI-R + ADOS[72]	1	Uncon obs	NA	NA	NA	Very low	274	297	83 (79, 87)	86 (81, 92)
SUBGROUP ANALYSIS – PRE-SCHOOL CHILDREN (≤ 5 YEARS)										
ADI-R[106;108;111;112]	4	Uncon obs	NA	NA	NA	Very low	382	186	70 (65, 74)	77 (71, 83)
3di	No study met the inclusion criteria for this review									
GARS	No study met the inclusion criteria for this review									
DAWBA	No study met the inclusion criteria for this review									
PIA	No study met the inclusion criteria for this review									
DISCO	No study met the inclusion criteria for this review									
ADOS[106;108;111;112]	4	Uncon obs	NA	NA	NA	Very low	382	186	84 (79, 87)	77 (71, 82)

ADI-R + ADOS[72]	1	Uncon obs	NA	NA	NA	Very low	274	297	83 (79, 87)	86 (81, 92)
SUBGROUP ANALYSIS – PRIMARY SCHOOL CHILDREN (6-- 11 YEARS)										
No study met the inclusion criteria for this review										
SUBGROUP ANALYSIS – SECONDARY SCHOOL CHILDREN (≥12 YEARS)										
No study met the inclusion criteria for this review										

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5.2.4 Evidence statement

Evidence relating to autism

Only studies examining the ADI-R, ADOS and 'ADI-R plus ADOS' pre-defined levels of accuracy for this review. No data was identified for the 3di, DISCO, DAWBA, PIA and GARS. Studies examining the CARS were excluded..

All studies: only the combination of ADI-R and ADOS meet the pre-defined levels of accuracy. The evidence was of very low quality.

Intellectual disability: only the ADOS and the combination of ADI-R and ADOS meet the pre-defined levels of accuracy. The evidence was of very low quality.

Pre-school (≤5 years) only: only the ADOS and the combination of the ADI-R and the ADOS met the pre-defined levels of accuracy. The evidence was of very low quality.

Primary school (6 – 11 years) only: no studies were identified for this age group.

Secondary school (≥12 years) only: no studies were identified for this age group.

Evidence relating to ASD

All studies: of all the diagnostic tools examined, only the 3di and the combination of ADI-R and ADOS met the pre-defined levels of diagnostic accuracy. The evidence was of very low quality.

Intellectual disability: only the combination of *ADI-R and ADOS* meet the pre-defined levels of accuracy. The evidence was of very low quality.

Pre-school (≤5 years) only: only the combination of ADI-R and ADOS meet the pre-defined levels of accuracy. The evidence was of very low quality.

Primary school (6 – 11 years) only: no studies were identified for this age group.

Secondary school (≥12 years) only: no studies were identified for this age group.

5.2.5 Evidence to recommendations

See section 5.6.5

5.3 Agreement between ASD specific tools

5.3.1 Methodological approach

After reviewing the evidence on the accuracy of diagnostic tools, it was evident that the studies were of very low quality. For that reason, evidence comparing the agreement between tools was not examined.

5.3.2 Description of included studies

No studies were included.

5.3.3 Evidence profiles

No evidence.

5.3.4 Evidence statement

No evidence.

5.3.5 Evidence to recommendations

See section 5.6.5

5.4 Other assessment tools to assist interpretation of the ASD-specific diagnostic tools

5.4.1 Methodological approach

The title and abstract (if available) of all 25,787 papers identified by the search strategies were screened for this question. A total of 31 studies were reviewed in full-text. All studies were ultimately excluded because while they provided information on the use of other assessments on children with ASD, they did not give any information on how the results of other assessments could be used to assist a diagnosis alongside another ASD specific tool. As such the GDG decided to develop recommendations by consensus only.

A list of the 31 excluded studies and the reasons for exclusion is found in Appendix G (Tables of excluded studies).

5.4.2 Description of included studies

No studies were included.

5.4.3 Evidence profiles

No evidence.

5.4.4 Evidence statement

No evidence.

5.4.5 Evidence to recommendations

See section 5.6.5

5.5 Agreement between single clinician and panel of clinicians to diagnose ASD or autism according to DSM-IV criteria

5.5.1 Methodological approach

The agreement between diagnosis by single clinician and a diagnostic team are reported as kappa scores. Kappa scores may be interpreted as follows[30]:

<0%	Poor
0-20%	Slight
21%-40%	Fair
41%-60%	Moderate
61%-80%	Substantial
81%-100%	Almost perfect (high agreement)

Ten studies were considered but only one was eligible for inclusion based on the following criteria:

Population: Children or young people under 19 years referred for a diagnostic assessment for ASD; or

Children or adolescents who had been given an ASD diagnosis where agreement between diagnostic methods was assessed.

Index: Single clinician

Comparator: Diagnostic team

Outcomes: The agreement between single clinician and diagnostic team.

The nine excluded studies and the reasons for exclusion are found in Appendix G – Tables of excluded studies).

5.5.2 Description of included studies

One study[114], carried out in Canada examined the agreement between a single clinician and a diagnostic team in diagnosing ASD based on clinical records and compared to DSM-IV criteria. The study was an uncontrolled observation design and was judged to be very low quality based on design. The study sample included a mix of age-groups from pre-school children to adults.

Further details regarding the included study are presented within the evidence tables (see Appendix H – tables of included studies).

5.5.3 Evidence profile

Table 5.3 reports the agreement (Kappa statistic) between single versus a panel of clinicians in diagnosing ASD.

Table 5.3 Agreement between single clinician and panel of clinicians to diagnose ASD, autism or non-ASD according to DSM-IV criteria

Diagnosis	Quality assessment						Summary of findings		
							Agreement		
	Studies	Design	Limitations	Inconsistency	Indirectness	Quality	Number	Age (months)	Kappa (%)
AGREEMENT BETWEEN SINGLE CLINICIAN VS PANEL OF CLINICIANS									
ASD[114]	1	Uncon obs	NA	NA	NA	Very low	143	29 - 482	.55
Autism[114]	1	Uncon obs	NA	NA	NA	Very low	143	29 - 482	.56
Non-ASD[114]	1	Uncon obs	NA	NA	NA	Very low	143	29 - 482	.81

5.5.4 Evidence statement

One very low quality study examined the agreement between a single clinician and a panel of clinicians to diagnose ASD, autism or atypical autism. Agreement was moderate for ASD and autism. The agreement for the same clinicians and panel considering a non-spectrum diagnosis was almost perfect.

5.5.5 Evidence to recommendations

See section 5.6.5

5.6 Stability of ICD-10 and DSM-IV criteria

5.6.1 Methodological approach

The stability of diagnoses over time is reported according to the proportion of individuals retaining their diagnosis at the second diagnostic assessment. Study design and quality are also reported. Studies were grouped according to age at first diagnosis; ≤ 24 months, 25–36 months, 37-48 months and 49-60 months. We have used these subgroups as early diagnosis is important is the management of ASD and using a single of category of pre-school (children under 5 years of age) would not provide reliable evidence on diagnostic stability. Data is reported, when available, for autism, ASD, and no spectrum diagnosis as these are the three option for children assessed for ASD.

In total, 49 studies were examined and 13 studies were eligible for inclusion based on the following criteria:

Population: Pre-school children diagnosed with autism, ASD or non-ASD according to DSM-IV or ICD-10

Outcomes: Proportion of children who kept their original diagnosis at the later assessment.

A list of the 36 excluded studies and the reasons for exclusion is found in Appendix G (Tables of excluded studies).

5.6.2 Description of included studies

Thirteen studies in total were included in the review. These studies were carried in Canada[115],Netherlands[116], the UK[117-119] and the USA[107;108;120-125]. All were uncontrolled observational studies and were graded as very low quality. Participants received their first diagnosis at ≤ 24 months in 4 studies[118;120 117;125], between 25 – 36 months in 9 studies[107;108;115;116;119;121-124]. No studies examined diagnosis at either 37 – 48 months or 49 - 60 months. DSM-IV was used in 9 studies[108;115;116;120-125] examined the stability while ICD-10 was examined in 5 studies[107;117-119].

Further details regarding individual studies are presented within the evidence tables (see Appendix H– tables of included studies).

5.6.3 Evidence profiles

Table 5.4 reports the proportion of children, by age, who retain a diagnosis of autism, ASD and non-ASD (non spectrum) using either the DSM-IV or ICD-10 criteria.

Table 5.4 Stability of diagnostic criteria over time (by age at first diagnostic assessment)

Diagnostic criteria	Quality assessment						Summary of findings			
							Diagnosis at Time 2			
	Studies (N)	Design	Limitations	Inconsistency	Indirectness	Quality	Age (months)	Autism % (95% CI)	ASD % (95% CI)	Non-ASD % (95% CI)
STABILITY IF DIAGNOSED AT ≤ 24 MONTHS										
AUTISM										
DSM-IV[120;125]	2 (64)	Uncon obs	NA	NA	NA	Very low	35.9 ± 3.8 - 46.9 ± 7.7	80.8 (64.1, 93.1)	19.2 (6.9, 35.9)	0
ICD-10[117;118]	2 (35)	Uncon obs	NA	NA	NA	Very low	42 - 85.4 ±8.5	83.9 (70.5, 93.8)	13.4 (4.5, 26.0)	3.8
OTHER ASD										
DSM-IV[120;125]	2 (24)	Uncon obs	NA	NA	NA	Very low	35.9 ± 3.8 - 46.9 ± 7.7	12.6 (1.8, 31.0)	87.4 (69.0, 98.2)	
ICD-10[118]	1 (3)	Uncon obs	NA	NA	NA	Very low	42	33.3	66.7	0
NON-SPECTRUM										
DSM-IV[120;125]	2 (32)	Uncon obs	NA	NA	NA	Very low	35.9 ± 3.8 - 46.9 ± 7.7	3.6	12.5 (1.7, 31.0)	85.8 (72.3, 95.3)
ICD-10[118]	1(34)	Uncon obs	NA	NA	NA	Very low	42	0	26.7	73.5
STABILITY IF DIAGNOSED AT 25 – 36 MONTHS										
AUTISM										
DSM-IV[108;115;116;121;122;124]	6(260)	Uncon obs	NA	NA	NA	Very low	45 ± 6.4 - 112.8 ± 15.6	75.1 (62.4, 85.9)	16.7 (10.2, 24.6)	10.1 (3.1, 20.6)
ICD-10[107;119]	2 (32)	Uncon obs	NA	NA	NA	Very low	45.8 ± 5.3 – 53	85.4 (71.8, 95.1)	11.4 (3.1, 24.1)	6.3
OTHER ASD										
DSM-IV[108;115;116;121;122;124]	6(260)	Uncon obs	NA	NA	NA	Very low	45 ± 6.4 - 112.8 ± 15.6	31.2 (13.0, 53.1)	34.7 (26.0, 44.0)	32.5 (15.9, 51.9)
DSM-IV[123a]	1 (73)	Uncon obs	NA	NA	NA	Very low	53.7 ± 7.9	82.2		17.8
ICD-10[107;119]	2 (32)	Uncon obs	NA	NA	NA	Very low	45.8 ± 5.3 – 53			

NON-SPECTRUM										
DSM-IV[108;115;116;124]	4 (142)	Uncon obs	NA	NA	NA	Very low	53 ± 8 - 112.8 ± 15.6	0	10.5 (0.1, 35.1)	92.8 (77.4, 99.8)
DSM-IV[123a]	1 (17)	Uncon obs	NA	NA	NA	Very low	53.7 ± 7.9	0	0	100
ICD-10[107;119]	2 (15)	Uncon obs	NA	NA	NA	Very low	45.8 ± 5.3 – 53	14.3	0	83.7 (63.1, 96.9)
STABILITY IF DIAGNOSED AT - 48 MONTHS										
AUTISM										
No studies met the inclusion criteria for this analysis										
OTHER ASD										
No studies met the inclusion criteria for this analysis										
NON-SPECTRUM										
No studies met the inclusion criteria for this analysis										
STABILITY IF DIAGNOSED AT 49 – 60 MONTHS										
AUTISM										
No studies met the inclusion criteria for this analysis										
OTHER ASD										
No studies met the inclusion criteria for this analysis										
NON-SPECTRUM										
No studies met the inclusion criteria for this analysis										

a This study combined Autism and other ASD into one category

5.6.4 Evidence statement

Eight studies of very low quality provided data for this review. Three studies included children first diagnosed using ICD-10 or DSM-IV at less than 24 months of age, 5 studies included children first diagnosed at between 25 and 36 months of age. No studies were identified for the other age groups, 37 to 48 months or 49 to 60 months of age.

Children aged less than 24 months at first diagnostic assessment using ICD-10/DSM-IV

All children, except a single case (1.1%), diagnosed as having ASD based on ICD-10/DSM-IV retained that initial diagnosis at the second assessment at least 12 months later.

However of children under 24 months who were thought not to have ASD, 25% were found to have ASD at the second assessment at least 12 months later.

Children aged between 25 and 36 months at first diagnostic assessment using ICD-10/DSM-IV

The majority of children, 90% (9.6%), diagnosed as having ASD based on ICD-10/DSM-IV retained that initial diagnosis at the second assessment at least 12 months later.

No child thought not to have ASD was found to have ASD at the second assessment at least 12 months later.

Children aged between 37 and 48 months at first diagnostic assessment using ICD-10/DSM-IV

No studies were identified for this analysis

Children aged between 49 and 60 months at first diagnostic assessment using ICD-10/DSM-IV

No studies were identified for this analysis

5.6.5 Evidence to recommendations

Relative value placed on the outcomes considered	The ASD Specific Diagnostic Assessment is the definitive assessment in the ASD pathway. It can provide a definitive diagnosis and also an essential assessment ("profile") of the child's strengths and weaknesses. The outcomes considered for the diagnostic tools were the accuracy and the agreement between tools because in this point in the pathway it was important to avoid both false positive and false negative results. It was important to determine whether a multi disciplinary team could establish a more accurate diagnosis than an individual health care professional. It was also important to determine the age at which a diagnosis of ASD can be reliably made using ICD-10 and DSM-IV criteria. It was possible that the accuracy of diagnosis might differ depending on a child's stage of development.
Trade-off between clinical benefits and harms	**ASD specific assessment tools** The GDG noted that although all of the studies addressing diagnostic tool accuracy were of very low quality, some of the tools (alone or in combination) reached the required minimum level of accuracy for some categories. The GDG acknowledged that there was a significant difference in the level of accuracy for the diagnostic tools and there was no evidence for some tools, The combination of ADI-R and ADOS was accurate in diagnosing ASD in pre-school children and children with an intellectual disability. The 3di was

	accurate in diagnosing ASD but the GDG considered that a study reporting 100% sensitivity was unlikely to representative of clinical practice. However taking into account the quality of the evidence (see below) the GDG considered that the clinical benefits of using these tools to reach a diagnosis remained uncertain, even for combinations and sub-groups that were accurate. The GDG acknowledged that both an ASD specific semi-structured interview and observation were beneficial in providing a useful systematic framework for information gathering to assist in the diagnostic assessment. The GDG also acknowledged the possible harms associated with the use of scores derived from these tools used in isolation to diagnose ASD in terms of the risk of giving a wrong diagnosis at the end of an ASD specific diagnostic assessment. Overall therefore the GDG recommended the use of a semi-structured interview and observation but did not extend their recommendation to include any specific published tool. **Multidisciplinary assessment versus single practitioner assessment** The GDG noted that only one study addressed this issue. It showed moderate diagnostic agreement between the diagnosis of an individual health care professional and a multidisciplinary team, but this study was of very low quality. In practice the GDG acknowledged that a diagnosis can be made by a single experienced health care professional. However, the label of ASD does not constitute a complete diagnostic assessment with an accompanying profile of the child or young persons' strengths and weaknesses that should be used to inform an effective management strategy. The GDG therefore concluded that a multi disciplinary team should also be engaged in the ASD diagnostic assessments and that such a team would be equipped to undertake the essential profiling of the child or young person's strengths and weaknesses. **Stability of diagnosis using ICD-10 and DSM-IV as diagnostic criteria** The evidence of stability indicates that diagnosis is reliable when established using ICD and DSM criteria in children in different age categories. The GDG consensus was that the diagnoses of ASD should be made in a consistent way to reduce professional disagreements and delay in the process. The GDG considered that the most effective way of achieving this was to consider the diagnostic threshold in the context of the ICD-10/DSM-IV criteria. The GDG noted that current practice in the NHS was not always to use these criteria, with individual health care practitioners and teams making diagnoses based on clinical experience alone. The result was health care professionals and ASD teams used varying diagnostic thresholds for ASD in the NHS. The GDG have sought to rectify this inconsistency by stating in their recommendations that any diagnosis should be made based on the ICD-10/DSM-IV criteria using clinical judgement.
Trade-off between net health benefits and resource use	The ASD specific instruments used in assessment have cost implications for training and use. There is insufficient evidence that one tool is better than another. However the GDG opinion was that training in an ASD specific tool for eliciting history and observation enhanced competence in ASD diagnostic assessment. The GDG was aware of evidence published in 2010, in the UK, training of local ASD teams in the diagnosis of ASD has led to a mean reduction in the time spent waiting for a diagnostic assessment[126] There are cost implications for the use of additional assessments. The GDG were unable to identify any evidence that could determine the cost effectiveness of carrying out additional assessments. However the GDG

	considered that clinical benefits justified the additional resource use The GDG view was that the value of a multidisciplinary team arriving at a diagnosis outweighed the additional costs of more than one person's involvement in deciding whether a child or young person has ASD. There was no published evidence identified that reported the cost effectiveness of monitoring, reviewing or referring children who are not immediately diagnosed. The potential costs associated with this are: the additional time required for professionals to make contact with other health care professional involved with the care of the child/young person and agencies outside the NHS and the cost of a more expert review. The GDG did not put a figure on these costs as there were no data on the proportion of children not diagnosed with ASD who would require this support, or additional referral to a more expert team i.e. a tertiary service. The assumption is that appropriate tertiary referral would improve the effectiveness of care because they will be better able to reach a firm decision about complex diagnostic cases.
Quality of evidence	**Accuracy of diagnostic tools used in isolation** Overall the studies on the accuracy of the diagnostic tools were all rated as "very low quality" with the exception of just two sub-group analyses on pre-school children (ADI-R and ADOS) being rated as "low quality". The body of evidence was greatest for ADI-R. The evidence included sub group analysis of children with ID and pre school age children. No studies reported acceptable levels of accuracy for both sensitivity and specificity. When additional studies were included in the review of "post hoc" referral only analysis ADI-R met the threshold for accuracy at identifying children with ASD but still did not meet the threshold for identifying children who did not have the condition. The evidence for ADOS did not meet the threshold for diagnostic accuracy for both sensitivity and specificity. Only one study included a sub-group analysis of children with a priori intellectual disability and for this group, the ADOS did meet the threshold for accuracy. However this was only one study and the reasons why it should be more accurate in this sub group are not easy to interpret. The evidence reported sub-group analysis of children in the pre-school (< 5 years). The ADOS met the threshold for accuracy for this sub group. No studies were identified for the other two age group, When additional studies were included that included the post-hoc 'Referrals' only group of children none of these studies met the criteria for accuracy in both sensitivity and specificity. Only one study was identified that considered the accuracy of 3di and GARS respectively. The GDG did not believe the results could be interpreted from this limited very low quality evidence. The results need to be considered with caution as the findings have not been replicated with other independent studies. No evidence was identified for the accuracy of DISCO. Prediction of ASD using a combination of ADOS and ADI-R was good although the overall quality was rated as "very low". The evidence reported that 85% of children were correctly identified as having ASD using ADI-R plus ADOS and 81% of children were correctly identified as not having ASD. When these instruments were evaluated on their own, the power to correctly identify children who did not have ASD improved but they were not as good at identifying children who had ASD.

	Overall the GDG recognised that the evidence supporting the use of these various diagnostic tools either individually or in combination as accurate instruments capable of establishing or ruling out a diagnosis of ASD was poor. The GDG nevertheless considered that consideration should be given to their use as a semi-structured means of gathering information from the ASD-specific Diagnostic Assessment interview and observation. **Assessments to interpret the ASD assessment** Although there was no evidence for the routine use of additional assessments as part of the ASD assessment, the GDG concluded that the clinical benefits outweighed the harms if specific assessments such as language/communication, cognitive and hearing assessment were carried out selectively depending on the needs of the individual child. **Multidisciplinary assessment versus single practitioner assessment** The GDG noted that this study had a small sample size and has not been replicated elsewhere. **ICD-10 and DSM-IV as diagnostic criteria** The GDG noted that selection bias could have had an impact on the data on stability of diagnosis using ICD/DSM reported in these studies. However they did not consider this to be so overwhelmingly important as to undermine the recommendation to use these criteria to diagnose ASD.
Other considerations	The GDG agreed, based on consensus, that for every child or young person undergoing an ASD-specific Diagnostic Assessment, the "core elements" of that assessment should be a detailed enquiry into the specific concerns raised, a medical history, enquiry about past care and educational experiences, a history and observation focussing on the developmental and behavioural features specified in the ICD-10 and DSM-IV ASD criteria. This core information might be sufficient to establish a diagnosis of ASD. The GDG acknowledged that there were no studies that would provide evidence of improved or diminished accuracy in diagnosing ASD using additional assessments to interpret the results of ASD specific tools. However, the GDG opinion was that it would be important to recognise cognitive impairment during the assessment. Cognitive impairment might explain deficits in social and communicative skills. It might also limit the child's or young person's ability to participate in the assessment. Recognition of cognitive impairment would also be an essential part of developing the "profile". Where necessary the GDG noted the importance of carrying out a formal language assessment for some children undergoing an ASD specific Diagnostic Assessment. In those with language impairments or if there were other reasons for concern assessment the GDG noted that a hearing assessment would be essential. Recommendations were therefore made on these The GDG considered that the diagnostic assessment of a child or young person with suspected ASD should include not only an attempt to establish an accurate diagnosis but also to provide an accurate assessment of the individual's profile and needs. . The GDG recommended therefore that as part of the ASD–specific Diagnostic Assessment every child and young person should also have an evaluation of their individual skills and impairments , the specific elements of which would be determined based on the individual need. The GDG recommended that this should lead to the development of a "profile" for each individual that would identify their personal strengths and weaknesses. The GDG consensus was that the health care professional undertaking the profile should consider gathering information about the child or young person in the following areas:

	intellectual ability and learning style, academic skills, speech language and communication, fine and gross motor skills, adaptive behaviour (includes self help skills), mental and emotional health including self esteem, physical health, sensory sensitivities, behaviour likely to affect participation in future support and management. Sensory sensitivities and behaviour are likely to affect participation in activities and life experiences. To inform management, the GDG noted that for children and young people with communication difficulties, it may be difficult to recognise physical and mental health problems. Effort should be made to assess these important concerns to the child and family to inform the profile and subsequent management. The GDG also recommended that each child or young person should undergo a formal risk assessment to examine the risks to and from them. Finally the GDG recommended that for each child a management plan should be developed based on the "profile" and taking account of other factors such as the family context. The GDG recognised that even after completion of a thorough ASD-specific Diagnostic Assessment, it would not always be possible to achieve diagnostic certainty. (see section 5.4 below) The evidence in relation to "stability of diagnosis" was pertinent to this. The GDG noted that there was evidence that false negative diagnosis of autism may occur in up to 25% of children under 24 months. However, the evidence in relation to the stability of diagnosis over time in different age groups was of very low quality. Nevertheless, based on their clinical experience the GDG agreed that diagnosis in children under 24 months may be difficult because of the developmental changes in early life. The GDG also concluded, based on their experience, that assessment and diagnosis were likely to be more difficult in children whose mental age was less than 18 months. Early life experiences (for example, extreme prematurity, or the experiences of "looked-after children") might be very relevant to the diagnostic assessment. For those who were "looked-after children" there was a possibility that relevant information might be difficult to obtain. Finally, those with complex mental health disorders were in the experience of the GDG sometimes difficult to assess and this might lead to diagnostic uncertainty. The GDG therefore made a recommendation that health care professionals undertaking a diagnostic assessment should be aware of these potential challenges. The experience of the GDG was that a failure to establish a clear diagnosis is often distressing to families and carers. As part of the diagnostic assessment, however, the individual child or young person will have undergone a thorough assessment of their strengths and weaknesses ("profiling") and this will enable the ASD Team and the parents/ carers to determine the support that the child or young person and family/carers will need. Thus the diagnostic assessment will have provided benefit even where there is continued diagnostic uncertainty. The GDG consensus is that, if a physical examination has not already been undertaken recently, then the ASD Team members undertaking the ASD-specific diagnostic assessment should consider whether a physical examination is necessary based on their clinical judgment. The physical examination of the child or young person may be necessary as part of the differential diagnosis, to consider coexisting conditions or to consider whether there are physical signs suggestive of a causative condition, that is, a condition strongly associated with ASD which could help determine a diagnosis of ASD. As part of the physical examination attention should be

focussed on identifying the skin stigmata of neurofibromatosis or tuberous sclerosis (Wood's light).

The GDG considered that a physical examination is not necessary for all children. However, it should always be undertaken in preschool children, in children and young people with an intellectual disability, and in those with dysmorphic features. It should be undertaken in children and young people where a concern about maltreatment, or self injurious behaviour arises. In these cases, other recently published NICE guidance on maltreatment and self harm should be followed.

The ASD Team

It was the GDG consensus that central to the diagnostic pathway there should be a dedicated multiprofessional group working together to carry out the diagnostic assessment, as outlined in the scope of the guideline. The ASD Team should include experienced, named health care professionals skilled in undertaking all aspects of the ASD diagnostic assessment and profiling. The GDG recognise that the ASD Team will usually be made up of professionals who also undertake assessments for children and young people with a wider range of social communication and developmental difficulties, but it should be a dedicated role for this group of professionals to consider all referrals for ASD specific diagnostic assessment and to undertake all components of the diagnostic assessment and profile.

Under this general model, a variety of models of service provision can exist. It should not be taken as a prescription for how all services should be organised. The ASD team should be made up of a core group of health care professionals but it should also have access to other health care professionals not within the core team. These other professionals should be skilled in undertaking assessments in children with coexisting conditions that make undertaking diagnostic assessment more complex, such as deafness, blindness, motor disorders and intellectual disability. the exact membership of the core team and other professionals will be determined by local considerations.

The GDG considered the role of the ASD team and agreed that members of the team should provide advice to non-expert professionals regarding referral as a means of ensuring that the right children and young people are referred to the ASD team for further assessment. They should also decide on the assessment needs of any child or young person who is referred, be skilled at communicating with children, young people and families and share information with them about the diagnostic process and other services available to them. This allays fears, promotes good understanding between professionals and families as well as acceptance of the findings of the diagnostic assessment.

Not all professionals in the ASD team need to be involved in the diagnostic process for every child or young person. The GDG recognise that while a very experienced health care professional could undertake some aspects of the assessment single-handedly (such as the ADI-R and the ADOS), a wider range of expertise is required to undertake the other aspects of assessments to develop a comprehensive profile of the child or young person.

For young people at the time of transition, the GDG agreed that good practice would be to involve professionals from adult services in the diagnostic assessment even where there is intellectual disability because it supports the specific needs of the young person and their family and

	enhances communication between services
Recommendations	3. There should be a multidisciplinary ASD team (the ASD team) which may include a: • paediatrician • child and adolescent psychiatrist • speech and language therapist • clinical or educational psychologist • occupational therapist. 4. The ASD team should: • provide advice to professionals about referring for ASD assessments • decide on the assessment needs of those referred • be skilled in communicating with children and young people with suspected or known ASD and with their parents and carers • develop the profile (see recommendation 51) and management plan for each child or young person • with parent or carer consent, share information from the ASD diagnostic assessment directly with relevant services, for example a school visit by an ASD team member • give information to families and carers about appropriate services and support (see recommendation 63). 6. The ASD team should either have the skills needed to carry out an ASD diagnostic assessment or have access to professionals that do, for assessing: • children and young people of all ages taking into account the cultural setting or language background **and** • children and young people with co-existing conditions such as deafness, blindness, motor disorders including cerebral palsy, intellectual disability, language disorders or additional mental health disorders. 7. If young people present at the time of transition to adult services, the ASD team should consider carrying out the diagnostic assessment jointly with the adult ASD diagnostic team, regardless of the young persons' intellectual ability. 36. Include the following elements in every ASD diagnostic assessment: • detailed enquiry about parent or carer concerns and if appropriate the child or young person's concerns • a medical history including prenatal, perinatal and family history and current health • the child's or young person's experiences of social care and education • a developmental history focussing on developmental and behavioural features consistent with ICD-10 or DSM-IV criteria (consider using an ASD-specific tool to gather this information) • assessment through interaction with and observation of the child or young person of their social and communicative skills and behaviours focussing on features consistent with ICD-10 or DSM-IV

criteria (consider using an ASD-specific diagnostic tool to gather this information).

37. Carry out a physical examination in:

- preschool children
- those with intellectual disability or a family history of intellectual disability
- those with dysmorphic features
- those in whom there is concern regarding physical maltreatment or neglect (see 'When to suspect child maltreatment' [NICE clinical guideline 89]) or self-injurious behaviour/self-harm (see 'Self-harm: the short-term physical and psychological management and secondary prevention of self-harm in primary and secondary care' [NICE clinical guideline 16])
- those with a history suggesting a neurological disorder including suspicion of epilepsy
- children or young people in whom you think it appropriate.

38. In the physical examination, look for:

- skin stigmata of neurofibromatosis or tuberous sclerosis using a Wood's light
- signs of injury, for example self-harm or child maltreatment (see NICE clinical guidelines 16 and 89 respectively).

41. Consider whether specific assessments are necessary to help the interpretation of the ASD history and observations, for example a cognitive or language assessment appropriate to the child or young persons' age and ability.

42. Consider which assessments are required to profile each child's or young person's skills and impairments, for example:

- intellectual ability and learning style
- academic skills
- speech, language and communication
- fine and gross motor skills
- adaptive behaviour (including self-help skills)
- mental and emotional health (including self esteem)
- physical health
- sensory sensitivities
- behaviour likely to affect participation.

43. Use information from all sources, together with clinical judgment, to diagnose ASD based on ICD-10 or DSM-IV criteria.

44. Do not rely on any single ASD-specific diagnostic tool without other sources of information to diagnose ASD.

45. Be aware that in some children and young people there may be uncertainty about the diagnosis of ASD, particularly in those with:

	• a chronological age of less than 24 months • a mental age of less than 18 months • a lack of available information about their early life (for example some looked-after or adopted children) • a complex comorbid mental health disorder (for example ADHD, conduct disorder, a possible attachment disorder) sensory impairment (for example blindness or deafness), or motor disorder such as cerebral palsy. 47. Be aware that in children and young people with communication difficulties it may be difficult to recognise functional problems or mental health problems. 51. Construct a profile for every child or young person who has had an ASD diagnostic assessment, including their strengths, skills, impairments and needs to create a needs-based management plan. This should cover learning, communication, self-care and other adaptive skills, behaviour and emotional health, taking account of the family context and needs. 52. Assess the risk of harm to and from the child or young person arising from their condition.

5.6.6 Research recommendations

PICO research question	What is the effectiveness and cost effectiveness of additional assessments (language, motor, psychiatric history or use of scales) in: • diagnosing ASD • differentiating ASD from other conditions • identifying common comorbidities in children and young people with signs and symptoms of ASD?
Why is this needed	
Importance to 'patients' or the population	Improved differential diagnosis (and identification of the common comorbidities) would improve acceptability and satisfaction for children and young people and their families and carers. Some of the comorbidities have proven treatments (for example, ADHD), so it may be possible to reduce morbidity.
Relevance to NICE guidance	The GDG considered this research area was of high importance for updates of key recommendations in the guideline
Relevance to the NHS	Costs from routine additional assessments (very variable in how common now – in child health SALT pretty common, IQ testing not common at all while reverse true in CAMHS). Also potential danger of this making the diagnostic process taken longer which goes against much of what the recommendations are trying to do.
National priorities	This is not an identified area of national priority
Current evidence base	The guideline has two recommendations that address this issue but no evidence to support these recommendations (Recommendations #41 and #51). Few if any studies on ASD address this question.
Equality	Those with the most complex needs might be thought a 'disadvantaged' group

	and this would help identify their range of needs and difficulties.
Feasibility	The GDG considered a study could be done in a 2-3 year time frame and at moderate cost only and would be fairly straightforward to undertaken. They did not identify any specific ethical or technical issues.
Other comments	None

5.7 Communicating diagnosis to the family

5.7.1 Introduction

Children, young people, parents and carers need to be treated with sensitivity and understanding throughout the ASD assessment process and , at the point of diagnosis. The purpose of this section is to make recommendations about how best to communicate a diagnosis of autism spectrum disorder to children, young people, parents and carers, based on available autism-specific evidence.

5.7.2 Methodological approach

The purpose of this review was to look at evidence for how to communicate an ASD diagnosis to children/families and carers.

No specific sub groups were considered for this question.

Examples are presented by outcome of interest with illustrative quotes in a modified GRADE table.

The title and abstract (if available) of all 25,787 papers identified by the search strategies were screened for this question. A total of 28 papers were reviewed in full-text. Nine studies were eligible for inclusion based on the following criteria:

Population: a)Children and young people under 19 years diagnosed with ASD; b). Parents/caregivers of ASD children and young people.

Outcomes: a) 'Good' practice: ways of communicating the diagnosis result that made parents feel satisfied/relieved in clinical practice; b) 'Poor' practice: ways of communicating that caused ASD families' negative emotion in clinical practice, such as agony, bewilderment, disbelieve of diagnosis result or timidity of communication with professionals; c) Parents' expectation: Parents' expectation of how a diagnosis should be communicated to them.

Study type: Controlled and uncontrolled observational studies.

A list of the 19 excluded studies and the reasons for exclusion is found in Appendix G (Tables of excluded studies).

5.7.3 Description of included studies

All of the included studies[127-135] were carried out in the UK. All studies were uncontrolled observational and were graded as very low quality. Three studies[128;131;132] used a questionnaire to solicit information, four studies[127;129;133;135] used interviews, one study[130] used both questionnaire and interview and the final study[134] used a focus group. All studies reported the views/experiences parents of children with ASD. No studies reported on children or young people's responses.

The authors of one study[135] summarised the views of participants but did not report verbatim quotes but we have retained this as it reported themes not covered in the other studies.

5.7.4 Evidence profile

Table 5.5 summarises examples identified in the evidence of good and poor practice in the communication of ASD diagnosis, and parents' expectations of how a diagnosis should be communicated to them.

Table 5.5 Examples of good and poor practice in the communication of ASD diagnosis

Examples	Study Quality						Supporting quotes from parents
	Number of studies	Study design	Limitations	Inconsistency	Indirectness	Quality	
GOOD PRACTICE							
A multidisciplinary team who listened to parents' views[128]	1	Uncon obs*	NA	NA	NA	Very low	*'Diagnosis for my son was made by a senior Clinical Medical Officer, a Behavioural psychologist and a Speech and Language Therapist when he was four and half years old. (It) involved a day-long series of tests and detailed information from myself and my husband. We were invited to a 'feedback' with the above people present and were asked what we thought was wrong with our son and then we were told he had autism. We were glad that P. had a diagnosis'*
Providing family with a clear and quick diagnosis result[131]	1	Uncon obs	NA	NA	NA	Very low	*'Why couldn't someone have spotted his autism earlier?... We look forward to the future in a much more positive and reassuring way because of the diagnosis. Life is much more relaxed and obviously understandable.'*
POOR PRACTICE							
Professionals' reluctance to give a diagnosis[133]	1	Uncon obs	NA	NA	NA	Very low	*'Whenever I have asked anyone for a definite diagnosis I have been told it is wrong to label children and a diagnosis isn't important. No one has used the word autism unless I force the issue –then they look shifty!'*
Told there is "nothing wrong" with a child [129]	1	Uncon obs	NA	NA	NA	Very low	*'At the beginning we thought perhaps it's Fragile X gene. This doctor did not know what I was doing, he said it was me who had the problem. We were told that she would never speak. They kept saying to me: perhaps she is probably deaf. I said that she was not because she could hear everything, she was not deaf because she had speech. You were called a liar. We went to the doctor time and time again, and they said no, there is nothing wrong with the child. The GP wrote in the medical records: her mother is neurotic, because he thought, she is off the wall this woman.'*
Delay in diagnosis[131]	1	Uncon obs	NA	NA	NA	Very low	*'The whole process is far too slow and seems to depend on the parents' persistence in pushing for a diagnosis. Months seem to go by waiting for appointment after appointment. This really prolongs the agony of what is, inevitably in any case, a painful process.'*
Professionals' reluctance to give a diagnosis of	1	Uncon obs	NA	NA	NA	Very low	*'I was fed up with professional pussyfooting around, afraid to say the dreaded word 'autism'. It seems that the very word autistic is taboo.'*

ASD[131]							
Inadequate explanation as to how a diagnosis was reached [127]	1	Uncon obs	NA	NA	NA	Very low	*'when I got an assessment of him (my son) from them (the professionals), really I just took it with a pinch of salt, I didn't take it very seriously because I thought the people that are writing about him (…) they didn't get to see the real Brian, I knew that they were seeing just the surface.'*
Inadequate response to queries during assessment[127]	1	Uncon obs	NA	NA	NA	Very low	*'You just didn't get any feedback (…) that was frustrating to me, because it was like, why the bloody hell can't you tell me what's going on here? [laughs] this is my child that I'm bringing to you.'*
Did not involve parents in the decision-making process[127]	1	Uncon obs	NA	NA	NA	Very low	*'They (professionals) know all the facts and all the details and they perhaps decide right we'll give you that fact, just one fact and perhaps not necessarily give you all the options to weigh up, I don't know, perhaps it's better [laughs] it's very complicated.'*
Giving people an impression that professionals have power and control over the parents[127]	1	Uncon obs	NA	NA	NA	Very low	*If I had said anything, as I felt I should have done at the time but didn't have the bottle to do it, I was thinking if I say anything, will that make them horrible to Adam? Will that make them against him? Will that affect a report on him? So you don't.'*
No prior warning of ASD before the disclosure of ASD[132]	1	Uncon obs	NA	NA	NA	Very low	*'More time and information should be given to parents at diagnosis. I was informed of the diagnosis and told I would be seen by the family services worker in a month. That was it. Not explanation. No hope. It was obvious that they knew what diagnosis they were likely to make prior to the play session but I had no prior warning. No one had the decency to tell me what might be wrong. At that point I needed to believe there was a future and I was appalled at the way I was treated. I should have had counselling there and then and lots of information given to me.*
Lack of information about the condition when conveying the diagnosis [134]	1	Uncon obs	NA	NA	NA	Very low	*'I don't feel I came away knowing anything about autism'*
Inappropriate manner when conveying the diagnosis[134]	1	Uncon obs	NA	NA	NA	Very low	*'The manner in which the diagnosis was given to us would have been, I suppose, in one sense, quite cold and calculating, it sort of accounted this is the problem, that's it, goodbye'*

Delay in diagnosis[134]	1	Uncon obs	NA	NA	NA	Very low	*'All you get is delay, after delay, after delay'*
PARENTS' EXPECTATIONS – how should diagnosis be communicated							
Reassure parents that there are things they can do[132]	1	Uncon obs	NA	NA	NA	Very low	*'I believe that when parents are told during diagnostic assessment that their child is autistic, they should be reassured that there are things they can do, e.g., Lovaas, PECS, change of diet, to make a huge difference. Obviously don't mislead them to think these things are a cure, but don't lead them to believe that the future is bleak, and doom and gloom, as I was.'*
Offer more than just the diagnosis[130]	1	Uncon obs	NA	NA	NA	Very low	*'The people that we went to, I think are very good at diagnosing, but I don't think that they really thought about the outcomes. They were thinking about the diagnosis right now and what this child had. …[They] mentioned absolutely nothing about what we could look for down the road with him and I don't even think that was on their minds at that point.'*
Open-mindedness[134]	1	Uncon obs	NA	NA	NA	Very low	*'a general openness all round'*
Provide written reports, especially of assessment[135]	1	Uncon obs	NA	NA	NA	Very low	The study authors reported participants views in summary only, without supporting quotes
Involve parents in discussion after the assessment, as this would help parents to understand professional 'findings'[135]	1	Uncon obs	NA	NA	NA	Very low	The study authors reported participants views in summary only, without supporting quotes
Talk to parents as 'equals', use language that can be understood and is not technical[135]	1	Uncon obs	NA	NA	NA	Very low	The study authors reported participants views in summary only, without supporting quotes
Take more opportunities to discuss the child's progress with the individual	1	Uncon obs	NA	NA	NA	Very low	The study authors reported participants views in summary only, without supporting quotes

professionals (e.g. individual reports should be discussed)[135]							
Only have professionals present who have involvement with the child[135]	1	Uncon obs	NA	NA	NA	Very low	The study authors reported participants views in summary only, without supporting quotes
Interview parents without the child being present[135]	1	Uncon obs	NA	NA	NA	Very low	The study authors reported participants views in summary only, without supporting quotes
Assess the child separately[135]	1	Uncon obs	NA	NA	NA	Very low	The study authors reported participants views in summary only, without supporting quotes
Know who is going to be present to prepare questions to ask[135]	1	Uncon obs	NA	NA	NA	Very low	The study authors reported participants views in summary only, without supporting quotes
Do not make a telephone call to parents to inform them of an appointment[135]	1	Uncon obs	NA	NA	NA	Very low	The study authors reported participants views in summary only, without supporting quotes
See the child in various settings[135]	1	Uncon obs	NA	NA	NA	Very low	The study authors reported participants views in summary only, without supporting quotes
Make appointments less formal; allow parents more time to ask questions[135]	1	Uncon obs	NA	NA	NA	Very low	The study authors reported participants views in summary only, without supporting quotes

*: Uncon obs: Uncontrolled observational study, such as case series.

5.7.5 Evidence statements

All the evidence was from the UK. All evidence was of low quality.

Poor practice

Two studies provided evidence of poor practice in communicating with families**.** Examples of poor practice were:

- Professionals' reluctance to give a diagnosis (2 studies)
- Incorrect diagnosis
- Delay in diagnosis (2 studies)
- No reply to parents' queries during assessment
- Not involving parents in the decision-making process.
- Giving people an impression that professionals have power and control over the parents.
- Not providing parents with necessary information (2 studies), such as how they reached the diagnosis
- No prior warning of ASD before the disclosure of ASD.
- Inappropriate manner when conveying diagnosis.

Good practice

Six studies provided evidence of good practice. Examples of good practice were:

- Multidisciplinary team that listens to parents' views
- Provision of a clear and quick diagnosis result

Parents' expectation

Three studies provided evidence of good practice. Examples of parents' expectations were:

Involving parents in decision-making process

- Involving parents in discussion after the assessment, as this would help parents to understand professional 'findings'
- Make appointments less formal; allow parents more time to ask questions.

Provide written reports and opportunities for discussion

- Provide written reports, especially of the assessment
- Parents should have more opportunities to discuss the child's progress with the individual professionals, for example, individual reports should be discussed

Other

- Talk to parents as 'equals'; use language that can be understood and is not technical
- Only have professionals present who have involvement with the child
- Interview parents without the child being present
- Assess the child separately
- More individualised professional involvement outside the clinic
- Do not make a telephone call to parents to inform them of an appointment.
- See the child in various settings
- Open-mindedness
- Letting the parents know who is going to be present to prepare questions to ask
- Reassure parents there are things they can do

5.7.6 Evidence to recommendations

Relative value placed on the outcomes considered	The following outcomes were identified as important for answering this question: examples of good practice, examples of poor practice and family/ carer expectations when receiving the diagnosis.
Trade-off between clinical benefits and harms	Evidence shows that when professionals have been either reluctant to give a diagnosis for fear of labelling the child or unable to arrive at a working, this has prevented parents from accessing vital services and support, created anxiety due to the uncertainty about their child's difficulties and hindered their understanding and management of their child. Gaining a diagnosis was described as 'a relief' to parents. Evidence also suggested that the diagnostic process worked best for parents when they were able to participate as equal partners, where explanatory language was not too technical, where they were given opportunities for input and provided with written information relating to the diagnosis and its implications. Parental confidence was boosted when a multi-disciplinary team were responsible for diagnosis. A lengthy diagnostic process was described by parents in one study as 'painful' . Evidence shows that parents value opportunities to receive an explanation of the diagnostic process (including timescales), discussion about the diagnosis and its implications for their child and family as well as receiving guidance and information about possible interventions to support and/or manage their child . Parents reported that receiving the diagnosis was emotionally debilitating, that they valued being gently prepared for it and it being shared in a sensitive way. A high percentage of parents in the studies stated they would have benefited from counselling at the time of diagnosis. Evidence suggested that parents value being signposted to sources of help and support. Before a child and family is referred back to primary care or on for further assessment, they require comprehensive feedback from the assessment. This should be based on the profile of strengths and weaknesses following assessment which should always be undertaken and shared with the family and carers regardless of the final diagnoses. Families and carers may have problems processing complex and distressing verbal information at a stressful time when they were expecting a definitive diagnosis. Therefore they should receive written reports as well as information in a face to face meeting with members of the assessment team. The GDG consensus was that the benefit of this intervention is reduction in the potential on-going distress to families and carers for whom a clear diagnosis is not reached.
Trade-off between net health benefits and resource use	No specific resource use issues were identified by the GDG for this question.
Quality of evidence	The evidence identified was qualitative, based on small scale studies, all within the UK. The evidence focused on the views of parents and not of the children and young people themselves. The quality if the evidence was very low. The GDG did not consider this evidence was sufficiently robust to directly influence individual recommendations for the NHS, but it provided an overview of the range of views and concerns raised by people at the time of receiving the diagnosis. Many of the reported views were familiar to the GDG both as parents and professionals. No viewpoints were extremely surprising and no comments were irrelevant to the NHS

Other considerations	The clinical question did not address the time at which discussing the possibility of ASD with parents, carers and should begin. However the GDG consensus was that the benefits of early preparation for the diagnosis outweighed the costs of the stress associated with naming the condition and therefore this discussion should be undertaken as early as possible with reasonable clinical judgement as to exactly when this should be. There was no evidence on how long health care professionals should take while communicating the diagnosis to children, young people and their carers but the GDG considered that it should not appear to families and carers to seem rushed because this would increase stress and reduce their ability to take in complex information about the diagnosis which can be distressing to the child or the family/ carer. The GDG agreed that it was important to include the child or young person when communicating the diagnosis of ASD. Those providing the diagnosis need to be aware that communicating the diagnosis raises complex feelings in those caring for children with ASD. These include relief that a diagnosis has been reached, as well as stress and anxiety that other members of the family (including themselves) should consider whether to be assessed for ASD; they should also be aware that the process of reaching a diagnosis may have been very long for the family, and that they may have lived with a child or young person with extremely challenging behaviour without a diagnosis during that time Therefore the health care professional communicating diagnosis needs to follow the lead of those listening as to the speed, depth of information and quantity of information provided in any consultation and provide an opportunity for the family to respond to the person who is talking to them. Taking account of these considerations, the GDG made recommendations specifically emphasising the need to involve parents and carers, explaining the diagnostic process and its conclusions, engaging in face-to-face discussion soon after the completion of the ASD-specific Diagnostic Assessment, discussing the risk of ASD occurring in future children and providing a detailed written report of the assessment and the evidence for its conclusions afterwards. The recommendations also addressed the importance of communication with other professionals following diagnosis.
Recommendations	54. After the ASD diagnostic assessment, discuss the findings in person with the parents or carers without delay. Explain the basis of conclusions even if the diagnosis is not yet certain. 55. When discussing the diagnosis with families, carers, children and young people, use generic guidelines for sharing and disclosing diagnosis to children and young people. 56. Discuss with the parents and/or carers how information should be shared with the child or young person. Take into account, for example, their age and ability to understand. 57. Provide information specific to the child or young person based on their profile. 58. When ASD is diagnosed, discuss with parents and/or carers the risk of ASD occurring in siblings and future children. 59. Provide a written report for the child or young person and parents and/or carers explaining the findings of the assessment and the basis for the conclusions drawn. 60. Share information from the diagnostic assessment with the GP and, with parental or carer consent (and if appropriate the consent of the child or young person), key professionals including those in education and social services.

	61. Offer a follow-up appointment with an appropriate member of the ASD team within 6 weeks of the assessment for further discussion.

5.8 Actions that should follow assessment for children and young people who are not immediately diagnosed with ASD

5.8.1 Introduction

For some children, there is continuing uncertainty as to the diagnosis of ASD. This section covers when to refer, when to gather further information, and when to undertake further assessment and observation.

5.8.2 Methodological approach

It was expected that no studies would be available since no empirical research evidence could address this type of question. A clinical trial, observational study or qualitative study would not be helpful since no specific intervention can be definitively linked to an ASD specific outcome. Therefore the GDG decided to use consensus methodology to answer this question, so no evidence was reviewed for this question.

5.8.3 Description of included studies

No systematic search of the evidence was undertaken

5.8.4 Evidence profile

No systematic search of the evidence was undertaken

5.8.5 Evidence statement

No systematic search of the evidence was undertaken

5.8.6 Evidence to recommendations

Relative value placed on the outcomes considered	The outcome of interest is the welfare of the child or young person who is not immediately diagnosed with ASD and for whom there s continued diagnostic uncertainty. No specific outcomes were predefined for this question as it was anticipated that no evidence would be identified to address this question. The focus of the GDG discussion in the absence of evidence was on reaching a consensus on the actions that should always be taken for children who are not diagnosed with ASD at the end of the assessment process.
Trade-off between clinical benefits and harms	The GDG consensus was that there was benefit in referral for a second opinion where there is diagnostic uncertainty, disagreement about the diagnosis or where there is a continued lack of agreement between professionals and parents/ carers. There is also benefit for children where further assessment for a specific condition or problem other than ASD is warranted and where assessment requires expertise beyond that of the multidisciplinary team. Referral to a more expert team may reduce the harms associated with delay in identifying the correct diagnosis and implementation of the appropriate specific interventions and support for that condition. The GDG consensus was that where there was continued diagnostic uncertainty but referral to a more expert team was not warranted, the child or young person should be reviewed and if necessary the assessment should be reviewed after an interval of time, not more than 6 months. The GDG consensus was that there is always benefit in having a plan in place

	for every child not immediately diagnosed because of the risk of missing important changes in signs and symptoms that would warrant further assessment. This plan needs to be agreed with parents and carers. The GDG consensus was that there may be benefit in undertaking observations of the child, young person if no definitive diagnosis has been reached but that did not have to happen for every child or young person. The consensus was that, if undertaken, any observations should be undertaken after the core assessments had been completed rather than earlier on the information gathering process. The observation can take place in a variety of settings, and health care professionals should listen to parents and carers about how the child behaves in different settings to determine the observation that would provide the most useful information, for example, school, nursery or in the home. The GDG also agreed that, where there is diagnostic uncertainty, it would be appropriate to consider seeking a referral for a second opinion from a more expert team. The GDG consensus was that the circumstances for seeking a referral included diagnostic uncertainty or a disagreement about the diagnosis within the ASD team or between the team and parents or carers. This would increase the likelihood of a firm diagnosis of ASD or another condition, speed up the initiation of appropriate intervention and reduce stress to the child and/or family. Referral is also warranted where the ASD team does not have access to the necessary expertise for a child with a complex co-existing condition, and uncertainty arising from a child or young person's failure to respond as expected to ASD specific support and interventions as these skills could not be expected to be available in every ASD Team. The GDG recommended that where there is remaining diagnostic uncertainty but a referral on is judged by the ASD Team not to be warranted, it may be beneficial to repeat the assessment after a period of time (not more than 6 months), consider observing the child in a different setting and that in the interim needs-based interventions should be provided. The GDG did not identify any potential harm in putting in place a plan to refer or monitor for children not immediately diagnosed with ASD.
Trade-off between net health benefits and resource use	There was no published evidence identified for this question that reported the cost effectiveness of referral to a more expert team in the case of diagnostic uncertainty, or monitoring and reviewing children who are not immediately diagnosed but not referred. The potential costs associated with this are the additional time required for professionals to make contact with other health care professional involved with the care of the child/young person and agencies outside the NHS. The GDG did not put a figure on the costs as there were no data on the proportion of children not diagnosed with ASD who would require referral or monitoring. There may be savings as a result of greater acceptance by families of the lack of a clear diagnosis of ASD, and greater welfare of the child as of referral to a more expert team, or enhanced monitoring over time, although the scale of these savings could not be estimated. It is the GDG's view that referral and enhanced monitoring of children with an uncertain diagnosis would be a cost effective used of NHS resources.
Quality of evidence	No evidence was identified that addressed this question
Other considerations	None

Recommendations	48. If after the ASD diagnostic assessment there is uncertainty about the diagnosis: • consider keeping the child or young person under review • carry out another ASD diagnostic assessment within 6 months • take account of information arising from any needs-based interventions provided in the interim. 49. If during the ASD diagnostic assessment, there were discrepancies between reported signs or symptoms and the findings of the ASD observation in the clinic setting, consider: • gathering additional information from other sources • carrying out further ASD-specific observation(s) in a different setting such as the school or nursery. 50. Consider obtaining a second opinion, including referral to a specialised tertiary ASD team if necessary, if after assessment there is: • continued uncertainty about the diagnosis • disagreement about the diagnosis within the ASD team • disagreement with parents or carers about the diagnosis • a lack of local access to particular skills and competencies required to reach a diagnosis in a child or young person who has a complex comorbidity, such as a severe sensory or motor impairment or mental health problem • a failure to respond as expected to any therapeutic interventions being provided.

1

6 Differential diagnosis

6.1 Introduction

Many neurodevelopmental and psychiatric disorders may present with symptoms that suggest the possibility of ASD but which are not ASD. These can be described as the differential diagnoses of ASD. It is essential to consider the differential diagnoses at each stage of the ASD pathway – when the possibility of ASD first arises and consideration is being given to referral to an ASD Team (see chapter 3 on Recognition), when the ASD Team is considering whether to proceed with an ASD-specific Diagnostic Assessment (see chapter 4 on Following referral), when undertaking an ASD-specific Diagnostic Assessment and when considering the diagnosis on completion of the assessment (see chapter 5 on Diagnostic assessment).

If there are concerns about a child or young person's development or behaviour and especially if the possibility of ASD has been raised, parents are anxious to know without delay what the nature of the problem may be. It is important to establish an accurate diagnosis, whether that be ASD or an alternative condition. An inaccurate diagnosis of ASD may result in the use of an inappropriate treatment strategy and may cause anxiety and distress to the child or young person and their parents/carers. This chapter addresses the most important disorders to be considered in children and young people presenting with possible ASD and how they may be differentiated from ASD. A differential diagnosis may also be a co-existing condition (see chapter 7 on Co-existing conditions).

Clinical Question:
What are the most important differential diagnoses of ASD?
What features observed during diagnosis reliably differentiate other conditions from ASD?

6.2 Identifying differential diagnoses

6.2.1 Methodological approach

To develop a shortlist of differential diagnoses, the GDG had to specify the criteria for 'important differential diagnoses' as this was the clinical question the review had to address. For the purposes of the review, they agreed 'important' should be defined as (a) the most common differential diagnoses and (b) those with a high impact for the child and/or family. However, since there is no standard index to reflect severity of impact, it was not possible to generate an evidence-based list of the highest impact differential diagnoses. The decision was therefore made only to review evidence for the most common differential diagnoses. GDG consensus discussion led to the identification of other differential diagnoses which were added to the list of diagnoses in terms of their clinical importance and likely impact.

The subgroups identified were the populations identified in the studies included in the review. The subgroups differ in how the children were selected for inclusion which depended on the type of clinic a child was referred to and therefore what they were referred for (suspicion of ASD, suspicion of another condition or a more general concern, or children referred because they had a positive screening result for ASD in a previous assessment). The prevalence of ASD will be different across these population groups.

Data for autism is reported separately from ASD as it was expected that some co-existing conditions would have different prevalence rates for each category and so it would not be appropriate to pool these data.

The outcome for these studies was the prevalence of the condition. The pooled percentage was calculated by combining the prevalence result of several studies that look at the same differential diagnosis of ASD, weighted by the size of each study. The value of I^2 indicates the heterogeneity between studies: the larger the value of I^2, the higher the inconsistency rate. However, where studies are of very low quality, the value of I^2 does not have to be reported (see the methodology section in chapter 2 on Development of the guideline]

After an initial search of 25,787 articles in the overall search, 56 were selected for on title and abstract and the papers requested for full review. Of these, 19 studies were eligible for inclusion based on the following criteria:

Population: Children or adolescents under 19 years referred for assessment because of clinically suspected ASD, a positive ASD screening test result, with developmental concerns or with behavioural concerns

Reference test: Final diagnosis of ASD made according to DSM-IV or ICD-10 criteria.

Outcomes: Prevalence of diagnoses other than ASD

A list of the 37 excluded studies and the reasons for exclusion is found in Appendix G – Tables of excluded studies).

The prevalence of alternative diagnoses were analysed and the results are presented for children with autism in an evidence profile (section 6.2.3) and a supporting evidence statement (section 6.2.4). The prevalence of coexisting conditions in children with ASD is in an evidence profile (section 6.2.5) and a supporting evidence statement (section 6.2.6).

Subgroup analyses are reported in relevant evidence statement in each evidence profile and statement after the complete analysis for all studies identified.

6.2.2 Description of included studies

Nineteen studies were included in this review. These studies were carried out in the Australia65;66;136, Canada137, Germany138, Israel139, Italy140, Japan141, Norway142, Sweden69;143, the Netherlands144;145, the USA72;73;107;146 and the UK147;148. All were uncontrolled observational and were graded as very low quality. Eight of the studies66;73;107;139;141;144;146;148 were in a preschool population, one study147 in primary school age children and none in secondary school age children. Five used a mixed population of preschool and primary school age children65;136;137;140;143, two primary and secondary69;145 while three included children or young people of all ages72;138;142.

Only one study reported145 the range of IQ. Four studies72;136;138;146 reported mean IQ scores but the proportion of children with intellectual disability was not reported. Four studies66;69;139;142 reported the proportion of children with intellectual disability but no separate outcomes were provided for each IQ group. Intellectual ability was not reported in the remaining studies.

6.2.3 Evidence profile - autism

Table 6.1 reports the prevalence of each alternative diagnosis in children with suspected autism. The conditions are reported under five categories identified by the GDG. Limitations, inconsistencies and indirectness are not reported in the table because the quality is very low.

1 **Table 6.1: Prevalence of alternative diagnoses in children with suspected autism**

	Quality assessment						Summary of findings		
							Number		Prevalence
	Studies	Design	Limitations	Inconsistency	Indirectness	Quality	Autism	Non-autism	Pooled % (95% CI)
Prevalence of alternative diagnoses in children with suspected autism									
ALL STUDIES									
Neuropsychiatric									
Behaviour problem[143]	1	Uncon obs*	NA	NA	NA	Very low	9	3	8
ADHD[143]	1	Uncon obs	NA	NA	NA	Very low	9	3	8
Emotional difficulties	No studies have been identified.								
Neurodevelopmental									
Language problem	No studies have been identified.								
Developmental disorder/delay[143 107]	2	Uncon obs	NA	NA	NA	Very low	35	7	6 (1, 15)
Neurological									
Rett's syndrome[107]	1	Uncon obs	NA	NA	NA	Very low	26	4	10
Medical									
Motor problem[107]	1	Uncon obs	NA	NA	NA	Very low	26	4	3
Other									
Abuse/neglect	No studies have been identified.								
SUBGROUP ANALYSIS - CHILDREN REFERRED ON SUSPICION OF AUTISM ONLY									
Neuropsychiatric									
Behaviour problem[143]	1	Uncon obs*	NA	NA	NA	Very low	9	3	8
ADHD[143]	1	Uncon obs	NA	NA	NA	Very low	9	3	8
Neurodevelopmental									
Developmental disorder/delay[143 107]	2	Uncon obs	NA	NA	NA	Very low	35	7	6 (1, 15)
Neurological									
Rett's syndrome[107]	1	Uncon obs	NA	NA	NA	Very low	26	4	10
Medical									
Motor problem[107]	1	Uncon obs	NA	NA	NA	Very low	26	4	3
Other									

Abuse/neglect	No studies have been identified.
SUBGROUP ANALYSIS - CHILDREN REFERRED FOR DEVELOPEMENTAL PROBLEMS	
No study met the inclusion criteria for this review	
SUBGROUP ANALYSIS – CHILDREN REFERRED FOR BEHAVIOURAL PROBLEMS	
No study met the inclusion criteria for this review	
SUBGROUP ANALYSIS - CHILDREN REFERRED WITH POSITIVE ASD SCREENING RESULTS	
No study met the inclusion criteria for this review	

1

6.2.4 Evidence statements –autism

Complete analysis – All studies

Neuropsychiatric problems

Two neuropsychiatric conditions [ADHD and behaviour problem] in children with suspected autism were identified from evidence. One study providing very low quality evidence reported on the prevalence of ADHD and one on behaviour problems. The prevalence for both is reported as 8%.

Neurodevelopmental problems

Only one neurodevelopmental diagnosis [developmental disorder/delay] in children with suspected autism was identified from evidence. Two studies providing very low quality reported the prevalence of intellectual disability. The pooled prevalence is reported as 6%.

Neurological problems

Only one neurological diagnosis [Rett's syndrome] was identified in children with suspected autism. Only one study providing very low quality evidence was identified. The prevalence is reported as 10%.

Medical problems

Only one medical diagnosis [a motor problem] in children with autism was identified from evidence. One study providing very low quality was identified. The prevalence for motor problem is reported as 3%.

Subgroup analysis - Children referred on suspicion of autism only

Neuropsychiatric problems

Two neuropsychiatric diagnoses [behaviour problem and ADHD] were identified from evidence. One study providing low quality evidence reported the prevalence of behaviour problem and one on ADHD. The prevalence for each is reported as 8%.

Neurodevelopmental problems

Only one neurodevelopmental diagnosis was identified from evidence. Two studies providing low quality evidence reported the prevalence of developmental disorder/delay. The pooled prevalence is reported as 6%.

Neurological problems

Only one neurological diagnosis was identified from evidence, which is Rett's syndrome. One study providing low quality evidence reported the prevalence of Rett's syndrome. The pooled prevalence for Rett's syndrome is reported as 10%.

Medical problems

Only one medical diagnosis was identified from evidence, which is a motor problem. One study providing low quality evidence reported the prevalence of a motor problem. The pooled prevalence for motor problem is 3%.

Subgroup analysis - Children and young people referred for developmental problems only

No study met the inclusion criteria for this review.

Subgroup analysis - Children and young people referred for behavioural problems only

No study met the inclusion criteria for this review.

Subgroup analysis - Children and young people referred for positive screening results only

No study met the inclusion criteria for this review.

6.2.5 Evidence to recommendations

See section 6.3.5

6.2.6 Evidence profile - ASD

Table 6.2 is the prevalence of each differential diagnosis in children with suspected ASD

Table 6.2: Prevalence of alternative diagnoses in children with suspected ASD

	Quality assessment						Summary of findings		
							Number		Prevalence
	Studies	Design	Limitations	Inconsistency	Indirectness	Quality	ASD	Non-ASD	Pooled % (95% CI)
Prevalence of alternative diagnosis in children and young people with suspected ASD									
ALL STUDIES									
Neuropsychiatric									
Behaviour problem[69;73]	2	Uncon obs	NA	NA	NA	Very low	75	117	24 (1, 80)
ADHD[72;138;140;141;144;145;147]	7	Uncon obs	NA	NA	NA	Very low	723	329	14 (6, 24)
Emotional difficulties[72;138;142]	3	Uncon obs	NA	NA	NA	Very low	551	204	6 (2, 10)
Neurodevelopmental									
Language problem[65;66;72;73;136;138-140;142;144;146;148]	12	Uncon obs	NA	NA	NA	Very low	946	780	21 (5, 43)
Developmental disorder/delay[65;66;69;72;73;137;138;141;142;144;146-148]	13	Uncon obs	NA	NA	NA	Very low	1041	713	15 (8, 23)
Neurological									
Down syndrome[72]	1	Uncon obs	NA	NA	NA	Very low	438	151	3
Foetal alcohol syndrome[72]	1	Uncon obs	NA	NA	NA	Very low	438	151	3
Medical									
Motor problem[73]	1	Uncon obs	NA	NA	NA	Very low	54	28	2 (2, 2)
Other									
Abuse/neglect[147]	1	Uncon obs	NA	NA	NA	Very low	13	37	26 (26, 26)
SUBGROUP ANALYSIS - CHILDREN REFERRED ON SUSPICION OF ASD ONLY									
Neuropsychiatric									
ADHD[72;138;140;143]	3	Uncon obs	NA	NA	NA	Very low	606	189	6 (2, 13)
Behaviour problem[73]	1	Uncon obs	NA	NA	NA	Very low	54	28	4
Emotional difficulties[72;138]	2	Uncon obs	NA	NA	NA	Very low	543	187	4 (3, 6)
Selective mutism[73]	1	Uncon obs	NA	NA	NA	Very low	54	28	1 (1, 1)

Neurodevelopmental									
Language problem[72;73;136;138;140;146]	6	Uncon obs	NA	NA	NA	Very low	701	284	9 (3, 17)
Developmental disorder/delay[72;73;138;146]	4	Uncon obs	NA	NA	NA	Very low	616	267	5 (3, 6)
Neurological									
No study met the inclusion criteria for this review									
Medical									
No study met the inclusion criteria for this review									
Other									
No study met the inclusion criteria for this review									
SUBGROUP ANALYSIS - CHILDREN REFERRED FOR DEVELOPEMENTAL PROBLEMS									
Neuropsychiatric									
Emotional difficulties[142]	1	Uncon obs	NA	NA	NA	Very low	8	17	16 (16, 16)
Neurodevelopmental									
Language problem[65;66;139;142]	4	Uncon obs	NA	NA	NA	Very low	207	429	41 (2, 89)
Developmental disorder/delay[65;66;137;142]	4	Uncon obs	NA	NA	NA	Very low	342	245	28 (21, 36)
Neurological									
No study met the inclusion criteria for this review									
Medical									
No study met the inclusion criteria for this review									
Other									
No study met the inclusion criteria for this review									
SUBGROUP ANALYSIS – CHILDREN REFERRED FOR BEHAVIOURAL PROBLEMS									
Neuropsychiatric									
Behaviour problem[69]	1	Uncon obs	NA	NA	NA	Very low	21	89	53 (53, 53)
ADHD[145]	1	Uncon obs	NA	NA	NA	Very low	75	40	35 (35, 35)
Neurodevelopmental									
Developmental disorder/delay[69]	1	Uncon obs	NA	NA	NA	Very low	21	89	28 (28, 28)
Neurological									
No study met the inclusion criteria for this review									
Medical									

No study met the inclusion criteria for this review									
Other									
No study met the inclusion criteria for this review									
SUBGROUP ANALYSIS - CHILDREN REFERRED WITH POSTITIVE ASD SCREENING RESULTS									
Neuropsychiatric									
ADHD[141;144;147]	3	Uncon obs	NA	NA	NA	Very low	42	100	17 (11, 23)
Tourette syndrome[147]	1	Uncon obs	NA	NA	NA	Very low	13	37	4 (4, 4)
Neurodevelopmental									
Language problem[144;148]	2	Uncon obs	NA	NA	NA	Very low	38	67	24 (17, 33)
Developmental disorder/delay[141;144;147;148]	4	Uncon obs	NA	NA	NA	Very low	62	112	12 (6, 19)
Neurological									
No study met the inclusion criteria for this review									
Medical									
No study met the inclusion criteria for this review									
Other									
Abuse/neglect[147]	1	Uncon obs	NA	NA	NA	Very low	13	37	26 (26, 26)

1 Uncon obs: Uncontrolled observational study, such as case series.

2

6.2.7 Evidence statement - ASD

Complete analysis – All studies

Neuropsychiatric problems

Six neuropsychiatric conditions [behaviour problem, ADHD, emotional difficulties, Tourettes syndrome, selective mutism and attachment disorder] were identified from evidence. Only data of the most prevalent differential diagnosis: abuse/neglect, behaviour problem, ADHD and emotional difficulties were reported here.

Three studies providing very low quality evidence reported on the prevalence of ADHD in children and young people suspected of having ASD, eight on ADHD and three on emotional difficulties. The pooled prevalence is 24%, 14% and 6% respectively.

Neurodevelopmental problems

Three neurodevelopmental diagnoses [language problem, developmental disorder/delay and disintegrative disorder] were identified from evidence. Only data of the most prevalent differential diagnosis: language problem and developmental disorder/delay are reported here.

Twelve studies providing very low quality evidence reported on the prevalence of language problem in ASD-suspicious children and young people, and fifteen on developmental disorder/delay. The pooled prevalence is 21% and 15% respectively.

Neurological problems

Two neurological diagnoses [Down syndrome and foetal alcohol syndrome] were identified from evidence. Only data of the most prevalent differential diagnosis, Down syndrome, is reported here. The evidence was very low quality and reported a prevalence of 3%.

Medical problems

Only one medical diagnosis was identified from evidence which is motor problem. One study provides very low quality evidence and reported a prevalence of 2%.

Other

One diagnosis was identified that did not fit the other categories, which was abuse/neglect. The study provides very low quality evidence. It reported the prevalence of abuse/neglect in children and young people suspected of having ASD of 26%.

Subgroup analysis - Children referred on suspicion of ASD only

Neuropsychiatric problems

Six neuropsychiatric diagnoses [ADHD, behaviour problem emotional difficulties, Tourette syndrome, selective mutism and attachment disorder] were identified from evidence. Only data of the most prevalent diagnoses, ADHD, behaviour problem, emotional difficulties and selective mutism, are reported here.

Three studies were identified for ADHD, one on behaviour problem, two on emotional difficulties and one on selective mutism. The evidence was very low quality. The pooled prevalence was 6%, 4%, and 1% respectively.

Neurodevelopmental problems

Three neurodevelopmental diagnoses [language problem, developmental disorder/delay and disintegrative disorder] were identified from evidence. Only data of the most prevalent differential diagnosis: language problem and developmental disorder/delay were reported here.

Six studies were identified for a language problem, and four on developmental disorder/delay. All were very low quality. The pooled prevalence was 9% and 5% respectively.

Neurological problems

No study met the inclusion criteria for this review.

Medical problems

No study met the inclusion criteria for this review.

Other

No study met the inclusion criteria for this review.

Subgroup analysis - Children referred on suspicion of developmental problems only

Neuropsychiatric problems

Only one neurological diagnosis was identified from evidence, which was emotional difficulty. The data was reported here.

One study reported on the prevalence of emotional difficulties. The evidence was very low quality. The pooled prevalence for emotional difficulties is 16%.

Neurodevelopmental problems

Four neurodevelopmental diagnosis were identified from evidence. Only data of the most prevalent differential diagnosis: language problem and developmental disorder/delay were reported here.

Four studies were identified for a language problem in children and young people referred for developmental problems, and four on developmental disorder/delay. The evidence was very low quality. The pooled prevalence was 41% and 28% respectively.

Neurological problems

No study met the inclusion criteria for this review.

Medical problems

No study met the inclusion criteria for this review.

Other

No study met the inclusion criteria for this review.

Subgroup analysis - Children referred on suspicion of behavioural problems only

Neuropsychiatric problems

Only two neuropsychiatric diagnoses was identified from evidence, which are behaviour problem and ADHD. The data of both diseases was reported here.

One study reported on the prevalence of behaviour problem in children and young people referred for behaviour problems, and one on ADHD. The evidence was very low quality. The pooled prevalence was 53% and 35% respectively.

Neurodevelopmental problems

Only one neurodevelopmental diagnosis of ASD was identified from evidence, which is developmental disorder/delay. The study reported on the prevalence of emotional difficulties in children and young people referred for behaviour problems. The evidence was very low quality. The pooled prevalence was 28%.

Neurological problems

No study met the inclusion criteria for this review.

Medical problems

No study met the inclusion criteria for this review.

Other

No study met the inclusion criteria for this review.

Subgroup analysis - Children and young people referred for positive screening results only

There were four studies looking at children referred after a positive result in a screening test for ASD. They each used a different screening test - ESAT, YACHT-18, CAHT and ASSQ.

Neuropsychiatric problems

Two neuropsychiatric diagnoses, ADHD and Tourette's syndrome] were identified from evidence.

Three studies reported on the prevalence of ADHD, and one on Tourette syndrome. The evidence was very low quality. The pooled prevalence was 17% and 4% respectively.

Neurodevelopmental problems

Two neurodevelopmental diagnoses [language problem and developmental disorder/delay] were identified from evidence.

Two studies reported on the prevalence of language problem, and four on developmental disorder/delay. The evidence was very low quality. The pooled prevalence was 24% and 12% respectively.

Neurological problems

No study met the inclusion criteria for this review.

Medical problems

No study met the inclusion criteria for this review.

Other

The study reported the prevalence of abuse/neglect. The evidence was very low quality. It reported the prevalence of 26%.

The evidence to recommendations section is at the end of the chapter.

6.2.8 Evidence to recommendations

See section 6.3.5

6.3 Identifying features that differentiate ASD from other conditions

6.3.1 Methodological approach

After an initial search of 25,787 articles in the overall search, 28 were selected for on title and abstract and the papers requested for full review. None of these papers have been included because all samples used in those studies have already been diagnosed as ASD or an alternative diagnoses before the test; so the accuracy of the differentiating features used in those studies would be falsely increased. Therefore GDG consensus has been used to answer this clinical question.

A list of the 28 excluded studies and the reasons for exclusion is found in Appendix G – tables of excluded studies.

Consequently, the GDG agreed to develop a table of features that differentiate ASD from the conditions identified in the previous section. This was developed from their own clinical knowledge and experience. A description of this process is reported in the evidence to recommendations section at the end of the chapter

6.3.2 Description of included studies

No studies were included.

6.3.3 Evidence profiles

No evidence.

6.3.4 Evidence profiles

No evidence.

6.3.5 Evidence to recommendations

Relative value placed on the outcomes considered	The GDG chose two outcomes to define whether a condition was important in the differential diagnosis of ASD: (1) the prevalence of that condition in children and young people with signs and symptoms considered suggestive of ASD, and (2) the impact of that condition on the child and parents or carers.
Trade-off between clinical benefits and harms	The GDG considered that the identification of conditions important in the differential diagnosis was relevant throughout the ASD pathway and was an essential element of the ASD-specific Diagnostic Assessment. The benefits to the child and family are the accurate and early recognition of those alternative conditions, potentially leading to timely and appropriate management. The potential harms from recognising a condition other than ASD might include distress to the child, young person or family on being informed of the diagnosis. The diagnosis might prove of greater concern to them than a diagnosis of ASD – for example if it emerged that the child or young person's condition was associated with significant morbidity or mortality. However, in general an accurate diagnosis is beneficial and may facilitate specific appropriate (for example treatment of epileptic encephalopathy might alleviate language regression) while avoiding ineffective treatment regimens. The GDG consensus was that the advantages of accurate diagnosis through consideration of important conditions clearly outweighed any disadvantages.
Trade-off between net health benefits and resource use	Health economic analysis could not be undertaken for this question due to the lack of evidence. The costs and benefits of identifying other diagnoses during the ASD specific assessment were considered. The GDG view is that although there would be an additional cost associated with establishing a diagnosis other than ASD (the resources needed to undertake an appropriate clinical review for relevant conditions in the differential diagnosis), this would be an effective use of clinical time in identifying other important conditions.
Quality of evidence	The evidence base for the various conditions to be considered in the differential diagnoses of ASD is not large and the quality of the evidence was low. The grouping of conditions into categories lead to some difficulties in comparing outcomes across the available studies. Sub group analysis by "reason for referral" reduced heterogeneity. But as the confidence intervals were still wide for the prevalence data for each group of conditions, the interpretation of the data was not straightforward. The GDG was concerned about the bias in these studies, for example due to pre-selection of samples and missing sample recruitment information. This meant that these studies were not robust and did not provide credible and clinically relevant data on the important conditions for consideration. It was not easy to determine how the findings should be applied in clinical practice.
Other considerations	The GDG recognised the importance of considering the differential diagnosis in any child or young person presenting with a developmental or behavioural concern, including those in whom ASD was suspected.

	The GDG concluded that the available studies did not adequately inform the need for a satisfactory and clinically relevant list of conditions to be considered in the differential diagnosis. They therefore chose to develop a list, based on in part on the findings from the evidence search but also on their clinical knowledge and experience. In doing so they also decided that it was inappropriate to rank the alternative diagnoses based on the quoted prevalence rates. The GDG also noted that studies of 'abuse/neglect' included information about attachment disorder. The diverse expertise and experience of the GDG allowed development of a list of conditions reflecting the wide experience of the membership. The list would take account of the frequency with which a condition presented as possible ASD and also on the clinical importance of recognising some specific disorders. The GDG agreed that this list of conditions to be considered in the differential diagnosis would facilitate accurate and timely recognition of those conditions with a similar presentation to ASD. The GDG also developed advice to support the decision-making process in differentiating between alternative diagnoses with similar features, This table does not form part of the main recommendations for this guideline. It is the result of GDG consensus and is designed to be referred to by health care professionals at different stages in the ASD pathway. For each condition listed, the characteristic key presenting features are specified. The table also shows the ways in which each condition typically differs from ASD. It covers key clinical features; the assessments and investigations that should have formed a part of the child's overall assessment, and highlights the relevant components or outcomes of those assessments that would contribute to the process of differentiation. The tables have been developed based on the combined clinical expertise of the GDG. While they are not informed by any systematic review of published literature, the GDG took note of the studies available in the evidence in which differentiating features were reported. [See appendix K] The GDG acknowledged the particular difficulties in differential diagnosis as the neuropsychiatric and developmental disorders can, and frequently do, co-exist with ASD. Attachment disorders present particular challenges. In 'looked after children', early developmental history, crucial in ASD diagnosis, may be difficult to obtain; re-examination over time in a different environment may clarify a diagnosis that is often dependent on experienced clinical judgement. Particular expertise may also be required for cases such as deafness and blindness in recognising what signs and symptoms can be attributed to the sensory impairment and what falls outside that attribution. In these situations, the GDG has recommended access to such expertise that may involve further and tertiary opinion from other professionals. Conditions such as epilepsy are more common in autism and need to be recognised as they require specific treatment. Epileptic encephalopathy is a particular clinical concern if there is a history of regression of developmental skills and has led to anxiety among clinicians about how to decide what tests should be done. A careful history noting whether autism is the presentation or whether there is cognitive regression plus motor impairment or other physical features in a child of two years or whether it is mainly language regression in a child of age three years are helpful pointers to the need for further investigations. Of course a child with physical symptoms and abnormal signs including seizures, requires further

	investigation beyond the scope of this guideline. Language delay, cognitive delay, motor inco-ordination or behavioural concerns in children and young people are all common presentations of ASD but are also all common neurodevelopmental problems and disorders in their own right. While there is overlap of symptoms and individual test scores by themselves (for example language or motor coordination test scores may not differentiate these conditions), the process of doing such tests and considering the particular diagnostic features of ASD by a professional with expertise, will help to make an accurate diagnosis. Intellectual disorder (ID) is the commonest co-existing condition with ASD and a difficult differential diagnosis in a young child. The evidence shows that the validity of the ASD specific tools for eliciting the history from an informant is limited below a mental age of 18 months (chapter 5). ASD diagnosis is often delayed in those with ID and yet from the treatment/intervention point of view, distinguishing the particular way that a child with ASD learns and communicates has important implications for child and family. The particular features of co-existing ASD in a child with ID may suggest an aetiological diagnosis for the ID, for example Fragile X (see chapter 7 on Co-existing conditions). No other equalities considerations were identified for this specific clinical question.
Recommendations	39. Consider the following differential diagnoses for ASD and if an alternative diagnosis is suspected carry out an appropriate assessment, including referral to other appropriate services: • neurodevelopmental disorders: specific language delay or disorder intellectual disability or global developmental delay developmental coordination disorder (DCD) • neuropsychiatric disorders: attention deficit hyperactivity disorder (ADHD) mood disorder anxiety disorder attachment disorders oppositional defiant disorder (ODD) conduct disorder obsessive-compulsive disorder (OCD) • conditions in which there is developmental regression: Rett's syndrome epileptic encephalopathy (EE) • other conditions: severe hearing impairment severe visual impairment (blind) maltreatment

	selective mutism.

7 Assessment of co-existing conditions

7.1 Introduction

It is important to ensure that both ASD and any relevant co-existing conditions are identified at the time of during the assessment. There are a number of disorders or diagnoses that co-occur in ASD at higher than expected rates and these are referred to as co-existing conditions. This differentiates them from other common health problems and conditions that effect other children and young people. They may also in some instances be regarded as risk factors. (see chapter 4 on Following referral) and may also be differential diagnosis (see chapter 6 on Differential diagnosis). The reasons why some disorders co-occur more commonly in people with ASD is not always well understood.

The importance of considering co-existing conditions in addition to the ASD diagnosis is that they may either be treatable in their own right or may influence the long-term outcome for the child/young person. When there is a focus on the diagnosis of an ASD, it is possible to neglect other diagnosable conditions.

The most important co-existing conditions are those that occur most frequently, have a high impact on present quality of life, or impact on the future development of the child or young person.

This chapter focuses on the co-existing conditions that any health care professional should think about when a child or young person when he/she is undergoing an ASD diagnostic assessment.

Clinical Question

Which are the common coexisting conditions that should be considered as part of assessment?

- Neurodevelopmental: speech and language problems, intellectual disability, coordination, learning difficulties in numeracy and literacy
- Neuropsychiatric disorders such as ADHD, OCD, anxiety, depression, Tourette's, Tic disorders;
- Medical problems such as functional gastrointestinal problems, tuberous sclerosis, neurofibromatosis

7.1.1 Methodological approach

The GDG aimed to review the evidence with respect to both symptoms and diagnosed disorders. The range of prevalence rates from different studies are reported.

An initial list (based on the literature reviews) of co-existing conditions (symptoms and diseases) was provided to the GDG who were asked to identify the most common coexisting conditions from this list and to add to this list if, by GDG consensus, important coexisting conditions were not represented in the evidence. In most cases, only the prevalence of diagnosed disorders will be reported. For example, if there were some

studies reported the prevalence of ADHD symptom in ASD children, not diagnosed ADHD disease, then the prevalence data won't be used for meta-analysis. The only three exceptions are: gastrointestinal problems, sleeping problem and intellectual disability.

Gastrointestinal problems and sleeping problem are considered to be important coexisting conditions of ASD by the GDG. However few studies have reported the prevalence of diagnosed gastrointestinal disease or sleeping problem. Therefore the GDG agreed that prevalence of gastrointestinal symptoms and sleeping problem symptoms could be used as proxies for prevalence of diagnosed gastrointestinal and sleeping problem.

In considering the evidence on global intellectual disability, the studies provided data on the proportion of children/young people with IQ<70. Current definitions of intellectual disability suggest two criteria: low cognitive ability, usually measured as IQ<70 and impairment in adaptive functioning. Virtually all children/young people with ASD show impairment in adaptive functioning and the GDG therefore believe it is reasonable to include studies reporting on those with IQ<70. A list of the 145 excluded studies with the reasons for exclusion is found in Appendix G – Tables of excluded studies.

After an initial search of 25,787 articles in the overall search, 193 were selected on title and abstract and the papers requested for full review. Four of these were unobtainable so 189 papers were reviewed in full text. In all, 38 studies were eligible for inclusion based on the following criteria:

Population: Children and young people with a diagnosis of ASD according to DSM-IV or ICD-10 criteria

Index: Coexisting conditions of ASD:

- Neuropsychiatric condition
- Neurodevelopmental condition
- Neurological condition
- Other medical condition

Outcomes: Prevalence of other medical (including psychiatric) disorders

A full list of the 151 excluded studies and the reason for exclusion is available (see Appendix G – tables of excluded studies).

The data for the prevalence of coexisting conditions in children with autism has been analysed and presented in an evidence profile (section 7.4) and a supporting evidence statement (section 7.5). The prevalence of coexisting conditions in children with ASD is in an evidence profile (section 7.6) and a supporting evidence statement (section 7.7). The data for autism from ASD has been separated as it was expected that some co-existing conditions would have different prevalence rates for each category and so it would not be appropriate to pool these data.

7.1.2 Description of included studies

In total, 38 studies were included in the review. All of the studies were uncontrolled observational in design and were graded as very low. The studies were carried out in Brazil [149], Canada [150], Czech Republic [151], Finland [152;153], France [154-156], Italy [157-159], Israel [160], Netherland [161], Japan [162;163], Portugal [164], Sweden [165], the U.K [166-170], the U.S.A [171-184], Turkey [185] and Venezuela [186]. One study was conducted in both Europe and the U.S.A[187].

One study[178] included children of preschool age and 3 studies[157;176;183] included primary school age. No study dealt exclusively with children of secondary school age. Seven studies[150;155;165;166;171;184;186] included mixed pre-school and primary school age children; thirteen studies[149;153;154;156;158;161;164;167;170;173-175;177] included mixed primary and secondary school; and twelve studies [151;152;159;160;163;168;169;172;179;181;182;185] included all age groups. Two studies [180;187] studies included adults (age>19). Age was not reported in the remaining studies.

Only one study[177] reported mean IQ scores but the proportion of children with intellectual disability was not reported. Fourteen studies[151;152;155;156;162;164;167;168;175;180;183-185;187] reported the proportion of children with intellectual disability but no separate outcome was provided for each IQ group. One study[159] only included children with intellectual disability while three studies[150;153;165] excluded children with intellectual disability. Intellectual ability was not reported in the remaining studies.

Further details regarding individual studies are presented within the evidence tables (see Appendix H – tables of included studies).

7.1.3 Evidence profile for autism

Table 7.1 summarises the study characteristics for each common coexisting condition that should be looked for as part of an ASD assessment. The table only reports prevalence data for conditions which the GDG identified a priori as important. The data could not be used to help to identify the conditions that were important because of the serious problems of heterogeneity that were identified.

Evidence statements report the prevalence data only for those conditions the GDG considered the most important coexisting conditions given the number and range of conditions identified in the literature, and that some conditions and symptoms are considered by the GDG elsewhere in the guideline (Chapter 1, Signs and Symptoms, Chapter 8 Medical Investigations).

Table 7.1 Prevalence of each co-existing condition in children or young people with autism

Coexisting condition	Quality assessment						Summary of findings		
							Sample size		Prevalence (Pooled, 95% CI)
	Studies	Design	Limitations	Inconsistency	Indirectness	Quality	Cases	Non-cases	
PREVALENCE OF EACH CO-EXISTING CONDITION IN CHILDREN OR YOUNG PEOPLE WITH AUTISM									
NEUROPSYCHIATRIC									
ADHD[175 149]	2	Uncon obs[#]	NA	NA	NA	Very low	43	74	41 (21, 63)
Self-injurious behaviour[155]	1	Uncon obs	NA	NA	NA	Very low	109	113	49
Anxiety[175]	1	Uncon obs	NA	NA	NA	Very low	63	38	62
ODD[175]	1	Uncon obs /	NA	NA	NA	Very low	6	80	7
Tic	No studies were identified.								
OCD[175]	1	Uncon obs	NA	NA	NA	Very low	35	59	37
Depression[175]	1	Uncon obs	NA	NA	NA	Very low	14	95	13
Seizures[152]	1	Uncon obs	NA	NA	NA	Very low	34	153	18
Tourette syndrome	No studies were identified.								
Conduct disorder	No studies were identified.								
NEURODEVELOPMENTAL									
Intellectual disability[152;155-157;162;168;175;183;184]	9	Uncon obs	NA	NA	NA	Very low	1618	414	76 (61, 89)
NEUROLOGICAL									
Cerebral palsy[152;156;169;184]	4	Uncon obs	NA	NA	NA	Very low	63	1318	5 (4, 6)
MEDICAL									
Sleep problem[160;174;183]	3	Uncon obs	NA	NA	NA	Very low	146	251	37 (11, 68)
Gastrointestinal problem[166]	1	Uncon obs	NA	NA	NA	Very low	3	93	3
Epilepsy[152;155-157;168;169;184]	7	Uncon obs	NA	NA	NA	Very low	342	1359	24 (8, 46)
A motor problem[152]	1	Uncon obs	NA	NA	NA	Very low	25	162	13
Vision deficits[152;156;184]	3	Uncon obs	NA	NA	NA	Very low	65	1283	7 (0, 26)
Auditory deficits[152;156;184]	3	Uncon obs	NA	NA	NA	Very low	29	1319	3 (0, 9)

Note:#: Uncon obs: Uncontrolled observational study, such as case series.

7.1.4 Evidence statements for autism

Neuropsychiatric conditions

Twelve neuropsychiatric coexisting conditions of autism [ADHD, adjustment disorder, aggression problem, anxiety, attention problem, bipolar disorder, depression, emotionally reactive, OCD, ODD, self-injurious behaviour, somatic complaints syndrome were identified from evidence. Only studies examining the prevalence of ADHD, self-injurious behaviour, anxiety, ODD, tic, OCD, depression and seizures are reported.

Two studies providing very low quality evidence reported on the prevalence of ADHD in autism children and young people, one on self-injurious behaviour, one on anxiety, one on ODD, one on OCD, one on depression and one on seizures. The prevalence of ADHD in children with autism was 41% (95%CI 21, 63), for self-injurious behaviour 49%, for anxiety 62%, for ODD 7%, depression 13% and for seizures 18%. No studies were identified for tics, Tourette's syndrome or conduct disorder in children with autism..

Neurodevelopmental conditions

Three neurodevelopmental coexisting conditions of autism [language problems, intellectual disability, regression and restricted interest] were identified from evidence. Only studies examining the prevalence of intellectual disability are reported. Nine studies providing very low quality evidence reported on the prevalence of intellectual disability in children with autism. The pooled prevalence was 776% (95%CI 61, 89)

Neurological conditions

Four neurological coexisting conditions of autism [cerebral palsy, seizures, hydrocephalus, meningitis] were identified from evidence. Only studies examining the prevalence of cerebral palsy are reported.

Four studies examined the prevalence of cerebral palsy in children with autism. The pooled prevalence was 5% (95%CI 4, 6)

Medical conditions

Eleven medical coexisting conditions of autism [Auditory deficits, epilepsy, gastrointestinal problems, chromosomal abnormalities, congenital disorder, genetic disorder, motor impairment, overweight (BMI>95th), perinatal condition, sleep problem, vision deficits] were identified from evidence. Only studies examining the prevalence of sleep problems, gastrointestinal problems, epilepsy, motor problem, vision deficits and auditory deficits are reported.

Seven studies providing very low quality evidence reported on the prevalence of epilepsy, three for sleep problems, three for auditory deficits, three for vision deficits and one each for gastrointestinal problems and motor problems. The pooled prevalence of epilepsy in children with autism was 24% (95%CI 8, 46), for sleep problems 37% (95%CI 11, 68), for vision deficits 7% (95%CI 0, 26), for auditory deficits 3% (95%CI 0, 9), gastrointestinal problems 3% and for motor problems 13%

7.1.5 Evidence to recommendations

See section 7.1.8

7.1.6 Evidence profile for ASD

Table 7.2 Prevalence of each co-existing condition in children with ASD

Coexisting condition	Quality assessment						Summary of findings		
							Sample size		Prevalence (Pooled, 95% CI)
	Studies	Design	Limitations	Inconsistency	Indirectness	Quality	Cases	Non-cases	
PREVALENCE OF EACH CO-EXISTING CONDITION IN CHILDREN OR YOUNG PEOPLE WITH ASD									
NEUROPSYCHIATRIC									
ADHD[153;161;170;172;173;176;182]	7	Uncon obs[#]	NA	NA	NA	Very low	1182	2191	45 (24, 67)
Self-injurious behaviour[155]	No studies have been identified.								
Anxiety[150;153;161;170;176;177;182]	7	Uncon obs	NA	NA	NA	Very low	357	2595	27 (10, 49)
ODD[153;161;170;176;182]	5	Uncon obs	NA	NA	NA	Very low	342	2520	23 (6, 47)
Tic[153;158;170;172;176;179]	6	Uncon obs	NA	NA	NA	Very low	248	2634	19 (2, 47)
OCD[161;170;176;179]	4	Uncon obs	NA	NA	NA	Very low	61	2277	8 (2, 17)
Depression[150;153;161;170;176;177]	6	Uncon obs	NA	NA	NA	Very low	58	2411	9 (3, 19)
Tourette syndrome[158;170;179]	3	Uncon obs	NA	NA	NA	Very low	15	211	12 (2, 28)
Conduct disorder[153;161;170;176]	4	Uncon obs	NA	NA	NA	Very low	17	2362	3 (0, 9)
NEURODEVELOPMENTAL									
Intellectual disability[151;159;164;167;171;176;180;185;187]	9	Uncon obs	NA	NA	NA	Very low	1256	2427	65 (38, 87)
NEUROLOGICAL									
Cerebral palsy[151;154;176;178]	4	Uncon obs	NA	NA	NA	Very low	91	2700	5 (1, 13)
MEDICAL									
Sleep problem[153;159;165]	3	Uncon obs	NA	NA	NA	Very low	64	49	61 (31, 88)
Gastrointestinal problems[181]	1	Uncon obs	NA	NA	NA	Very low	62	38	62
Epilepsy[151;154;163;164;176;178;186;187]	8	Uncon obs	NA	NA	NA	Very low	922	3812	15 (7, 26)
Seizures[171;178;180]	3	Uncon obs	NA	NA	NA	Very low	47	744	5 (2, 9)
A motor problem[151;154;167]	3	Uncon obs	NA	NA	NA	Very low	113	386	25 (0, 75)
Vision deficits[151;176;186]	3	Uncon obs	NA	NA	NA	Very low	77	2538	6 (0, 21)
Auditory deficits[151;154;176;179]	4	Uncon obs	NA	NA	NA	Very low	84	2446	8 (1, 20)

7.1.7 Evidence statements for ASD

Neuropsychiatric conditions

Thirteen neuropsychiatric coexisting conditions of ASD [ADHD, adjustment/reactive attachment/posttraumatic stress disorder, anxiety, behaviour problem, bipolar disorder, conduct disorder, depression, mutism, OCD, ODD, psychotic disorder, tic, Tourette syndrome] were identified from evidence. Only studies examining the prevalence of ADHD, anxiety, ODD, tic, OCD, depression, Tourette's syndrome and conduct disorder are reported.

Seven studies providing very low quality evidence reported on the prevalence of ADHD in ASD children and young people, seven on anxiety, five on ODD, six on tic, four on OCD, six on depression, three on Tourette's syndrome and four on conduct disorder. The pooled prevalence in children with ASD for ADHD was 45% (95%CI 24, 67), anxiety 27% (95%CI 10, 49), fro ODD 23% (95%CI 6, 47), for TICS 19% (95%CI 2, 47), for OCD 8% (95%CI 2, 17), depression 9% (95%CI 3, 19), and for Tourette's syndrome 12% (95%CI 2, 28), No studies were identified for self-injurious behaviour in children with ASD

Neurodevelopmental conditions

Four neurodevelopmental coexisting conditions of ASD [communication disorders, language problem, intellectual disability, regression] were identified from evidence. Only studies examining the prevalence of intellectual disability are reported. Nine studies providing very low quality evidence reported on the prevalence of intellectual disability in children and young people with ASD. The pooled prevalence was 65% (95%CI 38, 87).

Neurological conditions

Two neurological coexisting conditions of ASD [cerebral palsy, hydrocephalus] were identified from evidence. Only studies examining the prevalence of cerebral palsy are reported. Four studies reported on cerebral palsy in children and young people with ASD and the pooled prevalence was 5% (95%CI 1, 13).

Medical conditions

Fifteen medical coexisting conditions of ASD [asthma, auditory deficits, chromosomal abnormalities, congenital disorder, epilepsy, seizures, febrile convulsions, gastrointestinal problems, genetic disorder, mitochondrial respiratory chain disorder, motor impairment, overweight (BMI>95th), sleep problem, vision deficits, elimination disorder] were identified from evidence. Only studies examining the prevalence of sleep problem, motor problem, vision deficits and auditory deficits are reported.

Eight studies providing very low quality evidence reported on the prevalence of epilepsy in ASD children and young people, one on gastrointestinal problem, three on sleep problem in ASD children and young people, three on seizures, three on a motor problem, three on vision deficits and four on auditory deficits. The pooled prevalence for epilepsy was 15% (95%CI 7, 26), for sleep problems 61% (95%CI 31, 88, for seizures 5% (95%CI 2, 69), for motor problems 25% (95%CI 0, 75), for vision deficits 6% (95%CI 0, 21), for auditory deficits 8% (95%CI 1, 20) and for gastrointestinal problems 62%.

7.1.8 Evidence to recommendations

Relative value placed on the outcomes considered	The GDG agreed specific criteria for whether a disease or symptom should be considered a coexisting condition with ASD. These were: the prevalence in children and young people with ASD; the impact on quality of life; the ease of diagnosis (defined as diagnostic accuracy, and the cost-effectiveness of treatment of the condition if identified.
Trade-off between clinical benefits and harms	It was considered that the identification of important co-existing conditions was of clinical benefit because it would often affect how a child was cared for in all aspects of the diagnostic process and subsequent management.

	The GDG considered that systematic enquiry about coexisting conditions should be part of any clinical assessment of a child or young person with suspected or confirmed ASD. There are various known conditions associated with ASD that, if not recognised, could have an important impact on the welfare of the child or young person. There would be benefit for some children in the early identification of some co-existing conditions in children with suspected or confirmed ASD. Knowledge of such additional disorders would contribute to an understanding of the individuals 'strengths and weaknesses'. Some conditions would require specific medical or other intervention or modification of the overall treatment strategy. It might also lead to the identification of other family members with the condition and might have implications for genetic counselling. Most notable of these is Fragile X. The possible harm associated with assessing a child or young person for coexisting conditions might include prolongation of the ASD-specific Diagnostic Assessment. Looking for or confirming the presence of co-existing conditions in addition to ASD might cause distress to children and young people and to parents and carers. As with all stages of the ASD pathway the risk of such difficulties would be alleviated by good communication and close involvement of the child or young person and the parents or carers in the process. It GDG considered that overall the potential benefits of early identification of coexisting conditions outweigh the possible harms. The available evidence shows that a wide range of neuropsychiatric, neurodevelopmental, neurological and medical disorders and symptoms not reaching diagnostic threshold co-occur in children and young people with autism/ASD. The rates are given for each disorder or symptom and it is possible that any child/young person has more than one co-existing condition. Global intellectual disability, is likely the most common co-existing disorder. Neuropsychiatric disorders are also particularly common in children/young people with autism/ASD and amongst the most common of these are ADHD, anxiety disorders, behavioural problems subsumed under the heading of oppositional defiant disorder.
Trade-off between net health benefits and resource use	The GDG did not consider that routine enquiry aimed at finding clinical evidence for the presence of the specific co-existing conditions identified would add significantly to the time taken to undertake the normal clinical assessment in suspected ASD. Considering the possible benefits of recognising coexisting conditions, the GDG considered this to a be cost-effective use of a health care professional's time . However, any additional assessments triggered where such coexisting conditions are suspected or confirmed will only be cost-effective if the additional cost of these assessments (including assessments undertaken on individuals who turn out not to have the condition) can be justified by the health benefit of early identification and management (some conditions only). No evidence to support or refute the cost-effectiveness of early identification of coexisting conditions was identified. The GDG consensus was that use of health care resources to look for rare conditions in individuals without clinical manifestations to suggest their presence or to look for co-existing conditions for which no useful treatment existed could not be justified. All the conditions that appear on the list of

	coexisting conditions established by the GDG are important because either there are specific treatments of proven efficacy or they require support and management with clinically important benefits to the individual in terms of improved quality of life. The GDG considered that the use of this list as a guide to important coexisting conditions would be valuable and that undertaking further assessments on the basis of clinical judgement would be a cost-effective use of NHS resources.
Quality of evidence	Where there are multiple studies, the prevalence estimates for each disorder/symptom area vary widely. This reflects both differences in the populations studied and variation in the ways in which coexisting conditions were identified. The evidence on prevalence summarised in the literature is highly variable and is not exhaustive. The GDG considered that were insufficient studies resulting in a lack of replication of findings across studies and the probable underreporting of important coexisting conditions, so they were unable to judge how comparable the studies were with each other and compared with usual clinical practice in local areas in the UK. Furthermore in certain cases for example intellectual disability pooled prevalence statistic was in conflict with clinical experience although in this particular case they also noted that the confidence intervals for all children with ASD (as opposed to autism) were wide and the GDG considered that the true value would lie somewhere within this range.
Other considerations	The conditions listed in the table below have at least one of the following characteristics: the documented prevalence rate of the condition in children and young people with ASD is higher than that for the general population; the condition is likely to benefit from appropriate intervention(s); the condition is likely to have an important impact on quality of life. The names of the conditions in the table are taken directly from the literature except where the GDG considered a more generic term was appropriate such as mood disorder which is an interpretation by the GDG of the evidence for depression and genetic disorders instead of genetic abnormalities. The GDG consensus was that when assessing a child or young person with suspected or confirmed ASD, the health care professional should always consider the possibility of a co-existing condition and should undertake an appropriate systematic clinical enquiry with this in mind taking into account the history and presenting problem. The GDG noted that the communication difficulties associated with ASD might increase the risk of coexisting conditions going undetected. For example, mental health difficulties might be overlooked. The GDG therefore recommended that particular attention be given to information from other sources (including direct observation of the child or young person) and in different settings.
Recommendations	46. Consider whether the child or young person may have, or have symptoms of, any of the following coexisting conditions and if suspected, carry out appropriate assessments: • Neuropsychiatric: ADHD anxiety disorders and phobias

	mood disorders oppositional defiant behaviour tics and Tourette syndrome obsessive compulsive disorder self-injurious behaviour • Neurodevelopmental: global delay or intellectual disability motor coordination academic learning problems, for example literacy and numeracy speech and language disorder • Medical or genetic problems and disorders: epilepsy and epileptic encephalopathy chromosome disorders genetic abnormalities including fragile X tuberous sclerosis Duchenne muscular dystrophy neurofibromatosis • Functional problems: eating/feeding urinary continence/eneuresis bowels/encopresis sleep vision and hearing impairment.

1

8 Medical investigations

8.1 Introduction

ASD is a clinical syndrome in which the diagnosis is based on the presence of certain developmental and/or behavioural features. A number of disorders are known to occur more frequently in those with ASD than in the general population (chapter 7 on Co-existing conditions). Some of these co-existing conditions might when present be considered as causative of ASD.

In this chapter, consideration is given to the role of medical investigations that may identify causal conditions, specifically electroencephalography (EEG), brain-imaging techniques (MRI, CT), and blood and urine laboratory tests including genetic investigations. The role of such investigations in particular patient subgroups such as autistic regression is also addressed.

One difficulty arising with various biomedical investigations that have been studied in ASD is the proper interpretation of abnormal results. For several of the investigations, an 'abnormal result' may not point to a specific, recognised disorder and may not have treatment implications in their own right. With regard to EEG, which is undertaken as part of the assessment of epilepsy, it was recognised that abnormalities may occur more frequently in children and young people with ASD than in the general population but there may be no evidence of epilepsy. Furthermore, there is no standardised definition of what constitutes an 'abnormal EEG; leading to possible reporting variation between studies. Consideration needed to be given to the benefit or otherwise of EEG as part of the diagnostic assessment for epilepsy.

Likewise, it needed to be borne in mind that minor structural abnormalities may be reported on brain imaging but that are not necessarily associated with recognised disorder or any clinical consequences. As with EEGs, there is no standardised method for agreeing on what constitutes an abnormal scan and this may cause reporting variation.

Various genetic disorders are known to occur with markedly increased frequency in ASD – for example, Fragile X syndrome and tuberous sclerosis. Recently genetic investigations have revealed additional abnormalities that occur more commonly in those with ASD but not associated with a known syndrome. The situation is further complicated in relation to genetics, where in some cases, gene variants may increase the risk of ASD but individually confer a very small risk, while in other instances, genetic abnormalities may play a major causal role. Identification of the latter group of genetic abnormalities with ASD might be important in genetic counselling. There is substantial variability in the type and extent of genetic investigations undertaken. Furthermore, this is a field where technology is changing rapidly and new techniques are able to identify more subtle abnormalities than could be detected in earlier studies. However, a challenge of identifying more subtle abnormalities is that their clinical importance as a cause of ASD is often more uncertain.

Clinical Question

What should be the components of the diagnostic assessment?

- Biomedical investigations for diagnosis of ASD, e.g. EEG, brain scan, genetic tests, counselling; investigations for associated medical conditions.

8.1.1 Methodological approach to medical investigations

In order to examine the potential role of investigations, we looked for evidence from studies in which the investigations were carried out in children and young people with confirmed ASD. This would enable us to determine the frequency with which the investigations identified clinically relevant conditions.

We grouped the studies in the following ways

- Retrospective studies in which the investigations were routinely performed as part of the ASD diagnostic assessment (i.e. performed routinely)
- Retrospective studies in which the investigations were performed selectively based on clinical judgement
- Prospective research studies of the investigations in ASD (i.e., performed for research)

There was a risk that study populations might be affected by selection bias. Studies conducted for research purposes often have rigid eligibility criteria (for example, coexisting conditions) as such the findings cannot be generalised to clinical practice samples where additional co-existing conditions are likely to be common. Separate consideration of the above three study types would take account of the risk of bias.

The evidence profiles that follow present first the percentage of abnormal test results and second, the percentage of in whom a clinical condition was identified or confirmed by the investigation. The percentage reported in both cases relates to the total number in the studies, whether investigated or not.

The clinical relevance of these outcomes is as follows:

- the percentage of abnormal results is also important as these may lead to further investigation for co-existing conditions such as epilepsy or differential diagnoses such as Landau-Kleffner syndrome. This could have consequences both for the individual being investigated and for the use of NHS resources
- the percentage of children/young people who had a condition (potentially or actually) identified or confirmed by the biomedical investigation is important as this should ensure that all co-existing medical needs are identified and appropriate management can be initiated

StatsDirect was used to meta-analyse the data in proportions with 95% CI using a DerSimonian-Laird random effects model.

We have also analysed the results of the final outcome (number/percentage of children/young people who had a condition (potentially or actually) identified or confirmed by the biomedical investigation in an a priori subgroup of children with intellectual disability and also in a post-hoc subgroup of children with regression. This regression-only subgroup was studied because of the known association of language regression with neurological disorders such as epileptic encephalopathy, specifically Landau Kleffner Syndrome. When these subgroups were analysed we calculated both the prevalence of clinical findings in ASD children with regression and in ASD children without regression. These prevalence rates were then combined to present an odds ratio (OR) of this risk in ASD children with regression and then in children with intellectual disability.

After an initial search of 25,787 articles in the overall search, 88 were selected on title and abstract and the papers requested for full review. 37 studies (reported in 39 articles) were eligible for inclusion based on the following criteria

Population: Children or young people diagnosed with ASD according to DSM-IV or ICD-10 criteria

Index test: EEG, neuroimaging (MRI, CAT, CT, PET, SPECT), metabolic tests, blood tests, urine tests, and genetic investigations

Outcomes: the number/percentage of abnormal results; the number/percentage of children/young people who had a condition (potentially or actually) identified or confirmed by the biomedical investigation

A list of the 49 excluded studies and the reasons for exclusion is found in Appendix G (Tables of excluded studies).

We have analysed and presented the data for the percentage of abnormal results in separate evidence profiles for autism and ASD (section 8.4) and in a combined evidence statement (section 8.5). Data for the percentage of children/young people who had a condition (potentially or actually) identified or confirmed by the biomedical investigations are presented in separate evidence profiles (section 8.6) and a combined evidence statement (section 8.7). Subgroup analyses are reported in the relevant evidence statement (section 8.7)

8.1.2 Description of included studies

EEG

Twenty-four studies (in 26 articles) from Italy[157;188-191], Brazil[192;193], Canada[194;195], the Czech Republic[151;196], Israel[197;198], the UK[199], Japan[163;200]. India[201], Turkey[185;202] and the USA[203-209] examined the use of EEG in children or young people with autism / ASD. In six studies[157;188;194;195;197;198;203] EEG'S were routinely use, , in three studies [192;193;204;205] the EEG was performed on clinical judgement while in the remaining 15 studies[151;163;185;189-191;196;199-202;206-209] EEG's were used for research purposes. One of these studies[199] excluded children with a history of seizures while the remainder did not report excluding on the basis of clinical epilepsy.

Eight studies[157;163;190;198;199;201;206;209] examined EGGs in children / young people with autism. Five of these studies[157;190;198;199;206] included children with regression and two studies[157;190] included children with Intellectual disability.

Twenty-four studies dealt with EEGs in children / young people with ASD[151;185;188;189;191-197;200;202-205;207;208]. Six of the studies[151;191;196;197;207;208] included children with regression (one [207] compared those with language regression alone compared to those with both autistic and language regression) and two studies[196;210] included children with intellectual disability.

All studies were uncontrolled observational and were graded as very low quality.

Brain scans

Magnetic resonance imaging (MRI)

Ten studies from the UK[199], Italy[188], France[211], USA[203-205], India[201], Israel[198], Canada[194;195] and Turkey[185] with a total of 888 participants examined the use of magnetic resonance imaging (MRI) in children or young people with an ASD. In two studies[188;203] all participants were scanned, in five studies[194;195;198;199;204;205] scans were performed on clinical discretion (selected scanning) and in the final three studies[185;201;211] scans were performed on an Research-based basis.

Four studies[198;199;201;211] examined MRI in children / young people with autism. Two studies[198;199] included children / young people with regression and one study[211] included children with intellectual disability.

Six studies (from seven articles)[185;188;194;195;203-205] examined MRI in children / young people with ASD. No studies reported subgroup analyses for either regression or intellectual disability.

All studies were uncontrolled observational and were graded as very low quality.

Computed tomography (CAT/CT/PET/SPECT)

Five studies from Brazil[192;193], Canada[194;195], Israel[198], India[201] and the USA[205] with a total of 359 participants examined use of computed tomography in children or young people with an ASD. The samples of the studies ranged from 22 to 132 participants. In four studies [192-195;198;205] scans were performed on clinical discretion (selected scanning) (N = 337). One study [201] was research-based.

Two studies[198;201] examined computed tomography in children or young people with autism. One study[198] included children / young people with regression and no studies reported on subgroups with intellectual disability.

Three studies (from 5 articles)[192-195;205] examined computed tomography in children / young people with ASD. No studies reported subgroup analyses for either regression or intellectual disability.

All studies were uncontrolled observational and were graded as very low quality.

Metabolic tests

Twelve studies (from 14 articles) from the USA[203-205], Italy[157;188], Israel[198], Portugal[164], the Czech Republic[151], France[211], U.K [212], Canada[194;195] and Brazil[192;193] examined the use of metabolic tests in children or young people with ASD. One study [212] tested on a research basis. In six studies[157;164;188;192;193;203;211], all participants were tested while in another five studies[151;194;195;198;204;205] tests were performed on clinical discretion. Three studies [188;194;195;203] did not report the specific tests used. Two studies [151;192;193] reports screening for inborn errors of metabolism but provided no further details. One study [198] reported that the metabolic determination included determining the levels of ammonia, amino acids, lactic acid and pyruvic acid in blood as well as organic acids in urine. Another study[164] reported metabolic tests to look for amino acid and organic acid disorders, oligosaccharides and mucopolysaccharides, purine and pyrimidine disorders, creatine metabolism abnormalities and congenital glycosylation diseases. A third study [157] screened serum and urinary amino acids. A fourth[204] used urine / plasma inborn error screen. A fifth study [205] examined plasma amino acids and urine organic acids. The final study [211] examined plasma and urine amino and organic acid analysis, urine glycoaminoglycans quantitation, urine oligosaccharides, purine and pyrimidine analysis and creatine guanidoacetate urine analysis.

Three studies[157;198;211] examined metabolic testing in children / young people with autism. One study[198] included children / young people with regression and no studies reported on subgroups with intellectual disability.

Nine studies (from 11 articles) [151;164;164;188;192-194;203-205;212;213] examined metabolic tests in children / young people with ASD. No studies reported subgroup analyses for either regression or intellectual disability.

All studies were uncontrolled observational and were graded as very low quality.

Blood tests

Four studies from the USA[203;214] and Italy[157;215] examined the use of various blood tests in children or young people with ASD. In one study[157] participants were routinely given a complete blood count and blood chemistry obtained while in a second[203] serum uric acid levels were obtained. In the remaining two studies [214;215] participants with tested for serum IgE or for Mycoplasma, Chlamydia pneumoniae, HHV-6 for research purposes.

Two studies[157;215] examined blood tests in children / young people with autism. No studies reported subgroup analyses for either regression or intellectual disability.

Two studies [203;214] examined blood tests in children / young people with ASD. No studies reported subgroup analyses for either regression or intellectual disability.

All studies were uncontrolled observational and were graded as very low quality.

Urine tests

Two studies from the USA[203] and Finland[152] examined the use of urine tests in children and young people with ASD. All participants were routinely tested in two studies[152;203], and no studies were identified for children tested on clinical judgement or on a research basis. One study[152] did not report on the test used, another[203] examined uric acid levels.

A single study[152] examined urine tests in children / young people with autism. This study did not report subgroup analyses for either regression or intellectual disability.

A single study[203] examined urine tests in children / young people with ASD. This study did not report subgroup analyses for either regression or intellectual disability

All studies were uncontrolled observational and were graded as very low quality.

Genetic tests

Fifteen studies from Brazil[192;193;216], Canada[194;195;217], Finland[152], France[187], Israel[198], Italy[188;189], Taiwan[218] and the USA[180;203;204;219;220]. Genetic investigations were carried out as part of routine testing in 3 studies[152;188;203]. testing on clinical judgement in 5 studies[194;195;198;204;217;219] and testing for research purposes in seven studies[180;187;189;192;193;216;218;220]. The tests used were reported as follows; 17p11 FISH (fluorescence in situ hybridization)[203], aCGH-array[205], Chromosomal microarray, [180], Chromosome[205], Chromosome 15[203], Cytogenetic analysis[192;193;219;221], DNA[164;180;222], FISH (fluorescence in situ hybridization[204;216], Molecular analysis[216], Folic acid starvation / Southern Blot analysis[198], Fragile X[223], G banded chromosomes[222], G-banded Karyotype[180], Genetic[151;194], High Resolution Banding DNA[188], Karyotype[192;193;199;217;223], Molecular cytogenetics[188], Molecular/genetic[204], Polymerase chain reaction analysis[216], Prometaphase chromosomes (Karyotype)[203], PTEN gene sequencing[205], Rett gene sequencing[205] or were not reported.

Five studies[152;198;218-220] examined genetic tests in children / young people with autism. No studies reported subgroup analyses for either regression or intellectual disability.

Ten studies (from 12 articles)[180;187-189;192-195;203;204;216;217] examined genetic tests in children / young people with ASD. No studies reported subgroup analyses for either regression or intellectual disability.

All studies were uncontrolled observational and were graded as very low quality.

8.1.3 Evidence profile – percentage of abnormal results

Tables 8.1 and 8.2 present the percentage of abnormal results of biomedical investigations in children/young people with autism (Table 8.1) and ASD (Table 8.2), categorised by the reason the test was performed; routinely, on clinical judgement or as part of a research study.

1 **Table 8.1 Percentage of abnormal results of biomedical investigations in children/young people with Autism**

Biomedical investigation	Quality assessment							Summary of findings
	Studies (N)	Tested	Design	Limitations	Inconsistency	Indirectness	Quality	Percentage of total in studies including those who did not undergo the investigation (95% CI)
PERCENTAGE OF ABNORMAL RESULTS								
EEG								
Performed routinely[157;198]	2 (178)	100%	Uncon obs	N/A	N/A	N/A	Very low	11 (6, 63)
Performed based on clinical judgement	No studies were identified.							
Performed for research purposes[163;190;199;201;206;209]	6 (1432)	95.9%	Uncon obs	N/A	N/A	N/A	Very low	47 (20, 76)
MRI								
Performed routinely	No studies were identified.							
Performed based on clinical judgement[198;199]	2 (196)	21.4%	Uncon obs	N/A	N/A	N/A	Very low	0 (0, 1)
Performed for research purposes[201;211]	2 (99)	100%	Uncon obs	N/A	N/A	N/A	Very low	29 (7, 59)
CT/CAT/PET/SPECT								
Performed routinely	No studies were identified.							
Performed based on clinical judgement[198]	1 (132)	27.3%	Uncon obs	N/A	N/A	N/A	Very low	0
Performed for research purposes[201]	1 (22)	100%	Uncon obs	N/A	N/A	N/A	Very low	32
METABOLIC TESTS								
Performed routinely[157;211]	2 (123)	100.0%	Uncon obs	N/A	N/A	N/A	Very low	0 (0, 2)
Performed based on clinical judgement[198]	1 (132)	40.2%	Uncon obs	N/A	N/A	N/A	Very low	0
Performed for research purposes	No studies were identified.							
BLOOD TESTS								
Performed routinely[157]	1 (46)	100.0%	Uncon obs	N/A	N/A	N/A	Very low	0
Performed based on clinical judgement	No studies were identified.							
Performed for research purposes[215]	1 (43)	100.0%	Uncon obs	N/A	N/A	N/A	Very low	21
URINE TESTS								
Performed routinely[152]	1 (187)	100.0%	Uncon obs	N/A	N/A	N/A	Very low	0
Performed based on clinical judgement	No studies were identified.							
Performed for research purposes	No studies were identified.							

GENETIC TESTS								
Performed routinely[152].	1 (187)	100.0%	Uncon obs	N/A	N/A	N/A	Very low	12
Performed based on clinical judgement[198;219]	2 (1030)	32.4%	Uncon obs	N/A	N/A	N/A	Very low	3 (2, 4)
Performed for research purposes[218;220]	2 (816)	97.2%	Uncon obs	N/A	N/A	N/A	Very low	5 (1, 27)

Table 8.2 Percentage of abnormal results of biomedical investigations in children/young people with ASD

Biomedical investigation	Quality assessment							Summary of findings
	Studies (N)	Tested	Design	Limitations	Inconsistency	Indirectness	Quality	Percentage of total in studies including those who did not undergo the investigation (95% CI)
PERCENTAGE OF ABNORMAL RESULTS								
EEG								
Performed routinely[188;194;195;197;203]	4 (191)	100%	Uncon obs	N/A	N/A	N/A	Very low	7 (0, 25)
Performed based on clinical judgement[192;193;204;205]	3 (356)	43.8%	Uncon obs	N/A	N/A	N/A	Very low	10 (2, 21)
Performed for research purposes[151;185;189;191;196;200;202;207;208]	9 (3196)	43.8%	Uncon obs	N/A	N/A	N/A	Very low	40 (31, 49)
MRI								
Performed routinely[188;203]	2 (117)	100%	Uncon obs	N/A	N/A	N/A	Very low	3 (1, 7)
Performed based on clinical judgement[194;195;204;205]	3 (395)	22.0%	Uncon obs	N/A	N/A	N/A	Very low	2 (0, 8)
Performed for research purposes[185]	1 (81)	100%	Uncon obs	N/A	N/A	N/A	Very low	12
CT/CAT/PET/SPECT								
Performed routinely	No studies were identified.							
Performed based on clinical judgement[192-195;205]	3 (205)	43.9%	Uncon obs	N/A	N/A	N/A	Very low	7 (2, 38)
Performed for research purposes	No studies were identified.							
METABOLIC TESTS								
Performed routinely[164;188;192;193;203]	4 (322)	100.0%	Uncon obs	N/A	N/A	N/A	Very low	0 (0, 1)
Performed based on clinical judgement[151;164;194;195;204;205]	5 (610)	46.2%	Uncon obs	N/A	N/A	N/A	Very low	2 (0, 6)
Performed for research purposes[212]	1 (56)	100.0%	Uncon obs	N/A	N/A	N/A	Very low	100

BLOOD TESTS								
Performed routinely[203]	1 (32)	100.0%	Uncon obs	N/A	N/A	N/A	Very low	3
Performed based on clinical judgement	No studies were identified.							
Performed for research purposes[214]	1 (48)	100.0%	Uncon obs	N/A	N/A	N/A	Very low	58
URINE TESTS								
Performed routinely[203]	1 (32)	100.0%	Uncon obs	N/A	N/A	N/A	Very low	0
Performed based on clinical judgement	No studies were identified.							
Performed for research purposes	No studies were identified.							
GENETIC TESTS								
Performed routinely[188;203]	2 (117)	100.0%	Uncon obs	N/A	N/A	N/A	Very low	14 (7, 22)
Performed based on clinical judgement[194;195;204;217]	3 (187)	52.1%	Uncon obs	N/A	N/A	N/A	Very low	4 (1, 8)
Performed for research purposes[180;187;189;192;193;216]	5 (1651)	95.8%	Uncon obs	N/A	N/A	N/A	Very low	11 (3, 23)

8.1.4 Evidence statement – percentage of abnormal results

EEG

Six studies of very low quality provided data for routinely performed EEG, three for EEG performed based on clinical judgment, and 15 for research-based EEG. Of the studies looking at EEG performed routinely 11% (95%CI 6, 63) of children with autism and 7% (95%CI 0, 25) of children with ASD had abnormal results. Of studies examining EEG performed on clinical judgement 10% (95%CI 2, 21) of children with ASD had abnormal results and no studies examined EEG on clinical judgement in children with autism. When EEG was examined for research purposes 47% (95%CI 20, 76) of children with autism and 40% (95%CI31, 49) of children with ASD had abnormal results.

We did not perform any subgroup analyses for this outcome.

Brain scans

Magnetic resonance imaging (MRI)

Two studies of very low quality provided data for routinely performed MRI, five for MRI performed based on clinical judgment and three for research-based MRI. Of the studies looking at MRI performed routinely 3% (95%CI 1, 7) of children with ASD had abnormal results and no studies examined MRI on clinical judgement in children with autism. Of studies examining MRI performed on clinical judgement none of the children with autism and 2% (95%CI 0, 8) of children with ASD had abnormal results. When MRI was examined for research purposes 29% (95%CI 7, 59) of children with autism and 12% of children with ASD had abnormal results.

We did not perform any subgroup analyses for this outcome.

CT/CAT/PET/SPECT

Four studies of very low quality provided data for CT/CAT/PET/SPECT performed based on clinical judgment, one for research-based CT/CAT/PET/SPEC. No studies were identified for routinely performed CT/CAT/PET/SPECT. For CT/CAT/PET/SPECT performed based on clinical judgement, None of children with autism and 7% (95%CI 2, 38) of children with ASD had abnormal results. For research-based CT/CAT/PET/SPECT, 32% of children with autism received abnormal results and no studies examined CT/CAT/PET/SPECT in children with ASD for research purposes..

We did not perform any subgroup analyses for this outcome.

Metabolic tests

Six studies of very low quality provided data for routinely performed metabolic tests, six for tests performed based on clinical judgment and six for research-based metabolic tests. No abnormal results were found for routinely performed metabolic tests in children with autism or ASD. For metabolic tests performed based on clinical judgement, none of the children with autism and 2% (95%CI 0 – 6) of children with ASD had abnormal results. For research-based metabolic tests, no studies of children with autism were identified and 100% of participants had abnormal results.

We did not perform any subgroup analyses for this outcome.

Blood tests

Two studies of very low quality provided data for routinely performed blood tests and two for research-based tests. No studies were identified for blood tests performed based on clinical judgement. For studies of routinely performed tests, none of the children with autism and 3% of children with ASD had abnormal results. For research-based tests, 215 of children with autism and 58% of children with ASD had abnormal results.

We did not perform any subgroup analyses for this outcome.

Urine tests

Two studies of very low quality provided data for routinely performed urine tests. No studies were identified for urine tests performed based on clinical judgement or research-based urine tests. No abnormal results have been identified for urine performed routinely in either children with autism or ASD.

We did not perform any subgroup analyses for this outcome.

Genetic tests

Three studies of very low quality provided data for routinely performed genetic tests, 5 for genetic tests performed based on clinical judgement and 7 for research-based genetic tests. Of the studies looking at routinely performed genetic tests 12% of children with autism and 14% (95%CI 7, 22) of children with ASD had abnormal results. When tests were ordered on clinical judgement 3% (95%CI 2, 4) of children with autism and 4% (95%CI 1, 8) of children with ASD had abnormal results. In research-based studies 5% (95%CI 1, 27) of children with autism and 11% (95%CI 3, 23) of children with ASD had abnormal results.

We did not perform any subgroup analyses for this outcome.

8.1.5 Evidence to recommendations

See section 8.1.8

8.1.6 Evidence profile – percentage of children/young people who had a condition identified or confirmed by biomedical investigation

Tables 8.3 and 8.4 present the percentage of children/young people with autism (Table 8.3) and ASD (Table 8.4) who had a condition (potentially or actually) identified or confirmed by the biomedical investigation, categorised by the reason the test was performed; routinely, on clinical judgement or as part of a research study.

Table 8.3 Percentage of children/young people with autism who had a condition (potentially or actually) identified or confirmed by the biomedical investigation

Biomedical investigation	Quality assessment							Summary of findings
	Studies (N)	Tested	Design	Limitations	Inconsistency	Indirectness	Quality	Percentage of total in studies including those who did not undergo the investigation (95% CI)
PERCENTAGE OF CHILDREN/YOUNG PEOPLE WITH ASD WHO HAD A CONDITION (POTENTIALLY OR ACTUALLY) IDENTIFIED OR CONFIRMED BY THE BIOMEDICAL INVESTIGATIONS								
EEG								
Performed routinely[157;198]	2 (178)	100%	Uncon obs	N/A	N/A	N/A	Very low	4 (2, 26)
Performed based on clinical judgement	No studies were identified.							
Performed for research purposes[163;190;199;206;209]	5 (1410)	95.8%	Uncon obs	N/A	N/A	N/A	Very low	24 (10, 41)
MRI								
Performed routinely	No studies were identified.							
Performed based on clinical judgement[198;199]	2 (196)	21.8%	Uncon obs	N/A	N/A	N/A	Very low	0 (0, 1)
Performed for research purposes[211]	1 (77)	100.0%	Uncon obs	N/A	N/A	N/A	Very low	0
CT/CAT/PET/SPECT								
Performed routinely	No studies were identified for this analysis							
Performed based on clinical judgement[198]	1 (132)	27.3%	Uncon obs	N/A	N/A	N/A	Very low	0
Performed for research purposes[201]	No studies were identified.							
METABOLIC TESTS								
Performed routinely[157;211]	2 (123)	100.0%	Uncon obs	N/A	N/A	N/A	Very low	0 (0, 2)
Performed based on clinical judgement[198]	1 (132)	40.2%	Uncon obs	N/A	N/A	N/A	Very low	0
Performed for research purposes	No studies were identified.							
BLOOD TESTS								
Performed routinely[157]	1 (46)	100.0%	Uncon obs	N/A	N/A	N/A	Very low	0
Performed based on clinical judgement	No studies were identified.							
Performed for research purposes[215]	1 (43)	100.0%	Uncon obs	N/A	N/A	N/A	Very low	21
URINE TESTS								
Performed routinely[152]	1 (187)	100.0%	Uncon obs	N/A	N/A	N/A	Very low	0

Performed based on clinical judgement	No studies were identified.							
Performed for research purposes	No studies were identified.							
GENETIC TESTS								
Performed routinely[152].	1 (187)	100.0%	Uncon obs	N/A	N/A	N/A	Very low	9
Performed based on clinical judgement[198;219]	2 (1030)	32.4%	Uncon obs	N/A	N/A	N/A	Very low	3 (2, 4)
Performed for research purposes[218;220]	2 (816)	97.2%	Uncon obs	N/A	N/A	N/A	Very low	4 (0, 21)

Table 8.4 Percentage of children/young people with ASD who had a condition (potentially or actually) identified or confirmed by the biomedical investigation

Biomedical investigation	Quality assessment							Summary of findings
	Studies (N)	Tested	Design	Limitations	Inconsistency	Indirectness	Quality	Percentage of total in studies including those who did not undergo the investigation (95% CI)
PERCENTAGE OF CHILDREN/YOUNG PEOPLE WITH ASD WHO HAD A CONDITION (POTENTIALLY OR ACTUALLY) IDENTIFIED OR CONFIRMED BY THE BIOMEDICAL INVESTIGATIONS								
EEG								
Performed routinely[188;194;195;197;203]	4 (191)	100.0%	Uncon obs	N/A	N/A	N/A	Very low	7 (0, 24)
Performed based on clinical judgement[192;193;204;205]	3 (356)	43.8%	Uncon obs	N/A	N/A	N/A	Very low	4 (1, 11)
Performed for research purposes[151;189;191;196;200;202;207;208]	8 (3196)	99.6%	Uncon obs	N/A	N/A	N/A	Very low	23 (14, 34)
MRI								
Performed routinely[188;203]	2 (117)	100.0%	Uncon obs	N/A	N/A	N/A	Very low	3 (1, 7)
Performed based on clinical judgement[194;195;204;205]	3 (395)	22.0%	Uncon obs	N/A	N/A	N/A	Very low	0 (0, 1)
Performed for research purposes	No studies were identified.							
CT/CAT/PET/SPECT								
Performed routinely	No studies were identified for this analysis							
Performed based on clinical judgement[192-195;205]	3 (205)	43.9%	Uncon obs	N/A	N/A	N/A	Very low	0 (0, 2)

Performed for research purposes[201]	No studies were identified for this analysis							
METABOLIC TESTS								
Performed routinely[164;188;192;193;203]	4 (322)	100.0%	Uncon obs	N/A	N/A	N/A	Very low	0 (0, 1)
Performed based on clinical judgement[151;164;194;195;204;205]	5 (610)	46.2%	Uncon obs	N/A	N/A	N/A	Very low	1 (0, 6)
Performed for research purposes[212]	1 (56)	100.0%	Uncon obs	N/A	N/A	N/A	Very low	100
BLOOD TESTS								
Performed routinely[203]	1 (32)	100.0%	Uncon obs	N/A	N/A	N/A	Very low	3
Performed based on clinical judgement	No studies were identified for this analysis							
Performed for research purposes[214]	1 (48)	100.0%	Uncon obs	N/A	N/A	N/A	Very low	58
URINE TESTS								
Performed routinely[203]	1 (32)	100.0%	Uncon obs	N/A	N/A	N/A	Very low	0
Performed based on clinical judgement	No studies were identified for this analysis							
Performed for research purposes	No studies were identified for this analysis							
GENETIC TESTS								
Performed routinely[188;203]	2 (117)	100.0%	Uncon obs	N/A	N/A	N/A	Very low	14 (7, 22)
Performed based on clinical judgement[194;195;204;217]	3 (187)	52.1%	Uncon obs	N/A	N/A	N/A	Very low	3 (1, 7)
Performed for research purposes[180;187;189;192;193;216]	5 (1651)	95.8%	Uncon obs	N/A	N/A	N/A	Very low	10 (2, 24)

1

8.1.7 Evidence statement – percentage of children/young people who had a condition identified or confirmed by the biomedical investigation

EEG

All studies

In total, 6 studies of very low quality provided data for routinely performed EEG, three for EEG performed based on clinical judgment, and 13 for research-based EEG. In studies of routinely ordered EEG 4% (95%CI 2, 26) of children with autism and 7% (95%CI 0, 24) of children with ASD had a clinical diagnosis identified or confirmed (6 had clinical epilepsy, 16 had epilepsy and 2 had Landau Kleffner). In studies of EEG performed based on clinical judgement lead to a clinical diagnosis in none of the children with autism and 4% (95%CI 1, 11) of children with ASD (6 had clinical epilepsy, 2 had generalised epileptiform activity, three had unspecified generalised disorganization and 2 had unspecified hemispheric disorganisation).

Research-based EEG lead to a clinical diagnosis in 24% (95%CI 10, 41) of children with autism and 23% (95%CI 14, 34) of children with ASD (742 had epilepsy, 49 had epileptiform abnormalities, 41 had seizure disorders, 146 had epilepsy/epileptiform abnormalities/seizures, and 25 had Landau Kleffner syndrome).

Regression

One study of children / young people with autism and four studies of children / young people with ASD reported clinical epilepsy in the subset of those with regression compared to those without regression. The combined rate of clinical epilepsy in autism/ASD was higher in those with regression (73/318) than in those without regression (137/836). There was an increased risk of epilepsy in those with an ASD who regressed OR = 1.52 (95% CI 1.10, 2.09).

One study reported that language regression alone (N = 48) had an increased odds ratio of developing seizures OR = 4.5 (95%CI 1.6, 12.5) compared to language regression with autistic regression (N = 103)

Intellectual disability

Four studies of very low quality examined the link between intellectual ability and epilepsy in children with autism/ASD. 22.9% (83/362) of children with intellectual disability had clinical epilepsy compared with 10.3% (4/39) of children with no intellectual disability. Children with intellectual disability had an increased risk OR = 2.45 (95% CI 0.85, 7.13) of clinical epilepsy in these four studies

MRI

All studies

Two studies of very low quality provided data for routinely performed MRI, five for MRI performed based on clinical judgment and one for research-based MRI. Routinely performed MRI lead to a clinical diagnosis in 3% (95%CI 1, 7) of children with ASD (2 had macrocrania / partial agenesis of the corpos callosum and 1 had tuberous sclerosis) and no studies were identified for children with autism. No pathological findings have been identified for MRI based on clinical judgement or research-based MRI. In either autism or ASD

Regression

No studies were identified for this subgroup analysis.

Intellectual disability

No studies were identified for this subgroup analysis.

CT/CAT/PET/SPECT

All studies

Four studies of very low quality provided data for CT/CAT/PET/SPECT performed based on clinical judgment. No studies were identified for routinely performed or research-

based CT/CAT/PET/SPECT. No pathological findings have been identified for test performed based on clinical judgement in either autism or ASD.

Regression

No studies were identified for this subgroup analysis.

Intellectual disability

No studies were identified for this subgroup analysis.

Metabolic tests

All studies

Six studies of very low quality provided data for routinely performed metabolic tests, six for tests performed based on clinical judgment and 1 for research-based tests. No clinical findings have been identified for routinely performed test children with autism or ASD. Metabolic tests performed based on clinical judgement lead to a clinical diagnosis in none of the children with autism and 1% (95%CI 0, 6) of children with ASD (14 had hyperlactacidemia). Research-based metabolic tests lead to a clinical diagnosis in 100% of children with ASD(56 had indolyl-3-acryloylglycine) and there were no studies in children with autism.

Regression

No studies were identified for this subgroup analysis

Intellectual disability

No studies were identified for this subgroup analysis.

Blood tests

All studies

Two studies of very low quality provided data for routinely performed blood tests and two for research-based tests. Routinely performed blood tests lead to a clinical diagnosis in none of the children with autism and in 3% of children with ASD (1 had serum uric acid). No studies were identified for blood tests based on clinical judgment in either autism or ASD. Research-based blood tests lead to a clinical diagnosis in 21% of children with autism and 58% of children with ASD (28 had Mycoplasma, Chlamydia pneumoniae, HHV-6; 9 had allergological test - IgE > 200 Ku/l).

Regression

No studies were identified for this subgroup analysis.

Intellectual disability

No studies were identified for this subgroup analysis.

Urine tests

All studies

Two studies of very low quality provided data for routinely performed urine tests. No studies were identified for urine tests performed based on clinical judgment or for research-based urine tests in either autism or ASD. No pathological findings results from either routinely performed urine tests in either autism or ASD.

Regression

No studies were identified for this subgroup analysis.

Intellectual disability

No studies were identified for this subgroup analysis.

Genetic tests

All studies

Eleven studies of very low quality provided data for routinely performed genetic tests, 5 for genetic tests performed based on clinical judgement and 7 for research-based genetic

tests. Routinely performed genetic tests lead to a clinical diagnosis in 9% of children with autism and 14% (95%CI 7, 22) of children with ASD (8 cases of Down syndrome, 6 cases of suspected genetic abnormality NUD, 5 cases of Fragile X, 2 cases each of Tuberous sclerosis and Ito hypomelanosis each, 1 case each of mitochondriopathia, XYY syndrome, Klinefelter syndrome, Chromosome 46, XX dup(8)(p), Chromosome 17 deletion, Cohen syndrome, Brachmann-De-Lange syndrome, Rubinstein-Taybi syndrome, Usher syndrome, Wilson Turner syndrome, Alexander disease, Asrskog syndrome, Cardiofacial syndrome, CDI-I syndrome, 22-ring chromosomal syndrome, Mosiac ch abnormality (46XY, 47XYY), Interstital chromosomal deletion (2q23.3-2q24.2) and Partial deletion chromosom 11.)

Genetic tests performed based on clinical judgement lead to a clinical diagnosis in 3% (95%CI 2, 4) of children with autism and in 3% (95%CI 1, 7) of children with AAD. (13 cases of Fragile X, 11 cases of Mitochondrial respiratory chain disorder, 5 cases of 16p11.2 del, 3 cases of 2p16.3 del, 2 cases each of Rett syndrome / autism, 47XY, 47,XX,+21, 2q13 del, 13q12.11 del, 15q13.2q13.3 del, 15q13.2q13.3 dup, 21q dup , Xp22.31 del, 46,XY,dup(15)(q11.2q13), 47,XX,+mar(15), 47,XX,+21 each; 1 case each of Williams syndrome, Tuberous sclerosis, X-linked intellectual disability, XYY syndrome, 15q11-13 duplication, Inv/dup of pericentric region of chromosome 10, 47,XYY, 48, XY + mar1 + mar2 / 49,XY + mar1-3, aCGH 1q21.1single, copy 3 BAC loss, Atypical Rett syndrome, PTEN,530insT, PTEN,R130X, 47XY, +der(15) pter q15::p11 pter, 46,XY, inv (2)(p1q13)pat.3q+, Breakage, Trisomy 13, 15 inversion duplication, 47XXY, 46,XY,t(5;16)(p13.2;p13.2), 46,XX,inv(2)(p11;2q13), 46,XY,t(5;17)(q33;p13), 46,XY,t(3;6)(q26.2;q16.2), 46,XY,t(3;5)(q26.2;q22), 46,XX,t(6;7)(q13;q11.2), 46,XY,t(6;9)(q16.2;q13), Duplication (13)(q14.1q21.3), 47,XX,+mar.ish der(13) or der(21) (D13Z1/D21Z1+) [4]/46,XX [17], 46,XY,del (6)(q16.1q21), 46,XY,dup(15)(q11q13), 46,XY,del(10)(q26.3).ish del(10) (q telomere)(D10S2490–), 47,XY,+idic(15)(q13), 46,XY,?ins(6)(?p23?q13?q21), 46,XY,inv(9)(p11q13), 46,XY,inv(9)(p11q13), 47,XXY , 1q21.1 del, 1q43q44 dup, 2p21 del, 2q33.1 del, 3p22.1 del, 3q23 del, 3q29 dup, 4q23 del, 4q35.2 del, 6p21.32 dup, 6q16.1q21 del, 6q16.3 del, 7q11.22 del, 7q11.23 dup, 8pq mos dup, 8q23.3 del, 8q24.22q24.3 del, 9q34.2 dup, 10q11.21q11.23 dup, 10q26.3 del, 12p11.22 del, 12p13.33 del, 12q14.2 dup, 15q11.1 dup, 15q11.2 del, 15q11.2 dup, 15q11.2q13.1 dup, 15q14 del, 16p11.2 dup, 16p13.2 dup, 16q23.3 del, 7q12 del, 18p11.31p11.23 del, 119p13.13 dup, Xq12 de, Xq27.1 del, XXY dup, XYY dup, 45, X, 46,X,idic(Y)(Q11.21), 46,x,INV(Y)(p11.2q11.23), 46,XY, gonadal dysgenesis, 45,X/46,X,dic(X)(P11.2), 46,XX,del(8)(p23), 46,XY,fra(12)(q13), 47,XX,der(14)t(14:?)(q22:?), 46,XX,dup(15).46,XX,dup(15)(q11.2q13), 47,XY,+del(16)(q13q22), 46,XY,del(16)(q13q22), 46,XY,add(17)(q23), 46,XY,add(22)(q13).)

Research-based genetic tests lead to a clinical diagnosis in 4% (95%CI 0, 21) of children with autism and 10% (95% CI 2, 24) of children with ASD. (17 cases of Fragile X, 5 cases of Down syndrome, 4 cases of Provisionally unique syndrome, 3 cases of Sotos syndrome, 2 cases each of Tuberous sclerosis and Phenylketonuria, 1 case each of 7,46,XY,inv(7);[p12.2q31.3], Trisomy 8 mosaicism, Idic(15), Angelman syndrome, 46 XY, dup (22)(q12.1q11.23), 46 XX, del (9)(p24.1), Neurofibromatosis, 46 XY, trp(15)(111.2q12), Smith-Magenis, 47,XX, +invdup (15q11-q13)mat, 46,X,inv(Y)(p11;q11), 46,X,inv(Y)(q27.3).inv(Y)(p11;q11)1) ,46,XY,t(5;6)(q13:p23) ,ring chromosome 8,del 8q22,der 15,Acrocallosal syndrome, Robertsonian translocation, Chromosome inversion (inv 9) , Chromosomal Ygh+ and Polymorphic Y)

Regression

No studies were identified for this subgroup analysis.

Intellectual disability

No studies were identified for this subgroup analysis.

8.1.8 Evidence to recommendations

Relative value placed on the outcomes	The GDG agreed that any of the following would be important outcomes: • If routine testing of those with suspected or confirmed ASD identified

considered	an unsuspected coexisting condition • If selective testing (based on clinical judgement) of those with suspected or confirmed ASD confirmed a suspected coexisting condition • If routine testing of those with suspected ASD identified an alternative disorder to explain the signs or symptoms and thereby helped to rule out ASD • If selective testing (based on clinical judgement) of those with suspected ASD identified an alternative disorder to explain the signs or symptoms and thereby helped to rule out ASD
Trade-off between clinical benefits and harms	The evidence was from studies that considered the "yield" of a particular test or investigation. The yield of a test is the likelihood of a clinically important outcome being identified or confirmed from an abnormal result. For this clinical question the yield was determined by examining the results of tests carried out in children and young people with confirmed ASD. From this evidence the GDG extrapolated conclusions about the usefulness of these tests in identifying coexisting conditions or alternative (non-ASD) diagnoses in those in whom ASD is suspected or (in the case of coexisting conditions) **EEG** A usual reason for performing an EEG is to support a diagnosis of epilepsy when this is clinically suspected. Children and young people with ASD have an increased risk of epilepsy compared with the general population. Children with ASD and either intellectual disability or regression may have even higher rates of epilepsy. The risk of harm to a patient associated with performing and EEG is minimal. However, it is a somewhat time-consuming test, and for some children and young people with ASD co-operation may be difficult. It can also be distressing for some young people and in some cases the distress may lead to a lack of cooperation. Without cooperation the EEG recording may be of poor quality and may be difficult or impossible to interpret. A proportion of individuals in the general population have EEG abnormalities even though they do not have clinical epilepsy. They do not require anti-convulsant treatment. Several studies have found that children with ASD have epileptiform abnormalities in their EEGs but unless there are clinical manifestations of epilepsy treatment would not be indicated. Consequently it follows that an EEG would only be required if epilepsy was suspected based on clinical judgement. . Rarely, but importantly, epileptic encephalopathy (EE), may cause regression and thus is important to consider in the differential diagnosis of autistic regression. EE between 1 and 2 years, the common age for autistic regression, is associated with cognitive regression and often ataxia unlike autistic regression where the regression preserves motor skills and autistic symptoms are most obvious. Children with the rare EE condition known as Landau-Kleffner syndrome (LKS) present usually over 3 years of age. Language regression is the key symptom but behavioural symptoms may be present and overt epilepsy may be absent. A diagnosis of EE is supported by the finding of an abnormal EEG that worsens during sleep. Urgent diagnosis and treatment of Landau-Kleffner syndrome is important. The EEG is an essential component in establishing the diagnosis in this

condition. The GDG noted that Landau Kleffner syndrome was rare (0.3%) in studies where an EEG was performed routinely in children and young people believed to have ASD based on ICD-10/ DSM-IV criteria. In those thought to have ASD who underwent EEG selectively based on clinical concerns the diagnosis of Landau Kleffner syndrome was even more rare (0.001%). The GDG acknowledge that such a result where testing after clinical suspicions resulted in fewer cases identified is opaque. However the evidence base is not adequately robust to provide a clear explanation for this finding, except that it is a chance result given the rarity of the condition.

The GDG's considered view is that usually this rare condition would be suspected on clinical grounds and the EEG would only be performed to confirm the suspicion.

Neuroimaging

Neuroimaging - cranial computed tomography (CT/CAT/PET/SPECT) or magnetic resonance imaging (MR) can identify structural abnormalities of the brain. It is usually performed in order to establish a diagnosis on the basis of clinical suspicion. In children and young people with ASD certain coexisting conditions might be associated with abnormal brain structure – for example tuberose sclerosis. The GDG considered that for most such coexisting conditions it was likely there would be clinical suspicion of the disorder and neuroimaging could be undertaken selectively and only if clinically necessary.

The GDG noted that while there were no studies reporting the yield of routine cranial CT scanning in ASD, the yield using MR [in words] (an alternative sensitive imaging technique) was <3%. Importantly, among more than 1000 children studied (routinely, selectively or as part of a research protocol) only one child was found to have tuberous sclerosis as an unsuspected condition

Both procedures have potential harms associated with them. CT scanning is associated with patient exposure to ionising radiation. Patient cooperation is necessary during these procedures and general anaesthesia may be necessary for MRI.

For these reasons the GDG concluded that neuroimaging should only be performed in children and young people with suspected or confirmed ASD if there were specific clinical reasons to suspect a relevant coexisting or alternative condition and if the performance of the neuroimaging was necessary either to confirm the diagnosis or inform its management.

Metabolic and other blood and urine investigations

The GDG considered the evidence regarding the diagnostic yield from metabolic investigation in children and young people with ASD whether performed routinely or in clinically selected cases, or in a research context. Selected investigation and investigation in research studies did not identify any metabolic disorder in over 600 children tested. In fact 5 of 336 children and young people routinely investigated (no clinical concern) had an identified abnormality and in 4 of these the child had regression. However this was only reported as screen for inborn errors of metabolism so it is unclear what tests were used.

The GDG considered evidence regarding routine full blood count and selective measurement of plasma homocysteine measurement and noted that none of the children with ASD tested had an abnormal result.

	The GDG considered the evidence regarding urine testing in children with ASD. With routine testing only one of 32 was abnormal while with selective testing no child among 117 tested was found to be abnormal. In a research study urinary indoyl-3-acryloyglycine levels were not significantly different in children with ASD and controls. The GDG considered that none of these studies provided evidence to support routine metabolic screening of children with suspected or confirmed ASD or the performance of blood or urine tests routinely. The GDG did not consider there was evidence of benefit from such routine testing and there was potential harm in that venepuncture for blood tests is often a distressing procedure for children and young people. Blood and urine testing could only be justified in those in whom, based on clinical judgement, specific investigation was needed to look for a suspected coexisting or causative condition. **Genetic investigations** The GDG considered that the identification of clinical significant genetically based coexisting conditions was an important objective and a necessary component of the ASD-specific Diagnostic Assessment. A wide range of genetic investigations was available and the sophistication and power of these tests was increasing rapidly. It would be important to identify any genetic disorder that had medical implications, or that had an impact on the health of those with ASD or on their profile of strengths and weaknesses. In some cases recognition of such disorders might have important implications for genetic counselling of the wider family. The GDG considered the available evidence and concluded that for many known genetic disorders there would be associated recognisable phenotypic abnormalities such as dysmorphic features that would point to the need to perform genetic investigations (See Caglayan 2010 for a review of genetic syndromes associated with ASD). However, the GDG also noted that some recognised genetic disorders are less likely to have clear physical features (especially at certain times in development) and that a further pointer to a possible genetic origin was the presence of intellectual disability. Suspicion of a particular genetic disorder would in fact help in the selection of the specific genetic investigations most likely to be informative. Until recently, the genetic tests generally available have been karyotype and specific DNA tests eg for Fragile X. Recently, tests of higher resolution able to detect much smaller regions of imbalance have become available in some laboratories eg array CGH (comparative genomic hybridization), a technique for detecting abnormalities of genomic copy number (CNV). Those with ASD are found to have an increased rate of CNVs. Some appear to be specifically associated with ASD however, in other cases, the significance of the CNV is unclear and further research is needed. The GDG therefore concluded that genetic testing should not be routinely performed on all children and young people undergoing an ASD specific assessment, but should only be undertaken in those with dysmorphic features and/or intellectual disability. As technology is changing rapidly, the appropriate tests to undertake should be agreed with the regional Genetics Centre.
Trade-off between net health benefits and resource use	No evidence was identified regarding cost-effectiveness in relation to these various biomedical investigations. The GDG considered that without evidence of clinical and cost-effectiveness routine testing could not be recommended. The routine use of EEG testing and neuroimaging would have significant resource implications, particularly in relation to EEG technician and radiographer time and the time required for specialist doctors to interpret

	the results of these investigations. However the NICE guideline on epilepsy recommends that an EEG should be performed only to support a diagnosis of epilepsy in children. Similarly the GDG considered that given the low diagnostic yield with metabolic investigations and other blood and urine testing meant that they were not likely to be a cost effective use of resources. Finally, the GDG considered that, while there was no evidence regarding cost effectiveness, selective use of appropriate specific genetic investigations in children and young people with clinical features suggesting a genetic disorder was justified because genetic disorders identified might have important implications for the individuals and other family members, for example the identification of Fragile X.
Quality of evidence	The quality of the evidence in relation to the EEG and neuroimaging, metabolic and genetic testing was very low. The GDG noted that studies that identified co-existing conditions gave yields that would not in the GDG's view be seen in a general clinical sample. In both these sections where routine testing comes up with higher rates than clinical judgement, including the 95% CIs would be one way to highlight the lack of precision in the findings The GDG noted that where the evidence for routine testing for EEG reports a higher of abnormal results that the rates for clinical judgement, the wide confidence intervals indicate that the imprecision of these findings.
Other considerations	Regression of language and social communication and play skills with the signs and symptoms of autism in a child aged two years is unlikely to be due to epileptic encephalopathy although children with epileptic encephalopathy under 2 years do often regress—usually with more global symptoms and overt epilepsy. Autistic regression over 3 years of age is uncommon thus in children who present with language regression aged 3 years or older who may have behaviour problems but are less obviously autistic, and who may have fluctuating language loss, LKS should be considered. At all times, the possibility of epilepsy should be considered in a child with autism as an additional disorder and especially if there is intellectual disability.
Recommendations	53. Do not routinely perform any medical investigations as part of an ASD diagnostic assessment but consider the following in individual circumstances and based on clinical judgment: • electroencephalography (EEG) if there is suspicion of epilepsy (see 'The epilepsies: the diagnosis and management of the epilepsies in adults and children in primary and secondary care' [NICE clinical guideline 20]) • genetic tests, as recommended by your regional genetics centre, when there are specific dysmorphic features and/or evidence of intellectual disability.

8.1.9 Research recommendations

PICO research question	What are the effectiveness, cost effectiveness and acceptability to parents, carers, children and young people, of biomedical investigations (that is, EEG, brain imaging, genetic tests, metabolic tests or other blood or urine tests) for establishing aetiology, and/or of genetic counselling in children and young people with identified autism spectrum disorder?

Why this is needed	
Importance to 'patients' or the population	The area of research focuses not on diagnosis of ASD but on aetiology or genetic counselling, which are part of the wider diagnostic assessment, along with profiling. As yet, few genetic tests have obvious treatment implications and the value of these tests in improving the welfare of children and young people or the family is not well understood. As more genetic findings emerge, they might prove valuable in terms of explaining the underlying cause of a child's ASD but we have no evidence that this would improve outcomes.
Relevance to NICE guidance	Genetic counselling is currently an emerging area of research and will fill existing evidence gaps.
Relevance to the NHS	The costs would include not only laboratory investigation but also clinical time for appropriate consenting of families for example for genetic testing and interpretation of results. With regard to genetic tests, there is already a cost incurred for karyotype and DNA for Fragile X so any replacement test, for example for CGH array, would be offset.
National priorities	The GDG believe it is not a national priority area for the NHS
Current evidence base	Current evidence about the utility of biomedical investigations where there is no clear indicator (dysmorphology, intellectual disability, epilepsy suspected (for EEG)) does not allow us to judge whether such tests improve acceptability to families in terms of identifying a known aetiology or for future family planning.
Equality	With respect to other genetic testing, the GDG consensus is that there is lower uptake among disadvantaged groups.
Feasibility	A study on parental 'acceptability' and satisfaction about known/unknown aetiology would be feasible and of moderate cost only.
Other comments	None

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9 Information and support

9.1 Introduction

Children and young people with possible ASD and their carers need information they can understand and that is relevant to their circumstances. They may also require ongoing day-to-day support leading up to and throughout the assessment process. The chapter provides examples of information and support that are likely to be useful to children, young people and their families and carers from the point of referral, through assessment, at the point of diagnosis and beyond. Children and young people with possible ASD and their carers may need a variety of different kinds of ongoing support while waiting for and during the process of assessment for ASD, regardless of the outcome. This chapter aims to identify the kinds of day-to-day support that has helped others in this situation and to make recommendations about what should be offered during the process of referral, assessment and diagnosis. It does not cover specific types of therapeutic management available to children and young people while waiting for a diagnostic assessment as this was outside the scope of the guideline.

Clinical Questions

What information do children and young people, and their families/carers need during the process of referral, assessment and diagnosis of ASD?

What kinds of day-to-day, ongoing support (not specific to therapeutic interventions/management of ASD) should be offered to children and young people, and their families/carers, during the process of referral, assessment and discussion of diagnosis of ASD?

9.2 Information during the process of referral, assessment and diagnosis

9.2.1 Methodological approach

The purpose of this review was to find out what information children, young people and their carers need during the diagnostic process. The GDG agreed that the most appropriate evidence for this question would be identified in controlled and uncontrolled observational studies which describe the ASD family's needs/difficulties and feelings about certain given information.

Evidence of the views of patient or parent/carer experience from individual studies was extracted into evidence tables (see Appendix H) and summarised into modified GRADE evidence profiles below. In order to best reflect patients' opinions, as well as to avoid the risk of information loss/distortion, themes are reported in the modified GRADE evidence

profiles. These themes are supported by individual verbatim quotations from the included studies.

After an initial search of 25,787 references in the overall search, 41 papers were selected on title and abstract and requested for full review. Four studies were eligible for inclusion based on the following criteria:

Population: a) Children and young people under 19 years diagnosed with ASD ; b) Parents/caregivers of children and young people with ASD.
Outcomes: a) 'Good' information: information that could enhance family's understanding of ASD, improve family's mental health status and contribute to the child or young person's rehabilitation; b) 'Poor' information: information that has a negative impact on family's mental health and a child or young person's rehabilitation; c) Parents' and carers' expectation: expectation of the kind of information that should be provided to them.
Study type: Controlled and uncontrolled observational (qualitative) studies.
A list of the 37 excluded studies and the reasons for exclusion is found in Appendix G – Table of excluded studies.

9.2.2 Description of included studies

All of the four included studies[131;132;134;135] were carried out in the UK. All studies were uncontrolled observational in design so all were graded as very low quality. Two of the studies[131;132] used a postal questionnaire (a total of 1350 responses across both studies), one study[135] conducted structured interviews with 11 families and one study[134] conducted 15 focus groups involving a total of 70 parents. All studies reported from parents of children with ASD. No studies reported on children or young people's response. The authors of one study[135] summarised the views of participants but did not report verbatim quotes.

Further details regarding individual studies are presented within the evidence tables (see Appendix H – table of included studies).

9.2.3 Evidence profile

Table 9.1 summarises examples identified in the included studies of good and poor information provided during the diagnostic process, and the kinds of information parents would like to receive.

Table 9.1 Examples of information provided during the diagnostic process

Examples	Study Quality						Supporting quotes from parents
	Number of studies	Study design	Limitations	Inconsistency	Indirectness	Quality	
GOOD INFORMATION							
None identified							
POOR INFORMATION							
Not providing parents with information about what kinds of help are available[134]	1	Uncon obs*	NA	NA	NA	Very low	*'I didn't realized he could have had help'*
Delay in diagnosis[131]	1	Uncon obs*	NA	NA	NA	Very low	*'The whole process is far too slow and seems to depend on the parents' persistence in pushing for a diagnosis. Months seem to go by waiting for appointment after appointment. This really prolongs the agony of what is, inevitably in any case, a painful process.'*
Professions' reluctance to give diagnosis [131]	1	Uncon obs*	NA	NA	NA	Very low	*'I was fed up with professional pussyfooting around, afraid to say the dreaded word 'autism'. It seems that the very word autistic is taboo.'*
Information throughout the diagnostic process and at the time of diagnosis[132]	1	Uncon obs	NA	NA	NA	Very low	*'More time and information should be given to parents at diagnosis. I was informed of the diagnosis and told I would be seen by the family services worker in a month. That was it. Not explanation. No hope. It was obvious that they knew what diagnosis they were likely to make prior to the play session but I had no prior warning. No one had the decency to tell me what might be wrong. At that point I needed to believe there was a future and I was appalled at the way I was treated. I should have had counselling there and then and lots of information given to me.'*
PARENTS' EXPECTATIONS – what kind of information should be provided							
Comprehensive, basic information[131]	1	Uncon obs	NA	NA	NA	Very low	*'It would have helped us considerably if we had been provided, from the start, with a set of leaflets explaining the basic things parents need to know about, such as: statement of Special Educational Needs, respite care, local facilities and support groups, benefits and allowances, such as Disability Living Allowance etc., the roles and responsibilities of the numerous professionals involved, simple definitions of all the relevant terminology, advice on further reading.*

							It took us a long time to find out this sort of information, much of which was gleaned from other parents who had also found things out the hard way.'
Need for empathy/reassurance[132]	1	Uncon obs	NA	NA	NA	Very low	*'I believe that when parents are told during diagnostic assessment that their child is autistic, they should be reassured that there are things they can do, e.g., Lovaas, PECS, change of diet, to make a huge difference. Obviously don't mislead them to think these things are a cure, but don't lead them to believe that the future is bleak, and doom and gloom, as I was'*
Explanation of the clinical processes, especially at assessment[135]	1	Uncon obs	NA	NA	NA	Very low	The study authors reported participants views in summary only, without supporting quotes
Written advice on the services available[135]	1	Uncon obs	NA	NA	NA	Very low	The study authors reported participants views in summary only, without supporting quotes
Individualised advice for the child, not for the diagnosis[135]	1	Uncon obs	NA	NA	NA	Very low	The study authors reported participants views in summary only, without supporting quotes
More information on the child's progress and development[135]	1	Uncon obs	NA	NA	NA	Very low	The study authors reported participants views in summary only, without supporting quotes
Generalised information about ASD[134]	1	Uncon obs	NA	NA	NA	Very low	*'It would've been helpful just to have a very generalized, not a deep, I don't know I could have coped with loads and loads of leaflets.'*
Information about expectation of challenges/potential for progress for children with ASD[134]	1	Uncon obs	NA	NA	NA	Very low	*'I would have benefited from someone coming round…and telling me 'Don't expect this too soon', or 'Don't expect that behaviour"*

*: Uncon obs: Uncontrolled observational study, such as case series.

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9.2.4 Evidence statement

Good information

No papers provided evidence about good information.

Poor information

Three papers provided evidence about poor information in parents' opinion:

- No information about what kind of help is available

Parents' expectations – what kind of information should be provided

Four papers provided evidence about parents' expectation of information. The information can be classified into five groups: information about ASD, information about children with ASD, information about the diagnostic procedure, information about available support and information about available support organisations.

Information about ASD

- Simple definitions of all the relevant terminology
- Advice on further reading.

Information about the diagnostic procedure

- The roles and responsibilities of the numerous professionals involved
- Explanation of the clinical processes, especially at assessment

Information about Children with ASD

- Liaison with Education/The Educational Special Needs process
- Individualised advice about the child,
- Realistic expectations of the challenges that many children with ASD face, as well as the potential for progress and change
- Advice on treatment options available

Information of available support

- Benefits and allowances, such as Disability Living Allowance etc.
- Information about respite care

Information about available support organization

- Local facilities and support groups

Parents' expectation - when information should be provided to the family

Only one paper provides evidence for when should the information be provided to the family. Parents of younger children wanted information to be made available to them immediately at the time of diagnosis. The parents of the oldest children suggested that information should be phased over a period of time after the diagnosis.

9.2.5 Evidence to recommendations

Relative value placed on the outcomes considered	The GDG considered that evidence of 'good information, 'poor information' and 'parent expectations' should be identified for this question. Evidence from this review could then be extrapolated by the GDG to develop guidance what type of information children, young people and their carers need during the process of referral, assessment and diagnosis of ASD.
Trade-off between clinical benefits and	The GDG considered that evidence identified immediate and longer term benefits of providing accurate, appropriate and sympathetic information to a

harms	child, young person and family and carers. The potential harms identified were associated with the way that information may be given by health care professionals. It was the GDG's view that children, young people and their families require different kinds of information which needs to be tailored to their chronological and developmental age, their current health state and the impact of their condition on their lives. Parents in the studies reported the harms of poor information to be delays accessing services and therefore delay in developing a comprehensive understanding of their child. The information required can be summed up from the quote from a parent in one study who said they needed "the basic things parents need to know about autism", that is, its impact on the child and family and the availability of local and national services and supports. Parents reported the need for a named person that they could contact locally for further information. One parent summed up their experience as "finding out the hard way." Many parents quoted in the evidence were reported as wanting information on treatment (interventions and management). Parents also wanted diagnostic information to be individualised to the child's specific ASD profile, with information about what to expect with further child development milestones and what services and support were available locally. There were differences in how much information different parents wanted at what time. According to the only study which provided evidence on when to provide information, the responses differed by the age of the child. This pattern of results may reflect concerns in these parents about issues such as school transitions, especially those issues revolving around leaving school, which may not impact immediately on parents of younger children. The evidence supports the recommendations made by consensus within the GDG. The GDG consensus was also that children, young people and their carers require specific information about what would happen next. No evidence was identified that considered the value of specific types of day to day support, such as a telephone helpline. The GDG agreed that it was not possible to make a specific recommendation about which types of day to day support should be offered to children, young people and their families throughout the ASD pathway given the lack of evidence and the wide range of practice within the NHS.
Trade-off between net health benefits and resource use	The GDG considered that the provision of good quality information, given at the right time and individualised for the specific circumstances of the child or young person was not an expensive intervention, and the evidence from the qualitative studies showed that good information could have a very large impact on welfare, both of the child and carers, with positive impacts on the wider family. The provision of individualised information is good practice in many child development teams and is a relatively inexpensive means of keeping the family up to date with local resources and information that is directly relevant to their circumstances, such as the child's age and the severity of impairment. No cost-effectiveness evidence was identified that had considered the value of information in improving quality of life. However it was the GDG's opinion that sharing information specific to the child/ young person represented a good use of NHS resources by supporting the family to seek appropriate help early on and thereby increasing the child's welfare and reducing family stress.

Quality of evidence	The studies identified in the review only included the reported views of parents whose children were going through the process of diagnosis. No evidence was identified that reported the views of children and young people, or carers who were not also parents. Only four studies were identified that addressed this question, all of which came from the UK. They all reported qualitative evidence. The evidence came from small samples of self selected participants. There was not a sufficient evidence base on which to base recommendations for the NHS. But the results concurred with the views and experiences of the GDG members and there were no surprising findings.
Other considerations	The GDG agreed that families benefit from information about the support that is available to them, and that this support can be extremely important to them. This information could provide support, reduce stress and improve outcomes for the child and family while additional assessments or interventions are on-going. The information needs to be local, up to date and relevant to the specific circumstances of the child/ young person, Information about the child/young person also needs to be shared with other professionals involved in the care of the child or young person so that everyone is fully informed and can support the child and young family if further assessments are required, and to provide on-going support to meet the child/ young person and families' needs.
Recommendations	63. Provide information on support available locally for children and young people with ASD on an individual basis according to the family's needs. This may include: • contact details for: local and national support organisations (who may provide, for example, an opportunity to meet other families with experience of ASD, or information about specific courses for parents and carers and/or young people) advice on available social benefits education and social services • information to help prepare for the future for example, transition to adult services.

9.3 Support for children, young people, their families and carers

9.3.1 Methodological approach

The purpose of this review was to find out what kinds of day-to-day, on-going support should be provided to the family during the ASD diagnostic procedure.

The ideal population for this question should be children, young people and their carers who have been referred for assessment and possible diagnosis of suspected ASD, regardless of the final diagnosis. Due to the lack of evidence for this particular population, the GDG agreed that retrospective studies looking at children and young people who have been diagnosed ASD children/adolescents and their carers' past experience of the diagnostic procedure were appropriate to answer the question.

Evidence of the views of patient or parent/carer experience from individual studies were extracted into evidence tables (see Appendix H) and summarised into modified GRADE

evidence profiles below. In order to best reflect patients' opinions, as well as to avoid the risk of information loss/distortion, themes are reported in the modified GRADE evidence profiles instead of outcomes. These themes are supported by individual verbatim quotations from the included studies.

After an initial search of 25,787 references in the overall search, 18 were selected on title and abstract and the papers requested for full review. Four studies were eligible for inclusion based on the following criteria:

Population: Children and young people under 19 years adolescents diagnosed with ASD or their parents/caregivers.

Outcomes: a) 'Good' support: support that could have positive impact on families' welfare; b) 'Poor' support: support that have negative impact on the families' welfare; c) Parents' expectation: Parents' expectation of what kind of support that should be provided to them.

Study type: Controlled and uncontrolled observational studies.

A list of the 14 excluded studies and the reason for exclusion is found in Appendix G – Table of excluded studies.

9.3.2 Description of included studies

Three of the included studies were carried out in the U.K. [132;134;135] and one in the USA[224]. All studies [132;134;135;224] were uncontrolled observational design so all were graded as very low quality. One study conducted structured interviews with 11 families, one conducted short, open-ended interviews with five families, one conducted 15 focus groups with a total of 70 parents, and one was a postal questionnaire with a total of 55 responses. Although one study was conducted in the USA[224], the GDG felt that the experience might provide insights for the UK context. The study assessed the Vermont Rural Autism Project (VT-RAP), a 3-year federally and state-funded service program designed to enhance service delivery and create systems responsive to children with ASD and their families throughout Vermont. The VT-RAP assessment process made participating families an integral part of the assessment team with professionals participating in family activities and going into schools, as well as family's participating in the assessment.

All studies reported from parents of children with ASD. No studies reported on children or young people's response. The authors of one study[135] summarised the views of participants but did not report verbatim quotes.

Further details regarding individual studies are presented within the evidence tables (see Appendix H – table of included studies).

9.3.3 Evidence profile

Table 9.2 summarises examples identified from the included studies of good support, poor support and the kinds of support parents would like to receive.

Table 9.2 Examples of support provided during the diagnostic process

Examples	Study Quality						Supporting quotes from parents
	Number of studies	Study design	Limitations	Inconsistency	Indirectness	Quality	
GOOD SUPPORT							
Involving the school in child's assessment [224]	1	Uncon obs*	NA	NA	NA	Very low	*'It is a whole attitude shift and once you make that, things fall into place. I think that's what [VT-] RAP does. It pushes that button that gives people an attitude shift, I know it did for the school team….it made us feel like somebody was coming to our rescue. We dialled 911'*
Involving family in child's assessment [224]	1	Uncon obs	NA	NA	NA	Very low	*'We really felt like we were a part of the team, and somebody was listening to or questions. And while we always knew that a lot of the questions may not have answers, we felt that while there weren't answers there were a lot of people out there who could give us ideas.'*
Making individual team members to become more engaged in supporting ASD children [224]	1	Uncon obs	NA	NA	NA	Very low	*"It was wonderful having the SLP join the consulting team. She is learning, too. She goes right for it. She's a practical minded person and I value her opinion. She finds out if she doesn't know something, and there is good follow-through. Her involvement really benefited us'*
Facilitating a shift in the family's attitudes and behaviours [224]	1	Uncon obs	NA	NA	NA	Very low	*'[VT-RAP] was a complete asset to our son's future. It helped us look at him in terms of how the learns and doesn't learn. We [now] accommodate him instead of him accommodating us.'*
Support from school [134]	1	Uncon obs	NA	NA	NA	Very low	*'And since she's been at the school, they've [teachers] been very helpful, they've taught me a lot about the autism'*
Providing opportunities for ASD families to contact each other [134]	1	Uncon obs	NA	NA	NA	Very low	*'I feel quite lucky, because I did have that group for parents of newly diagnosed children'*
POOR SUPPORT							
Not providing any support [134]	1	Uncon obs	NA	NA	NA	Very low	*'It's that bad, it's that isolating, and I feel that shoved out of society'*
Lack of immediate help and support in	1	Uncon obs	NA	NA	NA	Very low	*'It's still slightly bizarre or surreal in my own mind, because I rang this number, which I thought would be answered immediately, and I*

times of crisis [134]							*was told that I was in a queuing system, could I be patient and wait, while this adolescent was waving a knife in front of me'*
Professionals not always easily contactable[134]	1	Uncon obs	NA	NA	NA	Very low	*'They need to be more available.'*
Little continuity or communication between the various services and authorities involved[134]	1	Uncon obs	NA	NA	NA	Very low	*'I find it very frustrating how social services, health and education…all work very much independently of one another'*
Offering support immediately after communicating the diagnosis[132]	1	Uncon obs	NA	NA	NA	Very low	*'More time and information should be given to parents at diagnosis. I was informed of the diagnosis and told I would be seen by the family services worker in a month. That was it. Not explanation. No hope. It was obvious that they knew what diagnosis they were likely to make prior to the play session but I had no prior warning. No one had the decency to tell me what might be wrong. At that point I needed to believe there was a future and I was appalled at the way I was treated. I should have had counselling there and then and lots of information given to me.'*
PARENTS' EXPECTATIONS – what kind of support should be provided							
Offer more guidance to help prepare for the future[135]	1	Uncon obs	NA	NA	NA	Very low	The study authors reported participants views in summary only, without supporting quotes
More practical support (e.g. review more frequently, offer intensive one-to-one sessions[135]	1	Uncon obs	NA	NA	NA	Very low	The study authors reported participants views in summary only, without supporting quotes
Offer more support, regardless of level of disability[135]	1	Uncon obs	NA	NA	NA	Very low	The study authors reported participants views in summary only, without supporting quotes
Co-ordinate information better (e.g. share feedback from clinic)[135]	1	Uncon obs	NA	NA	NA	Very low	The study authors reported participants views in summary only, without supporting quotes
Providing parents with support on demand[134]	1	Uncon obs	NA	NA	NA	Very low	*"It should be there all the time, whether you need it or not, before you get to that stage [breaking point]'*
Establishing a more coherent service,	1	Uncon obs	NA	NA	NA	Very low	*'Tri-agency alliances are a must'*

involving health, education and social services[134]							
Appointing someone as a 'key worker'[134]	1	Uncon obs	NA	NA	NA	Very low	*'Someone who is able to communicate between the agencies'*
Providing parents with respite care[134]	1	Uncon obs	NA	NA	NA	Very low	*'People who would befriend him…like a buddy system, where people would befriend and actually just sort of spend time…and actually take him outside the family environment…It alleviates some of the burden from me and my wife, and particularly my other children.'*

Uncon obs: Uncontrolled observational study, such as case series.

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9.3.4 Evidence statement

Good support

Two papers provided evidence for good support in clinical practice, one from the USA and one from the UK. Examples of good support:

- involving the school and the family in the child's assessment.
- providing opportunities to work on social skills (e.g. supporting them to turn take in a preferred activity or be involved in a specific task in a team game)
- facilitating a shift in the family's attitudes and behaviours
- support from school, such as providing advice, offering placements at school
- providing opportunities for the families to have contact with each other.

Poor support

Two papers reported poor support in clinical practice:

- the service did not provide parents with any support
- no provision of emergency or immediate support in times of crisis
- professionals are not always easily contactable
- little continuity or communication between the various services and authorities involved.

Parents' expectations - what kind of support should be provided

Two papers looked at what kind of support parents expect. The types of support parents expected are classified into three groups: support for the children, support for the family and support during the assessment.

Support for children with ASD

- Offer more support, regardless of level of disability

Support for the family

- Offer more guidance to help prepare for the future
- Provide more educational support
- Providing parents with some leaflets of different things about children with difficult problems
- Respite

Support for assessment

- Co-ordinate information better, for example, share feedback from the clinic
- Appointing someone as 'key worker'
- Establishing a more coherent service system, involving health, education and social services
- Written information on what problems to expect

- Offering support immediately after communicating the diagnosis

9.3.5 Evidence to recommendations

Relative value placed on the outcomes considered	The GDG considered that reports of 'good support, 'poor support and 'parent expectations' would be the most useful evidence for addressing this question.
Trade-off between clinical benefits and harms	The evidence that was identified for this question was from interviews with parents of children who had been through a diagnostic assessment for ASD. It illustrated the views of small groups of parents on what they valued in the support they received and what they would like to be different. The GDG took an overview of this evidence identified specific ideas and suggestions which they believed could be turned into practical recommendations for the NHS. The GDG also recognised that other were other views expressed in the evidence which were more difficult for individual clinical teams to implement and would require far-reaching and long term changes to the way that's services are organised in the NHS. The need for a more streamlined data processing to simplify communication between agencies was one such idea. The GDG strongly support this, but see it as a part of a wider need to improve communication between agencies and not specific to the needs of families and children with ASD. The GDG view is that the right support and intervention earlier on could have a very large impact on the welfare of the child/young person and family. One of the important themes reflected in the evidence and a viewpoint supported by the GDG is that there should enhanced communication between the assessment team and the child's educational setting. It was the consensus of the GDG that a visit to the school by a member of the assessment team or to have a teacher present during a follow-up meeting with parents after assessment would be a highly beneficial intervention given the problems that some families have with feelings of isolation and helplessness during and after assessment for ASD. Another theme supported by the GDG is services provision for the child/ young person during the diagnostic process. Where waiting for assessment and throughout the process, services should be in place to support the child's needs. It is outside the remit of this guideline to specify what these services should be. However, the GDG view is that they should not be delayed pending diagnosis and should be specific to the needs of the child or young person and their family. The role of a 'key worker' is mentioned in the qualitative evidence. The GDG view is that a coordinator role is valuable in acting as a link between the ASD team and the child/ young person and their family. The GDG view was that this role should be performed by someone within the ASD team and this may be different from a generic key worker role. The GDG view

	was that an ASD team member should be assigned this coordinator role to offer support and information during and immediately after a diagnostic assessment. The GDG concluded a case coordinator should be appointed once the decision has been reached to proceed to a full diagnostic assessment to support the child/ young person through the process. Provision of information about local support services specific to their age and circumstances should be provided to all children and families to improve their quality of life during and after diagnosis.
Trade-off between net health benefits and resource use	The evidence presented in this review suggests that the provision of support for children, young people and families is as a priority for the parents and families of children going through assessment. This is not always seen as the priority for the health care professionals undertaking the assessment because of the pressure to reduce waiting times for assessment and to see as many children as possible for assessment. From the families point of view, the welfare benefits of appropriate support during the process of assessment may mitigate the stress of waiting for a definitive diagnosis. Furthermore, if appropriate support and intervention can be accessed without the need for a definitive diagnosis of ASD support, then the pressure on professionals to speed up the process of assessment and reduce waiting times can be reduced. There are no health economic studies or externally verifiable data on the costs or outcomes of support for families during diagnosis. It is not possible to make a strong case for this support in the basis of evidence, but it is the GDG's opinion that the experience of assessment may be greatly improved by the early provision of appropriate support and advice to families. It is also the opinion of the GDG that non-therapeutic support is not costly and may reduce unnecessary and inappropriate use of other NHS resources by allowing the family to get advice on how and when to use the services that are already in place. It was the GDG's view that some of the health care resources should be identified to improve communication between health and education agencies, as well as social services and the voluntary sector involved in the assessment and on-going support of the child who has undergone a diagnosis for ASD, regardless of the final diagnostic category they are given. The GDG view is that the Case Coordinator role is integral to the team and therefore does not require additional professional time or health care resources, but a change in how professional time is used to improve communication and support for families. The GDG considered that the costs of professional time to liaise with educational colleagues was a cost-effective use of resources in both increasing the effectiveness of immediate and on-going support and management and reducing the need for unnecessary consultations as a result of the breakdown of communication between health and social care professionals.

Quality of evidence	The quality of the evidence was judged to be very low, because the studies were uncontrolled observational in design. The interview data concurred with the views of the GDG and there were no surprising findings. The limitations of using qualitative evidence only are that the views expressed relate to specific interventions which may not be reproduced widely in the NHS. It may also give too much weight to opinions and views that are not widely shared among parents and carers. However the GDG consensus was that the views expressed in the evidence reflected the views of many parents and carers going through diagnostic assessment in the NHS.
Other considerations	The GDG consensus is that, once a diagnostic assessment has been completed, regardless of the outcome, a model of enhanced communication between health and education should follow as it has a direct impact on the immediate support for the child or young person, and may set a good pattern for communication between health and education for the long term future. The follow up visit by a health care professional to the educational setting of the child or young person is already good practice in many parts of the NHS. The visit has a number of goals, the most important one of which is ensuring long term agreement professionals in health and education on how a child or young person's needs should be met in the immediate and long term future. It is the GDG's view that good communication between professionals is vital in ensuring that the messages that children, young people, families and carers receive from professionals is helpful and consistent, and that there is effective feedback from families to professionals without the need for a lot of unnecessary repetition. This should also ensure that changes to the child's and family's circumstances over time are well understood and incorporated into any management and support strategies across health and social care.
Recommendations	34. A case coordinator should be appointed from the ASD team for every child or young person who is to have an ASD diagnostic assessment. 35. The ASD case coordinator should: • act as a single point of contact for the parents or carers and for the child or young person undergoing an ASD diagnostic assessment, and for relevant professionals • make sure that parents, carers, children and young people have appropriate information and access to appropriate support during diagnostic assessment • explain to parents and carers the likely time and sequence of assessments. 62. After assessment and diagnosis of ASD, make sure the profile is made available to professionals in education and, and if appropriate, social care, so it can contribute to the child's or young person's individual education plan and other aspects of the needs-based management plan, through for example, a school visit by a member of the ASD team.

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10 Service descriptions and resource use

10.1 Introduction

The goal of diagnostic assessment for Autism Spectrum Disorder (ASD) is to identify children who have an ASD as quickly as possible so that they can access appropriate services and support. It is important that resource used in the recognition and diagnosis of ASD is efficient and effective because health care resources are always scarce. It is important to demonstrate that the recommendations developed for this guideline improve the way in which a diagnosis of ADS is arrived at and improves the experience of the process for children, young people, their families and carers. As with all health service decision-making, to do more of one thing means doing less of something else where resources are finite. The guideline development group has considered the impact of their decisions on resource use at every stage of the pathway, and has made its deliberations explicit in the translations of the evidence to recommendations. These deliberations have not, however, been made on the basis of externally verifiable evidence of cost-effectiveness because no evidence could be identified for any of the decision points in the care pathway. There are a number of reasons for this which requires some explanation.

The focus of the guideline is on recognition and diagnosis of ASD. In order to identify whether a diagnostic intervention (for example an ASD specific diagnostic tool such as the ADI-R or ADOS) is cost -effective, it is necessary to understand the consequence of diagnosing ASD to the individual and their family/ carers in terms of their welfare in the immediate and longer term. There is no clearly identifiable means of expressing 'effectiveness' when considering a behavioural/ developmental disorder or condition such as ASD. ASD manifests itself in children and young people with ASD very differently across the spectrum; between individuals, and within individuals as they grow older over time. ASD related disability is very difficult to quality employing the usual metrics of health economic evaluation (the quality adjusted life year) but this is not the only way of measuring health and well being. But the methods of economic evaluation used by NICE require consideration of outcomes in terms of the QALY to allow for explicit comparison of health care resource use across different areas of the NHS. For this guideline, an explicit unit of health outcome that could be translated into a QALY could not be identified because of the nature of the condition, either in the literature or by the members of the guideline development group.

Furthermore, at present there is not enough evidence that a single diagnostic "test" is sufficient for diagnosing ASD. There are developments in genetic testing which may result in a definitive test in the future but the present evidence does not support this. Therefore, an economic model that considered the diagnosis of ASD as a comparison between one test and another, or compared with current practice, was not appropriate. Also, the genetic tests which are considered in the guideline are not included in an economic model because they do not diagnose ASD. Their purpose is to diagnose other coexisting conditions or identify the cause of ASD in children and young people diagnosed with the condition. The value in identifying a cause of ASD is not easy to define or measure as it relates to decision-making about future family planning and the value to families of understanding why a child or young person has ASD.

An evaluation of biomedical and genetic tests for other conditions is not straightforward either since it would have to consider the effectiveness of identifying and managing conditions other than ASD, then consider the alternatives for management of that condition to arrive at a decision about whether it was cost effective to test children and young people with ADS for that condition. The studies that was identified for the clinical review of biomedical tests did not evaluate the effectiveness of a biomedical test in identifying a specific condition, but reported the 'yield' of a test in terms of how many abnormal results were identified. This evidence is one step removed from identifying a specific medical condition. Many of the abnormal results identified in these studies had no clinical significance. Even if the evidence had allowed the GDG to identify the accuracy (sensitivity and specificity) of a test in identifying a specific condition, to review the evidence for treating or managing other conditions in children with ASD would have been outside the scope of the guideline.

Finally, the aim of the diagnosis assessment is not only to arrive at a firm diagnosis of ASD but encompasses a far wider assessment of the child or young person's "profile" of strengths and weaknesses in order to inform future management. The assessment of strengths and weaknesses may require specific assessments but only in some children and young people. A literature search was not undertaken for this question. It was not possible to conceive a study design to could evaluate the effectiveness of assessments for profiling strengths and weaknesses to inform future management in children and young people with ASD. The recommendation is that the ASD team use their expertise and clinical judgement to consider which assessments to proceed with.

These problems in identifying or even conceptualising the type of evidence to inform recommendations are not confined to ASD alone and are somewhat generic to guidelines on developmental/behavioural and mental health conditions in childhood and adolescence. The complexity of the condition and the complexity of health care professionals' decision-making make it a difficult area for research that can directly inform a set of practical health care recommendations. Nevertheless decisions are made every day about how to recognise and diagnose ASD by individual clinicians and therapists. The postcode lottery for ASD diagnostic services across the NHS is a problem which this guideline has sought to address.

The GDG considered carefully how to make recommendations in the absence of evidence of clinical and cost effectiveness. One approach was to make its deliberations about the cost effectiveness of recommendations explicit throughout the translations in the guideline which has been done. The second is to describe what good ASD diagnostic services look like currently, that is, services that already follow many if not all of the recommendations in the guideline. The purpose is to give an idea of the ways that services might be configured to deliver the quality of care recommended in this guideline. It is not exhaustive, but shows how resources are currently used and which health care professionals are involved in which parts of the diagnostic pathway.

The service descriptions that follow are real services in the NHS covering inner city and rural/urban services, hospital and community based services, and a specialist regional referral unit that accepts referrals from other ASD teams for children and young people with especially complex diagnoses. These are not set up to be exemplars for service provision in the NHS, but to offer those who wish to set up a new service or to improve their service in line with the current guideline some examples of how this is being done elsewhere. The data on time taken to complete specific parts of the assessments in section 2 are estimates from one individual clinician working in that service. This data has not been verified by other evidence. The descriptions give examples of how resources can be used in different ways to achieve the same goals.

The rest of this chapter describes five current services in the NHS which could be seen as examples of good practice in ASD diagnostic assessment but that also give contextual information about how resources are employed currently, the pressure points for health services, and the forces at work which might increase or decrease costs for the NHS. The second section provides a systematic resource use analysis to describe how

services are configured in terms of the way that NHS personnel are deployed to do different kinds of tasks at different stages of the ASD diagnostic pathway.

As a whole this chapter is intended to give those who are not familiar with how multidisciplinary teams are organised; their workload; how they work together and decide which types of assessments and observations are required for different children and young people; how services are coordinated; the proportion of children and young people receiving non core elements of assessment, how they feed back information to families regarding diagnosis and address diagnostic uncertainty; and the support available during the process of diagnosis.

The first section describes how five services are configured. The second part considers resource use, but not the cost of these services. NHS tariffs for an ASD assessment are not published for the NHS. These services are not costed because the resource use is not exhaustive and only based on interviews with only one individual which the GDG did not believe was a sufficiently robust basis on which to derive cost data. A 'bottom up' cost analysis would require data on the costs of staff and the cost of overheads. The mean salary for specific health care professionals is published every year for the NHS in a publication called The Unit Costs of Health and Social Care. This provides an estimate of the midpoint on a salary scale for different ways of counting how health care professionals work, for example cost per contract hour, cost per patient related hour or per face to face patient contract. A generic 'per patient contact' data is reported differently for different professionals, making like for like comparisons difficult. In addition, the GDG were clear that the level of competency and expertise required in an ASD team implies health care staff costs which are higher than the midpoint on the salary scale. For each individual service, and individual cost analysis could be undertaken, requiring detailed understanding of the time taken to undertake each specific element of the diagnostic assessment. This data is not available for individual teams. The GDG was able to provide an estimate for what they guessed was the approximate amount of time taken to perform each task for illustration, but this estimate was not considered to be sufficiently robust as a basis for a cost analysis of an ASD assessment for the NHS. For that reason, cost data were not reported for this guideline

10.2 Descriptions of specific ASD diagnostic services

The following boxes describe specific services in England and Wales as reported by members of the GDG who work in these diagnostic services. They are based on descriptions given in interviews with five GDG members about the usual components for assessments and resource use of their services.

10.2.1 Service 1: outer city child development centre

The Social Communication Assessment (SoCA) pathway is one of several care pathways offered by the multidisciplinary Child Development Team. Our referrals come mainly from primary care (GPs and health visitors) and from speech and language therapists working in the community. The remainder come from hospital paediatricians, education (SENCOs or educational psychologists) and social care. Increasingly the referrals come on a CAF (Common Assessment Framework) form, especially those from health visitors and SLTs. At present, there is a two-stranded assessment service for children with possible autism spectrum disorders in the borough: children under the age of 6, and older children and young people who have additional significant learning disabilities, are seen in the CDC while children over 6 who do not have learning difficulties are seen by CAMHS. Although the distribution of resources across services means that this system is likely to continue for the foreseeable future, we are working towards a single point of entry for all referrals to the two services, to simplify matters for both referrers and families.

All CDC referrals are discussed at a weekly multidisciplinary referrals meeting lasting about an hour. Those children whose referrals suggest possible ASD are entered directly

into the SoCA pathway. Where the information in the referral indicates more isolated problems such as a specific language disorder or behavioural problems, the referral is passed on to the appropriate single service, such as SLT, or community based services able to offer behavioural support. If the referral is suggestive of an overall developmental delay the children are seen in a general CDT clinic; some of these children may later enter the SoCA pathway if their social communication difficulties become apparent at a later stage.

The core SoCA team comprises a consultant community paediatrician, SLT, OT and clinical psychologist. There is also input from an educational psychologist and specialist health visitor, and from the Early Support Keyworking service. We have a team meeting once a month, to discuss the children who are being, or have been, assessed. Ad hoc meetings are also convened to discuss operational issues.

A letter is sent to the parents of all children entered into the SoCA pathway within a week of the referral being received, including a leaflet about social communication disorders and the assessment process that the child will be offered. This assessment consists of two stages. The first, generic, stage applies to all children on the SoCA pathway. For each of these children we gather information about their general health, hearing, language, motor skills and sensory processing; in practice this entails appointments with a paediatrician (usually a specialist paediatric registrar), audiology, SLT and OT. Some of these assessments may already have taken place prior to referral and do not then need to be repeated. With parental consent we also request a report from the child's nursery or school, specifically asking for information about their functioning in the classroom setting and their peer relationships. Some children will also be offered a home visit from our specialist health visitor or from a Keyworker. If the child is already known to the educational psychology service the EP report is also obtained. For those children with significant developmental delay, or those with dysmorphic features, karyotyping and Fragile X assay is arranged; other biomedical investigations such as further blood tests or imaging are only arranged, after discussion with the consultant, if clinically indicated on the basis of the physical and neurological findings.

Once all the reports from the various assessments are available, each child is discussed at the SoCA team meeting, attended by all the core professionals and the educational psychologist. The amalgamated information, including general developmental history, medical history, and clinical observations from the different settings, is reviewed by the team, and compared against ICD-10 criteria. For some children, about a quarter to a third of the total, the diagnosis of ASD is clear at this stage. These children's parents are then invited to a feedback clinic with the consultant community paediatrician to discuss the assessments, the diagnosis is explained to the parents at that time, and the intervention to be offered is discussed and initiated. For a second, smaller, group of children, it will be equally clear that they do not have ASD; these parents are also offered a feedback appointment with either the consultant paediatrician or the specialist health visitor, and the appropriate care pathway put in place.

The remainder of the children do not have a clear cut diagnosis at the end of this stage and are offered a further, autism-specific, diagnostic assessment. This entails a semi-structured interview covering the developmental history and current behaviour, usually using the ADI-R, and a standardised play based observation of the child's social communication using the ADOS. The two components of the assessment are carried out concurrently, usually in one large clinic room, so that the parents are able to observe the ADOS while they themselves are being interviewed. The ADI-R is usually carried out by the consultant paediatrician and the ADOS by one or two other team members (SLT, OT and clinical psychologist). This part of the clinic takes about 2 hours. The family then have a break of about 45 minutes to an hour, while the team members score the ADOS and discuss their findings, in conjunction with the previous assessments carried out during the earlier generic stage of the process. The assessors then meet with the family to give immediate feedback, with an explanation of the diagnosis that has been reached and the reasons for this. In a small proportion of cases the diagnosis remains unclear: sometimes we arrange for one or two team members to go and observe the child in

school, in a social setting; for others it is agreed to monitor their progress and to repeat the ADOS in a year's time; very occasionally the child may be referred for a tertiary opinion.

At the end of the generic stage of assessment, some children may appear to have probable ASD but are developmentally too delayed for the autism specific diagnostic assessment. These children are offered therapeutic intervention and their progress monitored, with a view to offering a formal diagnostic assessment at a later stage.

We aim to complete the initial, generic, assessment within 12 weeks from referral and the diagnostic assessment within a further 6 weeks but are not able to meet this target at present because of a shortage of appropriately skilled and trained professionals. About 100 children a year are currently referred into the SoCA pathway; we run a total of 7 clinics a month; one child is seen in each ADOS/ ADI-R diagnostic clinic, and two are seen in each "stage 1 feedback" clinic, each appointment being for 1.5 hours.

When the professionals meet immediately after the diagnostic assessment, one of the therapists puts together a list of suggestions of activities to help the child; these are given to the parents during feedback. The parents are also given written information about autism, translated into other languages where appropriate, and information about the interventions that they will be offered, such as EarlyBird.

Report writing is done after the clinics: the professionals type their own sections of each report which are then pasted together, including a summary of the relevant background information and information from previous assessments, plus, where applicable, details of the information obtained from the ADI-R and the observations made in the ADOS. The recommendations already given to the parents are appended to the report. Reports are sent to the parents, GP, health professionals working with the child, and educational psychologist. A second copy of the report is given to the parents to share with their child's school or nursery.

10.2.2 Service 2: Rural/urban multi disciplinary multiagency team

Referral to specialist community child health services (community paediatricians, paediatric therapists and CAMHS) is via a single point of entry system from primary care, education and social care. Where there are concerns about a child's social communication skills, they may be referred initially to a variety of services, commonly, Speech and Language Therapy, community paediatrics or CAMHS, or a combination, depending on the referrers view of the main presenting problem. Referral meetings take place twice a month. Initial appointments are offered within the service referred to and further assessment and intervention is planned. If there are concerns about possible ASD, the initial clinician needs to make additional referrals whilst supporting the child and family. To start a diagnostic assessment, there needs to be agreement that this is appropriate between two professionals: a community paediatrician, a Speech and Language Therapist and an educational psychologist (from the Local Authority). By this stage most children will have a MDT involved and will be receiving appropriate therapy and school based interventions. If it is not clear that they should move into a diagnostic assessment, their progress can be monitored and the situation reviewed.

Referral for an ASD diagnostic assessment is made with explicit signed consent from both parents (where applicable). A lead professional is identified (one of the professionals already involved). The educational psychologist and SLT carry out any further more specialised assessments. This also involves observation at school or nursery. The community paediatrician completes a structured interview, generally using the Diagnostic Interview for Social and Communication Disorders (DISCO) with the parents. All educational psychologists and most SLTs and community paediatricians take part in these assessments according to a common approach supported by a toolkit document (which includes the care pathway, expectations of inputs from different professional groups and diagnostic criteria). In the last few years, there have been approximately 26 of these assessments per year (population of area covered – 200,000). The average time to complete the ASD diagnostic assessment is 18 weeks.

Each professional produces a report which is circulated to those involved in the assessment and parents. When each of the three professionals has completed their contribution, a final review meeting is held. Other professionals who are already involved with the child are also invited, for example, OT, or CAMHS professionals. In addition, members of staff from the nursery or school are also invited, although decisions concerning diagnosis are made by the main assessment professionals. Often the meeting is held at the school or nursery to facilitate this. The first part of the meeting is held with professionals only, to review all information on the child and, using ICD-10 criteria, determine whether an ASD diagnosis is met. If it is not, then an agreed narrative formulation (1-2 sentences) of the child's difficulties is written. Other co-morbid or alternative diagnoses may also be considered.

The outcome of the assessment is fed back to the parents in a one-to-one meeting with the lead professional. The family then join with the professionals to jointly agree a list of strengths and needs of the child and an action plan. The structure of the final review meeting is flexible to meet different families' needs - sometimes the whole meeting happens without the parents, and the outcome is fed back on a separate occasion (very shortly after the meeting has been held), together with the proposed strengths, needs and action plan, for their views and input. The family is given information about the diagnosis and local ASD support services including voluntary agencies. The notes of the meeting are typed up, together with all the assessment reports and details of how the child met the diagnostic criteria. This forms the final report and is sent to the parents, GP, school and MDT.

If there is uncertainty about the diagnosis, the case will be discussed with the steering group (local expert panel). Occasionally referrals are made to tertiary services.

10.2.3 Service 3: rural/ urban service

The diagnostic service comprises a psychiatrist, psychologist and a SLT as core, regular members. The multidisciplinary team also has regular input from junior doctors as part of their training and occasional input from nurses specialising in learning disabilities who may carry out some pre-clinic observations.

Referrals come from paediatrics and CAMHS so the children who have been referred will have already had some ASD diagnostic assessment. Referrers are generally seeking further assessment in terms of complex presentation, intellectual disability or a second opinion. Referrals are screened and discussed at our bi-monthly meeting by the psychiatrist and psychologist. The administrator also attends this meeting. If the referral is accepted, and mostly these are given the source of the referral, the administrator will allocate a clinic appointment and seek further information as deemed appropriate by the psychiatrist and the psychologist. Some referrals come with extensive information, others with less. The SLT is informed of the details of the child or young person and the clinic appointment and she liaises with her colleagues in speech and language therapy to arrange assessment and any intervention.

The multidisciplinary team administrator opens a file and follows up requests for further information. She also contacts the family with an appointment time and further information on the diagnostic assessment and what to expect. Families are advised to bring further information to the clinic appointments such as recent school reviews, and copies of any other reports. Not all families bring further information but when they do, this can be very helpful indeed.

On the day of the clinic assessment, the multidisciplinary team meets together to review the information before seeing the child/young person and family. The family and the child/young person meet with all multidisciplinary team members to introduce everyone and to describe the assessment process. The psychiatrist then conducts an interview with the parents/carers to obtain a developmental history. The psychologist and SLT carry out an ADOS assessment in most cases. They also carry out some assessment of their own based on the information received. The assessment can take approximately one to two hours. Following the interview and the assessments, these will be scored, rated and

discussed. If the outcome of the interview and ADOS clearly indicate ASD, the family will be given a diagnosis on the day. If the outcome is less clear, the family will be advised as to the next steps such as further assessments and/or observations. If ASD is clearly not indicated, the family will also be informed of this and similarly provided with advice as to any further steps.

The extent of further assessments can range from observation in a school/other setting of the child at break time/free time to assessments of speech, language communication skills and cognitive assessments. Those involving cognitive assessments are the most detailed and far ranging assessments we do.

Once diagnosis has been agreed, the family will have the opportunity to discuss this with one or two multidisciplinary team members. They will be informed as to the reason and evidence for diagnosis. They are also given information on local services, support groups, disability living allowance, courses, useful websites and resources. The local Autistic Society has developed a useful comprehensive handbook which is easily available at a small price to parents. Consent is sought to share information regarding diagnosis with other relevant agencies. Some of the local authorities are able to offer dedicated post-diagnostic intervention and support which has been very useful and a very welcome development. To date all families have consented to this referral following diagnosis.

10.2.4 Service 4: specialist hospital-based service

We receive referrals where there is a clinical query about a diagnosis from a paediatrician or child psychologist or paediatric neurologist who refers for another opinion. Once the referral has been received, we check who will remain involved at the local level as families may be referred from far away. Once a child has reached this level of service, there is certainly something wrong, so we don't want the local service to think that the child and family are no longer under their care. We then send the family an appointment with a questionnaire. No other agencies are involved at this stage. Children are usually over five years old and the referral could be years after the initial concerns about ASD were raised.

An administrator will collect all the information and reports from other agencies and there can be a delay if a number of services have been involved and have not provided a report. We collate information from previous assessments and develop an understanding of the developmental history. A child may have had a range of assessments at service level 2 or 3 but many of those assessments will be out of date and will have to be done again at this stage.

The first appointment is between three and a half and four hours. We see the parents / carers and the child together. The consultant psychiatrist will attend for an hour and a clinical psychologist will attend throughout. There is often a junior doctor and trainee psychologist in attendance. Preparation time is around one hour.

The assessment starts with a full family history and a full cognitive assessment and with structured questionnaires depending on the ability of the child. If the child has a lower cognitive ability, it is a much shorter assessment, so the entire assessment can take between 1 and 4 hours depending on this factor.

After that first appointment, there is an MDT meeting a week later for 90 minutes. Four people are usually involved. There are no structured referral criteria as this is a specialist service and all children present with complex features. If we suspect ASD, we will suggest the child is given another appointment to do an ADOS or ADI-R. The ADI-R can take 2 hours, and the ADOS 45 minutes, with half an hour to score. So we have two appointments to complete the assessment overall

Otherwise if not ASD suspected, the follow up appointments will depend on the needs of the child. In around 15% of the cases where ASD is suspected or where we have reason to believe that behaviour will be different outside the clinic, we will need to do a home or a school visit. Some children are so challenging that they can't come back to clinic so

we have to go off site to complete the assessment. So we have to allow a half to a full day for one or two people to do this (including a trainee).

We have a further MDT meeting for around half an hour. We then feed back to the family verbally at an appointment which takes one and a half hours. Then we write the reports (psychiatric report plus psychology report) which can take up to 3-4 hours per report. The administrative time required per referral is around 15 hours which is an improvement now we have electronic systems.

The child or young person will have a full cognitive assessment. A full family history is also taken.

10.2.5 Service 5: inner city service

We receive the majority of our referrals from either paediatricians or SLTs. Other referrers include CAMHS and schools and rarely GPs.

In response to very long waiting times for diagnostic assessment, we developed service with a single point of referral with three different types of assessment. The types depend on the level of complexity of the child's presentation described in the referral. There is a referral meeting every one or two weeks, with the service receiving 25-30 referrals per month. It takes 2 hours and 12– 15 referrals will be discussed. The referral meeting must have a minimum of 2 people, but ideally a consultant paediatrician, clinical psychologist and SLT. For every referral a decision is reached on whether the referral is appropriate what type of assessment should be carried out and by whom. The decision is based on information on the referral form and reports of any assessment that have already been carried out. Information from the school may be requested at this stage but not always received. While the child or young person is waiting to be seen, there will be interventions in place based on the child's presenting needs, as well as parents/carer support groups for families where no definitive diagnosis has yet been made but there is a clinical suspicion of ASD.

For the least complex children (typically under 5) we developed an observation/interview guideline which may be used by SLTs and paediatricians who are undertaking a communication assessment or a general developmental assessment. If both these professionals strongly suspect ASD and the child or young person has obvious signs or symptoms, then they will refer to the ASD diagnostic service and, if the team agrees with their initial views, one member of the multidisciplinary team will meet the paediatrician and/or SLT. During this meeting they will map the information gained about the child against the ICD-10 criteria for ASD whilst drafting a report. This meeting takes around 1 hour after which the parents, along with their child, will be invited to come and discuss the diagnosis and then agree a care plan for their child. The parents are meeting health care professionals that they are already involved with, which is an advantage. This is only a small percentage of cases, around 5%, and is referred to as a type 1 assessment.

For children where the signs and symptoms are not so clear, a type 2 assessment is more usual. For these children, an appointment will be arranged to attend the ASD diagnostic service. At the consultation, an informal ASD specific history is taken, and a structured play-based observation (using the ADOS) is carried out typically (for young children under 7) with the child and parents in the same room. The health care professionals (a paediatrician & SLT or clinical psychologist) involved in the assessment then meet to discuss whether the child meets the criteria for ASD, which takes up to 1 hour. The SLT or clinical psychologist will write up the ADOS which is used as a summary report and given to the parents on the same day. During this time a nursery nurse is available to support the family in a waiting room if required.

There is then detailed feedback to the family/ carers which is the same as feedback for a type 1 assessment. Information on ASD services and contact details are given out. If no blood tests were carried out at the general developmental assessment, then these may be organised after the diagnosis has been communicated to the family/ carers, but this does usually happen at an earlier stage.

Type 2 assessments are carried out for the majority of the cases referred to the diagnostic service, around 60% of all children and young people.

Type 3 assessments are for more complex cases. The children are usually older (over 7) and referrals usually come via the CAMHS service, schools and paediatricians. The professionals involved in these assessments are consultant paediatricians, SLTs & clinical psychologists. We also have a psychiatrist who offers a clinic session once a month for type 3 assessments, so we choose which children are appropriate on her behalf.

At the appointment with the child, we use the ADI-R or DISCO, to take a formal history from the parent or carer and, at the same time, carry out a detailed clinical assessment with the child in a separate room. The clinical assessment will include all or some of the following as is necessary: an observation of the child using ADOS, a cognitive assessment and a speech and language assessment. This can be very demanding on the child, so it may sometimes be necessary to complete the assessments on different days. In addition some children will require a school-based observation. The school observation can be completed by anyone on the diagnostic team. We do school observations on about half of the children we see for this type of assessment. A school observation will include observing a lesson, then transition into break time and then observing peer relationships in the unstructured environment of the playground. It takes about an hour plus travel time. The ADOS takes about 45 minutes, the language and cognitive assessments one hour each and the formal history typically takes 2.5 hours.

One appointment may be sufficient for the multidisciplinary team to make a diagnosis and give feedback to the child and family. For other's this may be different, for example there may be a longer clinical discussion which can involve consultation with other colleagues so an immediate diagnosis is not possible or when an additional appointment is need to complete the assessment.

For all types of assessment, once they have been completed, we write the report for parents that contain all the assessments, a report of the clinical history written by the paediatrician or psychologist and the observation. The report includes recommendations for management including referrals to new services if required. The SLT/psychologist types their own reports either on the day of assessment or the next day. The paediatricians dictate their report which is also written up the next day. The draft report is sent to parents/ carers which is followed-up by a face to face meeting with parents/ carers which lasts about an hour. It may require a longer meeting or a further follow-up appointment in some cases.

Each diagnostic assessment session is typically three and a half hours. The ideal is to do five assessments a week, but this can be constrained by the number of doctors who are available.

Administration takes about half a day per child.

All staff and referrers have received training in diagnostic assessment in ASD and receive regular training updates in diagnosis.

10.3 Estimating resource use for an ASD specific assessment

The resource use estimates reported in the tables below are measured in health care professionals' time to complete each task. It does not include the use of advocates or interpreters which are not routinely required by families and professionals. The resources included are:

- Time taken to discuss an individual referral
- The cost of additional assessments routinely undertaken on all or some children before a decision is taken to do an ASD specific assessment
- The time taken to prepare for the first appointment, and by whom

- Time in face to face meetings with the child and the family
- Report writing
- Multidisciplinary meetings to discuss and agree diagnosis
- Follow-up with parents/ carers
- Further tests and investigations
- Further observations of the child/ young person (including in some cases in nursery/school/home)

The estimate of the time spent on different kinds of activity related to the referral for and diagnostic assessment of ASD is based on interviews with five GDG members who work in child development diagnostic teams around the country. These estimates are based on their individual estimates of how long it takes to do individual tasks on average, accepting that these tasks can take a far longer time for some individual children and young people. Most diagnostic assessments take place in a local child health setting. Some families also have additional diagnostic assessments at more specialist level.

Based on the service descriptions above, the minimum time required is around 3- 4 hours to discuss the assessment with the child and family, undertake a clinical history, examine the child where appropriate, and complete any ASD specific interviews, observations and profiling. Across the five services examined in detail in the previous chapter, this time frame was fairly constant.

The tables below describe the services in terms of the components of assessment and who undertakes them in each service. The data is taken from discussions with one member of each of these teams and thus represents a snapshot of a service at one moment in time, from the perspective of one professional. Some of the descriptions are more detailed than others, based on the estimates provided by the individual GDG members describing their team.

The components of assessment are not all undertaken directly by the ASD assessment team. The resource use descriptions include all the components of assessment once a referral has been initiated. Therefore it represents the resource use for a child going through the pathway from referral to diagnosis, including assessments undertaken by professionals outside the ASD team rather than resource use for a specific ASD team.

1 **Table 10.1 Resource use for service 1**
2

Cost item	Professional	Time or Unit	% children
Main CDC referrals meeting			
	One or two consultant paediatricians	Part of a 1 hour meeting depending on number of referrals	100%
	Specialist HV key working manager	As above	100%
	Educational psychologist	As above	100%
	Administrator	As above	100%
	SLT/OT	As above	100%
Assessments by others	Audiology	½ hour	100%
	SLT – face-to-face contact`	1 hour	100%
Developmental assessment			
	General paediatric – medical and developmental assessment	OP visit, 1 hour	100%
	OT	1 hour	100%
	School report	1 hour	100%
	SENCO		
Administration	Medical secretary	30 minutes	100%
Monthly team meeting	Consultant paediatrician	15 minutes	100%
	Clinical psychologist	15 minutes	100%
	Clinical specialist OT	15 minutes	100%
	Highly specialist SLT	15 minutes	100%
	Educational psychologist	15 minutes	100%
	Specialist health visitor	15 minutes	
Preparation for first ASD assessment (note reading)	Community paediatrician + one or two other members of the ASD team	20 minutes	100%
ASD-specific diagnostic assessment	Consultant paediatrician	4 hours	70%
	One or two out of SLT/OT/Clinical psychologist	4 hours each	70%
Report writing	Consultant paediatrician	3 hours	70%
	One or two out of SLT/OT and clinical psychologist	2 hours each	70%
Additional assessments and investigations			
School visit	Consultant paediatrician	3 hours (1 hour travel)	25%
	SLT/OT/Educational psychologist	3 hours (1 hour travel)	25%
Feedback session	Consultant paediatrician + one	1 hour	

	other team member		
Biomedical tests if clinically indicated	Chromosome	per test	50%
	Fragile X	per test	50%
Follow-up appointment 2 to 4 weeks post diagnosis	Specialist health visitor or key worker (or sometimes lead professional)	1 hour	50%
Follow-up with consultant to review progress after about 6 months	Consultant paediatricians	1 hour	

SLT, speech & language therapist; OT, occupational therapist; SENCO, special educational needs co-ordinator

Table 10.2 Resource use for service 2

Cost item	Professional	Hours	% children
Administration	Medical secretary	3 hours	
Typical involvement prior to decision to proceed to ASD assessment	SLT	2 hours	80%
	Community paediatrician	2 hours	100%
	Educational psychologist	2 hours	100%
Decision to request formal assessment (including time to discuss decision with parents and gain consent to proceed)	Community paediatrician	30 minutes	100%
	Educational psychologist	30 minutes	100%
	SLT	30 minutes	100%
Formal ASD assessment	Community paediatrician	8 hrs incl admin	100%
	SLT assessment	8 hrs incl admin	90%
	OT (if involved)	8 hrs incl admin	20%
	Psychologist (education)	8 hrs incl admin	95%
	Psychologist (clinical) (if involved)	9 hrs incl admin	10%
Final meeting to agree outcome of assessment (located at school/ nursery)		(2hours for each involved professional)	100%
Notes of meeting typed up		Included above included above	
Biomedical tests	Fragile X		20%
	Chromosome		20%

SLT, speech & language therapist; OT, occupational therapist

Table 10.3 Resource use for service 3

Cost item	Professional	Hours	% children
Level of service			
MDT meeting prior to first appointment	Psychiatrist, Psychologist, secretary	1 hour	
Assessments by others prior to the clinic	School / nursery report		100%
	Educational psychologist report		100%
	community paediatrician Psychiatrist	OP clinic	100%
	SLT assessment	2 hours	80%
	OT/Health Visitor/ Nursery/ Social services		25%
Administration	Secretary		100%
Pre preparation for 1st appointment	Psychiatrist, Junior Dr	30 minutes	100%
	Psychologist	30 minutes	100%
	SLT	90 minutes	100%
First appointment and formal assessment	Psychiatrist, Junior doctor	2 hours	100%
	Psychologist	2 hours	100%
	SLT	2 hours	100%
Report writing	Psychiatrist, psychologist, SLT	3 hours	
School observation	Psychologist	half day	60%
follow-up appointment	Psychiatrist	30 minutes	100%
	Psychologist	30 minutes	100%
Biomedical tests	Chromosomal abnormalities		10%
	Genetics		10%

SLT, speech and language therapist; OT, occupational therapist

Table 10.4 Resource use for service 4

Resource use item	Professional	Hours	% children
Administration	Medical secretary	15 hours	100%
Preparation for first appointment	Consultant psychiatrist	1 hour	100%
	Clinical psychologist	1 hour	100%
First appointment	Consultant psychiatrist	1 hour	100%
	Clinical psychologist	4 hours	100%
	Junior medical doctor	4 hours	100%
	Psychology trainee*	4 hours	100%
Decision to request formal ASD assessment	Consultant psychiatrist	90 mins	100%
	Clinical psychologist	90 mins	100%
	Junior medical doctor	90 minutes	100%
Formal ASD assessment	Clinical psychologist	4 hours	70%
report writing	Psychiatric report	4 hours	70%
	Psychology report	4 hours	70%
Follow-up appointment	Consultant psychiatrist	90 minutes	70%
	Psychologist	90 minutes	70%
	Junior doctor	90 minutes	70%
	trainee psychologist	90 minutes	70%
School observation (15%)	Clinical psychologist	whole day	15%
Follow-up MDT meeting	Consultant psychiatrist	30 minutes	100%
	Clinical psychologist	30 minutes	100%
Biomedical tests	CG array		10%

Table 10.5 Resource use for service 5

The service reported in table 10.5 describes a service where children and young people referred to the service are offered a different kind of assessment based on the information received by the multidisciplinary team

Cost item	Professional	Time or Unit	% children
Referral meeting	Clinical Psychologist	10 minutes	100%
	Consultant paediatrician	10 minutes	100%
	SLT	10 minutes	100%
General developmental assessment	Consultant paediatrician	1 hour	60%
Biomedical tests	Fragile X		10%
	CG array		10%
Communication assessment	SLT	1 hour	60%
Type 1 assessment			
Professional discussion	Consultant paediatrician	1 hour	5%
	SLT	1 hour	5%
Follow-up with parent/carer	Consultant paediatrician	1 hour	5%
Type 2 assessment meeting			
Diagnostic Assessment	Paediatrician	3 hours	60%
	SLT/Clinical Psychologist	3 hours	60%
MDT meeting	Paediatrician	1 hour	60%
	SLT/Clinical Psychologist	1 hour	60%
Follow-up with parent/carer	SLT/Clinical Psychologist	1 hour	60%
	Paediatrician	1 hour	60%
Support for the child	Nursery nurse	2 hours	40%
Type 3 assessment			
Diagnostic assessment	Consultant paediatrician/psychiatrist	2.5 hours	35%
	Clinical Psychologist	2.5 hours	35%
	SLT	2.5 hours	35%
MDT discussion and report writing	Consultant paediatrician/psychiatrist	3.5 hours	35%
	Clinical Psychologist	3.5 hours	35%
	SLT	3.5 hours	35%
Follow-up with parent/carer	Consultant paediatrician/psychiatrist	1 hour	35%
school visit	SLT/Clinical Psychologist	1 hour	35%
administration	SLT/Clinical Psychologist	2 hours/half a day	Under 20%

10.4 Conclusion

Across the NHS, diagnostic assessment of ASD is undertaken by different health care professionals, in different settings and with different kinds of health care professional resources. This chapter used information from the GDG members to describe five ASD services operating at different levels of referral within the NHS. They are not representative of all models of services in England and Wales but provide some evidence of the organisation and personnel cost of services that operate differently to achieve the same aim. The core components are the same.

The purpose of this chapter was to explain the problems in doing any cost-effectiveness analysis for this guideline and to provide an overview of the way that some children's diagnostic services for ASD are currently configured around the country. It is compiled from discussions with one individual working in each service. It was not intended to be a fully comprehensive account of all the models of service that exist around the country, but to give a flavour of the ways that services are offered which adhere to many of the clinical and organisations recommendations developed in this guideline.

11 References, abbreviations and glossary

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11.2 Abbreviations

ABAS	Adaptive behaviour Assessment
ABC	Autism Behavior Checklist
ADHD	Attention deficit hyperactivity disorder
ADI-R	Autism Diagnostic Interview-Revised
ADOS	Autism Diagnostic Observation Schedule
ASD	Autism spectrum disorder
ASSQ	Autism Spectrum Screening Questionnaire
ATAC	Autism – Tics, AD/HD and other Comorbidities
BISCUIT	Baby and Infant Screen for Children with Autism Traits
BITSEA	Brief Infant-Toddler Social and Emotional Assessment
CAF	Common Assessment Framework
CAMHS	Child and Adolescent Mental Health Service
CARS	Childhood Autism Rating Scale
CAST	Childhood Asperger Syndrome Test
CCC	Children's Communication Checklist
CDC	Child Development Centre
CHECKLIST	Infant/Toddler Checklist of Communication and Language Development
CI	Confidence interval
CSI-4	Child Symptom Inventory-4
DAWBA	Development and Well-Being Assessment
DBC-ES	Developmental Behavior Checklist – Autism – Early Screen
DCD	Developmental Coordination Disorder
3di	Developmental, Dimensional and Diagnostic Interview
DISCO	Diagnostic Interview for Social and Communication Disorders
DSM	Diagnostic and Statistical Manual of Mental Disorders
ECI-4	Early Childhood Inventory-4
ESAT	Early Screening of Autistic Traits Questionnaire
ESCS	Early social communication scales
GADS	Gilliam Asperger's Disorder Scale
GARS	Gilliam Autism Rating Scale
GDG	Guideline development group
GRADE	Grading of Recommendations Assessment, Development and Evaluation
ICD	International Statistical Classification of Diseases and Related Health Problems
ITC	Infant/Toddlers Checklist
KADI	Krug Asperger's Disorder Index

MCDI	MacArthur Communicative Development Inventories
M-CHAT	Checklist for Autism in Toddlers - Modified
MDT	Multi-disciplinary team
OCD	Obsessive compulsive disorder
ODD	Oppositional defiant disorder
OT	Occupational Therapy/Therapist
PCQ	Parental Concerns Questionnaire
PDA	Pathological demand avoidance
PDD	Pervasive development disorder
PDD-MRS	Scale of Pervasive Developmental Disorder in Mentally Retarded Persons
PDDRS	Pervasive Developmental Disorder Rating Scale
PIA	Parent Interview for Autism
RBS	Repetitive Behavior Scale
SCQ	Social Communication Questionnaire
SDQ	Strengths and Difficulties Questionnaire
SEN	Special Educational Needs
SIGN	Scottish Intercollegiate Guideline Network
SLD	Specific language disorder
SLT	Speech and Language Therapy/Therapist
SRS	Social Responsiveness Scale
SSI	Screen for Social Intervention
STAT	Screening Tool for Autism in Two-year-olds
YACHT-18	Young Autism and other developmental disorders Checkup Tool

11.3 Glossary

Agreement	The degree to which more than one individual undertaking an assessment / scoring of an instrument agree with the outcome (diagnosis)
Attention deficit hyperactivity disorder (ADHD)	A developmental disorder with onset in childhood and with impairments in the ability to maintain attention to task combined with impulsive and hyperactive behaviour. Criteria for diagnosis defined in ICD10 and DSM IV.,
Autism spectrum disorder	A term, used synonymously with pervasive developmental disorder, to describe qualitative impairments in social reciprocity and social communication combined with restrictive repetitive interests and behaviours.
Best available evidence	The strongest research evidence available to support a particular guideline recommendation.
Bias	Influences on a study that can lead to invalid conclusions about a treatment or intervention. Bias in research can make a treatment look better or worse than it really is. Bias can even make it look as if the treatment works when it actually doesn't. Bias can occur by chance or as a result of systematic errors in the design and execution of a study. Bias can occur at different stages in the research process, e.g. in the collection, analysis, interpretation, publication or review of research data. For examples see Selection bias, Performance bias, Information bias, Confounding, Publication bias.
Biomedical test	A test carried out on the body or on a sample of body fluids defined by expected norms.
Blinding or masking	The practice of keeping the investigators or subjects of a study ignorant of the group to which a subject has been assigned. For example, a clinical trial in which the participating patients or their doctors are unaware of whether they (the patients) are taking the experimental drug or a placebo (dummy treatment). The purpose of 'blinding' or 'masking' is to protect against bias. See also Double blind study, Single blind study, Triple blind study.
Case control design	The comparison of cases with and without a particular disorder:\see case control study.
Case report (or case study)	Detailed report on one patient (or case), usually covering the course of that person's disease and their response to treatment.
Case series	Description of several cases of a given disease, usually covering the course of the disease and the response to treatment. There is no comparison (control) group of patients.
Case-control study	A study that starts with the identification of a group of individuals sharing the same characteristics (e.g. people with a particular disease) and a suitable comparison (control) group (e.g. people without the disease). All subjects are then assessed with respect to things that happened to them in the past, e.g. things that might be related to getting the disease under investigation. Such studies are also called retrospective as they look back in time from the outcome to the possible causes.

CG array	Comparative genomic hybridisation technique: a method of analysing samples for gene duplications and deletions.
Checklist	See Study checklist.
Child and adolescent mental health service	The service specialising in mental health for children and adolescents.
Child development centre	A location housing the facilities for assessment of usually young children with developmental problems, sometimes attached to a hospital or separately in the community, and part of the Child Health services.
Chronological age	The exact age in years and months of a child measured from birth.
Clinical effectiveness	The extent to which a specific treatment or intervention, when used under usual or everyday conditions, has a beneficial effect on the course or outcome of disease compared to no treatment or other routine care. (Clinical trials that assess effectiveness are sometimes called management trials.) Clinical 'effectiveness' is not the same as efficacy which establishes whether a treatment 'works' or not under ideal conditions..
Clinical impact	The effect that a guideline recommendation is likely to have on the treatment, or treatment outcomes, of the target population.
Clinical importance	The importance of a particular guideline recommendation to the clinical management of the target population.
Clinical question	This term is sometimes used in guideline development work to refer to the questions about treatment and care that are formulated in order to guide the search for research evidence. When a clinical question is formulated in a precise way, it is called a focused question.
Clinical trial	A research study conducted with patients which tests out a drug or other intervention to assess its effectiveness and safety. Each trial is designed to answer scientific questions and to find better ways to treat individuals with a specific disease. This general term encompasses controlled clinical trials and randomised controlled trials.
Clinician	A health care professional providing patient care, e.g. doctor, nurse, physiotherapist.
Cochrane Collaboration	An international organisation in which people find, appraise and review specific types of studies called randomised controlled trials. The Cochrane Database of Systematic Reviews contains regularly updated reviews on a variety of health issues and is available electronically as part of the Cochrane Library.
Cochrane Library	The Cochrane Library consists of a regularly updated collection of evidence-based medicine databases including the Cochrane Database of Systematic Reviews (reviews of randomised controlled trials prepared by the Cochrane Collaboration). The Cochrane Library is available on CD-ROM and the Internet.
Coexisting condition	A disorder which exists in association or together with the index disorder
Cognitive assessment	Assessment of IQ and learning using an intelligence test
Cognitive impairment	A deficit in some aspect of intellectual ability and / or learning
Cohort study	An observational study that takes a group (cohort) of patients and follows their progress over time in order to measure

	outcomes such as disease or mortality rates and make comparisons according to the treatments or interventions that patients received. Thus within the study group, subgroups of patients are identified (from information collected about patients) and these groups are compared with respect to outcome, e.g. comparing mortality between one group that received a specific treatment and one group which did not (or between two groups that received different levels of treatment). Cohorts can be assembled in the present and followed into the future (a 'concurrent' or 'prospective' cohort study) or identified from past records and followed forward from that time up to the present (a 'historical' or 'retrospective' cohort study). Because patients are not randomly allocated to subgroups, these subgroups may be quite different in their characteristics and some adjustment must be made when analysing the results to ensure that the comparison between groups is as fair as possible.
Cohort	A group of people sharing some common characteristic (e.g. patients with the same disease), followed up in a research study for a specified period of time.
Common Assessment Framework	A systematic questionnaire to record in a standardised way the additional needs that a child may have with the aim of determining how they should be met..It is intended to enable agencies to work together and is a key tool for the 'Every Child Matters' campaign.
Co-morbidity	Co-existence of a disease or diseases in the people being studied in addition to the health problem that is the subject of the study.
Confidence interval	A way of expressing certainty about the findings from a study or group of studies, using statistical techniques. A confidence interval describes a range of possible effects (of a treatment or intervention) that are consistent with the results of a study or group of studies. A wide confidence interval indicates a lack of certainty or precision about the true size of the clinical effect and is seen in studies with too few patients. Where confidence intervals are narrow they indicate more precise estimates of effects and a larger sample of patients studied. It is usual to interpret a '95%' confidence interval as the range of effects within which we are 95% confident that the true effect lies.
Confounder or confounding factor	Something that influences a study and can contribute to misleading findings if it is not understood or appropriately dealt with. For example, if a group of people exercising regularly and a group of people who do not exercise have an important age difference then any difference found in outcomes about heart disease could well be due to one group being older than the other rather than due to the exercising. Age is the confounding factor here and the effect of exercising on heart disease cannot be assessed without adjusting for age differences in some way.
Consensus methodology	The process of agreeing a particular course of action based on the collective views of a body of experts.
Consensus statement	A statement of the advised course of action in relation to a particular clinical topic, based on the collective views of a body of experts.
Control group	A group of patients recruited into a study that receives no treatment, a treatment of known effect, or a placebo (dummy

	treatment) - in order to provide a comparison for a group receiving an experimental treatment, such as a new drug.
Controlled observational study	A study to evaluate an intervention or test involving two (or more) groups of participants. One (the experimental group) receives the treatment, test or investigation that is being tested, and the other (the comparison or control group) receives an alternative or no intervention/test. The two groups are followed up to compare differences in outcomes.
Cost benefit analysis	A type of economic evaluation where both costs and benefits of health care treatment are measured in the same monetary units. If benefits exceed costs, the evaluation would recommend providing the treatment.
Cost effectiveness analysis	A type of economic evaluation comparing the costs and the effects on health of different treatments. Health effects are measured in 'health-related units', for example, the cost of preventing one additional heart attack.
Cost effectiveness	Value for money. A specific health care treatment is said to be 'cost-effective' if it gives a greater health gain than could be achieved by using the resources in other ways.
Cost-minimisation analysis	A form of cost-effectiveness analysis where the treatment alternatives are considered to be equally effective. Where treatments are equally effective the least costly is the most cost-effective
Cross-sectional study	The observation of a defined set of people at a single point in time or time period – a snapshot. (This type of study contrasts with a longitudinal study which follows a set of people over a period of time.)
Data set	A list of required information relating to a specific disease.
Decision analysis	Decision analysis is the study of how people make decisions or how they should make decisions. There are several methods that decision analysts use to help people to make better decisions, including decision trees.
Declaration of interest	A process by which members of a working group or committee 'declare' any personal or professional involvement with a company (or related to a technology) that might affect their objectivity e.g. if their position or department is funded by a pharmaceutical company.
Developmental age	An estimate of the functioning age equivalent of a child
Diagnosis	The identification of the nature and cause of symptoms in any individual.
Diagnostic study	A study to assess the effectiveness of a test or measurement in terms of its ability to accurately detect or exclude a specific disease.
Differential diagnosis	The conditions that may have similar features to each other and need to be considered in identifying a diagnosis
Disability Living Allowance	A benefit (non-means tested) intended to provide financial support to persons caring for anyone with a disability.
Double blind study	A study in which neither the subject (patient) nor the observer (investigator/clinician) is aware of which treatment or intervention the subject is receiving. The purpose of blinding is to protect against bias.
Echolalia	Frequent repetition of set words and phrases

Economic evaluation	A comparison of alternative courses of action in terms of both their costs and consequences. In health economic evaluations the consequences should include health outcomes.
Economic model	In health economics, a model is a theoretical construct that represents the costs and outcomes of alternatives for health care management. The economic model is a simplified framework designed to illustrate complex processes, often but not always using mathematical techniques.
Educational psychology service	The educational psychology service provides consultation and advice in relation to the education and development of children and young people. It is a statutory service. Educational psychologists have gained a psychology degree and undertaken postgraduate professional training, in educational psychology.
Effectiveness	See Clinical effectiveness.
Efficacy	The extent to which a specific treatment or intervention, under ideally controlled conditions (e.g. in a laboratory), has a beneficial effect on the course or outcome of disease compared to no treatment or other routine care.
Empirical	Based directly on experience (observation or experiment) rather than on reasoning alone.
Epidemiology	Study of diseases within a population, covering the causes and means of prevention.
Evidence based clinical practice	Evidence based clinical practice involves making decisions about the care of individual patients based on the best research evidence available rather than basing decisions on personal opinions or common practice (which may not always be evidence based). Evidence based clinical practice therefore involves integrating individual clinical expertise and patient preferences with the best available evidence from research
Evidence based	The process of systematically finding, appraising, and using research findings as the basis for clinical decisions.
Evidence table	A table summarising the results of a collection of studies which, taken together, represent the evidence supporting a particular recommendation or series of recommendations in a guideline.
Exclusion criteria	See Selection criteria.
Experimental study	A research study designed to test if a treatment or intervention has an effect on the course or outcome of a condition or disease - where the conditions of testing are to some extent under the control of the investigator. Controlled clinical trial and randomised controlled trial are examples of experimental studies.
Experimental treatment	A treatment or intervention (e.g. a new drug) being studied to see if it has an effect on the course or outcome of a condition or disease.
Fragile X	A condition in which there is a genetic abnormality in the X chromosome associated with intellectual disability mainly but not exclusively in boys.
Generalisability	The extent to which the results of a study hold true for a population of patients beyond those who participated in the research. See also External validity.
Genetic test	A test for genetic disorders which involves examination of an individual's DNA. In the context of ASD, it is often used to identify carriers of genes which code for specific coexisting

	conditions, or genetics sequences believed to be causative of ASD.
Global developmental delay	A term used to describe a delay in all aspects of development usually in young children before they are able to complete a standardised test of intellectual ability.
Gold standard	A method, procedure or measurement that is widely accepted as being the best available.
Grading of Recommendations Assessment, Development and Evaluation (GRADE)	A system for grading the quality of evidence and the strength of recommendations that can be applied across a wide range of interventions and contexts.
Grey literature	Reports that are unpublished or have limited distribution, and are not included in bibliographic retrieval systems.
Guideline recommendation	Course of action advised by the guideline development group on the basis of their assessment of the supporting evidence.
Guideline	A systematically developed tool which describes aspects of a patient's condition and the care to be given. A good guideline makes recommendations about treatment and care, based on the best research available, rather than opinion. It is used to assist clinician and patient decision-making about appropriate health care for specific clinical conditions.
Health economics	A branch of economics which studies decisions about the use and distribution of health care resources.
Heterogeneity	Or lack of homogeneity. The term is used in meta-analyses and systematic reviews when the results or estimates of effects of treatment from separate studies seem to be very different – in terms of the size of treatment effects or even to the extent that some indicate beneficial and others suggest adverse treatment effects. Such results may occur as a result of differences between studies in terms of the patient populations, outcome measures, definition of variables or duration of follow-up.
Hierarchy of evidence	An established hierarchy of study types, based on the degree of certainty that can be attributed to the conclusions that can be drawn from a well conducted study. Well-conducted randomised controlled trials (RCTs) are at the top of this hierarchy. (Several large statistically significant RCTs which are in agreement represent stronger evidence than say one small RCT.) Well-conducted studies of patients' views and experiences would appear at a lower level in the hierarchy of evidence.
Homogeneity	This means that the results of studies included in a systematic review or meta analysis are similar and there is no evidence of heterogeneity. Results are usually regarded as homogeneous when differences between studies could reasonably be expected to occur by chance. See also Consistency.
I^2	Statistical indication of the amount of heterogeneity between studies included in a meta-analysis.
In depth interview	A qualitative research technique. It is a face to face conversation between a researcher and a respondent with the purpose of exploring issues or topics in detail. Does not use pre-set questions, but is shaped by a defined set of topics or issues.

Inconsistency	The unexplained heterogeneity that is not adequately explained by the study investigators arises from Inconsistency of results or unexplained heterogeneity
Indirectness	A type of bias that can occur when a comparisons of intervention A versus B is not available, but A was compared with C and B was compared with C. Such studies allow indirect comparisons of the magnitude of effect of A versus B.
Information bias	Pertinent to all types of study and can be caused by inadequate questionnaires (e.g. difficult or biased questions), observer or interviewer errors (e.g. lack of blinding), response errors (e.g. lack of blinding if patients are aware of the treatment they receive) and measurement error (e.g. a faulty machine).
Intellectual disability	A broad concept of mental disability that encompasses mental retardation characterized by significantly impaired cognitive functioning and deficits in adaptive behaviours.
Isolated speech and language delay	A delay in speech or language or both without intellectual impairment or other developmental disorder
Literature review	A process of collecting, reading and assessing the quality of published (and unpublished) articles on a given topic.
Longitudinal study	A study of the same group of people at more than one point in time. (This type of study contrasts with a cross sectional study which observes a defined set of people at a single point in time.)
Looked after children	Children in the care of the local authority.
Methodological quality	The extent to which a study has conformed to recognised good practice in the design and execution of its research methods.
Methodology	The overall approach of a research project, e.g. the study will be a randomised controlled trial, of 200 people, over one year.
Morbidity	Disease or disability or poor health due to any cause
Mortality	Death.
Multicentre study	A study where subjects were selected from different locations or populations, e.g. a co-operative study between different hospitals; an international collaboration involving patients from more than one country.
Non-therapeutic support	General support without a therapeutic or healing aim.
Objective measure	A measurement that follows a standardised procedure which is less open to subjective interpretation by potentially biased observers and study participants.
Obsessive compulsive disorder (OCD)	Recurrent obsessional thoughts (ideas, urges or images that are unwanted and often distressing) or compulsive acts (behaviours/actions that have to be carried out repeatedly even if they make no sense)
Observation	A research technique used to help understand complex situations. It involves watching, listening to and recording behaviours, actions, activities and interactions. The settings are usually natural, but they can be laboratory settings, as in psychological research.
Observational study	In research about diseases or treatments, this refers to a study in which nature is allowed to take its course. Changes or differences in one characteristic (e.g. whether or not people received a specific treatment or intervention) are studied in

	relation to changes or differences in other(s) (e.g. whether or not they died), without the intervention of the investigator. There is a greater risk of selection bias than in experimental studies.
Odds ratio	Odds are a way of representing probability, especially familiar for betting. In recent years odds ratios have become widely used in reports of clinical studies. They provide an estimate (usually with a confidence interval) for the effect of a treatment. Odds are used to convey the idea of 'risk' and an odds ratio of 1 between two treatment groups would imply that the risks of an adverse outcome were the same in each group. For rare events the odds ratio and the relative risk (which uses actual risks and not odds) will be very similar. See also Relative risk, Risk ratio.
Oppositional defiant disorder	A persistent pattern of markedly defiant, disobedient, provocative
(ODD)	behaviour to those in authority, clearly outside the normal range of behaviour for a child of the same age . The individual may blame others for their own mistakes, lose their temper easily, and act in an angry, resentful or touchy manner.
Outcome	The end result of care and treatment and/ or rehabilitation. In other words, the change in health, functional ability, symptoms or situation of a person, which can be used to measure the effectiveness of care/ treatment/ rehabilitation. Researchers should decide what outcomes to measure before a study begins; outcomes are then assessed at the end of the study.
P value	If a study is done to compare two treatments then the P value is the probability of obtaining the results of that study, or something more extreme, if there really was no difference between treatments. (The assumption that there really is no difference between treatments is called the 'null hypothesis'.) Suppose the P-value was P=0.03. What this means is that if there really was no difference between treatments then there would only be a 3% chance of getting the kind of results obtained. Since this chance seems quite low we should question the validity of the assumption that there really is no difference between treatments. We would conclude that there probably is a difference between treatments. By convention, where the value of P is below 0.05 (i.e. less than 5%) the result is seen as statistically significant. Where the value of P is 0.001 or less, the result is seen as highly significant. P values just tell us whether an effect can be regarded as statistically significant or not. In no way does the P value relate to how big the effect might be, for this we need the confidence interval.
Pathological demand avoidance	proposed by Elizabeth Newsom at the University of Nottingham,. it is not a diagnosis in the DSM and ICD. It is considered to be part of the autism spectrum disorders but individuals with PDA are said to possess superficial social skills and to have a theory of mind. They often engage in manipulative, domineering behavior.
Peer review	Review of a study, service or recommendations by those with similar interests and expertise to the people who produced the study findings or recommendations. Peer reviewers can include professional and/ or patient/ carer representatives.

Pervasive development disorder	A term used in the ICD and DSM classifications to describe the group of disorders characterized by qualitative abnormalities in reciprocal social interactions and patterns of communication and by restricted stereotyped repetitive repertoire of interests and activities pervasive of the individuals functioning in all situations. ASD is the equivalent term sued in this guideline.
Power	See Statistical power.
Prevalence	Prevalence is a statistical concept referring to the number of cases of a disease that are present in a particular population at a given time.
Primary Care Trust	A Primary Care Trust is an NHS organisation responsible for improving the health of local people, developing services provided by local GPs and their teams (called Primary Care) and making sure that other appropriate health services are in place to meet local people's needs.
Primary care	Healthcare delivered to patients outside hospitals. Primary care covers a range of services provided by GPs, nurses and other health care professionals, dentists, pharmacists and opticians.
Prognostic factor	Patient or disease characteristics, e.g. age or co-morbidity, which influence the course of the disease under study. In a randomised trial to compare two treatments, chance imbalances in variables (prognostic factors) that influence patient outcome are possible, especially if the size of the study is fairly small. In terms of analysis these prognostic factors become confounding factors. See also Prognostic marker.
Prognostic marker	A prognostic factor used to assign patients to categories for a specified purpose – e.g. for treatment, or as part of a clinical trial, according to the likely progression of the disease. For example, the purpose of randomisation in a clinical trial is to produce similar treatment groups with respect to important prognostic factors. This can often be achieved more efficiently if randomisation takes place within subgroups defined by the most important prognostic factors. Thus if age was very much related to patient outcome then separate randomisation schemes would be used for different age groups. This process is known as stratified random allocation.
Prospective study	A study in which people are entered into the research and then followed up over a period of time with future events recorded as they happen. This contrasts with studies that are retrospective.
Protocol	A plan or set of steps which defines appropriate action. A research protocol sets out, in advance of carrying out the study, what question is to be answered and how information will be collected and analysed. Guideline implementation protocols set out how guideline recommendations will be used in practice by the NHS, both at national and local levels.
Publication bias	Studies with statistically significant results are more likely to get published than those with non-significant results. Meta-analyses that are exclusively based on published literature may therefore produce biased results. This type of bias can be assessed by a funnel plot.
Qualitative research	Qualitative research is used to explore and understand people's beliefs, experiences, attitudes, behaviour and interactions. It generates non-numerical data, e.g. a patient's description of their pain rather than a measure of pain. In health care, qualitative techniques have been commonly used in

	research documenting the experience of chronic illness and in studies about the functioning of organisations. Qualitative research techniques such as focus groups and in depth interviews have been used in one-off projects commissioned by guideline development groups to find out more about the views and experiences of patients and carers.
Quality adjusted life years (QALYs)	A measure of health outcome which looks at both length of life and quality of life. QALYS are calculated by estimating the years of life remaining for a patient following a particular care pathway and weighting each year with a quality of life score (on a zero to one scale). One QALY is equal to one year of life in perfect health, or two years at 50% health, and so on.
Quantitative research	Research that generates numerical data or data that can be converted into numbers, for example clinical trials or the national Census which counts people and households.
Quasi experimental study	A study designed to test if a treatment or intervention has an effect on the course or outcome of disease. It differs from a controlled clinical trial and a randomised controlled trial in that: a) the assignment of patients to treatment and comparison groups is not done randomly, or patients are not given equal probabilities of selection, or b) the investigator does not have full control over the allocation and/or timing of the intervention, but nonetheless conducts the study as if it were an experiment, allocating subjects to treatment and comparison groups.
Random allocation/Randomisation	A method that uses the play of chance to assign participants to comparison groups in a research study, for example, by using a random numbers table or a computer-generated random sequence. Random allocation implies that each individual (or each unit in the case of cluster randomisation) being entered into a study has the same chance of receiving each of the possible interventions.
Randomised controlled trial	A study to test a specific drug or other treatment in which people are randomly assigned to two (or more) groups: one (the experimental group) receiving the treatment that is being tested, and the other (the comparison or control group) receiving an alternative treatment, a placebo (dummy treatment) or no treatment. The two groups are followed up to compare differences in outcomes to see how effective the experimental treatment was. (Through randomisation, the groups should be similar in all aspects apart from the treatment they receive during the study.)
Referral	The process of passing from one service or stage in the health service to another.
Retrospective study	A retrospective study deals with the present/past and does not involve studying future events. This contrasts with studies that are prospective.
Review	Summary of the main points and trends in the research literature on a specified topic. A review is considered non-systematic unless an extensive literature search has been carried out to ensure that all aspects of the topic are covered and an objective appraisal made of the quality of the studies.
Risk assessment	The process of quantifying the probability of a harmful effect.
Risk ratio	Ratio of the risk of an undesirable event or outcome occurring in a group of patients receiving experimental treatment

	compared with a comparison (control) group. The term relative risk is sometimes used as a synonym of risk ratio.
Royal Colleges	In the UK medical/nursing world the term royal colleges, as for example in 'The Royal College of….', refers to organisations which usually combine an educational standards and examination role with the promotion of professional standards.
Safety netting	The provision of support for patients in whom the clinician has some uncertainty as to whether the patient has a self-limiting illness and is concerned that their condition may deteriorate. Safety netting may take a number of forms, such as dialogue with the patient or carer about symptoms and signs to watch for, advice about when to seek further medical attention, review after a set period, and liaising with other healthcare services
Sample	A part of the study's target population from which the subjects of the study will be recruited. If subjects are drawn in an unbiased way from a particular population, the results can be generalised from the sample to the population as a whole.
Sampling frame	A list or register of names which is used to recruit participants to a study.
Sampling	Refers to the way participants are selected for inclusion in a study.
School transitions	The process of moving from one school year to another and particularly from primary to secondary or secondary to further education.
Secondary care	Care provided in hospitals.
Selection bias	Selection bias has occurred if, the characteristics of the sample differ from those of the wider population from which the sample has been drawn or there are systematic differences between comparison groups of patients in a study in terms of prognosis or responsiveness to treatment.
Selection criteria	Explicit standards used by guideline development groups to decide which studies should be included and excluded from consideration as potential sources of evidence.
Semi-structured interview	Structured interviews involve asking people pre-set questions. A semi-structured interview allows more flexibility than a structured interview. The interviewer asks a number of open-ended questions, following up areas of interest in response to the information given by the respondent.
Sensitivity	In diagnostic testing, it refers to the chance of having a positive test result given that you have the disease. 100% sensitivity means that all those with the disease will test positive, but this is not the same the other way around. A patient could have a positive test result but not have the disease – this is called a 'false positive'. The sensitivity of a test is also related to its 'negative predictive value' (true negatives) – a test with a sensitivity of 100% means that all those who get a negative test result do not have the disease. To fully judge the accuracy of a test, its Specificity must also be considered.
Single blind study	A study in which either the subject (patient/participant) or the observer (clinician/investigator) is not aware of which treatment or intervention the subject is receiving.
Social communication disorder	A descriptive term for a problem in social interaction and social communication but not currently a diagnosis-this may change in DSM V.

Specificity	In diagnostic testing, it refers to the chance of having a negative test result given that you do not have the disease. 100% specificity means that all those without the disease will test negative, but this is not the same the other way around. A patient could have a negative test result yet still have the disease – this is called a 'false negative'. The specificity of a test is also related to its 'positive predictive value' (true positives) – a test with a specificity of 100% means that all those who get a positive test result definitely have the disease. To fully judge the accuracy of a test, its Sensitivity must also be considered.
Standard deviation	A measure of the spread, scatter or variability of a set of measurements. Usually used with the mean (average) to describe numerical data.
Statistical power	The ability of a study to demonstrate an association or causal relationship between two variables, given that an association exists. For example, 80% power in a clinical trial means that the study has a 80% chance of ending up with a P value of less than 5% in a statistical test (i.e. a statistically significant treatment effect) if there really was an important difference (e.g. 10% versus 5% mortality) between treatments. If the statistical power of a study is low, the study results will be questionable (the study might have been too small to detect any differences). By convention, 80% is an acceptable level of power. See also P value.
Stereotypes	Repetitive, stereotyped, purposeless movements, actions, body patterns, speech patterns. They include hand flapping, clapping, slapping, fluttering, rocking, or facial movements.
Structured interview	A research technique where the interviewer controls the interview by adhering strictly to a questionnaire or interview schedule with pre-set questions.
Study checklist	A list of questions addressing the key aspects of the research methodology that must be in place if a study is to be accepted as valid. A different checklist is required for each study type. These checklists are used to ensure a degree of consistency in the way that studies are evaluated.
Study population	People who have been identified as the subjects of a study.
Study quality	See Methodological quality.
Study type	The kind of design used for a study. Randomised controlled trial, case-control study, cohort study are all examples of study types.
Subject	A person who takes part in an experiment or research study.
Survey	A study in which information is systematically collected from people (usually from a sample within a defined population).
Syndrome	The association of several clinically recognizable features, signs (observed by a physician), symptoms (reported by the patient), phenomena or characteristics that often occur together,
Systematic error	Refers to the various errors or biases inherent in a study. See also Bias.
Systematic review	A review in which evidence from scientific studies has been identified, appraised and synthesised in a methodical way according to predetermined criteria. May or may not include a meta-analysis.

Systematic	Methodical, according to plan; not random.
Systemic	Involving the whole body.
Target population	The people to whom guideline recommendations are intended to apply. Recommendations may be less valid if applied to a population with different characteristics from the participants in the research study – e.g. in terms of age, disease state, social background.
Tertiary centre	A major medical centre providing complex treatments which receives referrals from both primary and secondary care. Sometimes called a tertiary referral centre. See also Primary care and Secondary care.
Triple blind study	A study in which the statistical analysis is carried out without knowing which treatment patients received, in addition to the patients and investigators/clinicians being unaware which treatment patients were getting.
	Unconjugated hyperbilirubinaemia arises if the liver cannot handle the amount of unconjugated bilirubin presented to it. This can occur as a result of excessive red blood cell breakdown – (haemolysis) and/or because of immaturity of the liver enzymes involved in conjugation.
Uncontrolled observational study	A type of study where there is no control group.
Univariate analysis	Analysis of data on a single variable at a time
Validity	Assessment of how well a tool or instrument measures what it is intended to measure. See also External validity, Internal validity.
Variable	A measurement that can vary within a study, e.g. the age of participants. Variability is present when differences can be seen between different people or within the same person over time, with respect to any characteristic or feature which can be assessed or measured.
Yield	The outcome of a biomedical test that can suggest clinically relevant findings.

Appendix A

Scope of the guideline

1 NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

SCOPE

1 Guideline title

Autism spectrum disorders in children and young people: recognition, referral and diagnosis

1.1 Short title

Autism spectrum disorders in children and young people

2 The remit

The Department of Health has asked NICE: 'to develop a clinical guideline in relation to the initial recognition, referral and diagnosis of autism spectrum disorders in children and adolescents'.

3 Clinical need for the guideline

3.1 Epidemiology

a) Autism spectrum disorders are lifelong neurological conditions. The way they are expressed in individual people will differ at different stages of their lives and in response to interventions. The number of identified cases of children and young people with all disorders in the autism spectrum (which includes autism, Asperger's syndrome and atypical autism) has risen in the past decade. The prevalence for all autism spectrum disorders (ASDs) ranges from 60 per 10,000 to more than 100 per 10,000 in the UK. The prevalence for autism is reported to range from 20 to 40 per 10,000. These numbers have had a significant impact on referrals to diagnostic services.

b) The main areas of functioning affected in people with ASD as defined by the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) are:

- qualitative impairments in social interaction

- qualitative impairments in communication
- restricted, repetitive and stereotyped patterns of behaviour, interests and activities.

c) Other features commonly found are a lack of cognitive and behavioural flexibility; altered sensory sensitivity; sensory processing difficulties, stereotyped mannerisms; emotional dysregulation, and a limited range of interests and activities.

d) These features may be along a continuum from minimal to severe. The presence of features of the autism spectrum may have minimal impact on a person's ability to function in the world, and 'condition' is a more appropriate term than 'disorder'. For a diagnosis of ASD to be made there must be both the presence of impairments (as defined by the World Health Organization) and an impact on the person's functioning.

e) The two major diagnostic classification systems (DSM-IV and ICD-10) use similar but not identical criteria. They both use the term pervasive developmental disorder (PDD), which encompasses autism, Asperger's syndrome and atypical autism (or PDD-NOS [not otherwise specified]). For the purposes of this clinical guideline the term ASD is used instead of PDD because it is more widely understood.

f) Children and young people with ASD are more likely to have associated mental health and medical health problems, other developmental disorders and adaptive impairments. 'Diagnostic overshadowing' means there may be a tendency to overlook symptoms of ASD in these groups and attribute them to being part of an intellectual disability. Children with a diagnosed intellectual disability have been identified as a specific group in which ASD may be under-diagnosed.

3.2 Current practice

a) There is wide variation in rates of identification and referral for diagnostic assessment, waiting times for diagnosis, models of multiprofessional working, assessment criteria, diagnostic practice, and biomedical investigation and genetic counselling for children and young people with features of ASD. These factors contribute to delays in reaching a diagnosis and subsequent access to appropriate services.

b) Healthcare professionals usually make the diagnosis of ASD in a child or young person. By working jointly with social care and educational professionals in a range of environments, healthcare professionals share information regarding the diagnosis and agree on a plan for future support and/or interventions for each child or young person. When the process works well, professionals and carers communicate right from the start, laying the foundation for a long-term understanding between children, carers and the professionals supporting their needs. However, practice varies and in some parts of the country waiting lists for multiprofessional specialist assessment are longer than 2 years.

c) Diagnosis is a process that can have a variable time frame involving different competencies amongst the professionals involved. However, flexibility in approach to diagnosis is not always a feature of current diagnostic assessment in the NHS.

d) The current use of biomedical investigations to rule out other conditions and thresholds for genetic counselling referral varies markedly. Opinion also varies on the value of biomedical investigations in the diagnostic assessment of autism and coexisting conditions.

e) Children and young people with other existing conditions featuring intellectual, physical or sensory disability and/or mental health problems may not be recognised as having symptoms of ASD, and there may be overlaps between a developmental disorder and a coexisting condition. Children's social circumstances (for instance, 'looked after' children) may also affect how quickly features of ASD are recognised.

f) Some of the behaviours that define ASD may also feature in other communication disorders and learning disabilities (such as childhood attachment disorders), as well as being the result of other conditions (such as epilepsy or acquired brain injury) or childhood experiences (such as trauma or maltreatment). Children and young people may be wrongly diagnosed as having a mental illness when they have features of ASD, or, conversely, they may be misdiagnosed with autism when they have another condition. Misdiagnosis can lead to delays in children and young people receiving the care and support that they need.

g) The process and content of information-sharing varies widely, for instance in the provision of information and support for the family while awaiting diagnosis and immediately after.

h) Clinical guidance for diagnosis has been published for the NHS in Scotland: 'Assessment, diagnosis and clinical interventions for children and young people with autism spectrum disorders' (Scottish Intercollegiate Guidelines Network [SIGN 98] 2007). The National Service Framework for Children, Young People and Maternity Services (2004) included an 'Autism exemplar', which described the 'patient journey' of a 3-year-old boy with ASD and built on guidance in the National Autism Plan for Children (NAP-C). The Autistic Spectrum Disorder Strategic Action Plan for Wales (2008) focused on the role of strategic health plans to develop services and interagency cooperation between health and education for children and young people with ASD. The Department of Health published the consultation document 'A better future' (2009) on designing services to improve support for adults with autistic spectrum conditions. The National Audit Office is currently undertaking a study, 'Supporting people with autism through adulthood' focusing particularly on the transition from adolescence to adulthood.

i) This guideline is needed to make services more child and family/supporter centred and to help reduce variation in professional practice by improving initial recognition of the features of ASD and the timing and process of diagnostic assessment to enable longer-term future care.

4 The guideline

The guideline development process is described in detail on the NICE website (see section 6, 'Further information').

This scope defines what the guideline will (and will not) examine, and what the guideline developers will consider. The scope is based on the referral from the Department of Health.

The areas that will be addressed by the guideline are described in the following sections:

4.1 Population

4.1.1 Groups that will be covered

a) Children and young people from birth up to 18 years until their 19th birthday.

b) Specific subgroups of children in whom ASD is known to be less likely to be recognised.

- Children diagnosed with an intellectual disability, because the components of a core diagnosis may be different for children in this group.

4.1.2 Groups that will not be covered

a) Adults (19 and older).

4.2 Healthcare setting

a) Primary, secondary and tertiary care by healthcare professionals who have direct contact with, and make decisions concerning, the care of children and young people.

b) This is an NHS guideline. It will comment on the interface with other services, such as social services and the voluntary sector. But it will not include recommendations relating to services provided exclusively by these agencies, except relating to care provided in those settings by healthcare professionals funded by the NHS. The guideline may include some recommendations for education services, either directly or indirectly, relating to collaborative working with NHS professionals.

4.3 Clinical management

4.3.1 Key clinical issues that will be covered

a) Signs and symptoms (features of ASD) that should prompt professionals working with children and/or parents or carers to consider ASD in a child or young person. These will include signs and symptoms that should trigger referral for specialist assessment.

b) Information requirements from other agencies.

c) The components of diagnostic assessment after referral, including:

- methods of assessing ASD
- diagnostic thresholds for ASD
- assessment of the most common coexisting conditions and differential diagnoses, including other developmental disorders
- speech and language disorders, intellectual disabilities, and mental health problems
- clinical evidence for and cost effectiveness of (which test should be done on whom and for what purpose):
  - biomedical investigations (including sequencing and number of tests)
  - genetic assessments (such as karyotype, fragile x, comparative genomic hybridization [CGH] array)
  - neuroimaging (computed tomography [CT], magnetic resonance imaging [MRI], single photon emission computed tomography [SPECT], positron emission tomography [PET])
  - electroencephalograms [EEGs]
  - metabolic tests.

d) The information and day-to-day support (such as a telephone helpline) appropriate for children, young people and parents/carers during the process of referral, assessment and diagnosis of ASD.

e) Ineffective diagnostic interventions and approaches.

4.3.2 Clinical issues that will not be covered

a) Population screening or surveillance.

b) The basic components of any routine paediatric or mental health assessment not specific to ASD.

c) The role and competencies of different professions in the recognition and diagnosis of ASD.

d) Specific models for running a diagnostic service.

e) Interventions and ongoing management of ASD, including specific therapeutic interventions during diagnosis.

f) Reassessment and review of diagnosis.

4.4 Main outcomes

a) Diagnostic accuracy of clinical and other features for the recognition of ASD.

b) Diagnostic accuracy of biomedical investigations in ASD.

c) Identification of coexisting conditions.

d) Health-related quality of life, measured in quality-adjusted life years (QALYs) if possible.

e)Children and young people's views and the views of their parents and carers of the process of referral, assessment and diagnosis, and their support and information needs.

f) A clinical pathway that describes the components of an effective diagnostic service, based on an ethos of multiprofessional working.

4.5 Economic aspects

Developers will take into account both clinical and cost effectiveness when making recommendations involving a choice between alternative diagnostic and biomedical investigations. A review of the economic evidence will be conducted and analyses will be carried out as appropriate. The preferred unit of effectiveness is the QALY and the costs considered will usually only be from an NHS and personal social services (PSS) perspective. Further detail on the methods can be found in 'The guidelines manual' (see 'Further information').

4.6 Status

4.6.1 Scope

This is the final scope.

4.6.2 Timing

The development of the guideline recommendations will begin in September 2009.

5 Related NICE guidance

• When to suspect child maltreatment. NICE clinical guideline 89 (2009). Available from www.nice.org.uk/CG89

• Attention deficit hyperactivity disorder. NICE clinical guideline 72 (2008) Available from www.nice.org.uk/CG72

• Depression in children and young people. NICE clinical guideline 28 (2005). Available from www.nice.org.uk/CG28

6 Further information

Information on the guideline development process is provided in:

• 'How NICE clinical guidelines are developed: an overview for stakeholders', the public and the NHS'

• 'The guidelines manual'.

These are available from the NICE website (www.nice.org.uk/guidelinesmanual). Information on the progress of the guideline will also be available from the NICE website (www.nice.org.uk).

Appendix B

Declarations of interest

The Guideline Development Group were asked to declare any possible conflicts of interest which could interfere with their work on the guideline. The interests that were declared are as follows:

GDG Member	Interest Declared	Type of Interest	Decisions Taken
Gillian Baird	Published research on ASD prevalence and screening, including a total population screening study that informed the work of the national screening committee	Personal, non-pecuniary	NCC-WCH Clinical Co-Director facilitated discussions on related topics while declaration considered. Not considered a conflict of interest by the NCC-WCH/NICE and GB chaired all GDG discussions from 29-03-10
	Involved in the development of the DSM-IV-V and ICD-10-11	Personal, non-pecuniary	Declare and can participate in discussions on all topics
Tony Charman	Published research on screening tools, diagnostic instruments, interventions and the prevalence of autism	Personal, non-pecuniary	Declare and can participate in discussions on all topics
	Holding office in the following groups and professional bodies: member of the Scientific Advisory board of the charity Research Autism; Chair of the Advisory Group to the All Party Parliamentary Group on Autism; Invited expert on a number of panels convened by the MRC and the NAS in the UK and NIH in the USA	Personal, non-pecuniary	Declare and can participate in discussions on all topics
	Involved in the development and testing CHAT, Q-CHAT screening instruments	Personal, non-pecuniary	Declare and can participate in discussions on all topics
	European Science Foundation COST Action: Enhancing the Scientific Study of Early Autism (ESSEA); a 'network' grant that involves work on early screening and early intervention	Non-personal, pecuniary	Declare and can participate in discussions on all topics

GDG Member	Interest Declared	Type of Interest	Decisions Taken
	amongst other activities		
Diana Howlett	Leads steering group of the North Somerset Autism Strategy Group that endorses a multiagency approach to assessment and diagnosis of ASD. This approach could be changed in light of new guidance.	Personal, non-pecuniary	Declare and can participate in discussions on all topics
Anne Marie McKigney	Involved in small research project to map and evaluate the current diagnostic process used for assessment of ASD in children and young people in Gwent (2010)	Non-personal, pecuniary	Declare and can participate in discussions on all topics
	Member of Aneurin Bevan Health Board) Working Party on Assessment and Diagnosis for Autism Spectrum Disorder - 2003. This approach could be changed in light of new guidance	Personal, non-pecuniary	Declare and can participate in discussions on all topics
	Member of focus group looking at the assessment and diagnosis of children with ASD in Wales, as part of the Welsh Assembly Government ASD Strategic Action Plan.	Personal, non-pecuniary	Declare and can participate in discussions on all topics
Ann Le Couteur	Royalties on sales of Autism Diagnostic Interview paid to Newcastle University (from Western Psychological Services (WPS)).	Non-personal pecuniary	Declare and can participate in discussions on all topics
	Lecture given on Diagnostic Assessment and Interventions and Comorbid Disorders	Personal non-pecuniary	Declare and can participate in discussions on all topics
	Lecture given on 'Diagnostic Assessment and Interventions and Comorbid Disorders' (Romania, November 2009)	Personal non-pecuniary	Declare and can participate in discussions on all topics
	Lecture given on 'Autism Spectrum Disorders: Assessments and Interventions' (Association for Child and Adolescent Mental Health Emmanuel Millar Lecture and Day Conference, March 2010)	Personal non-pecuniary	Declare and can participate in discussions on all topics
	Moderator Question and Answer Session on 'Meeting the global challenge of screening and diagnosis of autism spectrum disorders' (IMFAR conference, May 2010)	Personal non-pecuniary	Declare and can participate in discussions on all topics
	Costs for reviewing Autism Diagnostic Interview-Revised (ADI-R) paid to Newcastle University.	Non-personal, pecuniary	Declare and can participate in discussions on all topics
	Holding office in the following groups and professional bodies: Member of Medical Research Council Review of Autism Research (2000-01); NAP-C advisor to National Service Framework Disabled Children External Working	Personal non-pecuniary	Declare and can participate in discussions on all topics

GDG Member	Interest Declared	Type of Interest	Decisions Taken
	Group (2001-03); Member of the All Party Parliamentary Group on Autism; Member of Dept for Education and Skills Autism Research Co-ordination Group; Member of the Scientific Advisory Committee, Research Autism; External advisor and expert peer reviewer for the Scottish Intercollegiate Guidelines Network ASD guideline (2006-07); External advisor and expert peer reviewer for the New Zealand ASD Guideline (2007-08); Independent Autism expert advisor to the North East Autism Consortium: A multi-agency strategic planning group responsible for the commissioning of services for adults (14+) with ASD; Dept of Health Adult Autism Strategy External Reference Group - Member of Health subgroup & Dept of Health North of England Stakeholders Group (2008-10); The UK Brain Bank for Autism & Developmental Disorders Member of Research Advisory Group; Member of National Advisory Board for Transition to Adult Services & Adulthood for Young People with ASC; Patron of the South Tyneside ASD support Group; Patron of the Tyne & Wear Autistic Society.		
	Published research on screening tools, diagnostic instruments, interventions and the prevalence of autism	Personal, non-pecuniary	Declare and can participate in discussions on all topics
Jamie Nicholls	GP tutor for Southend-on-Sea area, a paid post (one session per week) and responsible for arranging the continuing professional education for the primary care practitioners in local area	Personal, pecuniary	Declare and can participate in discussions on all topics
	Member of the Scientific & Advisory Committee of Research Autism. Given lectures and written educational articles on autism directed mainly towards education in primary care	Personal, non-pecuniary	Declare and can participate in discussions on all topics
Lorraine Scott	Member of diagnostic Forum In Northern Ireland that aims to develop advice on standards for assessment and diagnosis of Autism Spectrum Disorders (ASD)	Personal, non-pecuniary	Declare and can participate in discussions on all topics
Emily Simonoff	Published research on screening tools, diagnostic instruments, interventions and the prevalence of autism	Personal, non-pecuniary	Declare and can participate in discussions on all topics

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Appendix C

Registered stakeholder organisations

For a list of registered stakeholder organisations please see the NICE website:
http://guidance.nice.org.uk/CG/Wave15/78/SHRegistration/SHList/pdf/English

Appendix D

Review questions

Signs and symptoms

1. a) What are the signs and symptoms that should prompt a health care or other professional in any context to think of ASD?

1. b) When should a child or young person be referred for a diagnostic assessment?

Diagnostic assessment

2. In children with suspected ASD (based on signs and symptoms) what information assists in the decision to refer for a formal ASD diagnostic assessment?

a) Are there screening instruments that are effective in assessing the need for a specialist ASD assessment?

b) What information about the child and family increases the likelihood of a diagnosis of ASD and would assist in the decision to refer for a formal ASD diagnostic assessment?

part 1: General risk factors

part 2. Risk of ASD in co-existing conditions

c) Information from other sources as contextual information: information about how the child functions in different environments such as school and home; social care reports (i.e. 'Looked After' children); other agencies

3. What should be the components of the diagnostic assessment? When should they be undertaken, in what subgroups and in what order?

a) Assessment tools specific to ASD: e.g. Autism Diagnostic Interview-Revised (ADI-R), Developmental, Dimensional and Diagnostic Interview (3di), Diagnostic Interview for Social and Communication Disorders (DISCO), Autism Diagnostic Observation Schedule (ADOS), Gilliam Autism Rating Scale

b) Other assessment tools that help the interpretation of the specific ASD tools (e.g. ADI-R, 3di, DISCO, ADOS, Gilliam Autism Rating Scale): an assessment of intellectual ability; an assessment of receptive and expressive language etc.

c) Biomedical investigations for diagnosis of ASD e.g. EEG, brain scan, genetic tests, physical examination; genetic counselling; investigations for associated medical conditions

4.a) What are the most important differential diagnoses of ASD?

4.b)What features observed during diagnosis reliably differentiate the important differential diagnoses from ASD?

5. How should information be integrated to arrive at a diagnosis?

a) Is the diagnostic assessment more accurate and reliable when performed by a multidisciplinary team or a single practitioner?

b) What is the stability of an ASD diagnosis over time?

c) What is the agreement of an ASD diagnosis across different diagnostic tools?

6. How should the findings of the diagnostic assessment be communicated to children and young people, and their families/carers?

7. What actions should follow assessment for children and young people who are not immediately diagnosed with ASD?

Coexisting conditions

8. Which are the common coexisting conditions that should be considered as part of assessment?

- Neurodevelopmental: speech and language problems, intellectual disability, coordination, learning difficulties in numeracy and literacy;
- Neuropsychiatric disorders such as ADHD, OCD, anxiety, depression, Tourette's, Tic disorders;
- Medical problems such as functional gastrointestinal problems, tuberosclerosis, neurofibromatosis

Information and support

9. What information do children and young people, and their families/carers need during the process of referral, assessment and diagnosis of ASD?

10. What kinds of day-to-day, ongoing support (not specific to therapeutic interventions/management of ASD) should be offered to children and young people, and their families/carers, during the process of referral, assessment and discussion of diagnosis of ASD?

Appendix E

Protocols

See separate file

Appendix F

Search strategies

See separate file

Appendix G

Excluded studies

See separate file

Appendix H

Included studies

See separate file

Appendix I

Diagnostic criteria

Permission to reproduce ICD-10 and DSM-IV criteria pending.

Appendix J

Diagnostic tools

Autism Diagnostic Interview-Revised (ADI-R)

(Le Couteur *et al.* 2003; Lord *et al.* 1994; Rutter *et al.* 2003).

The ADI-R is a semi-structured investigator-based interview undertaken with parents/main caregiver. The format of the interview is designed to provide a framework for a lifetime differential diagnosis of pervasive development disorder/autism spectrum disorder (ASD) defined within the internationally accepted diagnostic systems (DSM-IV-TR and ICD-10). The interview emphasises the need to record descriptions of specific behaviours in the three key domains necessary for a diagnosis of autism/ASD (with sections focussing on regression and special skills) and some other relevant clinical behaviours. The interview can be used for individuals of the mental age of 2 years and above. It takes around 2 to 3 hours to administer and training is required. The published algorithm provides a threshold for autism/non-autism only. With increasing awareness of the autism spectrum the original authors and a number of other ASD research groups, are re-analysing ADI-R datasets to propose new diagnostic algorithm(s) threshold cut-off scores for autism and ASD (Buitelaar *et al.* 1999; Le Couteur *et al.* in preparation). The interview does not cover the more subtle and milder symptoms of the broader autism phenotype.

The ADI-R format records information about current behaviours (defined as the last three months), lifetime and early childhood ratings. The interview is now available in thirteen languages.

Autism Diagnostic Observational Schedule (ADOS)

(Lord *et al.* 2000).

The ADOS is a widely used semi-structured, standardised play- and activities-based assessment focusing on the three behavioural domains necessary for a differential diagnosis of ASD and/or other neurodevelopmental disorders:

- communication
- social interaction
- play/imaginative use of materials and repetitive behaviours

These observations compliment the information gained from other assessment procedures such as the developmental history and direct observations. It takes 30-45 minutes to administer. Training in the use of pre-determined social contexts is required and once trained regular reliability checks are necessary. There are four modules for use with individuals ranging from pre-school children without useful speech through to verbally able adults. The module choice controls for levels of expressive language. The ADOS publications report high levels of reliability of items across modules. The exception is coding of items such as repetitive behaviours and sensory abnormalities which may occur less frequently during a live individual assessment.

Diagnostic algorithms summarise the ratings for social behaviour and communication in relation to DSM IV and ICD-10 diagnostic criteria with separate thresholds for autism and

ASD. The ADOS is available in several languages, but further work may well be required to consider particular social and cultural factors. This assessment provides useful clinical and research information that can inform intervention planning, and although the instrument was originally developed as a diagnostic tool, it has also been used as an outcome measure (Aldred *et al.* 2004; McConachie *et al.* 2003).

Developmental Diagnostic and Dimensional interview (3di)

(Skuse *et al.* 2004)

This is a computerised interview assessment procedure that is designed to be administered by a trained interviewer with a parent informant using a laptop computer. A structured computer-generated report is available at the end of the interview together with algorithms using a dimensional framework of symptom and diagnostic profiles for autism and common non-autistic co-morbidities. The focus is on current functioning. Parents can be sent a pre-interview package of questionnaires to complete. This information can be entered onto the computer and allow an abbreviated face-to-face interview lasting 45 minutes, compared with 90 minutes for the full interview. The interview was devised to assess autistic traits, social impairment and co-morbidity in children of normal ability and is not recommended for use in pre-school children.

Diagnostic Interview for Social and Communication Disorders (DISCO)

(Leekam *et al.* 2002, Wing *et al.* 2002).

The DISCO is a clinical interview schedule based on Wing and Gould's original theoretical proposal that autism is a spectrum of conditions with a particular emphasis on the triad of impairments. It was designed to collect information on development and behaviour for individuals of all ages and levels of ability. The interview evolved from the earlier Handicaps, Behaviours and Skills schedule (HBS) (Wing and Gould, 1978; 1979) and is used to elicit information relevant for the broader autism spectrum, other associated developmental disorders and co-morbid conditions. A set of algorithms and information on developmental skills and atypical behaviours can be derived from the interview but these are not clinical diagnoses (Leekam *et al.* 2002; Wing *et al.* 2002). The semi-structured interview is undertaken with parents/main caregivers. It takes approximately 3 hours to administer and specific training is required.

CARS

To be completed

GARS

To be completed

DAWBA

To be completed

PIA

To be completed

Appendix K

Differential diagnosis advice for healthcare professionals

The GDG also developed this advice to support the decision-making process in differentiating between alternative diagnoses with similar features. For each condition listed, the characteristic key presenting features are specified. The table also shows the ways in which each condition typically differs from ASD. It covers key clinical features; the assessments and investigations that should have formed a part of the child's overall assessment, and highlights the relevant components or outcomes of those assessments that would contribute to the process of differentiation.

Key presenting features that may overlap with ASD	Main features to differentiate from ASD	Assessments or investigations to differentiate from ASD	Special notes / diagnostic pitfalls
Neurodevelopmental disorders			
Specific language disorder/impairment			

A specific language disorder will present with:
• Predominantly impaired use and/or understanding of language
• Play and imagination may be delayed
• There may be associated impairment of social communication
• Beyond the preschool period, there may be an impact on the child's ability to develop and maintain peer friendships
	A child with specific language impairment would usually show:
	• Compensatory development of non-verbal communication
	• The quality of play and imagination should be normal
	• Social motivation and cooperative in assessment
	• Relative strengths in reciprocal social interaction and empathy
	• A clear positive approach to peer friendships, at least in the preschool years
	
	There would usually be an absence
		The pattern of language testing may be helpful:
		
		• In specific language impairment:
		  ○ Expressive language can be more impaired than receptive
		  ○ Pattern of responses to tests can often reveal greater problems with grammatical structures than in other areas
		• In ASD:
		  ○ Expressive language can be better than receptive
		  ○ Single word noun vocabulary may be extensive but with
			ASD and speech and language impairment may coexist

Key presenting features that may overlap with ASD	Main features to differentiate from ASD	Assessments or investigations to differentiate from ASD	Special notes / diagnostic pitfalls
	of: • Echolalia • Rigid repetitive behaviours • Stereotyped mannerisms • Abnormal responses to sound and other senses • Over focussed intense interests	impaired abstract concepts ○ Sentence structure can be better than comprehension of paragraphs ○ Cognitive assessment may also be very useful, leading to a profile of the child's skills and deficits, and the balance between verbal and non-verbal abilities ○ Pattern of responses to tests may give an uneven profile across different subtests# ○ Use of language may be more limited than capability suggests, for example single words or minimal phrases for needs despite ability to construct sentence or excessive talking that lacks reciprocity	
Intellectual disability/global developmental delay			
• Delayed use and understanding of language • Delayed or absent play skills • Limited social interactions and peer relationships	In severe intellectual disability: • The delay is likely to be across all areas of development, with a more even developmental profile on IQ testing • The child would be expected to show more social intent and interest, consistent with developmental level • Imitation present In ASD there may be:	Tests of intellectual/cognitive function will distinguish the generally low cognitive level from the often uneven profile found in ASD. Tests of adaptive impairment eg Vineland or ABAS may not distinguish since adaptive skills are often much more impaired in ASD that would be predicted from the IQ.	• ID can co-occur with ASD • It is still important to diagnose ASD, if present, in a child with a severe overall intellectual impairment as this will influence educational and learning strategies • It is also relevant when considering aetiological investigations and genetic counselling.

Key presenting features that may overlap with ASD	Main features to differentiate from ASD	Assessments or investigations to differentiate from ASD	Special notes / diagnostic pitfalls
	• Relative strength in areas that do not depend on language and social understanding • More marked impairment of language / communication / play / flexibility • More marked sensory sensitivities and interests In ASD with SLD: • IQ profile may be quite evenly delayed but the child is more likely to be aloof / withdrawn / self injurious/ritualistic or to show very challenging behaviour		If a child has a severe intellectual disability, the impairment of social communication may not become apparent until later in age than usual, because the latter is related to the child's overall developmental level
Developmental coordination disorder (DCD)			
• Clumsiness / poor motor coordination • History of delayed motor milestones, (can also be present in ASD but not the majority) • Lack of awareness of personal and other's space • In some, peer relationships are often poor	In DCD: • Play is normal • Language is not typically delayed or disordered • Good communicative intent • The organisational difficulties and motor planning difficulties are the predominant area of difficulty	Occupational Therapy assessment: there are numerous standardised tools for assessing DCD, Observations in school setting: motor and social functioning in playground / classroom	DCD and ASD can co-occur Those who receive an early DCD diagnosis because of delayed motor milestones may not have their social impairment recognised until much later
Neuropsychiatric disorders			
Attention deficit hyperactivity disorder (ADHD)			
• Poor attention • Impulsive behaviour • Increased level of physical activity • Butting into other children's games and other	In ADHD: • The child's overactive behaviour is characterised by fidgety, restless behaviour • Inattention and distractibility are relatively pervasive and do not	• Careful developmental history • Observation and/or good accounts of the child in different settings, for example home and school, including situations likely to elicit distractibility and disorganised	ADHD commonly co-exists with ASD (see chapter 7 on Co-existing conditions)

Key presenting features that may overlap with ASD	Main features to differentiate from ASD	Assessments or investigations to differentiate from ASD	Special notes / diagnostic pitfalls
adults'/children's conversations • Lack of awareness of danger • A history of poor social skills and problems with peer relationships	occur only in situations where the child is not interested or motivated • The child understands the rules or social norms, for example putting your hand up in class to get the teacher's attention or answer a question but act impulsively so that they may shout out because they are excited about knowing the answer, or simply because an idea has popped into their mind, irrespective of whether the moment is appropriate • Dangerous behaviour is driven by impulsivity and there is an understanding of the potential dangers • The child is able to demonstrate social reciprocity and appropriate non-verbal communication • They do not usually react with marked distress to stimuli to which they are over sensitive. In ASD: • Typically the child can be engaged in, or concentrate on, certain subjects or topics for a sustained period if that topic has a particular interest for them (although focus on computer games is common in ADHD) • The child does not understand the social rules and norms, nor why they should conform to such rules; behaviour is very self-directed	behaviour • Specific rating scales for ADHD	

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	• The child may not understand common dangers and so act in a dangerous way: this is distinct from the" acting without thinking" seen in a child with ADHD.		
Mood disorder			
Depression may present with: • Withdrawn behaviour • Reduced or very limited verbal output • Lack of interest in typical activities for the developmental age	In depression: • Usually an episodic course, with a history of more 'normal' social behaviour (the child can show social interest in activities etc) when not depressed or severely anxious • The change in social functioning should be temporally related to other depressive symptoms. • May not be pervasive: it may be less evident in some settings.	A careful early developmental history is essential as is a mental state examination Elicit accounts of behaviour and/or observation in different settings and semi-structured interviews with the child/young person and parents to elicit the current mental state and any changes that have occurred. Look for any events (loss, trauma, bullying) that may be associated with a change in behaviour and functioning.	At times these disorders can be hard to distinguish on presenting behaviour alone; they may also co-occur (see chapter on Co-existing conditions)
Anxiety disorder			
Anxiety may be associated with: • Repetitive anxious behaviour (e.g. repetitive questioning or demanding reassurance). Social phobia may present with: • Social avoidance: 'anticipatory anxiety'	In anxiety: • The repetitive questions etc will usually have an anxious quality e.g. "you won't leave me mummy?." • However this usually does NOT have a repetitive/stereotyped quality to it, so that questions do not have to be answered in exactly the same way. In social phobia: • Typically they are less anxious with people they know. • Anxiety often occurs in situations of public performance where they		

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	think they may be judged. for example reading aloud in the classroom, meeting others at parties, changing clothes for PE • They have an interest in and care about the opinions of others in such situations • The characteristic feature is the anxious content, compared with the intensity (and insistent quality) of the repetitive behaviour seen in the child with ASD (”What time is news at Ten?”).		
Attachment disorders			
• Overfriendly, disinhibited and indiscriminately socially intrusive behaviour - i.e. no evidence of socially appropriate hesitancy or initial shyness with strangers • OR , emotionally withdrawn behaviour with minimally expressed attachment behaviours to parent/carer eg seeking or responding to comfort. • • Abnormal behaviour at separation and reunion with parent/carer • Limited response to other peoples distress • Children who have experienced deprivation may show self-stimulatory and self-comforting behaviours that are repetitive and stereotyped	In ASD: • Behaviour may lack normal boundaries but this is less likely to be in order to gain social attention. For example: child with ASD child might treat adult rather like an object- climbing up over an adult to reach something behind the adult rather than climbing onto the strange adult’s lap to gain attention -attachment disorder). • Social communicative behaviours such as eye contact are poorly regulated in ASD rather than avoidant as in emotionally withdrawn attachment. • Children with ASD can show behaviours that suggest appropriate separation anxiety but the greeting and farewell behaviour has an unusual quality • Children with attachment disorders	Developmental and social history is essential.* * • History of emotional or physical neglect • Physical evidence of abuse / neglect, but may not be easily available. • Careful history taking is essential, and observation of the child with parents; • Information from other professionals e.g. health visitors, nursery staff. school teachers or social worker is essential Clinical judgement is often the crucial factor in distinguishing between a maltreated child and one with ASD In those with continuous ‘good parenting’, an attachment disorder would be unlikely. For those children who have experienced significantly disrupted	There is an overlap between the behaviour seen in a maltreated child and that seen in a child with attachment disorder; the two may also co-exist. In all cases, consider whether liaison with social services is needed See NICE guidelines on recognition of maltreatment (http://guidance.nice.org.uk/CG89)

Key presenting features that may overlap with ASD	Main features to differentiate from ASD	Assessments or investigations to differentiate from ASD	Special notes / diagnostic pitfalls
	show relatively normal imaginative play (when given access to developmentally appropriate toys) • Children with attachment disorders usually do not show over-intense or unusual interests • In attachment disorder, the child may make a lot of rapid progress when exposed to a more nurturing environment, including nursery, school or foster placement	and/or inconsistent parenting and care during their preschool years, attachment disorder is more likely but may co-exist with ASD	
Oppositional defiant disorder (ODD)			
• Oppositional behaviour is common in children with ASD. • Children with ODD may have impaired or limited peer relationships • Children with ODD may show limited empathy or concern for others including lack of remorse	In ODD: • The child usually understands that their behaviour is undesirable, even unacceptable but they persist with it. • The behaviour often has a deliberate quality • The behaviour may have clear benefits for the child • When children are motivated to alter their behaviour they may do so • Should be able to show evidence of social-communicative understanding/ competence so that he/she will have some awareness of the impact of their behaviour. • Does not usually show stereotyped or repetitive behaviour The child with ASD: • May have little if any awareness of	Assessment of the quality of communication and social interaction in situations when the child is enjoying him/herself and not trying to avoid demands	Oppositional behaviours are developmentally normal at times. ODD may co-exist in ASD as a separate disorder. Pathological demand avoidance (PDA) has been described as a particular subgroup of ASD with passive early onset, obsessive behaviours which are often person focussed with superficial social interest in whom the most striking feature is refusal to comply (excessive demand avoidance) even to events which the child enjoys.

Key presenting features that may overlap with ASD	Main features to differentiate from ASD	Assessments or investigations to differentiate from ASD	Special notes / diagnostic pitfalls
	the impact of their behaviour on others- their prime focus will be exclusively focussing on the behaviour/ interest that they are wanting to pursue • The child with ASD is often upset when it is pointed out to them they have hurt other people		
Conduct disorder			
• Individuals with CD can be described as callous/ unemotional and have limited empathy • Individuals with ASD may behave in an antisocial manner, particularly if they are annoyed or feel that others have 'broken rules'	Children with conduct disorder: • Show evidence of 'competence' in some areas of their social relationships • Do not have early social communication problems. • Their antisocial behaviour may show evidence of 'theory of mind', i.e., they may use sophisticated strategies to avoid detection. In ASD: • The child fails to understand the impact of their behaviour on others • They may become distressed when the impact is explained to them	Observation in different settings and interviews Developmental and social history is essential. Interview child/young person to assess their understanding of their behaviour and their motivation to behave in an antisocial fashion	Conduct disorder with callous/unemotional traits can co-occur with ASD
Obsessive compulsive disorder (OCD)			
• Obsessive, ritualistic and repetitive behaviour patterns	In OCD: • Onset of symptoms tends to be later than ASD usually after age 4 • Behaviours may be associated with distress for the child/ young person • Rituals are less likely to be associated with obsessional	Early developmental and social history is important; children with OCD generally have normal social communicative development OCD typically does not start before mid childhood Interviewing child to gain a better account of the behaviour is	OCD can co-occur with ASD

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	thinking (the child with ASD is not undertaking a ritual to avoid or compensate for obsessional thoughts) • The content of obsessions and rituals is often associated with avoiding harm and magical thinking (If I do this then my mother will be safe) In ASD: • The child is unlikely to be upset by their obsessions or rituals (unless they are disrupted) • Routines often relate to a dislike of disrupting a particular pattern of everyday activity, e.g., the way food is served on the plate, which route is taken going to school	necessary.	
Conditions in which there is developmental regression:			
Rett's syndrome			
• Regression of developmental skills before or around the first birthday, associated with lack of speech and loss of social communication behaviour • Stereotyped hand movements and hyperventilation are common	• Mainly affects girls • Motor regression, ataxia, loss of purposeful hand movements and oro-motor skills • Fall off of head growth • Characteristic "hand-wringing" movements of hands • often social interest is a relative strength (i.e. relative to level of cognitive impairment)	Specific diagnostic genetic test, MecP2 mutation, can confirm Rett's in most cases.	Those with milder symptoms (i.e. the ones who are more mobile) are more likely to have a co-occurring diagnosis of ASD. However, diagnosis is still made in the same way in milder cases on motor impairment, hand stereotypies, regression etc (although not all the features may be present) and MECP2.
Epileptic encephalopathy (EE)			
• Age of onset and site of electrical activity are critical in type of regression and outcome with	In LKS: • Onset typically between 2 and 7 years old, after a period of typical	• History of onset and symptoms • Presence of overt epilepsy • EEG in EE shows specific findings	Differentiation from autistic regression may not be easy and specialist assessment is

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epileptic encephalopathy (EE) • Broad developmental regression with hyperactivity and social impairment is found in EE in younger children < 2 years • Regression of language rather than regression to autism is found in Landau-Kleffner syndrome (LKS) epileptic encephalopathy usually in children >3 years of age although social withdrawal may be found • Overt seizures may not be present • • Absence seizures may be mistaken for a lack of interest in the child's surroundings	development • Onset over a period of a few days • Loss of previously acquired words • Loss of understanding of language • Symptoms may fluctuate • Non-verbal communication is preserved • Auditory agnosia: an inability to recognise and interpret environmental sounds • Social interest and play are usually preserved • Absence of mannerisms, rigid behaviour, sensory abnormalities, preoccupations and over focussed interests	which worsen in sleep eg localised in LKS to the perisylvian region.	recommended if any concern about epilepsy. Ref NICE epilepsy guidelines
Other conditions			
Severe visual impairment (blind)			
• Behaviours that involve vision are absent: eye gaze, postures, facial expressions, communicative gestures • The normal stage of echolalia / repeating others' speech is prolonged in blind children compared to their sighted peers • Delayed transition from non-specific babble to meaningful use of objects' names • Delayed development of abstract language • Delayed development of pretend	Blind children: • Show appropriate social curiosity • Make an effort to communicate • Show social reciprocity • Language development may be delayed but follows a broadly similar pattern to typically developing children • Seek to share information and experiences • More able to generalise their learning and to use environmental cues to expand their understanding	• Competence in assessing blind/severely partially sighted children/YP as the key presenting features need to be assessed relative to typically developing blind children.	ASD and severe visual impairment (especially if due to a brain as opposed to eye disorder) co-occur Joint attention behaviours are visually dependant so other diagnostic features assume greater importance

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play and perseveration of sensory based, exploratory play • Narrower range of interests compared to sighted children Repetitive mannerisms may be present	• Demonstrate empathy • Usual exploratory play with toys apart from delayed pretend play • Can be interested in new topics by others • Show normal flexibility in life events Different repetitive mannerisms eg not hand flapping, though may show eye poking and rocking (blindisms)		
Severe hearing impairment			
• Delayed language development: affects both use and understanding of language • Social isolation and awkwardness due to the child not picking up on the usual nuances of social communication	The following are not usually impaired or found in peripheral hearing loss • Non-verbal communication • Reciprocal communication • Play and imagination • Socially interest and initiation of peer interaction • Rigid repetitive behaviours, stereotyped mannerisms, abnormal responses to other senses and over focussed intense interests	• Formal and careful hearing testing is essential - bearing in mind that bright hearing impaired children are very visually alert	• ASD can co-occur with hearing impairment
Selective mutism			
• Lack of speech, especially in social settings • There may be a history of language delay / disorder • Anxiety is common, leading to controlling behaviours	• History of appropriate quality of communication and social interaction in some circumstances, typically at home, where the child usually talks • Normal non-verbal communication • Good imaginative play • Anxiety may lead to controlling behaviours but not rigid and repetitive behaviours or routines • Absence of stereotyped mannerisms, abnormal sensory	Observation in different settings	Consider language assessment ASD and selective mutism may co-exist

Key presenting features that may overlap with ASD	Main features to differentiate from ASD	Assessments or investigations to differentiate from ASD	Special notes / diagnostic pitfalls
	responses or over focussed intense interests		

1