Healthcare Improvement Scotland

SIGN

# SIGN 145 • Assessment, diagnosis and interventions for autism spectrum disorders

*A national clinical guideline*

*June 2016*

Evidence

## KEY TO EVIDENCE STATEMENTS AND RECOMMENDATIONS

### LEVELS OF EVIDENCE

| | |
|---|---|
| $1^{++}$ | High-quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias |
| $1^{+}$ | Well-conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias |
| $1^{-}$ | Meta-analyses, systematic reviews, or RCTs with a high risk of bias |
| $2^{++}$ | High-quality systematic reviews of case-control or cohort studies<br>High-quality case-control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal |
| $2^{+}$ | Well-conducted case-control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal |
| $2^{-}$ | Case-control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal |
| 3 | Non-analytic studies, eg case reports, case series |
| 4 | Expert opinion |

### RECOMMENDATIONS

Some recommendations can be made with more certainty than others. The wording used in the recommendations in this guideline denotes the certainty with which the recommendation is made (the 'strength' of the recommendation).

The 'strength' of a recommendation takes into account the quality (level) of the evidence. Although higher-quality evidence is more likely to be associated with strong recommendations than lower-quality evidence, a particular level of quality does not automatically lead to a particular strength of recommendation.

Other factors that are taken into account when forming recommendations include: relevance to the NHS in Scotland; applicability of published evidence to the target population; consistency of the body of evidence, and the balance of benefits and harms of the options.

**R** For '**strong**' recommendations on interventions that '**should**' be used, the guideline development group is confident that, for the vast **majority** of people, the intervention (or interventions) will do more good than harm. For **'strong'** recommendations on interventions that **'should not'** be used, the guideline development group is confident that, for the vast **majority** of people, the intervention (or interventions) will do more harm than good.

**R** For **'conditional'** recommendations on interventions that should be '**considered**', the guideline development group is confident that the intervention will do more good than harm for **most** patients. The choice of intervention is therefore more likely to vary depending on a person's values and preferences, and so the healthcare professional should spend more time discussing the options with the patient.

### GOOD-PRACTICE POINTS

✓ Recommended best practice based on the clinical experience of the guideline development group.

NICE accredited
www.nice.org.uk/accreditation

NICE has accredited the process used by Scottish Intercollegiate Guidelines Network to produce clinical guidelines. The accreditation term is valid until 31 March 2020 and is applicable to guidance produced using the processes described in SIGN 50: a guideline developer's handbook, 2015 edition (**www.sign.ac.uk/guidelines/fulltext/50/index.html**). More information on accreditation can be viewed at **www.nice.org.uk/accreditation**

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Every care is taken to ensure that this publication is correct in every detail at the time of publication. However, in the event of errors or omissions corrections will be published in the web version of this document, which is the definitive version at all times. This version can be found on our web site **www.sign.ac.uk.**

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Scottish Intercollegiate Guidelines Network

# Assessment, diagnosis and interventions for autism spectrum disorders

A national clinical guideline

June 2016

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# Contents

# 1 Introduction

## 1.1 THE NEED FOR A GUIDELINE

Since SIGN 98: Assessment, diagnosis and clinical interventions for children and young people with autism spectrum disorders was published in July 2007, there have been significant developments in interagency working attributable to the Getting it Right for Every Child (GIRFEC) approach now enshrined in the Children and Young People (Scotland) Act 2014.[1,2] The Scottish Strategy for Autism (2011) has provided a ten-year framework to progress implementation, planning and outcomes for adult and children and young people's services with a view to developing effective joint pathways for service delivery.[3]

This guideline updates SIGN 98 to reflect new evidence for managing children and young people and to incorporate evidence which applies to adults and older people. The inclusion of adults is in response to the increasing understanding that autism spectrum disorder (ASD) is a lifelong condition in which the core features of ASD persist whilst manifesting differently according to different age stages. Depending on the severity of autistic difficulties, ASD may not be evident as a presentation throughout preschool, primary, or secondary school years or in adulthood. It may not be recognised because of associated coexisting conditions. Variable environmental factors, for example relatively smaller class size in primary school years, or family 'scaffolding' of social impairment in childhood or adolescence or, in adults, unmasking of symptoms and signs of ASD due to loss of informal carers, will also influence this dynamic.[4] Alternatively the signs and symptoms of ASD may not always have been recognised by parents, carers, the individual themselves or other professionals,[5] so may not present until adulthood, or perhaps even older adulthood. There is therefore a need for a guideline which reflects the whole age range.

This is a highly prevalent condition. A community survey in England in 2007 estimated around 1% of adults have ASD.[6] Prevalence in children is also around 1%.[7,8] A study in greater Glasgow of children 0–6 years old reported a prevalence of autism of 11.1 per year per 10,000 children (0.1%) in 2007.[9] ASD is recognised more commonly in boys than girls, at a ratio of approximately 4:1, although this varies across the spectrum.[10]

Prompt diagnosis and appropriate intervention, specialised educational programmes, and structured support may help a person with ASD maximise his or her potential. Since the publication of SIGN 98, services across Scotland have adhered to the majority of the recommendations on assessment and diagnosis.[11,12] It is hoped that this update will contribute further to a reduction in variation in practice and improve services for people of all ages with ASD.

### 1.1.1 UPDATING THE EVIDENCE

This guideline updates SIGN 98 to reflect evidence published between 2006 and 2014.

For sections not included in the update, and sections where no new evidence was found, text and recommendations are reproduced verbatim from SIGN 98. The original supporting evidence was not reappraised by the current guideline development group.

The evidence review underpinning the sections on adults used the key questions and evidence identified to develop the National Institute for Health and Care Excellence (NICE) guideline 142, Autism: recognition, referral, diagnosis and management of adults on the autism spectrum.[13] Further searches were conducted to identify studies published after publication of NICE 142.

See section 13 for further details of the literature search and Annex 1 for details of the key questions addressed in this update.

### 1.1.2 SUMMARY OF UPDATES TO THE GUIDELINE, BY SECTION

The following list details the sections which have been revised with new evidence, to reflect new legislation, or to incorporate advice on adults with ASD. The remaining sections were not included in the selective update and are reproduced verbatim from SIGN 98.

| | | |
|---|---|---|
| 2 | Key recommendations | New |
| 3 | Definitions and concepts | Updated |
| 4 | Recognition, assessment and diagnosis | |
| 4.1.1 | Introduction | Updated |
| 4.1.3 | Surveillance | Updated |
| 4.1.4 | Secondary screening | Minor revision |
| 4.1.6 | Identifying adults for assessment | New |
| 4.1.7 | Instruments to aid identification of adults with ASD | New |
| 4.1.8 | Gender differences across the age ranges | New |
| 4.2.2 | Specialist assessment | Updated |
| 4.2.3 | Components of specialist assessment | Updated |
| 4.3 | Individual profiling | Updated |
| 4.4 | Conditions associated with ASD | Updated |
| 4.5 | Biomedical investigations | Updated |
| 4.6 | Prognostic indicators in childhood | Updated |
| 5 | Principles of intervention | Minor revision |
| 6 | Non-pharmacological interventions for children and young people | |
| 6.1 | Parent-mediated interventions | Updated |
| 6.2.1 | Support for early communication skills | Updated |
| 6.2.2 | Interventions for social communication and interaction | Updated |
| 6.3.1 | Intensive behavioural and developmental programmes | Completely revised |
| 6.3.2 | Specific interventions for ASD | New |
| 6.3.3 | Cognitive behavioural therapies | New |
| 6.3.4 | Auditory integration training | Updated |
| 6.3.5 | Occupational therapy and sensory integration therapy | Completely revised |
| 6.3.6 | Music therapy | Updated |
| 6.3.7 | Sleep management | Updated |
| 6.3.8 | Facilitated communication | No new evidence identified |
| 6.3.9 | Additional interventions to address behavioural challenges | Updated |
| 6.4 | Nutritional interventions | Updated |
| 6.5 | Other interventions | New |
| 7 | Non-pharmacological interventions for adults | New |
| 8 | Pharmacological interventions for children and young people | |
| 8.2 | Second-generation antipsychotics | Completely revised |
| 8.3 | Methylphenidate | Updated |
| 8.4 | Noradrenergic reuptake inhibitors | New |
| 8.5 | Antidepressants | New |
| 8.6 | Naltrexone | No new evidence identified |
| 8.7.1 | Secretin | Updated |
| 8.7.2 | Oxytocin | New |
| 8.8 | Melatonin | Completely revised |

| | | |
|---|---|---|
| 9 | Pharmacological interventions for adults | New |
| 10 | Service provision | No new evidence identified |
| 10.4 | Support during transition | Updated |
| 11 | Provision of information | |
| 11.2 | Checklist for provision of information | Minor revision |
| 11.3 | Sources of further information | Updated |
| 12 | Implementing the guideline | Completely revised |
| 13 | The evidence base | New |

## 1.2 REMIT OF THE GUIDELINE

### 1.2.1 OVERALL OBJECTIVES

This guideline provides recommendations based on current evidence for best practice in the assessment, diagnosis and interventions for children, young people, adults and older adults with ASD. It includes screening and surveillance, diagnosis and assessment, clinical interventions and service provision, as well as recommendations for research and audit.

### 1.2.2 TARGET USERS OF THE GUIDELINE

This guideline will be of interest to healthcare professionals and other multiagency colleagues who work with children and adults with ASD, as well as people with ASD, their parents, carers, relatives, partners and others with whom they interact.

### 1.2.3 AIM AND ETHOS OF THE GUIDELINE

The aim of this guideline is to provide the evidence base and recommendations to inform clinical service provision, in particular, assessment and clinical intervention. It is the hope of the guideline development group that the concept of 'ASD-friendly' services is a constant throughout this guideline. The involvement of parents, family, carers and the individual with ASD is important to the success of any intervention. Healthcare professionals should be given adequate time for discussion with patients and carers, and there should be continuity of care across services.

### 1.2.4 PATIENT VERSION

Patient versions of this guideline are available from the SIGN website, www.sign.ac.uk

## 1.3 STATEMENT OF INTENT

This guideline is not intended to be construed or to serve as a standard of care. Standards of care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge and technology advance and patterns of care evolve. Adherence to guideline recommendations will not ensure a successful outcome in every case, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care aimed at the same results. The ultimate judgement must be made by the appropriate healthcare professional(s) responsible for clinical decisions regarding a particular clinical procedure or treatment plan. This judgement should only be arrived at following discussion of the options with the patient, covering the diagnostic and treatment choices available. It is advised, however, that significant departures from the national guideline or any local guidelines derived from it should be fully documented in the patient's case notes at the time the relevant decision is taken.

### 1.3.1 INFLUENCE OF FINANCIAL AND OTHER INTERESTS

It has been recognised that financial interests in, or close working relationships with, pharmaceutical companies may have an influence on the interpretation of evidence from clinical studies.

It is not possible to completely eliminate any possible bias from this source, nor even to quantify the degree of bias with any certainty. SIGN requires that all those involved in the work of guideline development should declare all financial interests, whether direct or indirect, annually for as long as they are actively working with the organisation. By being explicit about the influences to which contributors are subjected, SIGN acknowledges the risk of bias and makes it possible for guideline users or reviewers to assess for themselves how likely it is that the conclusions and guideline recommendations are based on a biased interpretation of the evidence.

Details of those involved in developing this guideline can be found in section 14.

### 1.3.2 PRESCRIBING OF LICENSED MEDICINES OUTWITH THEIR MARKETING AUTHORISATION

Recommendations within this guideline are based on the best clinical evidence. Some recommendations may be for medicines prescribed outwith the marketing authorisation (MA) also known as product licence. This is known as 'off label' use.

Medicines may be prescribed 'off label' in the following circumstances:

- for an indication not specified within the marketing authorisation
- for administration via a different route
- for administration of a different dose
- for a different patient population.

An unlicensed medicine is a medicine which does not have MA for medicinal use in humans.

Generally 'off label' prescribing of medicines becomes necessary if the clinical need cannot be met by licensed medicines within the marketing authorisation. Such use should be supported by appropriate evidence and experience.[14]

"Prescribing medicines outside the conditions of their marketing authorisation alters (and probably increases) the prescribers' professional responsibility and potential liability."[14]

The General Medical Council (GMC) recommends that when prescribing a medicine 'off label', doctors should:

- be satisfied that such use would better serve the patient's needs than an authorised alternative (if one exists)
- be satisfied that there is sufficient evidence/experience of using the medicines to show its safety and efficacy, seeking the necessary information from appropriate sources
- record in the patient's clinical notes the medicine prescribed and, when not following common practice, the reasons for the choice
- take responsibility for prescribing the medicine and for overseeing the patient's care, including monitoring the effects of the medicine.

Non-medical prescribers should ensure that they are familiar with the legislative framework and their own professional prescribing standards.

Prior to any prescribing, the licensing status of a medication should be checked in the summary of product characteristics (SPC) or the British National Formulary for Children.[14,15] The prescriber must be competent, operate within the professional code of ethics of their statutory bodies and the prescribing practices of their employers.[16]

### 1.3.3 ADDITIONAL ADVICE TO NHSSCOTLAND FROM HEALTHCARE IMPROVEMENT SCOTLAND AND THE SCOTTISH MEDICINES CONSORTIUM

Healthcare Improvement Scotland processes multiple technology appraisals (MTAs) for NHSScotland that have been produced by NICE in England and Wales.

The Scottish Medicines Consortium (SMC) provides advice to NHS boards and their Area Drug and Therapeutics Committees about the status of all newly licensed medicines and any major new indications for established products.

SMC advice relevant to this guideline is summarised in section 12.4.

# 2 Key recommendations

The following recommendations were highlighted by the guideline development group as the key clinical recommendations that should be prioritised for implementation.

## 2.1 DIAGNOSTIC CRITERIA

R **All professionals involved in diagnosing ASD in children, young people or adults should consider using the current version of either ICD or DSM. The classification system used for diagnosis should be recorded in the patient's notes.**

## 2.2 RECOGNITION, ASSESSMENT AND DIAGNOSIS

R **As part of the core programme of child health surveillance, healthcare professionals can aid early identification of children requiring further assessment for ASD and other developmental disorders. Clinical assessment should incorporate a high level of vigilance for features suggestive of ASD, in the domains of social interaction and play, speech, language and communication difficulties and behaviour.**

✓ The assessment of children and young people with developmental delay, emotional and behavioural problems, psychiatric disorders, impaired mental health or genetic syndromes should include surveillance for ASD as part of routine practice.

R **Healthcare professionals should consider that females with ASD may present with a different symptom profile and level of impairment than males with ASD.**

R **A diagnostic assessment, alongside a profile of the individual's strengths and weaknesses, carried out by a multidisciplinary team which has the skills and experience to undertake the assessments, should be considered as the optimum approach for individuals suspected of having ASD.**

✓ Specialist assessment should involve a history-taking element, a clinical observation/assessment element, and the obtaining of wider contextual and functional information.

## 2.3 NON-PHARMACOLOGICAL INTERVENTIONS FOR CHILDREN

✓ Parent-mediated intervention programmes should be considered for children and young people of all ages who are affected by ASD, as they may help families interact with their child, promote development and increase parental satisfaction, empowerment and mental health.

✓ Behavioural interventions may be considered to address a wide range of specific behaviours, including those that challenge, in children and young people with ASD, both to reduce symptom frequency and severity and to increase the development of adaptive skills.

## 2.4 NON-PHARMACOLOGICAL INTERVENTIONS FOR ADULTS

✓ Psychosocial interventions should be considered for adults with ASD if indicated for managing coexisting conditions.

# 3 Definitions and concepts

## 3.1 DEFINITIONS

Autism spectrum disorder is a complex developmental condition, behaviourally defined, that includes a range of possible developmental impairments in reciprocal social interaction and communication, and also a stereotyped, repetitive or limited behavioural repertoire. Sensory differences may also be a presenting feature.[4] ASD may occur in association with any level of general intellectual/learning ability, and manifestations range from subtle problems of understanding and impaired social function to severe disabilities.[17]

Impairments in each of the areas relevant to ASD diagnoses occur along a continuum from minimal to severe and categorical diagnoses inevitably involve defining a cut off. Diagnostic classification in itself should not be the basis for decisions about provision within education, or need for social care and support.[18] Some affected individuals advocate that it is inappropriate to describe them as having a disorder and consider that autism spectrum condition (ASC) is a more appropriate term.

## 3.2 DIAGNOSTIC CRITERIA

There are two major diagnostic classification systems in current use, the International Classification of Diseases, version 10 (ICD-10) and the Diagnostic and Statistical Manual of Mental Disorders 5th edition (DSM-5).[4,19] Because DSM-5 is the most recent classification system, published in 2013 (whilst ICD-10 was published in 1993) this guideline has referred only to DSM-5 in terms of the current approach to diagnostic classification. Given that ICD-11 is not due for publication until 2017, it is uncertain to what extent the two systems will correspond.

The most important difference between ICD-10 and DSM-5 is that ICD-10 uses the concept of pervasive developmental disorders (PDD). Whilst the conditions of childhood autism and Asperger's syndrome are included in PDD, the concept of an autism spectrum is not. A further important difference is that the two conditions of childhood autism and Asperger's syndrome in ICD-10 are determined by the concept of a "triad of impairments", which DSM has now reduced to a dyad of impairments. Thus, the new DSM-5 dimension of "persistent deficits in social communication and social interaction across multiple contexts" reflects the view that problems with reciprocal social interaction and communication overlap and cannot be reliably distinguished. The second diagnostic dimension of the DSM-5 dyad of restricted, repetitive patterns of behaviour, interests, or activities is unchanged from the triad, but has been operationalised. Another significant difference between DSM-5 and ICD-10 is that, because the disorder spectrum concept has now been fully integrated into autism classification, the condition of Asperger's syndrome (or Asperger's disorder from DSM-IV)[20] is no longer used. In addition, domain B of DSM-5 classification adds in new clinical signs of stereotypical speech and also hyper- or hyporeactivity to sensory input or interest in sensory aspects of the environment.[4]

Studies included in the guideline were conducted before the introduction of DSM-5 and discussion of the evidence base reflects the use of DSM-IV.

Three studies all found that the use of DSM-IV and ICD-10 criteria for autism improve the reliability of the diagnostic process.[21-23] The studies consistently found that:

- using either DSM-IV or ICD-10 increases the reliability of the diagnostic process. The effect is even greater when inexperienced practitioners are making the diagnosis **2+**
- the current criteria for Asperger's syndrome and autism have poor discriminant validity.

**R** **All professionals involved in diagnosing ASD in children, young people or adults should consider using the current version of either ICD or DSM. The classification system used for diagnosis should be recorded in the patient's notes.**

# 4 Recognition, assessment and diagnosis

## 4.1 RECOGNITION IN PRIMARY CARE

### 4.1.1 INTRODUCTION

Autism spectrum disorder can be recognised for the first time at any age, despite the fact that it is a lifelong disorder that starts in early life. Some people will not present to a health professional until later in life. It is important to be aware of the possibility of an ASD diagnosis not only in primary care but also in education, social work and employment settings. People may present at any time but particularly at times of change or stress, for example moving to university, after the death of a spouse or at times of work or life stress.

In keeping with the principles of GIRFEC and the Children and Young People (Scotland) Act 2014, children in Scotland are offered a programme of immunisation, screening, surveillance, health promotion and parenting support through the mechanism of the universal child health review.[1,2,24,25] In 2014, NHSScotland reintroduced a 27–30 month universal child health review within this programme.

This child health review remains broadly aligned to Health for All Children (Hall 4), which states that every child and parent should have access to a universal or core programme of preventative preschool care, but that formal screening should be confined to the evidence-based programmes agreed by the UK National Screening Committee.[26] Hall 4 does not recommend formal universal screening for speech and language delay, global developmental delay or ASD, but states that staff should elicit and respond to parental concerns as part of child health surveillance. The report emphasises the need for an efficient preliminary assessment, or triage process, to determine which children may need referral for fuller assessment and/or intervention.

Identifying adults for assessment is discussed in section 4.1.6.

### 4.1.2 SCREENING

Screening has been defined by the UK National Screening Committee as "a public health service in which members of a defined population, who do not necessarily perceive they are at risk of, or are already affected by a disease or its complications, are asked a question or offered a test, to identify those individuals who are more likely to be helped than harmed by further tests or treatment to reduce the risk of a disease or its complications".[27]

Any screening test must have a known specificity (analogous to the risk of false positives) and sensitivity (analogous to the risk of false negatives) within the population to which it is being applied. A systematic review has not identified any research into screening instruments for ASD that meet the rigorous criteria for a robust population screening test.[28] **2+**

Population screening for ASD is not recommended.[29] False positive or false negative results from inappropriate use of screening tests may delay correct diagnosis. The decision about the need for referral and further assessment should be made on clinical grounds.

**R** **Population screening for ASD is not recommended.**

Identifying adults for assessment is discussed in section 4.1.6.

### 4.1.3 SURVEILLANCE

Outwith the scheduled opportunities for surveillance of children within the universal child health review, primary care is well placed to offer opportunistic surveillance for older children and adults.

Child health surveillance takes a broad clinical approach involving partnership between parents, children and health professionals. Child health surveillance can contribute to the early recognition and diagnosis of ASD.[30] Surveillance for ASD should follow general developmental surveillance and should be considered by all professionals working with children and young people.

Responding to concerns raised by parents plays a role in surveillance, and healthcare professionals should be aware that parental concerns about the absence of normal developmental features are as important as the presence of abnormal features.[31-34] **3**

The recognition of children requiring further assessment for ASD requires a high level of vigilance for features indicative of abnormal development, both at any specific age and as they emerge over a period of time. A number of instruments have been designed to identify children with an increased likelihood of ASD. Reviews by NICE found that none of these instruments met an acceptable level of diagnostic accuracy (defined as sensitivity and specificity of at least 80%).[5,35] Different instruments demonstrated a variety of levels of sensitivity and specificity, and the evidence is insufficient to determine whether any particular instrument is effective in detecting children at risk of ASD.[5,35] **2++** **2+**

These instruments can provide a useful structure for considering relevant clinical features during surveillance by healthcare professionals. They are not meant to formally assess children or be used to provide a diagnosis of ASD, but are useful for information gathering.[5,35] **2+** **4**

Surveillance remains dependent on the use of clinical knowledge and skills to identify unusual patterns of development. Not all children with ASD will be identified during child health surveillance, and parents should be encouraged to return for further assessment, if they remain concerned about the development of their child.

Regression (a loss or reduction) in language or social skills under the age of three years is a particularly strong predictor which should prompt referral for assessment for ASD.[5] There is also evidence of an increased risk of autism (unadjusted relative risk (RR) range 31.3 to 91.9), and ASD (unadjusted RR range 7 to 17) in children with intellectual disability.[5] Further features and risk factors which should alert healthcare and education professionals to the possibility of ASD are shown in Annexes 2 and 3. **2++**

**R** **As part of the core programme of child health surveillance, healthcare professionals can aid early identification of children requiring further assessment for ASD and other developmental disorders. Clinical assessment should incorporate a high level of vigilance for features suggestive of ASD, in the domains of social interaction and play, speech, language and communication difficulties and behaviour.**

**R** **Children under three years of age who have regression in language or social skills should be referred for assessment for ASD.**

**R** **Instruments may be used for information gathering, but they should not be used to make or rule out a referral for an assessment for ASD.**

### 4.1.4 SECONDARY SCREENING

Secondary screening of children and young people thought to be at high risk may be appropriate, for example for children referred to services because of developmental delay, emotional and behavioural problems or certain genetic syndromes (*see section 4.1.3 and Annexes 2 and 3*). Siblings of individuals with ASD also have an increased risk (RR 13.40, CI 6.93 to 25.92).[5] **2++**

Secondary screening is dependent on an awareness that a child is at higher risk of ASD and the application of sound clinical knowledge and skills. Several structured instruments for use in secondary screening have been examined in a number of studies using relatively small cohorts.[36-42] With all these instruments, the findings of the studies have not been replicated outwith the study settings. See Annex 4 for a list of instruments. **2+**

The use of these instruments can be considered as a supplement to the clinical assessment of at-risk children and may improve the reliability of the process used to screen for ASD. A single specific instrument cannot be recommended as each one is designed for use within a limited age group, and often focuses on one particular ASD, for example Asperger's syndrome.

✓ The assessment of children and young people with developmental delay, emotional and behavioural problems, psychiatric disorders, impaired mental health or genetic syndromes should include surveillance for ASD as part of routine practice.

✓ Healthcare professionals should consider informing families that there is a substantial increased risk of ASD in siblings of affected children.

✓ For adults, ASD should be considered as part of an assessment if they have developmental delay, failure to meet adult milestones (work, development of intimate relationships or independence from parents), emotional and behavioural problems, intellectual disability or genetic syndromes.

### 4.1.5 TIMING OF DIAGNOSIS

Assessment is part of a continuum which occurs from the point of recognition to the time of diagnosis and can occur at any age. In children under two years old typical ASD behaviours may not be evident.[30] **4**

The evidence regarding the minimum age at which ASD can be reliably diagnosed is not clear.

- The diagnosis of autism is always more reliable and stable than the diagnosis of other autism spectrum disorders, regardless of age, and can be reliably diagnosed between the ages of 2–3 years by experienced healthcare professionals.[43,44]
- In children later identified as having ASD, features reported when they were under two years of age may have been non-specific.[45] **3**

**R** **ASD should be part of the differential diagnosis for preschool children displaying absence of age-appropriate developmental features, as typical ASD behaviours may not be obvious in this age group.**

✓ Regardless of the findings of any earlier assessments, referral for further assessment for ASD should be considered at any age.

Features which alert to the possibility of ASD in older children are given in Annex 2.

### 4.1.6 IDENTIFYING ADULTS FOR ASSESSMENT

No relevant studies were identified on specific signs and symptoms suggestive of ASD in adults. Using expert opinion, NICE suggested that the presence of at least one of the following signs or symptoms should prompt ASD assessment:[13]

- persistent difficulty in social interaction
- persistent difficulty in social communication
- stereotypic (rigid and repetitive) behaviours, resistance to change (in, for example, diet, routine or environment) or restricted interests. **4**

NICE suggested there are a number of factors associated with the presence of ASD:[13]

- problems with staying in education or finding and sustaining employment
- difficulty in initiating or sustaining social relationships
- history of a neurodevelopmental condition (including intellectual disability and attention deficit hyperactivity disorders (ADHD)) or a mental disorder.

A number of studies considered prevalence of previously undiagnosed ASD in adults presenting to a variety of mental health services. The results, however, were inconsistent.

In a cross-sectional study, there was a higher prevalence of ASD in patients attending a youth mental health service (aged 15–25, n=476) than in community samples (3.4% confirmed diagnosis versus 1% in the community).[46] A further 7.8% were reported to be exhibiting traits of ASD, based on assessment by non-specialist clinicians. A small study of 46 patients with schizophrenic psychotic disorders reported a high ASD prevalence rate of 41%.[47] No studies were identified on the prevalence of ASD in patients diagnosed with depression. **3**

A systematic review of eight small retrospective studies reported the prevalence of ASD amongst adults with anorexia nervosa, bulimia disorder and other eating disorders was 8–37%. Six of the eight studies were from the same community sample. The most recent studies reported a prevalence of 18–28%.[48] The variation in prevalence may reflect issues with the case-identification instruments used as there is no specific instrument for this patient group. There is also a risk of inaccurate diagnosis due to the potential effects of starvation on cognition. **3**

A study conducted in a gender clinic in London reported that among the 92 participants the prevalence of autistic traits, based on assessment with the Autism Spectrum Quotient (AQ) was 5.5% (3 male to female and 2 female to male transsexuals) compared to reports of clinical diagnoses of 0.5–2.0% in the general population.[49] **3**

Further indicators of possible ASD in adults are listed in Annex 2.

✓ Healthcare professionals should be aware of indicators for ASD in adults presenting with other conditions.

### 4.1.7 INSTRUMENTS TO AID IDENTIFICATION OF ADULTS WITH ASD

A systematic review by NICE identified studies using the Autism Spectrum Quotient-10 (AQ-10), the Autism Screening Questionnaire/Social Communication Questionnaire (ASQ/SCQ), the Autism Behaviour Checklist (ABC) and the Pervasive Developmental Disorder in Mental Retardation Scale (PDD-MRS) for case identification in adults. Most were appraised to be at high risk of bias.[13] No high-quality studies published after the NICE guideline have been identified. **2++**

Studies into the use of AQ-10 to identify adults with autism reported good sensitivity and specificity.[13] It is freely available and only takes a few minutes to complete.[13] The AQ instrument requires self completion so may not be suitable for people with an intellectual disability. Therefore, it is recommended for use in people with an intelligence quotient (IQ) greater than 70.[13] **4**

No other studies of instruments for this group were of sufficient quality to inform a recommendation. It is preferable to use the indicators listed in Annex 2 to identify who should be referred for assessment.

**R** **The use of the Autism Spectrum Quotient-10 instrument may be considered to help identify adults with possible ASD capable of self completing the instrument, who should be referred for assessment.**

### 4.1.8 GENDER DIFFERENCES ACROSS THE AGE RANGES

The number of females presenting with ASD is consistently under-reported due to misdiagnosis.[50-53] A possible explanation for this is that the instruments used are not sufficiently sensitive or specific enough to identify ASD characteristics in females. How presentations of ASD vary between males and females remains to be completely determined. Research regarding the possible different symptom profile of females is in its infancy and is susceptible to sampling issues due either to gender stereotyping at diagnosis or better adaptation by females potentially leading to under-representation of females in clinical samples.[50,53]

Studies have highlighted the potential differences in the way females with ASD may present compared to males:

- Both males and females with ASD experience pervasive difficulties in developing and maintaining friendships, but females may show more of a desire to have friends and fit in with their peer group than males.[51]
- Both males and females with ASD show impairments in play behaviour, however this skill may be less impaired in females with ASD. Females with ASD may mask social play deficits by imitating their typically developing peers.[51] Female interests may be in more socially accepted domains than males (for example, horses, dolls or pop stars) therefore seeming less unusual or impairing.[51,53] **2++ 2+ 4**
- Females with ASD may have better coping skills than males with ASD which may lead to fewer females being diagnosed, even when they have equivalently high levels of autistic traits to males who do receive a diagnosis.[50] This may lead to females being older when ASD is considered as a potential diagnosis.[53]
- Females with ASD may show less severe signs of repetitive and restricted behaviours and interests than males with ASD. This may be evident from six years onwards but not before age six.[53]
- There may be a higher incidence of disordered eating in females with ASD than males with ASD.[51]
- Females with ASD may show less impairment in theory of mind tasks than males with ASD.[51]
- There may be differences in the communication profile and executive functioning skills between males and females with ASD although there is conflicting evidence about what the specific differences are.[51]
- Research indicates that in the absence of intellectual disability or behavioural issues, females are less likely than males to meet diagnostic criteria for ASD. This is hypothesised to be due to females presenting with a different phenotype; displaying less restricted interests and stereotyped behaviours.[53] If ASD is accompanied with an intellectual disability, however, the female to male ratio is 1:2. As restricted interests and stereotyped behaviours are common in people with intellectual disability, this ratio may reflect an over-representation of ASD in females with low IQ. Alternatively, this may support the hypothesis that females with a higher IQ have better adaptation and compensation abilities which prevent ASD symptoms reaching a diagnostic threshold.[50]

**R** **Healthcare professionals should consider that females with ASD may present with a different symptom profile and level of impairment than males with ASD.**

## 4.2 METHODS OF ASSESSMENT

### 4.2.1 INITIAL ASSESSMENT

The initial presentation can be to a wide range of professionals in primary care, education or social services. Important information can be gathered at this stage that may suggest the need for specialist assessment. Those involved in carrying out the initial assessment should be aware of the core features of ASD as well as of the wide range of different possible presentations, depending on the individual's level of communication and intellect, personality, gender differences, family and educational supports.

Key areas to explore at this stage include:

- the nature of the problem: are the presenting features of the type represented by the diagnostic criteria for ASD?
- the severity of the problem (dysfunction and/or distress in a number of contexts including individual, family, educational or workplace, or severity in one such context).

✓ If, on the basis of initial assessment, it is suspected that the individual may have ASD, they should be referred for specialist assessment.

### 4.2.2 SPECIALIST ASSESSMENT

Specialist assessment is conducted by professionals who have sufficient expertise and training to establish a diagnosis of ASD and to conduct the individual profiling. Professionals need to give regard to the balance between their competencies and the complexity of the clinical presentation.[5,54] The aim of specialist assessment is to gather and record information that enables diagnosis and to formulate a multiagency management plan, leading to the development of an appropriate programme of supportive intervention. Such an assessment is necessarily comprehensive and may take place over a period of time.[18]

A diagnosis of ASD may be seen as a lifelong 'label'. For this reason, it is of equal importance that clinicians diagnose, and not diagnose, accurately. Specialist healthcare professionals must ensure that they are sufficiently informed and experienced to confidently diagnose in the majority of cases and that they collaborate, where possible, with relevant multiagency colleagues, so as to achieve diagnostic consensus. Healthcare professionals should also have a low threshold of referral to more specialised colleagues in cases of diagnostic disagreement or subtle presentation.

The process of assessment and diagnosis aims to review functioning in relevant domains, make diagnoses as appropriate and facilitate seamless, multiagency intervention. It should acknowledge that other conditions (for example specific language impairment in a three year old, first onset depression in a 13 year old, or acute psychosis in a young adult) may present in a superficially similar way to ASD and also that there is significant potential for an individual to present with more than one condition.

Research evidence on multidisciplinary compared to single assessment is limited. NICE identified one low-quality study which compared clinical diagnosis by a single practitioner with that of a panel. It reported agreement between the individual healthcare professional and the multidisciplinary team. Expert opinion, however, advocates the use of multidisciplinary assessment by experienced professionals to ensure diagnostic accuracy and profiling of the skills, difficulties and subsequent needs of the individual. This should aid tailored care planning and interventions for the individual and their carers.[5,13]



✓ The use of different professional groups in the assessment process is recommended as it may identify different aspects of ASD and aid accurate diagnosis.

R **A diagnostic assessment, alongside a profile of the individual's strengths and weaknesses, carried out by a multidisciplinary team which has the skills and experience to undertake the assessments, should be considered as the optimum approach for individuals suspected of having ASD.**

✓ Specialist assessment should involve a history-taking element, a clinical observation/assessment element, and obtaining wider contextual and functional information.

✓ Specialist assessment should be available for any individuals who need it. Specialist teams should assess if their service is being used equitably. Apparent inequalities should be investigated and addressed.

✓ An assessment of mental health needs, well being and risk should be considered for all individuals with ASD presenting to any agency.

### 4.2.3 COMPONENTS OF SPECIALIST ASSESSMENT

*History taking (parent/carer/informant interview)*

History taking is an important component of any ASD assessment, including those of adults or older people. Without it, evidence of ASD-like behaviour cannot be put into context. Use of ASD-specific history-taking instruments can be useful in this process, although healthcare professionals should be mindful of the need for a global perspective on the circumstances of an individual, taking into consideration the possibility of coexisting conditions and possible differential diagnoses.

A clinical history should include:

- a history of the individual's prenatal, perinatal and developmental history (including social and emotional factors) up to the patient's age at assessment. This should include a detailed enquiry into evidence of any problems in social relationships at home, in education or work settings
- a description of the current problems experienced by the individual and other informants (eg relative, nursery staff, teachers, educational psychologists, employers). The focus should be on eliciting features consistent with the diagnosis of ASD
- a family history including evidence of any ASD, speech and language difficulties, psychiatric disorders, intellectual disability, epilepsy, developmental neurological problems or addictions
- a description of who is in the family (eg use of a genogram) and any history of family problems (eg parental separation/divorce) or significant life events (eg loss) which might be affecting the individual's behaviour.

A framework for an ASD-specific developmental history is important and a version is available in the National Autism Plan for Children and for adults from the Royal College of Psychiatrists.[18,55]

ASD-specific diagnostic instruments may be used to supplement the process of clinical history taking, for example the Autism Diagnostic Interview-revised (ADI-R),[56,57] the Diagnostic Interview for Social and Communication Disorders (DISCO)[58] and the Developmental, Dimensional and Diagnostic Interview (3di).[59]

The ADI-R has been shown to be a reliable diagnostic instrument.[56,57,60] It should be used with caution in children with a developmental level below the age of two years. It can be used as an information gathering instrument to complement and guide clinical judgement.[61] **2+**

The 3di and DISCO allow structured data collection in relation to ASD and other conditions. The published data on the 3di suggests that it is a reliable and valid ASD diagnostic interview schedule when compared to the ADI-R.[59] **2+**

These instruments were developed and tested on child populations but can be valuable in supporting diagnosis in adults and older people.[13]

*Clinical observation/assessment (individual assessment/interview)*

The experience of interacting with an individual, in order to elicit clinical evidence of ASD that is compatible with ICD-10 or DSM-5, is a significant professional task, which cannot be undertaken without a substantial amount of clinical experience. Such skills are not exclusive to disciplines. The crucial elements are training and experience.

Assessments of individuals for ASD cannot be rushed. It may not be possible to obtain sufficient evidence in one session and the individual may require observation in different settings, for example at school (especially in unstructured activity such as break time) as well as the clinic.[18] **4**

ASD-specific diagnostic instruments may be used to supplement the process of clinical observation, as part of the diagnostic assessment.

The Childhood Autism Rating Scale (CARS) is an older instrument which encompasses history and observation of spontaneous behaviours relevant to autism.[62,63] It has recently been updated to CARS-2.

The Autism Diagnostic Observation Schedule–Generic (ADOS-G), has been shown to be a reliable diagnostic instrument and can be used to supplement clinical history.[64] It provides standard contexts to elicit relevant social and communicative behaviours, rather than relying on what is spontaneously manifested by a child or young person. ADOS-G has an excellent diagnostic validity, if controlled for expressive language level.[64] For detection of autism versus non-ASD disorders, ADOS-G had a sensitivity of 67–91% and specificity of 65–95% for communication and social domain scores and 82–94% sensitivity, 55–81% specificity for social affective and repetitive restricted behaviour domain scores.[65] The ADOS-G has been updated to the ADOS-2.[66] **2+**

A comparison of instruments concluded that the use of a combination of ADOS and ADI-R was similar in accuracy to the 'gold standard' multidisciplinary assessment, although the quality of the studies was poor.[61] NICE recommend that diagnosis is not based on any autism-specific diagnostic instrument alone.[5] **2+ 4**

**R** **Healthcare professionals involved in specialist assessment should take an ASD-specific developmental history and should directly observe and assess the individual's social and communication skills and behaviour.**

**R** **Consider the use of a structured instrument to assist information gathering in the assessment of an individual with possible ASD.**

✓ In adults, the developmental history may not be available, but could be sought from a parent, sibling, or any person who knew the individual well as a child. Diagnostic assessment should always be undertaken even in the absence of an informant for early developmental history.

*Contextual and functional information*

Current legislative developments place a strong emphasis upon assessment as a collaborative process linked to a cycle of planning, intervention and review. GIRFEC provides explicit structures for gathering assessment information.[1] Helpful information about an individual's functioning should be gathered from a variety of settings and people, such as education provision, employment, relatives and carers. Frameworks and instruments for information gathering to guide education professionals are available (eg social responsiveness scale for teachers, GIRFEC assessment pathways).

This type of information increases understanding as to how an individual functions in groups, in unstructured settings, and when performing real-life tasks. It may point professionals towards difficulties that are not evident in one-to-one observations, or in more structured assessment contexts.

✓ Information about individual's functioning outside the clinic setting, should routinely be obtained from as many available sources as is feasible.

## 4.3 INDIVIDUAL PROFILING

People with ASD vary considerably in their individual strengths and difficulties. More detailed assessment of communication, neuropsychological functioning, motor and sensory skills, and adaptive functioning may be helpful.

### 4.3.1 COMMUNICATION SKILLS

By definition, all individuals with ASD have an impairment in communication which ranges from profound comprehension problems and lack of speech to subtle pragmatic or functional use of language difficulties, such as failure to understand sarcasm or use of metaphor. Receptive and expressive language skills are generally equally impaired.[67] A wide range of speech and language and communication assessments are available but there is limited evidence to support the use of one assessment instrument over another.[68-70] **3**

'Theory of mind' (a spontaneous ability to impute the thoughts of others) is not a diagnostic marker for ASD but relates to communication and linguistic development. It may be of value as part of an assessment to inform intervention. Verbal abilities should be taken into account to avoid overinterpreting deficits in theory of mind.

**R** **All children and young people with ASD should have a comprehensive evaluation of their speech and language and communication skills, which should inform intervention.**

✓ Assessment of speech, language and communication may be indicated for adults with ASD particularly in the presence of intellectual disability.

✓ Healthcare professionals should note that an individual's level of comprehension may be at a lower developmental level than that suggested by their expressive language skills.

### 4.3.2 COGNITIVE, NEUROPSYCHOLOGICAL AND ADAPTIVE FUNCTIONING ASSESSMENT

Consideration of the wider developmental level is an essential part of the assessment process. A cognitive or neuropsychological assessment will not confirm ASD but it may be helpful to use these tools to establish a profile of relative strengths and difficulties. This may be useful in identifying intellectual disability (as a differential or coexisting diagnosis) and to benchmark which developmental and social skills should be expected in the context of a person's level of ability.[71] This information may also be useful when considering what interventions are most appropriate and effective.[71] **4**

Individuals with ASD will have a range of impairments in intellectual, neuropsychological and adaptive skills. Assessments are useful for individual profiling but are not diagnostic instruments.[72-77] An assessment of adaptive functioning allows for information regarding the child's typical functioning at home or at school. This may be different from their cognitive abilities and highlights functional impairments and areas where support may be required. Some impairments, such as theory of mind[73,75,77] and executive function[74] are not specific to ASD, although they may be more severe in this group. The degree of impairment is also influenced by levels of speech and language, communication and verbal mental age. This applies equally to adults.[13] **3 4**

Insights from these assessments may promote understanding by caregivers, therapists, education and social work staff in optimally supporting the individual with ASD to reach their potential.

**R** **Individuals with ASD should be considered for assessment of intellectual, neuropsychological and adaptive functioning.**

### 4.3.3 MOTOR AND SENSORY SKILLS

There was insufficient evidence to make recommendations about occupational therapy or physiotherapy assessments. However, DSM-5 includes hyper- or hyporeactivity to sensory input within its diagnostic criteria.[4]

✓ Sensory behaviours should be taken into account when profiling the needs of individuals with ASD.

✓ Occupational therapy and physiotherapy assessments should be considered where relevant.

## 4.4 CONDITIONS ASSOCIATED WITH ASD

Individuals with ASD can experience the full range of developmental, medical and mental health problems that are experienced by those who do not have ASD. Clinicians should not assume that any problems are inevitable aspects of ASD. Clinical features of ASD may overlap and coexist with symptoms of other disorders. It is essential that any differential or comorbid diagnoses are identified during the assessment period to ensure that appropriate interventions and support are put in place to address all aspects of the clinical presentation.[71]

Parent-reported sleep problems are more frequent in children and young people with ASD.[78-81] **2+**

There are some clinical conditions which seem to occur more frequently in children and young people with ASD, regardless of intellectual ability. Children with autism experience higher rates of mental ill health and behaviour problems.[38,82] In particular, there is evidence that anxiety and depression[83-87] and ADHD[88,89] are more common. **2+**

The prevalence of epilepsy is higher in the population with ASD than in the general population and people with ASD have a higher risk of mortality than the general population. The pooled estimate for the percentage of participants with epilepsy in a systematic review of outcomes in ASD was 1.8% (95% CI 0.4 to 9.4%) for studies in which the majority of individuals did not have an intellectual disability and for whom the mean age at follow up was less than 12 years, and 23.7% (95% CI 17.5 to 30.5%) in studies for whom the majority of individuals had an intellectual disability and the mean age of follow up was more than 12 years. The pooled estimate for the standardised mortality ratio was 2.8 (95% CI 1.8 to 4.2%).[90] **2++**

Children and young people with ASD have elevated rates of visual impairment and hearing impairment.[86,91,92] As these associations have been described in the main in children and young people with intellectual disabilities, the extent of the specific association across the ASD spectrum is uncertain. **2+**

There is also evidence that neuromotor problems, such as clumsiness[93] and tics[89,94] are commonly experienced by children and young people with ASD. **2-**

Children and young people with ASD display the same attachment behaviours as children who do not have ASD. However, children and young people with ASD are more likely to be insecurely attached, affecting their responsiveness in contact with caregivers.[95] **2+**

Equally, children with ASD that has not been recognised may initially present to clinical services with a separate problem, for example epilepsy,[96] a sleep disorder, or school refusal, suggesting that ASD should always be considered as part of a wider clinical presentation, irrespective of the reason for referral.

A case-control study found no evidence that children with autism were more likely than children without autism to have had defined gastrointestinal disorders at any time before their diagnosis.[97] Parent-reported gastrointestinal symptoms, in particular frequent vomiting and constipation, were more common after diagnosis in one study. Parents also reported higher rates of food selectivity.[98] **2+**

✓ Healthcare professionals should recognise that children and young people with ASD may also have additional developmental disorders, medical problems or emotional difficulties/disorders and should have access to the same range of therapeutic interventions as any other child.

**R** **Healthcare professionals should be aware of the need to routinely check for coexisting problems in children and young people with ASD. Where necessary, detailed assessment should be carried out to accurately identify and manage coexisting problems.**

It is important to recognise that these associated conditions also apply to adults.[13] **4**

## 4.5 BIOMEDICAL INVESTIGATIONS

ASD can be associated with a wide range of underlying conditions including genetic abnormalities. Medical investigations however should not be routinely performed but may be considered on an individual basis that takes into account findings on physical examination, such as dysmorphism and neurocutaneous stigmata, congenital anomalies and intellectual disability or suspicion of epilepsy.[5] The autism spectrum is highly variable and can be investigated with an ever increasing range of genetic techniques such as microarray comparative genomic hybridisation (CGH), whole exome and whole genome sequencing. However, the clinical judgement to understand how to incorporate these techniques into an individual's assessment requires a systematic approach.[99] The genetic alterations giving rise to ASD phenotypes arise from chromosomal syndromes, such as Turner and Down's syndrome, large segmental cytogenetic alterations, single gene disorders and copy number variants.[99]

Chromosomal microarray has largely replaced microscopy-based karyotyping and in various clinical situations microarray-CGH yields a typical pathogenic copy number variant detection rate of 10% for autism and ASD (higher detection rates with concomitant intellectual disability).[100]

A wide range of these techniques were assessed by NICE and all studies were deemed to be of low quality.[5] Routinely performed genetic tests led to a clinical diagnosis in 9% of individuals with autism and 14% with autism spectrum disorder (95% CI 7 to 22).[5] Recent reviews on the role of genetic investigations in ASD state that rare neurometabolic conditions in ASD are mostly single gene disorders and in patients with suspected ASD a first and second tier approach for investigations as regards ASD is advocated (*see Table 1*).[99,101,102]

*Table 1: First and second tier genetic investigations for possible ASD [101]*

| **First tier** |
|---|
| Three-generation family history with pedigree analysis |
| Initial evaluation to identify known syndromes or associated conditions<br>• examination with special attention to dysmorphic features<br>• if specific syndromic diagnosis is suspected, proceed with targeted investigations<br>• if appropriate clinical indicators are present, perform metabolic and/or mitochondrial testing (alternatively, consider referral to a metabolic specialist) |
| Chromosomal microarray: oligonucleotide array-comparative genomic hybridisation or single-nucleotide polymorphism array |
| DNA testing for fragile X (to be performed routinely for male patients only)* |
| **Second tier** |
| *MECP2* sequencing to be performed for all females with ASD |
| *MECP2* duplication testing in males, if phenotype is suggestive |
| *PTEN* testing only if the head circumference is >2.5 SD above the mean |
| Brain magnetic resonance imaging only in the presence of specific indicators (eg microcephaly, regression, seizures, and history of stupor/coma) |
| *MECP2*, methyl-CPG-binding protein 2; *PTEN*, phosphatase and tensin homolog; SD standard deviation.<br>*DNA testing for fragile X in females if indicators present (eg family history and phenotype). |

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Investigations are not only carried out to aid diagnosis through establishing aetiology, but also to exclude treatable conditions, to identify coexisting conditions and to establish baseline information prior to starting treatment. The evidence does not support the use of routine magnetic resonance imaging (MRI) of the brain.[103-105] Whilst epilepsy is common in individuals with ASD,[13,106] there is no indication for an electroencephalogram (EEG) in the absence of other clinical criteria.[13,107]

A fifth to a third of preschool children with ASD have a history of regression in acquired language skills during their second year of life. A total loss of acquired language skills is associated with a high probability of ASD when this occurs in children under the age of three.[108] When children undergo language regression over the age of three, they are more likely to experience seizures and the differential diagnosis should include consideration of an acquired epileptic dysphasia/Landau Kleffner dysphasia.[108] Other conditions such as Rett syndrome may appear superficially similar to ASD,[109] and other neurodegenerative conditions such as mitochondriopathies may need to be considered and investigated.[110]

3

The same approach to investigations should be considered in adults as appropriate.[13] | 4

**R** **Where clinically relevant, the need for the following should be reviewed for all individuals with ASD:**

- **examination of physical status, with particular attention to neurological and dysmorphic features**
- **chromosomal microarray**
- **examination of audiological status**
- **investigations to rule out recognised aetiologies of ASD** (eg tuberous sclerosis)**.**

✓ Advice on further testing should be sought from the local genetics service.

## 4.6 PROGNOSTIC INDICATORS IN CHILDHOOD

In one small study, early joint attention and imitation skills were found to be predictive of preschool language levels.[111] High IQ and language skills at an early age were also found to predict better eventual outcome in communication and social competence domains,[112-116] although social impairments and repetitive behaviours may persist.[115] | $2^{+}$

Improvements in adaptive behaviour and decline in atypical features have been reported for adolescents with ASD and a high IQ, with poorer outcomes evident in social impairment and social skills for young people with intellectual disability.[117,118] Nine percent of individuals with a measured verbal IQ over 70 at the age of 2 years no longer met diagnostic criteria for ASD when followed up at 19 years of age.[119] | 3

A well-conducted systematic review of the diagnostic stability of ASD considered distinct from autistic disorder prior to DSM-5 diagnostic criteria found that autistic disorder is a reasonably stable diagnosis but other autism spectrum disorders have very variable stability between studies and clinicians, when using this diagnosis, need to inform parents of its instability. To what extent this remains relevant under the diagnostic criteria in DSM-5 requires long term, large population cohort studies.[120] | $2^{++}$

Early language regression before three years of age, in children referred for paediatric neurology assessment, or referred for ASD assessment, has a high probability of being associated with an ASD diagnosis.[108,121] The majority of children with ASD who are reported to regress subsequently regain the lost skills.[122] Regression does not appear to be associated with a worse prognosis during preschool years.[45,121] | $2^{+}$

There have been no good-quality studies of later childhood or adolescent onset regression and it is not clear whether the phenomena are clinically the same.

Evidence for prognostic indicators in adulthood has not been reviewed.

# 5 Principles of intervention

Following a diagnosis of ASD, individuals, parents, relatives, carers, and professionals want effective interventions to be available and need information to help make decisions about what form these could take.

There are many different interventions for people with ASD in everyday use, some of which are not evidence based.[123]

Following a baseline assessment, the potential balance of risks and benefits from any intervention needs to be considered for each individual, and discussed as appropriate with them and their parents, relatives or carers, so that they can make an informed decision. Individuals with ASD, their parents, relatives, carers, and healthcare professionals should, as far as possible, plan how they intend to evaluate the benefits from any intervention. This will help them to make a decision about whether or not to continue after any trial period.

Everyone is entitled to benefit from their education and have positive wider life experiences. ASD symptoms can constitute a significant barrier and psychoeducational interventions for ASD are employed in this context. Parents, educationalists, health professionals, social workers and the voluntary sector may employ pragmatic, eclectic, individualised interventions to optimise a person's functioning, by promoting development of skills, or adapting the environment to compensate when skills are not present.[124] Many of these approaches are based on theoretical principles germane to ASD. Some are derived from generic considerations such as visual support to communication, or behavioural approaches to reduce behaviour that challenges. Others are derived from more autism-specific considerations such as the difficulty in 'mentalising' experienced in ASD, whereby the individual experiences difficulties understanding the motivations and perspectives of others. Where appropriate, the guideline comments on these interventions as good practice points, recognising that many are in use in everyday practice in the UK and have widespread practitioner support.

Given the highly individualised nature of behavioural interventions, single-case research is a widespread and increasingly rigorous way of testing and developing the field. It is encouraging that scientifically and statistically rigorous methods are being developed for collating and analysing this data, but it is still a developing area which needs replication, further peer review and consensus.

Where evidence-based interventions are available, they should be delivered by personnel with the appropriate skills and training, according to the protocols used in the original research.

# 6 Non-pharmacological interventions for children and young people

## 6.1 PARENT-MEDIATED INTERVENTIONS

Parent-mediated intervention programmes are used to both advance the development and communication of an affected child and to offer practical advice and support to parents.[125,126,127,128]

A well-conducted Cochrane review of parent-mediated early intervention for young children (aged 1–6 years) with ASD identified 17 studies, all of which had a risk of bias and used a variety of interventions, intensity and treatment duration.[129] Results were inconsistent and inconclusive. There was a statistically significant benefit from parent-child interaction for joint attention. Small improvements were also seen in language comprehension and expression and reduction in parental stress, although these results need to be substantiated by further, larger randomised controlled trials (RCTs). **1++**

✓ Parent-mediated intervention programmes should be considered for children and young people of all ages who are affected by ASD, as they may help families interact with their child, promote development and increase parental satisfaction, empowerment and mental health.

## 6.2 COMMUNICATION INTERVENTIONS

### 6.2.1 SUPPORT FOR EARLY COMMUNCIATION SKILLS

Many children and young people with ASD have little or no speech. Those who do have speech have difficulties in using language effectively (pragmatic language impairment or social communication difficulty).

*Parent- and clinician-led interventions*

The manner in which the communication impairment is manifest is influenced by the child's acquisition of joint attention and early interaction skills, which are a precursor to communication through language. Many of the strategies implemented to support communication are designed and managed by speech and language therapists, working in combination with a wide range of professionals and in partnership with parents. Parent-led interventions incorporate features such as working on joint attention and communicative intent (*see section 6.1*). Clinician-mediated interventions target early purposeful communication skills such as joint attention, motivation to communicate, understanding and using language communication.

Meta-analysis of RCTs of parent-mediated communication-focused treatment (PACT) reported no reduction in autism symptoms, compared to treatment as usual, but there was benefit for parent-child social communication.[130] **1++**

*Visual supports*

Alternative/augmentative communication, also referred to as visual supports, are employed in day-to-day educational support and at home to enhance both understanding of expectations and routines and to support the child in expressive communication. Visual supports may be objects of reference, photographs, picture symbols, signs and gestures and may be displayed in a variety of ways, including using electronic technology.[131]

*Picture Exchange Communication System*

The Picture Exchange Communication System (PECS) is a programme devised to develop social and communication skills in children with ASD using picture symbols. Staff trained in using the system teach the use of symbols to communicate in a progressive programme of up to six phases which draws on specific applied behavioural analysis techniques. Individuals learning PECS do not need to master prerequisite skills such as eye contact or gestures[132] and PECS can be used with children with or without intellectual **3**

disability.[132,133] Two meta-analyses reported small to moderate improvements in communication.[132,133] Learners with ASD alone (with or without comorbid speech impairment) had better outcomes than learners with ASD and comorbid intellectual disability.[133] A small number of studies showed a reduction in behaviour that challenges,[133] and a few reported speech improvements.[132,133] The best outcomes were amongst those who completed all six phases of PECS.[132,133] Most evidence of benefit was amongst preschool age children, although some studies also included adolescents and adults.[133] It was most beneficial for those with a specific developmental profile (low joint attention, low motor imitation and high object exploration).[132,133] **3**

*Environmental visual supports to assist understanding*

A number of studies were identified that assessed the efficacy of interventions to directly support social communication and interaction through the use of visual timetabling, operationalising through short stories or the use of speech bubbles or cartoons. The number of participants in each study was very small and the study populations were heterogeneous, making it difficult to generalise from their findings.[134-141] The evidence for interventions supporting communication was heterogeneous with a small number of studies looking at different aspects, for example intelligibility,[142] reading and writing as a visual support to communication.[143,144] **1⁻, 3**

**R** **Interventions to support communicative understanding and expression in individuals with ASD, such as the Picture Exchange Communication System and the use of environmental visual supports** (eg in the form of pictures or objects)**, should be considered.**

✓ Choice of interventions to support communication in children and young people with ASD should be informed by effective assessment.

### 6.2.2 INTERVENTIONS FOR SOCIAL COMMUNICATION AND INTERACTION

A Cochrane review of five RCTs of 196 young people of average or above average intelligence with ASD (aged 6 –21 years) showed that social skills groups improve overall social competence (weighted mean difference between treatment and control groups 0.47, 95% CI 0.16 to 0.78, p=0.003).[145] All the studies had some risk of bias, and the review concluded that further studies are needed to substantiate these results. Eleven studies were identified in another systematic review which showed short-term benefit in parent-reported social skills, although the quality of the studies was low and inconsistency in outcome measures across the studies makes it difficult to generalise skills beyond the intervention setting.[146] **1⁺⁺**

Three systematic reviews of studies into the use of computer-based interventions (CBI) concluded that, although the studies identified were small and of low quality, CBI showed promising results for social skills-related outcomes.[147-149] Results were seen across an age range of three to 29 years and IQ between 55 and 99. **2⁻, 2⁺**

Although it is difficult to synthesise the evidence due to heterogeneity, the interventions are linked to theories about underlying core deficits in ASD. They fall into a number of areas, for example offering additional support to verbal-social initiations, such as tactile prompting, or visual reinforcement, to help children with ASD acquire an alternative to a theory of mind. Studies also looked at peer training, to support the social interaction and communication of the child with ASD and buddy programmes that aim to elicit more appropriate social skills in students with ASD, in comparison to a passive proximity approach.

The evidence does not clarify which of these approaches is the most effective but many of them are currently in everyday educational use for children with ASD.

**R** **Interventions to support social communication should be considered for children and young people with ASD, with the most appropriate intervention being assessed on an individual basis.**

✓ Adapting the communicative, social and physical environments of children and young people with ASD may be of benefit (options include providing visual prompts, reducing requirements for complex social interactions, using routine, timetabling and prompting and minimising sensory irritations).

## 6.3 BEHAVIOURAL/PSYCHOLOGICAL INTERVENTIONS

Behavioural and other psychological interventions for people with ASD may be divided into three main groups:

- intensive behavioural and developmental programmes aimed at improving overall functioning and altering outcome
- interventions which aim to address specific behavioural difficulties associated with ASD, such as sleep disturbance, or to increase positive behaviours such as initiating social contact with peers
- a range of other behavioural/psychological interventions which do not fall readily into the other two groups.

### 6.3.1 INTENSIVE BEHAVIOURAL AND DEVELOPMENTAL PROGRAMMES

Early intensive behavioural intervention (EIBI) programmes aim to engage the child with ASD in a structured learning programme that is highly individualised, taking into account the idiosyncratic motivations and specific metacognitive and learning needs of each child. Although programmes vary widely in the emphasis given to different skills (verbal behaviours, pivotal responses, play, joint attention, etc) they tend to start with very basic skills (sitting, looking, listening) and over time work towards more complex metacognitive skills such as self monitoring or theory of mind. EIBI programmes involve varying levels of parental involvement. Generalisation of skills from prompted to spontaneous use is a key element.

EIBI programmes attempt to address a comprehensive range of behaviours associated with ASD, rather than focusing on one specific aspect such as communication, social skills or interaction. Given that ASD is a pervasive condition, these comprehensive programmes are necessarily intensive. They vary considerably in terms of technologies and emphasis but are all based on applied behaviour analysis (ABA).[146] Programmes have evolved considerably since early models such as the University of California, Los Angeles (UCLA) project,[150] and reviews of comprehensive, ABA-based and intensive programmes increasingly include developmental programmes such as the Learning Experiences and Alternative Program for Preschoolers and their parents (LEAP) and the Early Start Denver Model (ESDM).[146,151,152] EIBI programmes are manualised, intensive and target a comprehensive range of skills for training, practice and generalisation.

It is important to distinguish ABA, which has a wide range of applications at varying intensities, from EIBI, which is one application of ABA. EIBI programmes should not be referred to as 'ABA for autism', as this is not an accurate label.[151] Modern EIBI programmes are best described as behavioural and developmental programmes.

Programmes usually start when the child with ASD is three or four, with some reviewed studies starting at 18 months. They aim to build the prerequisite learning skills required to be ready for starting primary school. EIBI therefore describes comprehensive teaching programmes, rather than interventions that aim to reduce symptoms. While such ABA principles have been applied widely in community, hospital and educational settings for many years to address deficits and delays in learning resulting from a wide range of neurological conditions, they are not typically comprehensive or high intensity. Early models of EIBI for children with ASD typically required up to 30 or more hours per week, but more recent reviews include programmes ranging from 13–28 hours per week.[146] A number of more specific ABA-based interventions are also available (for example PECS) which do not require the same level of intensity (*see section 6.2.1*).

Ten well-conducted systematic reviews assessed the quality of trials on EIBI as low to moderate due to the complexities of conducting long-term studies in this area.[146,151-159] Early intervention based on high-intensity behaviour analysis over extended timeframes, whether delivered by parents or clinicians, was associated with improvement in cognitive functioning, language skills, adaptive behavior, including social competence and daily living skills relative to community controls in some groups of young children. Not all improvements were maintained at long-term follow up.[146] Only one systematic review concluded there was no impact.[156] This may be due to the inclusion of a study which compared high-intensity clinic-based ABA with high intensity parent-delivered ABA. Both programmes produced positive impact but the difference was not significant, diluting the gains found in the other included studies, and invalidating the author's conclusions.[159] The reviews show a steady improvement in study quality over time, although there are problems with small sample sizes, non-randomisation and partial blinding.[146,151-158] While these are relevant to any research in this area, they constitute biases that make it possible that the conclusions may change in the light of further evidence.

**1**$^{++}$
**2**$^{++}$
**2**$^{+}$

EIBI, based on the principles of ABA delivered with an intensive (>15 hours per week) and comprehensive (ie addressing numerous areas of functioning) approach can positively affect some children with ASD.[146] A Cochrane review concluded that while EIBI cannot be recommended universally it should be considered on a case-by-case basis.[158] There were no clear predictors identifying which children will respond or not, and while intensity or total hours were moderately correlated with some outcomes,[154,157] such correlations were not always significant.[158] **1++ 2++ 2+**

While it has been shown that EIBI is superior to no intervention or treatment as usual, the evidence does not warrant the provision of universal EIBI. It does however justify rigorous cost-effectiveness research, which currently is of poor quality and does not support wide application of this approach.[151] EIBI may not be cost effective when considered on the level of an individual early years service, but the cost effectiveness of it may change when considered on a societal level.[151]

Although interventions can be very intensive, no difference was found between EIBI and controls on measures of parental stress, parental anxiety, parental depression or parental positive perceptions.[159] No harms arising from EIBI were reported.[146] **1++ 2++**

There are risks of misuse by personnel who are not properly trained or supervised, which apply to any technique or intervention model. None of the papers specifically compared personnel across different competence levels, and it would be ethically difficult to do so. Robust frameworks exist for ensuring the safety of individuals receiving support and intervention, including person-centred approaches, values-based services, regular service review as well as competence and supervision frameworks, and these apply to ABA approaches as much as any other. In Scotland practitioners with comprehensive ABA skills are not widely available outside certain branches of clinical psychology, but health, education and social-care staff can access training to support children with communication difficulties which will involve ABA competencies, such as task analysis, shaping, fading or functional analysis. Specific ABA programmes such as PECS may be supported locally by speech and language therapists, psychologists and educational staff.

**R** **Access to support from staff trained in applied behaviour analysis-based technologies** (eg Picture Exchange Communication System, discrete trial training, task analysis, prompting, fading or shaping) **to build independence in adaptive, communication and social skills should be considered for children with ASD.**

### 6.3.2 SPECIFIC INTERVENTIONS FOR ASD

The Treatment and Education of Autistic and Related Communication Handicapped Children (TEACCH) approach involves the development of a programme around the individual's skills, interests and needs. A meta-analysis reported that TEACCH had small effects on perceptual, motor, verbal and cognitive skills. Improvements in social and maladaptive behaviours were moderate to large.[160] Effects on communication, activities of daily living and motor functioning were non-significant or small. The studies included in the study were small or of poor quality and outcomes were heterogeneous. Further research is needed to determine efficacy and the duration, intensity and setting required to implement TEACCH. **2+**

Social Stories™ are short individualised stories which describe a social situation or skill to help individuals with ASD. They are commonly used to enable individuals to understand socially-expected behaviours. Ten criteria guide story development tailored to each individual. These criteria ensure that the story structure and content is descriptive, meaningful and safe for its audience. The use of Social Stories™ has been studied mostly through single-subject research design, which is appropriate to highlight the individualised nature of the intervention.[161-163] While the studies showed considerable variation, most reported only a small clinical effect on behaviour. Social Stories™ may be easy to implement and require few resources, but those using them should be aware that the potential for improvement may be limited. **3**

### 6.3.3 COGNITIVE BEHAVIOURAL THERAPIES

Mental health difficulties are more prevalent among individuals with ASD than the typically developing population (*see section 4.4*), and there has been a number of reviews of cognitive behavioural therapy (CBT) for co-occurring mental health conditions in ASD.[146,151,164,165] CBT for children and adolescents with ASD has consistently shown positive effects for reduction in anxiety (clinician-rated anxiety Cohen's *d* effect size (*d*)=1.19, parent-rated anxiety *d*=1.21, child-reported anxiety *d*=0.68).[146,151,164,165] Outcomes were better when rated by clinicians or parents compared to ratings by children themselves. Despite some evidence of beneficial outcomes, important theoretical questions remain about whether anxiety in ASD is a true comorbidity or a manifestation of core ASD symptoms.[164] The studies were in children with IQ >70. No evidence was identified on whether CBT is beneficial for children presenting with a combination of ASD and intellectual disability. **2++** **2+**

Adaptations that take account of an individual's ASD presentation were employed in every study reviewed. These adaptations are not condition specific but reflect individual needs. Noteworthy adaptations include involving carers/parents, considering the impact of limited emotional insight, using concrete and visual material to support communication and structure sessions, considering the sensory environment and incorporating the person's interests.

A systematic review of cognitive skills training in children and adolescents with ASD reported improvements in theory of mind (*d*=0.75), imitation (*d*=0.2), play (joint engagement with mother *d*=0.67), emotion recognition (*d*=0.75) and initiations of joint attention (*d*=0.23).[166] Generalisation of skills learned being applied to different situations was demonstrated to be a problem for individuals with ASD across the studies, with few showing any change in non-taught measures. **1++**

Matching interventions to patients is likely to require expertise in needs assessment and patient/family engagement, to identify where emotional disorder is the result of environmental factors, skills deficits or cognitive distortions, so as to advise on suitability of behavioural, skills training or CBT interventions.

A cost-utility analysis, assessing the relative cost effectiveness of group CBT and individual CBT (relative to individuals remaining on a waiting list) for the management of anxiety in children and young people with autism found that, over the 38 weeks of the analysis, group CBT was the most cost-effective intervention of the options within this economic model (cost-effective relative to waiting list at £13,910 per quality adjusted life years (QALY) for group CBT versus £97,367 per QALY for individual CBT).[151]

**R** **Cognitive behavioural therapy may be considered, using a group format where available and appropriate, to treat anxiety in children and young people with ASD and who have average verbal and cognitive ability.**

✓ The delivery of cognitive behavioural therapy should be adapted for people with ASD.

✓ Cognitive behavioural therapy can be considered as a means of treating a coexisting condition if recommended in guidelines for that condition.

### 6.3.4 AUDITORY INTEGRATION TRAINING

Auditory integration training (AIT) is offered to children with ASD on the premise that they experience discomfort when listening to certain sound frequencies. In AIT the participant listens to modulated music tapes through headphones for specified time periods. A well-conducted Cochrane review identified seven small RCTs analysing AIT with a variety of outcome measures. Results for or against the use of AIT were inconclusive. Three of the trials reported no long-term benefits of AIT, while three small studies reported improvement in the Aberrant Behaviour Checklist total score.[167] **1++**

### 6.3.5 OCCUPATIONAL THERAPY AND SENSORY INTEGRATION THERAPY

Occupational therapists (OT) work with individuals and their carers to assess skills in the areas of self care, leisure and accessing an educational curriculum. They may draw on an understanding of sensory processing and motor skill development to generate solutions and strategies. The aim is to enable the individual to maximise his or her potential with activities of daily living. This could include reducing the impact of sensory sensitivities, if necessary.

Sensory integration therapy (SIT) is a theory and approach developed by OTs that targets difficulties with sensory processing and motor skills. It is a manualised clinic-based intervention that is child directed and aims to elicit adaptive responses to sensory experience. Three systematic reviews reported insufficient high-quality evidence to support the use of SIT.[168-170] Two small, low-quality RCTs reported positive effects using goal attainment scaling as an outcome measure.[168] **1+**

Sensory-based interventions (SBI) are usually classroom based, devised, but often not directly administered, by OTs. These use sensory strategies such as deep touch pressure or movement breaks (and possibly equipment such as weighted vests or therapy balls) to influence a child's state of arousal and adaptive behaviour. Studies of SBIs identified in a systematic review were of low quality and showed limited consistent improvement.[168] **1+**

✓ Children and young people affected by ASD may benefit from occupational therapy, advice and support in adapting environments, activities and routines in daily life.

### 6.3.6 MUSIC THERAPY

Music therapy may help children with ASD to improve their skills in social interaction, verbal communication, initiating behaviour, and social-emotional reciprocity, compared to placebo or standard care, in the short- to medium-term. The ten studies included in a Cochrane review were small (with a total of 165 participants) and of moderate quality and the authors concluded that, while results are positive, larger trials are needed to confirm the results.[171] **1++**

Music therapy is delivered by practitioners with specialised academic and clinical training.[171] **1++**

### 6.3.7 SLEEP MANAGEMENT

By the age of one year most children are able to sleep through the night. If after this time a child is regularly unable to sleep, or has a period of good sleep which is disrupted, then this constitutes a sleep problem. Sleep disturbance is reported to be a common problem for children and young people with ASD.

One moderate-quality RCT compared cognitive behavioural therapy, melatonin, combined melatonin and CBT to a placebo pill in children aged 4–10 years with ASD and sleep problems (40 in each arm of the trial). Participants in the CBT arm received four weeks of family therapy. All three active arms showed improvements in sleep onset latency (SOL), total sleep time, waking after sleep onset and sleep efficiency compared to placebo at 12 weeks, based on actigraph data.[172] The best results were reported for the combination of CBT and melatonin with a 22% increase in total sleep time from baseline (0.07% placebo), increase in naptime 67.85% (3.3% placebo) and sleep efficiency 20% (1.12% placebo) and a reduction in SOL of 60.75% (-0.02% placebo). Cognitive behavioural therapy alone saw improvements in: total sleep time 9.31%; SOL 60.75%; naptime 37.14% and sleep efficiency 11.26%. **1+**

Due to paucity of evidence NICE used expert opinion to recommend the development of a sleep plan to address sleep problems and establish a regular night-time sleep pattern. Behavioural interventions should be tried before a pharmacological intervention.[151] **4**

An RCT of the use of weighted blankets compared to placebo to improve sleep in children with ASD did not find any significant difference in SOL (mean difference 2.1), sleep efficiency (mean difference -0.3) or night-time waking (mean difference -0.2).[173] The intervention was well received by children and parents, however, with 48% of children using the weighted blanket choosing the 'really liked' category in the assessment questionnaire, compared to 31% placebo. Fifty-one per cent of parents felt that their child's sleep had very much improved/much improved compared to 16% placebo, and that their child was calmer (35 *v* 14%). Limitations of the study were that the participants' diagnosis of ASD was not assessed directly by the research team. **1⁻**

Melatonin for sleep management is covered in section 8.8.

✓ Behavioural therapy should be considered for children and young people with ASD who experience sleep problems.

✓ Children with ASD who present with signs of possible obstructive sleep apnoea, or sleep disordered breathing (loud snoring, choking or periodic stopping of breathing during sleep) should be referred to sleep medicine services for assessment.

### 6.3.8 FACILITATED COMMUNICATION

Facilitated communication is defined by the American Psychological Society as "a process by which a facilitator supports the hand or arm of a communicatively impaired individual while using a keyboard or typing device".

Two systematic reviews of facilitated communication conclude that there is no evidence to validate claims that the person with autism is being helped to communicate, although there is extensive evidence of communications that are generated by the facilitator.[174,175] Given the ethical implications of these findings in relation to the integrity and dignity of children and young people with ASD, the American Psychological Association has passed a resolution against the use of facilitated communication for people with ASD on ethical grounds.[176] **1⁺⁺**

**R** **Facilitated communication should not be used as a means to communicate with children and young people with ASD.**

### 6.3.9 ADDITIONAL INTERVENTIONS TO ADDRESS BEHAVIOURAL CHALLENGES

A range of behavioural challenges may present in individuals with ASD (for example self injury, aggression, passivity and lack of engagement). NICE concluded that existing programmes to target core features of autism that can result in behaviours that challenge are variable in availability and quality. Confounding factors in studies may include specific skills deficits or sensory problems which may contribute to a particular behaviour pattern, along with the social and physical environment.[151] **2⁺⁺**

A systematic review identified a range of behavioural and educational interventions addressing behaviours that challenge. They varied in scope, target and intensity so it was not possible to determine which components linked to clinically meaningful changes in functioning.[152] Although common behavioural interventions result in positive behavioural outcomes across a wide range of target areas,[151,152] further RCTs are required with sufficient duration to ascertain which components of interventions are effective and have a sustainable effect on outcomes. **2⁺⁺**

✓ Behavioural interventions may be considered to address a wide range of specific behaviours, including those that challenge, in children and young people with ASD, both to reduce symptom frequency and severity and to increase the development of adaptive skills.

✓ Healthcare professionals should be aware that some behaviours that challenge may be due to an underlying lack of skills development in the child/young person and may also represent an individual's strategy for coping with their difficulties and circumstances.

✓ Healthcare professionals should be aware that factors in the social and physical environment may contribute to positive behaviours or those that challenge.

## 6.4 NUTRITIONAL INTERVENTIONS

A systematic review of gluten-free and/or casein-free diets identified three RCTs which reported no improvement in measures of language, attention, activity level, sleep, or bowel habits. Two further studies reported some improvements in behavior but the results may have been compromised by placebo effect and high attrition rates. All the studies had small sample sizes, so further research is needed to confirm results.[177] **1+**

A Cochrane review of omega-3 fatty acids supplementation for people with ASD identified two RCTs which were not sufficiently robust to draw any conclusions.[178] A further RCT published since the Cochrane review is also underpowered.[151,179] One low-quality trial of omega-3 for sleep problems identified by NICE reported a statistically significant negative treatment effect for omega-3 compared to a healthy diet control group (standardised mean difference (SMD) 1.11, 95% CI 0.21 to 2.00).[151] **1++** **1-**

A Cochrane review of combined vitamin B6 and magnesium intervention for children and young people with ASD found insufficiently robust studies to meet the criteria set for the review and therefore no recommendation can be made.[180] **1++**

As with all children and young people, nutritional interventions may be required for children and young people with ASD who also have significant food selectivity and dysfunctional feeding behavior.

✓ Gastrointestinal symptoms in children and young people with ASD should be managed in the same way as in children and young people without ASD.

✓ Advice on diet and food intake should be sought from a dietician for children and young people with ASD who display significant food selectivity and dysfunctional feeding behaviour, or who are on restricted diets that may be adversely impacting on growth, or producing physical symptoms of recognised nutritional deficiencies or intolerances.

## 6.5 OTHER INTERVENTIONS

Systematic reviews of complementary therapies, acupuncture and animal-assisted interventions reported that evidence for the use of complementary and alternative therapies for individuals with ASD is sparse and no strong conclusions could be drawn.[181-183] **2-** **2+**

Meta-analysis of small trials of various physical activities concluded that exercise for individuals with ASD may be beneficial for improving motor skills and social interaction. Further, larger, more rigorous trials are needed to support the findings.[184] **2+**

# 7 Non-pharmacological interventions for adults

Psychosocial interventions aimed at improving outcomes have been developed using a variety of models. Most have been developed for children and young people, and there is less evidence about their efficacy in adulthood. This can create the false impression that adulthood is less of a challenge for people with ASD, but there is evidence that adult outcomes are poor and adult developmental milestones such as work, intimate relationships or independence from parents are often not achieved.[185] A review found that studies suggest that 30–84% of adults with ASD might have some form of diagnosable mental illness.[185]

Interventions for adults should be regularly monitored, ideally with objective measures of change in target behaviours, to monitor positive and negative outcomes and adherence to the intervention.[13] Healthcare professionals working with adults with ASD should assess caregiver needs as well as the needs of the individual with ASD.[13] Parents or carers supporting people with ASD may experience higher levels of carer burden during the individual's transition to and in early adulthood.[186] The involvement of carers will also support assessment and intervention objectives.

Psychosocial interventions target a range of outcomes, including adaptive behaviours, communication, social skills, employment, quality of life and comorbid mental health difficulties, and the approaches used overlap considerably. Social programmes involve communication and behavioural elements while most communication programmes involve behavioural elements.[13]

Research into the needs and experiences of adults with ASD is limited. Where there are gaps in the evidence base for adults, it may be possible to extrapolate carefully from the evidence about interventions for children and young people.

## 7.1 COMMUNICATION INTERVENTIONS

Two uncontrolled studies looking at communication skills training in adults, both with ASD and severe to profound intellectual disability were identified by NICE.[13] Samples were small and no conclusions could be drawn. No further, more recent evidence was identified. **2++**

## 7.2 FACILITATED COMMUNICATION

A single uncontrolled study on facilitated communication with adults found no significant improvement in target behaviours.[13] Given that potential harms have been associated with this intervention, it is not recommended that services provide facilitated communication.[13] **2++**

See section 6.3.8 for further advice on facilitated communication.

**R** **Facilitated communication should not be used as a means to communicate with adults with ASD.**

## 7.3 SOCIAL SKILLS INTERVENTIONS

Difficulties with relationships and social participation are widespread among adults with ASD. The skills required to initiate and maintain relationships are beneficial in other areas, for example employment, wider participation in society and help seeking.[13] One RCT and two observational studies on social skills interventions were identified in the NICE review.[13] Also included were studies looking at adolescents (mean age >15 years; one RCT and three observational studies) and one RCT in adults with intellectual disability.[13] No further, more recent studies were identified. **2++**

The RCT in adults with ASD evaluated an emotion recognition training computer programme and found no benefit compared to treatment as usual. The two observational studies of social skills groups for adults with ASD reported improvements in social interaction, as did the RCT in adolescents with ASD which found a significant effect of their group intervention compared to a waiting list control. However, the three observational studies of social skills groups for adolescents all failed to find evidence of benefit. All of the above studies involved participants with average IQ. The RCT of social adjustment training for adults with intellectual disability found no improvement in behaviour that challenges.[13] **2++**

Evidence for interventions targeting social interaction skills is limited. Based on the available evidence and the pervasive impact of social interaction difficulties, NICE recommended that group-based social skills programmes should be considered for adults with ASD with and without intellectual disability who have identified problems with social interaction. They further recommend that individual programmes should be available for those who find groups difficult.[13] **4**

## 7.4 BEHAVIOURAL INTERVENTIONS

One RCT and three uncontrolled studies looking at adaptive functioning, one of which looked at childcare skills, were identified. The studies included adolescents (>15 years) and adults with intellectual disability. There were no studies addressing behavioural therapies for behaviour that challenges, and the evidence for adaptive skills was limited and low quality. NICE used expert opinion to recommend that behavioural interventions should be considered for adaptive functioning and behaviour that challenges.[13] **2++ 4**

One further meta-analysis which addressed behavioural interventions for academic skills, adaptive skills, behaviour that challenges, social skills, phobic avoidance and vocational skills[187] reviewed 48 studies, reporting on interventions for 110 participants, with quality varying from low (n=32) to high (n=7). The review included adolescents, and single-case studies. Interventions for problem behaviour, academic skills and phobic avoidance were reported by fewer than five studies each, limiting the reviewers' ability to draw conclusions from these articles. Studies looking at adaptive behaviour and social skills were the most frequent, and some evidence of benefit was reported in these domains. **3**

Conclusions must be made with caution given that it is a meta-analysis of single-case studies, and because the quality of many of the studies included in the review was low.

It is not possible to make definitive recommendations on the basis of the evidence considered. However, it is recognised that behavioural interventions are an important option to consider when addressing behaviour that challenges and adaptive functioning in adults with ASD. Further advice is available in NICE 11, Challenging behaviour and learning disabilities: prevention and interventions for people with learning disabilities whose behaviour challenges.[188]

## 7.5 COGNITIVE BEHAVIOURAL THERAPIES

Cognitive behavioural therapy has sometimes been seen as inaccessible for people with ASD because of the abstract and emotional nature of the approach. A number of adaptations have been developed and can improve accessibility for people with ASD and/or intellectual disability.[13] One RCT of CBT for adults with ASD, comparing interventions for obsessive-compulsive disorder (OCD) with treatment as usual found no treatment effect.[13] The study did not report adapting their intervention and that the lack of treatment effect may suggest that modification is necessary. **2++**

The NICE guideline development group used expert opinion to recommend that CBT should be offered to individuals presenting with both ASD and intellectual disability who are at risk of victimisation, or those with or without intellectual disability who experience problems associated with anger or aggression. Where individuals with ASD experience problems such as anxiety or depression which are typically treated with CBT clinicians should consider using the following adaptations:[13]

- a more concrete and structured approach with a greater use of written and visual information, which may include worksheets, thought bubbles, images and 'tool boxes'
- placing greater emphasis on changing behaviour, rather than cognitions, and using the behaviour as the starting point for intervention
- making rules explicit and explaining their context
- using plain English and avoiding excessive use of metaphor, ambiguity and hypothetical situations
- involving a family member, partner, carer or professional (if the person with ASD agrees) to support the implementation of an intervention
- maintaining the person's attention by offering regular breaks and incorporating their special interests into therapy if possible, such as using computers to present information.

**4**

A further five small studies addressing CBT for adults with ASD were identified. Two were RCTs[189,190] and the others were quasi-experimental or preliminary trials.[191-193] Comparison across studies was not possible because the target of the intervention in each study was different, covering OCD; depression and stress; anxiety, depression and rumination; quality of life and self esteem; or cognitive and social impairments.

**1+**
**1-**
**2-**

One RCT found twice as many responders in their CBT group, but overall improvement was similar to their anxiety management control group.[189] These overall improvements were similar to those reported in non-ASD trials of CBT for OCD (aggregated effect sizes of 1.12 to 1.45).[189] Noting that it is unusual to find anxiety management being as effective as CBT in non-ASD trials, the authors speculated that perhaps education about emotions and anxiety management has a more powerful impact on people with ASD, given their relative deficits in emotion recognition and self reflection. In the other RCT, non-blinded outcome measures indicated significant improvements in depression, anxiety, rumination and positive affect for the mindfulness group, whilst their waiting list control group showed no change at all on these measures.[190] A preliminary RCT reported that both the CBT group and a recreational activity control group showed significant improvement on a measure of quality of life which was maintained at follow up, but found no difference in any of their measures of psychiatric symptoms.[191]

**1+**
**1-**

No harms were reported in the studies and one reported that more participants requested CBT than anxiety management, suggesting that these approaches seem to be acceptable to adults with ASD.[189] No individuals with intellectual disability were included. One study recommends involving carers and supportive individuals in the intervention.[189]

**1+**

There is insufficient evidence to recommend any specific model of psychosocial intervention. However, a diagnosis of ASD should not prevent anyone from receiving these interventions. Therefore, if an individual with ASD experiences a symptom or condition that would usually be treated with CBT or related psychosocial intervention (for example anxiety), then they should receive the intervention recommended by guidelines for that symptom or condition. It is important not to assume that complex intervention is required; interventions to improve emotional literacy, distress tolerance, relaxation skills or general adjustment could be considered as first line.

✓ Psychosocial interventions should be considered for adults with ASD if indicated for managing coexisting conditions.

# 8 Pharmacological interventions for children and young people

## 8.1 GENERAL PRINCIPLES

Any pharmacological intervention considered for children and young people with ASD should not be viewed in isolation but seen as a possible component of a multistranded package of care.

There are no controlled long-term studies demonstrating that pharmacological interventions affect the core difficulties or outcomes in children and young people with ASD. There is little evidence directly comparing pharmacological and non-pharmacological approaches.

Pharmacological interventions may be considered when appropriate, for management of coexisting psychiatric or neurodevelopmental conditions in individuals with ASD. Pharmacological approaches may also be considered as a short- to medium-term intervention for specific severe symptoms occurring in children and young people with ASD. Interventions for other coexisting medical conditions, for example epilepsy, which may be required for children and young people with ASD, are not discussed in this guideline.

Only medications available in the UK are discussed. No pharmacological interventions have ASD as a licensing indication, and there are few drugs specifically licensed for use in children and adolescents.[194] Prescribing medicines in this situation therefore brings extra responsibilities (*see section 1.3.2 for further advice on prescribing of licensed medicines outwith their marketing authorisation)*.

An assessment of the need for pharmacological intervention should include an appraisal of the child's environment (school and home) and daily routines (for example sleep, daily activities, meals etc). Changes in these areas may be worth attempting before using medication and are likely to complement the effects of any appropriate medication prescribed. It is possible that management of coexisting conditions with medication may enhance the ability of children and young people to benefit from other approaches.

### 8.1.1 FRAMEWORK FOR USE OF MEDICATION

The balance of potential risks and benefits arising from any pharmacological intervention needs to be carefully considered for each individual child and discussed as appropriate with them and their parents/carers so that they can make an informed decision.

If a trial of pharmacological intervention is agreed, there should be careful pretreatment assessment of the child's overall symptoms and functioning, and definition of the 'target symptoms', that is those symptoms potentially responsive to the drug. There should be agreement about how symptoms and any emergent side effects of treatment will be measured, as well as the monitoring arrangements and expected duration of any trial of medication. Children and young people, their parents/carers and healthcare professionals, should, as far as possible, plan how they intend to make a decision about whether or not to continue with medication, after any trial period.

✓ Pharmacological intervention for children and young people with ASD should only be undertaken by doctors with appropriate training and access to pharmacy or other support as required.

## 8.2 SECOND-GENERATION ANTIPSYCHOTICS

In children with ASD aripiprazole (2.5–15 mg per day) can be effective in reducing irritability (mean improvement 6.17 points on ABC irritability subscale), and hyperactivity (mean improvement 7.93 point on ABC hyperactivity subscale) compared to placebo over eight weeks.[195] This effect did not continue when used as maintenance therapy, with no significant difference in time to relapse between aripiprazole and placebo.[196] Use of apriprazole was associated with greater risk of developing adverse effects, with the likelihood of sedation 4.28 times higher, drooling 9.64 times higher and tremor 10.26 times higher than the control group.[195] Other studies found weight gain, somnolence, vomiting, and extrapyramidal effects to be common.[152,196]

**1**$^{++}$
**2**$^{+}$

From a body of moderate-quality evidence (four RCTs and two case series), a systematic review concluded that risperidone improved behaviour that challenges and repetitive behaviour compared to placebo.[152] Weight gain, sedation and extrapyramidal effects were associated with use of risperidone.[152] Adverse effects remained similar over a six-month period.[197] Hyperprolactinemia is also a common side effect in boys aged from 10 to 20 years, which may have an effect on lumbar-spine bone mineral density.[198,199]

**1+**
**1++**
**2+**

A meta-analysis comparing both efficacy and adverse effects of aripiprazole and risperidone concluded that short-term (6–10 weeks) efficacy is similar for both in reducing behavioural disturbances associated with autism, with or without intellectual disability.[200] There was also little difference between the two interventions in terms of weight gain.[201]

**1+**
**2+**

A review of the effects of antipsychotic medication after three to four weeks, and to discontinue treatment if there is no clinically important response at six weeks is recommended.[151]

**4**

A cost-utility analysis of risperidone, aripiprazole and placebo for the management of behaviour that challenges (including irritability) in children and young people with ASD over eight weeks reported that risperidone in tablet form was the most cost-effective intervention.[151] Aripiprazole was not cost effective. Risperidone is available as a generic medicine, and the same cost-effectiveness conclusions may be assumed to apply to other antipsychotics with similar acquisition costs. While costs of clinical management were considered for inclusion in the analysis, the only differentiating factor between the treatment arms was the medicine acquisition cost. Costs relating to behaviour that challenges were not included due to a lack of reliable data. Although this is a limitation with the model, this could be considered conservative since any improvement in behaviour may lead to reduction in associated costs.

Evidence for use of other antipsychotics for autistic behaviours is of low quality. Potential harms are associated with the drugs and it is recommended that they should not be used in children to manage autistic behaviours.[151]

**1++**
**4**

**R** **Antipsychotics** (including second-generation antipsychotics) **should not be used to manage the core symptoms of autistic spectrum disorders in children and young people.**

**R** **Second-generation antipsychotics may be considered to reduce irritability and hyperactivity in children and young people with autistic spectrum disorders in the short term** (eight weeks)**. Patients and their carers should be advised of potential side effects before treatment is started.**

**R** **Children prescribed second-generation antipsychotics should be reviewed after three or four weeks of medication. If there is no clinically important response at six weeks treatment should be stopped.**

### 8.2.1 RISPERIDONE ADJUNCTIVE THERAPIES

Used as adjunctive therapies to risperidone, galantamine and celecoxib may reduce irritability, lethargy and social withdrawal in children with ASD.[202,203] Memantine showed a reduction in stereotypical behaviour and irritability and riluzole reduced irritability, stereotypical behaviour and hyperactivity.[204,205] In all four studies the diagnosis of ASD may be unreliable as there was a lack of clarity over the baseline characteristics in terms of treatment history. The high rates of administration of risperidone used in these Iranian trials are unfeasible in Scotland.

**1+**

## 8.3 METHYLPHENIDATE

There is evidence that methylphenidate reduces hyperactivity in children up to 14 years with ASD and coexisting ADHD (with a mean IQ in the intellectual disability range).[206] After eight weeks' follow up 49% of the 72 participants responded to methylphenidate, with a 30% reduction in hyperactivity in parent or teacher rating scales, and 'much improved' or 'very much improved' reporting on the Clinical Global Impression (CGI) scale. Adverse effects (appetite decrease, difficulty falling asleep, irritability and emotional outbursts) were more common in children receiving methylphenidate compared to those on placebo.[206] In one study from a specialist paediatric clinic, response to methylphenidate and level of side effects were not significantly different in children with ADHD and ASD compared with children with ADHD alone.[207] The use of a test dose is worthwhile to assess whether methylphenidate will be tolerated.[206,208] No further RCTs of a larger sample size have been published. Smaller RCTs and uncontrolled studies support the efficacy of methylphenidate for the reduction of ADHD-like symptoms.[209] **1+**

There is no evidence about the use of other stimulant medication for ADHD symptoms in children and young people with ASD.[209] If methylphenidate is not tolerated use of other medication could be considered with reference to SIGN guideline 112 on attention deficit and hyperkinetic disorders in children and young people.[210]

**R** **Methylphenidate may be considered for management of attention difficulties/hyperactivity in children or young people with ASD.**

✓ Use of a test dose to assess if methylphenidate is tolerated could be considered in children prior to any longer trial.

✓ Side effects should be carefully monitored (see SIGN guideline 112 on attention deficit and hyperkinetic disorders in children and young people).[210]

## 8.4 NORADRENERGIC REUPTAKE INHIBITORS

One RCT studying the use of atomoxetine demonstrated reduced ADHD symptoms in children with ASD compared to placebo. Further studies are required to establish the efficacy and safety profile of this intervention.[211] **1+**

## 8.5 ANTIDEPRESSANTS

### 8.5.1 SELECTIVE SEROTONIN REUPTAKE INHIBITORS

Trials of fluoxetine, fluvoxamine, fenfluramine and citalopram showed no significant difference in CGI or obsessive-compulsive disorders for children with ASD compared to placebo.[212] Citalopram was associated with higher rates of seizures and fenfluramine increased withdrawal, sadness, stereotypical movements, appetite reduction and weight loss. No adverse effects were found with use of fluoxetine or fluvoxamine.[212] No evidence for the use of selective serotonin reuptake inhibitors (SSRIs) to improve the core features of ASD has been identified.[151] Insufficient evidence was identified to determine the efficacy of SSRIs to reduce repetitive behaviours in children with ASD.[152] **1++**

SSRIs may be considered for children with common coexisting conditions such as depression for which there is established evidence for their use.[213,214,152]

**R** **Selective serotonin reuptake inhibitors should not be used to manage core features of ASD** (eg repetitive behaviours) **in children and young people.**

**R** **Selective serotonin reuptake inhibitors should be considered for children and young people with symptoms of coexisting conditions on a case-by-case basis.**

### 8.5.2 TRICYCLIC ANTIDEPRESSANTS

A well-conducted Cochrane review identified three small studies on the use of tricyclic antidepressants (TCAs) for symptoms of ASD, two of which were in children and one in children and young adults.[215] Findings were inconsistent. For tianeptine, parents and teachers reported improvements but this was not supported by clinician ratings. Two studies on clomipramine showed improved outcomes for core features of ASD but mixed results for hyperactivity. All three studies reported adverse effects such as drowsiness and fatigue. Further evidence is needed before a recommendation on the use of TCAs for core symptoms of ASD can be made. This should not preclude the use of TCAs for coexisting conditions in people with ASD, and appropriate guidance should be followed. | 1++

## 8.6 NALTREXONE

All studies identified related to children less than eight years of age and naltrexone did not improve symptoms of autism.[216-219] | 1+

## 8.7 HORMONAL INTERVENTIONS

### 8.7.1 SECRETIN

Secretin (human or porcine) as a single dose, or in multiple doses, for up to six months does not improve ASD symptoms, and no subgroup of children who benefit has been identified.[152,220] | 1++

R **Secretin is not recommended for the management of symptoms of ASD in children and young people.**

### 8.7.2 OXYTOCIN

Small pilot studies of oxytocin demonstrated positive findings on eye gaze and emotion recognition but effects on repetitive behaviours were inconsistent and no effect was seen in CGI. Further, larger studies are needed to determine efficacy.[221] | 1++

## 8.8 MELATONIN

Melatonin (3 mg controlled release) is effective in reducing sleep problems in children with ASD. In a four-way trial melatonin increased total sleep time by 17.31%, reduced SOL by 44.33% and increased naptime by 51.51% over baseline at 12 weeks.[151,172] In the same study melatonin in combination with CBT was most effective, with 84.62% of the children meeting a standard sleep criterion of SOL of 30 minutes or less or a reduction of SOL by 50% after 12 weeks, compared to 39.92% for the melatonin group, 10.34% for CBT and no reduction for the placebo group[172] (*see section 6.3.7 for results from the other arms of the trial*). | 1+

A further RCT of immediate-release melatonin (0.5 mg increased incrementally to 12 mg over four weeks) in children with ASD showed melatonin was effective for SOL measured by a sleep diary, but effects on total sleep time were non-significant.[151] | 1+

Neither study reported any statistically significant adverse effects from the use of melatonin.[35,172] | 1+

The melatonin prolonged-release tablet, Slenyto, is licensed for use in children with autism who experience insomnia, however it is not recommended for use in NHSScotland by the Scottish Medicines Consortium *(see section 12.4)*. Prescribing of Circadin for children is considered as off-label use and prescribing of any other melatonin products would be unlicensed use *(see section 1.3.2)*.[194]

R **In children with ASD who have sleep difficulties which have not resolved following behavioural interventions, a trial of melatonin to improve sleep onset should be considered.**

- ✓ Use of melatonin should follow consultation with a paediatrician or psychiatrist with expertise in the management of sleep medicine in children and/or ASD, and be in conjunction with behavioural interventions.
- ✓ Melatonin prescription should be reviewed regularly in the context of any emerging possible side effects and/or reduced therapeutic effect.
- ✓ Children with ASD who present with signs of possible obstructive sleep apnoea, or sleep-disordered breathing (loud snoring, choking or periodic stopping of breathing during sleep) should be referred to sleep medicine services for assessment.
- ✓ Obtain an adequate baseline sleep diary before any trial of melatonin.

  Continue sleep hygiene measures (bedtime and wake-up routine, avoidance of day-time sleep) and a sleep diary, during any medication trial.

Prescribing of Circadin for children is considered as off-label use and prescribing of any other melatonin products would be unlicensed use (*see section 1.3.2*).[194]

# 9 Pharmacological interventions for adults

## 9.1 GENERAL PRINCIPLES

The evidence considered in this section addresses pharmacological interventions for the core symptoms of ASD. Many adults with ASD have coexisting conditions, such as anxiety, depression or ADHD. While some of the therapies may not have evidence to support their use for managing symptoms of ASD, this should not preclude their use in adults with ASD for the management of a coexisting condition. In these cases, advice should be sought from guidance relevant to the particular condition.

✓ Adults with ASD who are prescribed any pharmacological therapies should be reviewed regularly to ensure the intervention is of benefit, being used appropriately, and for any signs of adverse events or interactions with other medications.[13]

## 9.2 ANTIPSYCHOTICS

Meta-analysis of two small open label RCTs on the use of risperidone in adults with ASD showed benefit in reducing behaviour that challenges.[13] One of the trials also reported improvement in repetitive behaviours and symptom severity. A small RCT (n=36) comparing haloperidol to placebo found no significant treatment effect for autistic behaviours. This study had a 21% drop out rate compared to 3% in the placebo arm due to fatigue, dystonia and depression.[13] **1++**

A more recent systematic review on psychopharmacological interventions for behaviour that challenges in adults with ASD and intellectual disability did not find any further studies.[222] **1++**

Due to the lack of trials in adults with ASD, NICE identified studies of adults with intellectual disabilities and extrapolated the findings for adults with ASD. Some patients within the trials had coexisting psychiatric conditions. The results were inconsistent, but suggest risperidone may improve symptom severity and behaviour that challenges. Three studies of zuclopenthixol in adults with learning disability had conflicting results. Cis-clopenthixol may be superior to haloperidol for behaviour management. One observational study of olanzapine showed an improvement in challenging behavior amongst adolescents with intellectual disability, but reported weight gain as a side effect.[13] **2++**

Side effects were considered to be tolerable. Statistically significant weight gain was reported in two of the risperidone studies. Studies were short term, between three to 12 weeks' intervention and up to 24 weeks' follow up, so long-term data on the effects of antipsychotics in adults with ASD are unavailable. It is recommended that effects of the medication are reviewed after three to four weeks and treatment discontinued if there is no clinically important response at six weeks.[13] **2++ 4**

R **Antipsychotic medication should be considered for addressing behaviour that challenges in adults with ASD when psychosocial or other interventions could not be delivered due to the severity of behaviour that challenges.**

R **Antipsychotics should be prescribed by a specialist and quality of life outcomes monitored carefully. Review the effects of medication after three to four weeks and discontinue if there is no indication of clinically important response at six weeks.**

## 9.3 PHARMACOTHERAPY TO IMPROVE COGNITION

No trials were identified on pharmacotherapy to improve cognition in adults with ASD. Two small observational studies in children reported inconsistent results.[13] Evidence on memantine and galantamine as risperidone adjunctive therapies in studies in children is detailed in section 8.2.1. **2++**

## 9.4 METHYLPHENIDATE

No evidence was identified on the use of methylphenidate for the core symptoms of ASD in adults. It has been found to have benefit in reducing hyperactivity in children with ASD and ADHD (*see section 8.3*).

## 9.5 NORADRENERGIC REUPTAKE INHIBITORS

No evidence was identified on the use of noradrenergic reuptake inhibitors for the core symptoms of ASD in adults. Evidence from studies in children is also limited (*see section 8.4*).

## 9.6 ANTIDEPRESSANTS

Studies on the efficacy of SSRIs in managing symptoms of ASD in adults are small, heterogeneous and of short duration (12 weeks).[212] Improvements were found in CGI, obsessive-compulsive behaviours and aggression with fluvoxamine, and in CGI and anxiety with fluoxetine.[212] One study of fluvoxamine compared to placebo also reported a statistically significant reduction on repetitive behaviours and autistic behaviours.[13,222] A further study on the effects of fluoxetine in adolescents with ASD reported improvements in CGI ratings for overall clinical severity and compulsive behaviours, but 26% of participants had side effects that impacted on functioning. A study of sertraline reported a reduction in repetitive behaviours, autistic behaviours, maladaptive behaviours and overall symptom severity.[13] **1++**

One study comparing clomipramine to placebo reported no effect on core symptoms of ASD and had a 34% dropout rate due to side effects.[13]

There is a lack of recent good-quality evidence to support a recommendation on the use of antidepressants for the core symptoms of ASD. This should not preclude their use for other conditions in adults with ASD.

✓ Adults with ASD who have coexisting mental ill health that may respond to antidepressants should be offered treatment, with close monitoring for response and adverse effects.

## 9.7 ANXIOLYTICS

No evidence was identified on the use of anxiolytics for the core symptoms of ASD in adults. Their use in adults with ASD and anxiety should follow appropriate guidance on the management of anxiety.

## 9.8 ANTICONVULSANTS

No evidence was identified on the use of anticonvulsants for the core symptoms of ASD in adults. Studies in children were of low quality and had mixed results.[13] There is insufficient evidence on which to base a recommendation. **1++**

## 9.9 NALTREXONE

No evidence was identified on the use of naltrexone for the core symptoms of ASD in adults. Limited evidence suggests that it is not effective in children (*see section 8.6*).

## 9.10 HORMONAL INTERVENTIONS

### 9.10.1 SECRETIN

No studies on the use of secretin for managing symptoms of ASD in adults were identified. Studies in children did not find it to be of benefit (*see section 8.7.1*).

**R** **Secretin should not be considered for the management of symptoms of ASD in adults.**

### 9.10.2 OXYTOCIN

No good-quality evidence was identified on the use of oxytocin for the core symptoms of ASD in adults. Four placebo-controlled trials were identified but each had fewer than ten participants per arm and results were inconsistent.[13] **2++**

## 9.11 MELATONIN

No evidence was identified on the use of melatonin in adults with ASD to improve sleep problems. RCTs in children have shown improvements in sleep time and sleep-onset latency, particularly when used with CBT (*see sections 8.8 and 6.3.7*).

**R** **In adults with ASD who have sleep difficulties which have not resolved following behavioural interventions, a trial of melatonin to improve sleep onset may be considered.**

✓ Use of melatonin should follow consultation with a psychiatrist with expertise in the management of sleep medicine and/or ASD, and be in conjunction with behavioural interventions.

✓ Obtain an adequate baseline sleep diary before any trial of melatonin.

✓ Continue sleep hygiene measures (bedtime and wake-up routine, avoidance of day-time sleep) and a sleep diary, during any medication trial.

✓ Melatonin prescription should be regularly reviewed in the context of any emerging possible side effects and/or reduced therapeutic effect.

✓ Adults with ASD who present with signs of possible obstructive sleep apnoea, or sleep disordered breathing (loud snoring, choking or periodic stopping of breathing during sleep) should be referred to sleep medicine services for assessment.

Melatonin products are not licensed for use in the UK, with the exception of Circadin which is licensed as monotherapy for the short-term treatment of primary insomnia characterised by poor quality of sleep in patients who are aged 55 or over (*see section 1.3.2 for advice on prescribing of licensed medicines outwith their marketing authorisation*).[14] Circadin has not been accepted for use in NHSScotland by the SMC (*see section 12.4)*.

# 10 Service provision

Autism spectrum disorder is a lifelong condition and individuals with ASD have varying needs across their lifespan. To allow people to live as independently as possible, services need to take a wide, varied and adaptable approach.

The Scottish Strategy for Autism (2011) sets out a ten-year plan for service provision to improve the lives of people with ASD and their carers.[3] The strategy advocates partnership working with a range of services such as social care, education, housing, employment and other community-based services to provide a holistic joined-up approach. The Strategy is aligned with the Scottish Government's national practice model, GIRFEC 2012,[1] which has been supported in statute by the Children and Young People (Scotland) Act 2014.[2] The framework and legislation outline duties for services, which significantly impacts on the provision of autism services. This includes duties for public bodies to co-ordinate planning, design, and delivery of services for children and young people with a focus on improving well-being outcomes and to report collaboratively on how they are improving such outcomes. The provision of services that are collaboratively organised and delivered successfully is complex and has significant implications for co-ordination and strategic management processes.

Services for adults are available from ASD-specific providers, for example Scottish Autism, the National Autistic Society and Autism Initiatives. In addition, a significant number of non-specialist voluntary organisations offer services to adults with ASD. Services take a wide range of formats and include outreach services, support in the local community and 24-hour housing support and care at home. Some general service providers are now providing specialist residential services, which has enabled people who were previously placed out of area to return to their home communities. Some providers have developed their own organisational ASD strategies and have looked at designing environments which respond to the specific needs of individuals with ASD.

As well as support from service providers there are also a range of options to support independent living available through volunteer organisations, family support groups and peer support groups (*see section 11.3*). Employment support services are available both through mainstream services and more specific services. Advocacy is available mainly through mainstream advocacy services.

## 10.1 TRAINING

Despite the increasing awareness of, and interest in, the nature of ASD, there remain some gaps in training for professionals working with people with ASD. This can cause service delivery to be less effective.

The small body of evidence on training points to improvement in attitudes of mainstream teachers towards the inclusion of children with ASD in their classes,[223,224] increased levels of parental confidence in relation to service provision,[17] and in benefits in knowledge for medical staff from evidence-based educational interventions.[225]

4

The Autism Training Framework outlines the skills and knowledge required at different levels within the health- and social-care workforce to achieve key outcomes for people with ASD. It describes the knowledge and skills required by generic health- and social-care workers who will occasionally encounter a person with ASD, through to those who provide highly specialist interventions in ASD services.[54]

**R** **All professions and service providers working in the ASD field should review their training arrangements to ensure that staff have up-to-date knowledge and adequate skill levels.**

## 10.2 INTERVENTIONS AND MEETING SUPPORT NEEDS

Education services are a key resource in the provision of support and intervention to reduce the impact of ASD on children, young people and their families. The co-ordination of services and collaboration between services as outlined in GIRFEC and related legislation is paramount for the provision of effective interventions and support. Most local authorities have ASD strategies in place to provide a range of educational input and support.[226]

Families with children who have ASD often experience high stress levels as a consequence of their care-giving responsibilities, the child's cognitive impairment and the need for long-term support.[227-230] Education and skills interventions have been shown to lead to significant improvements in the self-reported mental health of parents of preschool children.[128] **4** **1+**

**R** **Education and skills interventions for parents of preschool children with ASD should be offered.**

✓ Education and skills interventions should be offered to parents of all children and young people diagnosed with ASD.

Informal social support is important to absorb family stress.[231,232] It is important to consider the needs of siblings of children and young people with ASD. Supporting parents through provision of training in communication with their children is discussed in section 6.1.[228]

## 10.3 INFORMATION PROVISION AND SUPPORT FOR PARENTS/CARERS

See section 11 for advice on provision of information and support.

## 10.4 SUPPORT DURING TRANSITION

Transitions, at all stages from preschool through adulthood and into older adulthood, are challenging for people with ASD. However, evidence regarding best practice around transition is very limited. A single study was identified in which telephone interviews with parents were used to capture their perceptions of transition and the support needed.[233] Parents reported that increased social work contact with families during periods of transition was valued.

Professionals should be aware that difficulties during transition may arise because the high level of support being provided prior to such transition was unrecognised. Reassessing support needs and planning ahead prior to a transition may allow appropriate new support to be put in place.

Although individual support needs will vary, some basic aspects may be generally applicable. For example, a survey of supervisors of adults with ASD employed within a supported work environment, indicated that the support strategies used were based on principles largely applicable to all young people, including clear guidance, mentoring and regular reviews.[234] **4**

Principles of good transitions are outlined by the Scottish Transitions Forum (*see section 11.3.2*)

✓ Families and services should plan ahead to reduce the impact of transitions.

✓ Social work contact with families should be instituted or extended during periods of transition.

✓ Families should be advised of relevant legislation under the Adults with Incapacity (Scotland) Act 2000,[235] the Adult Support and Protection (Scotland) Act 2007,[236] and the Children and Young People Act (Scotland) 2014.[2]

# 11 Provision of information

## 11.1 PROVIDING INFORMATION AND SUPPORT

Provision of information should always be viewed as a two-way process. The concerns and questions which children, young people, adults with ASD, and their parents/carers wish to raise should be identified during assessment, and be responded to as far as possible.

A limited amount of evidence was identified where either outcomes were not described in terms of parent satisfaction,[237] there was no information on the diagnostic instrument used to classify the children studied,[238] or the number of subjects was unclear.[239] The principles which emerged were that parents felt more satisfied if at the time of diagnosis sharing they were given good-quality written information, with an opportunity to ask questions[238] and that parents value a multidisciplinary diagnostic assessment.[239]

4

Information on the diagnostic process and the implications for children, young people, adults and parents should be explained along with information on the roles of the various professions involved. Parents and carers need to have their early concerns acknowledged and to receive support in the management of their child or the adult in their care.[238,240-242]

It is essential that parents or carers of individuals diagnosed with ASD, and the individual themselves, receive clear, accurate and appropriate written and verbal information about the condition including short- and long-term consequences. The information should be appropriate to the patient's age, ability level and cultural background and should be provided at a pace that suits the circumstances.

Where feasible and appropriate childcare should be made available for a short time during sharing of the diagnosis. This will allow parents or carers to focus fully on the information being given and allow for questions.

Consideration should be given as to how the diagnosis should be shared. This may require seeing children, young people and adults, their parents and carers separately, sequentially or simultaneously. For young people and adults their own engagement and understanding of the diagnosis will be important in negotiating appropriate supports.

Assessment is a particularly stressful period for the individual, their parents and carers and links forged with local professionals at this time can be helpful following diagnosis.

Surveys of parents report the importance placed on the quality of the communication skills of the professionals disclosing the diagnosis.[238,240-242] A negative experience could affect parental or carer satisfaction and cause added stress. Healthcare professionals should be aware that the absence of clearly-defined terminology and uncertainty of diagnosis is difficult for parents or carers. This can be challenging when the individual has a mixture of difficulties. Where a diagnosis can be clearly made the use of straightforward terminology in communication to parents and carers is important. When the diagnosis is uncertain (borderline according to current diagnostic criteria) then healthcare professionals should explain this situation to parents and carers. In all circumstances healthcare professionals should work with the family to identify how services can meet the needs of the child or adult.

Children, young people and adults, their parents or carers should have the opportunity to ask questions following the diagnosis. Follow-up arrangements should be offered once there has been time to reflect on the implications of the diagnosis.[17]

Professionals should recognise that children, young people and adults, their parents or carers may have a significant adjustment reaction to the diagnosis and for some this adjustment period may be prolonged and difficult.

ASD affects all aspects of the child's or adult's and the family's life and the importance of social support and family networks were noted.[228,231,232,241,243] Families are required to take on multiple roles when their child is diagnosed including at times, the roles of cotherapist, and advocate. Supporting family involvement in these roles is crucial and will impact on the success of any intervention.

A number of studies comment on the issue of encouraging families to participate in any decisions related to their child and the importance of feeling that their opinions are valued.[238,240-242]

The sample checklist in section 11.2 suggests the type of information individuals with ASD or their families/carers may require.

**R** **Professionals should offer individuals, parents and carers good-quality written information and an opportunity to ask questions when sharing information about the individual with ASD.**

**R** **Information should be provided in an accessible and understandable form.**

✓ For adults with ASD appropriate consent must be obtained before information is shared with carers.

✓ The information shared should relate to the individual's particular ASD presentation.

✓ People with ASD and their families/carers require support and high-quality verbal and written information at time of diagnosis. This should include a written report of the outcome of the various assessments and the final diagnosis. Copies of the letters sent to the various professionals who have been asked to assess their child or the adult may also be included.

✓ Professionals involved in sharing of an ASD diagnosis and information provision should receive ongoing education and training.

✓ Individuals with ASD and their parents, relatives or carers should be encouraged to continue to learn about ASD and about any useful interventions and support.

## 11.2 CHECKLIST FOR PROVISION OF INFORMATION

This section gives examples of the information patients/carers may find helpful at the key stages of the patient journey. The checklist was designed by members of the guideline development group based on their experience and their understanding of the evidence base. The points are provided for use by health professionals when discussing ASD with patients and carers and in guiding the production of locally-produced information materials. The checklist is neither exhaustive nor exclusive.

| **Before assessment** | |
|---|---|
| Initial professional concerned (eg health visitor, teacher, GP) should: | • explain to child/young person/adult and parent/carer that a person's behaviour shows various 'clinical clues' that may suggest the possibility of ASD or a social interaction or social communication difficulty (*see Annex 2*)<br>• discuss the advantages and disadvantages of further assessment with the individual (as appropriate) and/or parent/carer, as they see it, and check there is agreement to organise this |
| Person(s) making referral for further assessment should: | • include all relevant information regarding any concerns, the individual's current situation and details of any professionals involved<br>• explain the patient/parent/carer's understanding of the reason for referral<br>• consider providing the patient/parent/carer with a copy of the referral letter<br>• initiate general management/behaviour strategies and family support in the interim, if necessary by involving multiagency colleagues |
| The specialist team receiving the referral should: | • ensure that the patient and parents/carers receive information about the process which will follow referral, including likely timescale of any preassessment and assessment phases, and who will be involved<br>• if corresponding with professional colleagues to arrange assessments, consider copying correspondence to families<br>• consider developing protocols to gather as much relevant information preassessment as possible, in order to reduce assessment duration<br>• inform the parent/carer that they are welcome to bring a supporter to the assessment if they wish<br>• explain that, if any part of the assessment is to be video recorded, the team will obtain written consent of the patient and/or carer (as appropriate) to retain the recording |
| **At the assessment appointment(s)** | |
| The specialist team should: | • check the current understanding of the patient and parents/carers, as appropriate about the reasons for referral and their level of agreement with the concerns of the referring professional<br>• explain the proposed assessments and agree with patient and parent/carer how these will be organised and which colleagues will be involved<br>• repeat explanations and revise arrangements as needed<br>• if a diagnosis of ASD or any differential diagnosis is not confirmed, provide an explanation and respond constructively to any requests for a second opinion<br>• ensure that any identified unmet needs are signposted to the appropriate services |

| At any feedback appointment(s) | |
|---|---|
| The specialist team should:: | • allow sufficient time for explanation and discussion of the assessment findings and be sensitive to the potential distress that may arise in the patient and parent/carer and their possible needs to be seen separately<br>• find out what the patient and family understand about diagnosis and add information as appropriate (eg if a diagnosis of ASD has been made, a member of the team should explain how the referred patient's presentation fits into ICD-10 or DSM-5 criteria)<br>• include the diagnostic criteria used (ICD-10 or DSM-5) in the written feedback report<br>• offer basic information based on current knowledge about causation, intervention and prognosis, any investigations indicated, and the probable steps to provide appropriate multiagency supportive intervention<br>• provide information about what written feedback will be made available, and check with the patient and parent/relative/carer (as appropriate) how it should be shared with relevant multiagency colleagues<br>• if any part of the assessment has been video recorded, obtain written consent from the patient and parent/relative/carer (as appropriate) to retain the recording<br>• if the patient is considered unable to have the outcome of the assessment explained to them at feedback, discuss with the parent/carer how this might be undertaken at a later date and the best timescale<br>• in cases of diagnostic uncertainty, discuss with the patient and parent/relative/carer (as appropriate) how and when to best review/repeat the assessment, or options for further specialist assessment |
| **Supportive intervention following diagnosis of ASD** | |
| Multiagency multiprofessionals (integrated and collaborative and in partnership with the family) should: | • involve relevant multiagency colleagues (education, social work, voluntary sector, careers advisors, employers, as appropriate)<br>• tailor intervention to the requirements of the individual and family, working in partnership<br>• provide further information as needed, eg about impairments or coexisting conditions<br>• discuss potential educational approaches with the parent/carer and patient (as appropriate), including additional support for learning<br>• have in place arrangements for liaising/sharing required information with education services<br>• discuss wider family/sibling support, provision of respite, and the role of social work assistance<br>• provide information about:<br>- entitlement to social security benefits<br>- potential voluntary/community supports<br>- available parent training opportunities<br>- recommended sources of further information<br>• organise for the family to have a named contact for ongoing assistance (consider implementing the National Autism Plan for Children's recommendation for a key worker).[18] |

## 11.3 SOURCES OF FURTHER INFORMATION

**Autism Initiatives**
11 Granton Square, Edinburgh EH5 1HX
Tel: 0131 551 7260
www.autisminitiatives.org • E-mail: hos@aiscotland.org.uk

Autism Initiatives is a parent-led charity offering support to people with autism and their families.

**Autism Network Scotland**
Level 6, Curran Building, The University of Strathclyde, 101 St James Road, Glasgow G4 0NS
Tel: 0141 444 8146
www.autismnetworkscotland.org.uk • Email: autism.network@strath.ac.uk

Autism Network Scotland connects and communicates with those interested in the field of ASD. It signposts ASD professionals and practitioners, people with ASD, their families and carers toward examples of good practice, resources and information.

**Healthtalk.org**
www.healthtalk.org

Healthtalk.org provides free, reliable information about health issues, by sharing real-life experiences.

**National Autistic Society Scotland**
NAS Scotland, Central Chambers, 1st Floor, 109 Hope Street, Glasgow G2 6LL
Tel: 0141 221 8090
www.autism.org.uk • Email: scotland@nas.org.uk

The National Autistic Society Scotland works throughout Scotland to provide a wide range of quality, personalised support services for people with ASD and their families and carers.

**NHS inform**
Caledonia House, Fifty Pitches Road, Cardonald Park, Glasgow G51 4EB
Tel: 0800 22 44 88
www.nhsinform.co.uk • Email**:** nhs.inform@nhs24.scot.nhs.uk

NHS Inform is the national health information service for Scotland.

**Research Autism**
25 Nutford Place, London W1H 5YQ
Tel: 020 3490 3091
www.researchautism.net • Email: info@researchautism.net

Research Autism provides information on high-quality, independent research into new and existing health, education, social and other interventions.

**Scottish Autism (Autism Advice line)**
Hilton House, Alloa Business Park, Whins Road, Alloa FK10 3SA
Tel: 01259 222 022
www.scottishautism.org • Email: autism@scottishautism.org

Scottish Autism provides a team of autism advisors trained and experienced in working with people on the autism spectrum and who can offer personalised help and support.

**SWAN - Scottish Women's Autism Network**
www.autismnetworkscotland.org.uk/swan • Email: swan.scotland@gmail.com

SWAN works in partnership with Autism Network Scotland and offers peer support and networking opportunities to women with autism.

### 11.3.1 LOCAL SUPPORT GROUPS AND TELEPHONE HELPLINES

www.nhsinform.co.uk/support-services
Tel: 0800 22 44 88

The Support Service Directory on the NHS inform website provides details of local support groups.

### 11.3.2 PROFESSIONAL RESOURCES

**NHS Education for Scotland learning resource on autism spectrum disorders for GPs and primary care practitioners**
www.asd.nes.scot.nhs.uk

A learning resource designed for any professional who is working in the healthcare system at the primary-care level (eg general practitioners; allied health professionals, dentists, optometrists, public health nurses, district nurses, practice nurses, and dental nurses.

**NHS Education for Scotland e-learning module 'Practical Strategies for the Primary Care Practitioner'**
www.knowledge.scot.nhs.uk/home/learning-and-cpd/learning-spaces/autism-spectrum-disorder.aspx

This is a learning module that provides practitioners with advice about adapting routine consultations in primary care to accommodate the needs of people with ASD their families and carers.

**Scottish Strategy for Autism Menu of Interventions**
www.gov.scot/Resource/0043/00438221.pd**f**

This is a non-evidence-based, multi-agency guide to interventions and supports for people with ASD, in line with the Scottish Autism Strategy recommendations for good autism provision.

**Scottish Transitions Forum**
www.scottishtransitions.org.uk

The Scottish Transitions Forum aims to improve the experience of people with additional support needs, as they go through life transitions, particularly the transition of young people from school or college to adult life.

# 12 Implementing the guideline

This section provides advice on the resource implications associated with implementing the key clinical recommendations, and advice on audit as a tool to aid implementation.

## 12.1 IMPLEMENTATION STRATEGY

Implementation of national clinical guidelines is the responsibility of each NHS board and is an essential part of clinical governance. Mechanisms should be in place to review care provided against the guideline recommendations. The reasons for any differences should be assessed and addressed where appropriate. Local arrangements should then be made to implement the national guideline in individual hospitals, units and practices.

Implementation of this guideline will be encouraged and supported by SIGN. The implementation strategy for this guideline encompasses the following tools and activities.

## 12.2 RESOURCE IMPLICATIONS OF KEY RECOMMENDATIONS

No recommendations are considered likely to reach the £5 million threshold which warrants full cost impact analysis.

## 12.3 AUDITING CURRENT PRACTICE

A first step in implementing a clinical practice guideline is to gain an understanding of current clinical practice. Audit tools designed around guideline recommendations can assist in this process. Audit tools should be comprehensive but not time consuming to use. Successful implementation and audit of guideline recommendations requires good communication between staff and multidisciplinary team working.

The guideline development group has identified the following as key points to audit to assist with the implementation of this guideline:

- Are children undergoing universal child health surveillance activities being assessed for ASD?
- Are children presenting with developmental delay, emotional and behavioural problems, or genetic syndromes, receiving surveillance for ASD as part of their routine practice?
- Are individuals being diagnosed with ASD using ICD-10 or DSM-5?
- What is the number of females being diagnosed with ASD and the age of females at diagnosis compared to males?
- What is the number of patients with ASD who have a coexisting condition?
- Is there adequate linking from diagnosis of ASD in individuals into intervention and support services?
- Are individuals, parents and carers offered written information at the time of diagnosis?
- Are individuals with ASD and sleep difficulties being offered therapy?
- Are parent-mediated intervention programmes being offered and appraised?
- Are there interventions in place to support communication?
- Do children have access to support from staff trained in ABA-based interventions?
- Is there access to group CBT/tailored CBT for children and young people with ASD and anxiety?
- Are patients with ASD treated with second-generation antipsychotics reviewed after three weeks?
- What is the number of staff who have received ASD training in line with the Autism Training Framework?[54]

An audit tool designed to measure adherence to assessment recommendations in SIGN 98 is available.[11]

## 12.4 HEALTH TECHNOLOGY ASSESSMENT ADVICE FOR NHSSCOTLAND

In June 2007 the Scottish Medicines Consortium (SMC) advised that methylphenidate prolonged-release capsule (Medikinet XL®) is accepted for restricted use within NHSScotland as part of a comprehensive treatment programme for attention deficit hyperactivity disorder (ADHD) in children over six years of age when remedial measures alone prove insufficient.

Melatonin prolonged-release tablets (Circadin) are not recommended for use within NHSScotland as monotherapy for the short-term treatment of primary insomnia characterised by poor quality of sleep in patients who are aged 55 or over due to a lack of submission from the holder of the marketing authorisation (August 2008).

Melatonin prolonged-release tablets (Slenyto) are not recommended for use within NHSScotland for the treatment of insomnia in children and adolescents aged 2–18 with autism spectrum disorder (ASD) and/or Smith-Magenis syndrome, where sleep hygiene measures have been insufficient. The submitting company's justification of the treatment's cost in relation to its health benefits was not sufficient and the company did not present a sufficiently robust clinical and economic analysis to gain acceptance by SMC (September 2019).

# 13 The evidence base

## 13.1 SYSTEMATIC LITERATURE REVIEW

The evidence base for this guideline was synthesised in accordance with SIGN methodology. A systematic review of the literature was carried out using an explicit search strategy devised by an Evidence and Information Scientist. Databases searched include Medline, Embase, Cinahl, PsycINFO and the Cochrane Library. The year range covered was 2006–2014. Internet searches were carried out on various websites including the US National Guidelines Clearinghouse. The main searches were supplemented by material identified by individual members of the development group. Each of the selected papers was evaluated by two members of the group using standard SIGN methodological checklists before conclusions were considered as evidence.

### 13.1.1 LITERATURE SEARCH FOR PATIENT ISSUES

At the start of the guideline development process, an Evidence and Information Scientist conducted a literature search for qualitative and quantitative studies that addressed patient issues of relevance to diagnosis and interventions for patients with ASD. Databases searched include Medline, Embase, Cinahl and PsycINFO, and the results were summarised by the SIGN Patient Involvement Officer and presented to the guideline development group.

### 13.1.2 LITERATURE SEARCH FOR COST EFFECTIVENESS

The guideline development group identified key questions with potential cost-effectiveness implications where it was judged particularly important to gain an understanding of the additional costs and benefits of different intervention strategies, based on the following criteria:

- treatments which may have a significant resource impact
- opportunities for significant disinvestment or resource release
- the potential need for significant service redesign
- cost-effectiveness evidence could aid implementation of a recommendation.

A systematic literature search for economic evidence for these questions was conducted using Medline, Embase, NHS Economic Evaluation Database (NHS EED) and Health Economics Evaluation Database (HEED), covering the years 2010–2014. Papers were selected and evaluated by a Health Economist, and considered for clinical relevance by guideline group members.

Interventions are considered to be cost effective if they fall below the commonly-accepted UK threshold of £20,000 per quality-adjusted life year (QALY).

The key questions are listed in Annex 1.

## 13.2 RECOMMENDATIONS FOR RESEARCH

The guideline development group was not able to identify sufficient evidence to answer all of the key questions asked in this guideline (*see Annex 1*). The following areas for further research have been identified:

- Studies into case identification instruments using populations that have not previously encountered the diagnostic journey or already been diagnosed with ASD. These populations may not have the insight to complete the questionnaire in the same way. A supporting question would be, do individuals with undiagnosed ASD complete questionnaires in the same way as individuals with diagnosed ASD?
- Studies into the adaptation and/or development of identification and screening tools for children and adults with ASD who have an intellectual disability.
- Research into the impact of the professional make-up of the diagnostic team and the assessment processes used on the speed and quality of diagnosis.
- A study to ascertain whether the identification of ASD in adults with an eating disorder provides patient benefit through improved management options.
- A study to determine the diagnostic utility of the combined use of ADI-R and ADOS in children.
- Studies on the accuracy of neuropsychological assessment tools in the diagnostic process for identifying ASD.
- Further research into the benefits of social-skills groups with consistent definitions of interventions, target populations and outcome measures, particularly those related to improvements in quality of life.
- Research into PECS, including measures of treatment fidelity, maintenance and generalisation, and speech and communication outcomes compared to other interventions for people with ASD. The potential influence of pretreatment variables (eg joint attention) should be taken into account.
- Studies on the efficacy of computer-based interventions to improve social skills and identify individual characteristics which may predict the effectiveness of CBI. The research should consider the preferences and abilities of the individual with ASD, and whether the software can be customised to their needs.
- Further research into EIBI with improved methodological rigour and long-term follow up.
- Studies on the cost effectiveness of EIBI.
- A study of the impact of high-intensity interventions on families and siblings.
- A study into the factors associated with decline in benefit of EIBI (between the ages 3 and 4 and age 5 and 6), including what the associated factors may be (for example starting school, or condition-related factors), whether a decline is found in neurotypical and other conditions, and whether the decline resolves over time.
- Studies of the short- and long-term efficacy of psychological therapies compared to placebo, attention control or pharmacological interventions. Better measures of outcomes, particularly self-reported outcomes (for example quality of life, symptoms and emotional distress) are needed to support research into these interventions. Studies should consider cost effectiveness and efficacy of modifications to therapies to adapt to ASD (for example inclusion of parents, longer sessions, more frequent sessions).
- Studies of Social Stories™ to include data on generalisation and maintenance of skills.
- Studies into who benefits from skills-based interventions – younger children, older children or adults.
- An RCT of auditory integration therapy, with explicit methodology and validated outcome measures. The trial should demonstrate how AIT has modulated the music delivered, what type of filtering has been involved to attenuate sounds at selected frequencies, and how they have been modulated.
- Controlled trials with large sample sizes to evaluate the efficacy of sensory integration and sensory-based interventions.
- RCTs on behavioural interventions to reduce behaviour that challenges with outcomes measured over long follow-up periods.
- A study into the neurophysiological mechanisms by which sensory regulation influences psychological state and behaviour in ASD.
- An adequately powered, blinded RCT on the efficacy of gluten-free and casein-free diets. Monitoring of adverse dietary impacts should be included.

- An adequately powered, blinded RCT on the efficacy of omega-3 supplementation for improving outcomes related to ASD symptomatology and quality of life.
- Interventions that employ complementary and alternative therapies for ASD should be evaluated through well-designed trials if there is a theoretical plausible hypothesis as to why they might have benefit.
- RCTs for physical exercise interventions in ASD.
- An RCT to establish the efficacy and safety of atomoxetine for reducing ADHD symptoms in people with ASD.
- An RCT to clarify the nature and extent of increased side effects from stimulant use in patients with ASD compared to those with ADHD (non ASD).
- Studies to determine the influence of gender on the efficacy of long-acting psychostimulants.
- Large RCTs to determine the efficacy and safety of TCAs for improving core symptoms of ASD. The effects of TCAs on coexisting conditions common in people with ASD should also be studied.
- A large RCT, with female participation, to determine the efficacy of oxytocin in improving ASD symptoms.
- Long-term study of the efficacy, safety and cost effectiveness of melatonin compared to behavioural interventions for managing sleep problems.
- Any studies into the presentation, assessment and management of ASD in older adults, to ascertain the nature and extent of ASD in this age group.

Standardised outcome measures specific to ASD are required to ensure comparisons can be made across studies.

## 13.3 REVIEW AND UPDATING

This guideline was issued in 2016 and will be considered for review in three years. The review history, and any updates to the guideline in the interim period, will be noted in the review report, which is available in the supporting material section for this guideline on the SIGN website: www.sign.ac.uk

Comments on new evidence that would update this guideline are welcome and should be sent to the SIGN Executive, Gyle Square, 1 South Gyle Crescent, Edinburgh, EH12 9EB (email: sign@sign.ac.uk).

# 14 Development of the guideline

## 14.1 INTRODUCTION

SIGN is a collaborative network of clinicians, other healthcare professionals and patient organisations and is part of Healthcare Improvement Scotland. SIGN guidelines are developed by multidisciplinary groups of practising healthcare professionals using a standard methodology based on a systematic review of the evidence. Further details about SIGN and the guideline development methodology are contained in 'SIGN 50: A Guideline Developer's Handbook', available at **www.sign.ac.uk**

This guideline was developed according to the 2015 edition of SIGN 50.

## 14.2 THE GUIDELINE DEVELOPMENT GROUP

| | |
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The membership of the guideline development group was confirmed following consultation with the member organisations of SIGN. All members of the guideline development group made declarations of interests. A register of interests is available in the supporting material section for this guideline at **www.sign.ac.uk**

Guideline development and literature review expertise, support and facilitation were provided by the SIGN Executive.

| | |
|---|---|
| Mr Euan Bremner | *Project Officer* |
| Ms Karen Graham | *Patient Involvement Officer* |
| Ms Karen King | *Distribution and Office Co-ordinator* |
| Mr Stuart Neville | *Publications Designer* |
| Miss Gaynor Rattray | *Guideline Co-ordinator* |

All members of the SIGN Executive make yearly declarations of interests. A register of interests is available on the contacts page of the SIGN website **www.sign.ac.uk**

### 14.2.1 ACKNOWLEDGEMENTS

SIGN would like to acknowledge the guideline development group responsible for the development of SIGN 98: Assessment, diagnosis and clinical interventions for children and young people with autism spectrum disorder, on which this guideline is based.

SIGN is grateful to the following former members of the guideline development group:

| | |
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| Ms Jane Ansell | *Chief Executive, Sleep Scotland, Edinburgh* |
| Dr Jill Ogston | *Clinical Psychologist, Child and Adolescent Mental Health Service, Ayrshire Central Hospital* |
| Dr Andrew Watson | *Consultant Psychiatrist, NHS Lothian* |


## 14.3 CONSULTATION AND PEER REVIEW

A report of the consultation and peer review comments and responses is available in the supporting material section for this guideline on the SIGN website. All expert referees and other contributors made declarations of interests and further details of these are available on request from the SIGN Executive.

### 14.3.1 SPECIALIST REVIEW

This guideline was reviewed in draft form by the following independent expert referees, who were asked to comment primarily on the comprehensiveness and accuracy of interpretation of the evidence base supporting the recommendations in the guideline. The guideline group addresses every comment made by an external reviewer, and must justify any disagreement with the reviewers' comments.

SIGN is very grateful to all of these experts for their contribution to the guideline.

| | |
|---|---|
| Professor Gillian Baird | *Consultant Paediatrician (Neurodisability), Guy's and St Thomas Trust, London* |
| Professor Simon Baron-Cohen | *Professor of Developmental Psychopathology, Director, Autism Research Centre, Cambridge University* |
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| | |
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| Dr Gillian Scott | *Trainee Psychiatrist, Kirklands Hospital, Bothwell* |
| Professor Fred Volkmar | *Irving B. Harris Professor, Child Study Center, Yale University School of Medicine, New York* |

### 14.3.2 PUBLIC CONSULTATION

The draft guideline was also available on the SIGN website for a month to allow all interested parties to comment.

### 14.3.3 SIGN EDITORIAL GROUP

As a final quality control check, the guideline is reviewed by an editorial group comprising the relevant specialty representatives on SIGN Council to ensure that the specialist reviewers' comments have been addressed adequately and that any risk of bias in the guideline development process as a whole has been minimised. The editorial group for this guideline was as follows. All members of SIGN Council make yearly declarations of interest. A register of interests is available on the SIGN Council membership page of the SIGN website **www.sign.ac.uk**

| | |
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| Dr Iris Clarke | *Allied Health Professions* |
| Dr Roberta James | *SIGN Programme Lead; Co-Editor* |
| Professor John Kinsella | *Chair of SIGN; Co-Editor* |
| Professor Ronan O'Carroll | *British Psychological Society* |
| Dr Werner Pretorius | *Royal College of Psychiatrists in Scotland* |
| Dr Karen Ritchie | *Healthcare Improvement Scotland* |
| Mr Alan Timmins | *Royal Pharmaceutical Society* |

# Abbreviations

| | |
|---|---|
| **3di** | Developmental, Dimensional and Diagnostic Interview |
| **ABA** | applied behaviour analysis |
| **ABC** | Autism Behaviour Checklist |
| **ADHD** | attention deficit hyperactivity disorder |
| **ADI-R** | Autism Diagnostic Interview-revised |
| **ADOS-G** | Autism Diagnostic Observation Schedule-Generic |
| **AIT** | auditory integration training |
| **AQ** | Autism Spectrum Quotient |
| **ASC** | autism spectrum condition |
| **ASD** | autistic spectrum disorder |
| **ASQ/SCQ** | Autism Screening Questionnaire/Social Communication Questionnaire |
| **ASSQ** | Autism Spectrum Screening Questionnaire |
| **AUC** | area under the curve |
| **CARS** | Childhood Autism Rating Scale |
| **CAST** | Childhood Asperger Syndrome Test |
| **CBI** | computer-based interventions |
| **CBT** | cognitive behavioural therapy |
| **CGH** | comparative genomic hybridisation |
| **CGI** | Clinical Global Impression |
| **CHAT** | Checklist for Autism in Toddlers |
| ***d*** | Cohen's *d* effect size; small ($d$ =0.2), medium ($d$ =0.5), and large ($d \geq 0.8$) |
| **DISCO** | Diagnostic Interview for Social and Communication Disorders |
| **DSM** | Diagnostic and Statistical Manual of Mental Disorders |
| **EEG** | electroencephalogram |
| **EIBI** | early intensive behavioural interventions |
| **ESDM** | Early Start Denver Model |
| **GIRFEC** | Getting it Right for Every Child |
| **GMC** | General Medical Council |
| **Hall 4** | Health for all children, 4th edition |
| **HEED** | Health Economics Evaluation Database |
| **ICD** | International Classification of Diseases |
| **ICER** | incremental cost effectiveness ratio |
| **IQ** | intelligence quotient |
| **LEAP** | Learning Experiences and Alternative Program |
| **MA** | marketing authorisation |

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| **M-CHAT** | Modified Checklist for Autism in Toddlers |
| ***MECP2*** | methyl-CPG-binding protein 2 |
| **MRI** | magnetic resonance imaging |
| **MTA** | multiple technology appraisal |
| **NHS EED** | NHS Economic Evaluation Database |
| **NICE** | National Institute for Health and Care Excellence |
| **NPV** | negative predictive value |
| **OCD** | obsessive-compulsive disorder |
| **OR** | odds ratio |
| **OT** | occupational therapist |
| **PACT** | Parent-Mediated Communication-focused Treatment |
| **PDD** | pervasive developmental disorder |
| **PDD-MRS** | Pervasive Developmental Disorder in Mental Retardation Scale |
| **PECS** | Picture Exchange Communication System |
| **PEDS** | Parents Evaluation of Developmental Status |
| **PPV** | positive predictive value |
| ***PTEN*** | phosphatase and tensin homolog |
| **QALY** | quality-adjusted life years |
| **RCT** | randomised controlled trial |
| **RR** | relative risk |
| **SBI** | sensory-based intervention |
| **SD** | standard deviation |
| **SIGN** | Scottish Intercollegiate Guidelines Network |
| **SIT** | sensory integration therapy |
| **SMC** | Scottish Medicines Consortium |
| **SMD** | standardised mean difference |
| **SOL** | sleep onset latency |
| **SPC** | summary of product characteristics |
| **SSRI** | selective serotonin reuptake inhibitors |
| **STAT** | Screening Tool for Autism in Two-Year Olds |
| **TCA** | tricyclic antidepressant |
| **TEACCH** | Treatment and Education of Autistic and Related Communication Handicapped Children |
| **UCLA** | University of California, Los Angeles |

# Annex 1

## Key questions addressed in this update

This guideline is based on a series of structured key questions that define the target population, the intervention, diagnostic test, or exposure under investigation, the comparison(s) used and the outcomes used to measure efficacy, effectiveness, or risk. These questions form the basis of the systematic literature search.

| Guideline section | Key question | |
|---|---|---|
| 4.1.3, 4.1.5, Annex 3 | 1 | Which of the following factors are useful in helping to identify a child or adolescent at increased risk of autism/ASD?<br>• preterm infants, adverse events in utero or trauma at birth<br>• familial history of autism/ASD<br>• children whose parents have mental health problems<br>• maternal use of antidepressants or anticonvulsants<br>• adolescents who have eating disorders<br>• additional educational or support needs/ specific learning disorders<br>• groups at risk of exclusion, eg ethnic minorities<br>• living in urban versus rural areas |
| 4.6 | 1a | Is there evidence that specific findings at the time of ASD diagnosis can reliably predict prognosis? |
| 4.1.3 | 2 | Is the use of a structured assessment tool more effective than an unstructured review for early identification of children with potential autism/ASD at the 27–30 month health check?<br>If so, which structured tool is the most robust for early identification? Does efficacy differ depending on the gender of the child?<br>Tools: ASQ, Modified Checklist for Autism in Toddlers (M-CHAT), Parents Evaluation of Developmental Status (PEDS), SureStart Language Scale, Strengths and Difficulties Questionnaire<br>Outcomes: to prompt referral. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) |
| 4.2.2 | 3 | Does multidisciplinary or single practitioner assessment of children and adolescents with suspected autism/ASD provide more accurate diagnosis, a more comprehensive profile, and most efficiency in terms of the length of time taken for the assessment and speed of assessment to feedback on diagnosis?<br>If multidisciplinary assessment is better, which healthcare professionals should be involved?<br>Consider: cost/health economics<br>Consider: rural versus urban |
| 4.2.3 | 4 | In children or adolescents with suspected autism/ASD is diagnosis more reliable if both ADOS and ADI-R are used, compared to a single tool or neither?<br>Which interview tool is most effective?<br>Which observational tool is most effective?<br>Does efficacy differ depending on the gender of the child/adolescent?<br>Consider: the level training for professionals using the tool |

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| 4.1.6 | 5 | Are there differences in the way girls with autism/ASD present and respond to interventions compared to boys?<br><br>Consider: triad/dyad of symptoms |
| 4.3.2 | 6 | Are there neuropsychological assessment tools for children and adolescents that can accurately detect autism/ASD?<br><br>Executive function tests:<br>• NEPSY-Theory of Mind, Memory for faces, Affect recognition<br>• Deliskaplan, Executive Function System (DKEFS)<br>• Behavioural Assessment of Dysexecutive Syndrome (BADS)<br>• Others: Weschler Intelligence Scale for Children (WISC)<br>• Weschler Adult Intelligence Scale (WAIS)<br>• Weschler Memory Scales (WMS/CMS)<br>• BRIEF Neuropsychological Cognitive Examination<br>• Happé Stories<br><br>Outcomes: sensitivity, specificity, PPV, NPV |
| 4.5 | 7 | In children and adolescents with suspected ASD, does genetic testing aid accurate diagnosis, speed of diagnosis, and inform appropriate follow up? |
| 6.2, 6.3.2, 6.3.9, 6.5 | 8 | In children and adolescents with autism/ASD, are any of the following interventions effective in improving outcome?<br>• Social Stories™<br>• computer-based interventions<br>• social skills groups<br>• Picture Exchange Communication System (PECS)<br>• Treatment and Education of Autistic and Related Communication Handicapped Children (TEACCH)<br>• interventions for behaviour that challenges<br>• see additional search terms on page 62<br><br>Outcomes: improved communication and social interaction, quality of life, behavioural improvement, repetitive interests/activities; reduction in overall autistic behaviours |
| 6.3.1 | 9 | In children and adolescents with autism/ASD, are early intensive behaviour interventions effective in improving outcome?<br><br>Outcomes: improved communication and social interaction, repetitive interests/activities, reduction in overall autistic behaviours, behavioural improvements, adaptive functioning, quality of life |
| 6.3.3 | 10 | In children and adolescents with autism/ASD do psychological therapies improve outcome?<br>• cognitive behavioural therapy<br>• cognitive remediation therapy<br><br>Comparison: other interventions, no therapy<br><br>Outcomes: improvement in mental health and social functioning, improved communication and social interaction, repetitive interests/activities; reduction in overall autistic behaviours, behavioural improvement, quality of life<br><br>Consider: cost effectiveness |

| | | |
|---|---|---|
| 6.3.5 | 11 | In children and adolescents with autism/ASD, does sensory integration therapy improve outcomes?<br><br>Comparison: other interventions, no therapy<br><br>Outcomes: improvement in repetitive interests/activities; reduction in overall autistic behaviours, behavioural improvement, sensory profiles/sensory modulation, quality of life |
| 6.3.7, 6.4, 8.8 | 12 | In children and adolescents with autism/ASD and sleep problems, do any of the following interventions improve outcomes:<br>• cognitive/behavioural interventions<br>• sleep programme<br>• referral to a sleep counsellor<br>• omega-3 fatty acids supplementation<br>• melatonin<br><br>Outcomes: improvements in sleep patterns, sleep hygiene and sleep problems, daytime learning and daytime behaviour, quality of life |
| 6.4 | 13 | In children and adolescents with autism/ASD, do the following nutritional interventions improve outcome, compared to children without ASD:<br>• omega-3 fatty acids supplementation<br>• gluten-free and casein-free diets<br><br>Outcomes: improvement in repetitive interests/activities; reduction in overall autistic behaviours, behavioural improvement, gastrointestinal symptoms and growth quality of life |
| 8 | 14 | In children and adolescents with autism/ASD, does use of, or discontinuing the use of, any of the following pharmacological therapies improve outcomes?<br>• risperidone<br>• aripiprazole<br>• antidepressants and anxiolytics<br>• SSRIs, fluoxetine, sertraline<br>• tricyclic antidepressants<br>• anticonvulsants<br>• hormonal interventions<br>• SNRIs<br>• antihistamines and antioxidants<br>• secretin<br>• stimulants<br><br>Outcomes: improvement in repetitive interests/activities; reduction in overall autistic behaviours, behavioural improvement, improvements in mental health, side effects, IQ, improvement in communication and social interaction, quality of life<br><br>Consider: cost effectiveness |

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|---|---|---|
| 10<br><br>(no new evidence identified) | 15 | Are particular models of service delivery more effective than others in improving outcomes in children, adolescents or adults with autism/ASD?<br>• ASD-specific service versus general service<br>• multidisciplinary service/agency versus single agency<br>• clinical integrated pathway compared to single service<br>• single-day assessment clinics<br><br>Outcomes: improvement in repetitive interests/activities, reduction in overall autistic behaviours, behavioural improvement, IQ, improved communication and social interaction, quality of life, improved reliability and validity of diagnosis, reduction in waiting times |
| 4.1.6 | 16 | What is the effectiveness of screening for ASD in adults who have mental ill health, eg recurrent severe depression, a family history of ASD, or other developmental disorders?<br><br>Outcomes: speed of diagnosis, quality of life |
| 4.1.6 | 17 | What signs or symptoms should prompt any professional who comes into contact with an adult with possible autism/ASD to consider assessment?<br><br>Outcomes: to prompt referral, sensitivity, specificity, PPV, NPV, area under the curve (AUC) |
| 4.1.8 | 18 | What are the most effective methods/tools for case identification in autism/ASD in adults?<br><br>Comparison: DSM or ICD |
| 4.2.2 | 19 | In adults with possible autism/ASD, what are the key components of, and the most effective structure for, a diagnostic assessment? To answer this question, consideration should be given to:<br>• the nature and content of the clinical interview and observation (including an early developmental history where possible)<br>• formal diagnostic methods/ psychological instruments (including risk assessment)<br>• biological measures<br>• the setting(s) in which the assessment takes place<br>• who the informant needs to be (to provide a developmental history)<br>• comorbidities<br><br>Outcomes: sensitivity and specificity, PPV, NPV, reliability, validity, AUC |
| 7 | 20 | For adults with autism/ASD, what are the benefits and/or potential harms associated with different psychosocial interventions (for example, applied behavioural analysis, cognitive behavioural therapy, mentoring, social groups, and befriending schemes)?<br><br>Comparison: treatment as usual, waitlist control, other interventions<br><br>Outcomes: improved social interaction, communication, repetitive interests/activities, reduction in overall autistic behaviours, improved management of behaviour that challenges, outcomes involving treatment of coexisting conditions |
| 9 | 21 | For adults with autism/ASD, what is the effectiveness of biomedical interventions:<br>• pharmacotherapy (eg antipsychotics, antidepressants, anticonvulsants)<br>• vitamins and dietary supplements (eg omega-3 fatty acid supplements, vitamin $B_{12}$, vitamin A)<br>• hormones (eg oxytocin, secretin, melatonin)<br><br>Comparison: placebo, other interventions<br><br>Outcomes: improved social interaction, communication, repetitive interests/activities; reduction in overall autistic behaviours, improved management of behaviour that challenges, outcomes involving treatment of coexisting conditions, side effects |

| **Additional search terms for KQ 8:** | |
|---|---|
| Animal/pet therapy | Precision teaching |
| Art therapy | Psychotherapy; autogenic training |
| Auditory integration therapy | Psychodynamic psychotherapy |
| British sign language | SCERTS® |
| Child's talk | Self awareness training |
| Communication/language training; augmentive communication | Sensory integration therapy |
| DDAT (Dyslexia, Dyspraxia, Attention Deficit Treatment Centre) Developmental skills | Sexual health |
| Dolphins | Social communication training |
| EarlyBird | Sonrise OPTIONS |
| Facilitated communication | SPELL |
| Gentle teaching; growing minds; intensive interaction | SPIRALS |
| Hanen Parent Programme | Talking mats |
| Heavy metal chelation | Teaching methods; brain gym |
| HELP | Theory of mind training |
| Holding therapy | Tomatis method |
| Hyperacusis prevention | Total communication |
| Light and sound therapy | Verbal behaviour |
| Makaton | Visual language |
| Movement programmes; physical exercise | Visual therapies; colorimetric therapy; Irlen lenses/glasses; orthoptics |
| Parent programmes | White noise |
| Portage | Ward Infant Language Screening Test Assessment Acceleration Remediation (WILSTAAR) |

# Annex 2

## Indicators of possible ASD

| **Preschool children**[244] |
|---|
| • delay or absence of spoken language<br>• looks through people; not aware of others<br>• not responsive to other people's facial expression/feelings<br>• lack of pretend play; little or no imagination<br>• does not show typical interest in or play near peers purposefully<br>• lack of turn-taking<br>• unable to share pleasure<br>• qualitative impairment in non-verbal communication<br>• does not point at an object to direct another person to look at it<br>• lack of gaze monitoring<br>• lack of initiation of activity or social play<br>• unusual or repetitive hand and finger mannerisms<br>• unusual reactions, or lack of reaction, to sensory stimuli. |
| **School-age children**[18] |
| **Communication impairments:**<br>• abnormalities in language development including muteness<br>• odd or inappropriate prosody<br>• persistent echolalia<br>• reference to self as 'you', 'she' or 'he' beyond three years<br>• unusual vocabulary for child's age/social group<br>• limited use of language for communication and/or tendency to talk freely only about specific topics<br>• qualitative impairment in non-verbal communication.* |
| **Social impairments:**<br>• inability to join in play of other children or inappropriate attempts at joint play (may manifest as aggressive or disruptive behaviour)<br>• lack of awareness of classroom 'norms' (criticising teachers, overt unwillingness to co-operate in classroom activities, inability to appreciate or follow current trends)<br>• easily overwhelmed by social and other stimulation<br>• failure to relate normally to adults (too intense/no relationship)<br>• showing extreme reactions to invasion of personal space and resistance to being hurried. |
| **Impairments of interests, activities and/or behaviours:**<br>• lack of flexible co-operative imaginative play/creativity<br>• difficulty in organising self in relation to unstructured space (eg hugging the perimeter of playgrounds, halls)<br>• inability to cope with change or unstructured situations, even ones that other children enjoy (school trips, teachers being away etc). |
| **Other factors:**<br>• unusual profile of skills/deficits<br>• any other evidence of odd behaviours including unusual responses to sensory stimuli. |

*Based on the expert opinion of the guideline development group

**Adolescents***

These indicators are in addition to those in younger children. Difficulties are likely to be more subtle in older individuals or those without intellectual disability.

**General picture:**

- long standing difficulties in social behaviours, communication and coping with change, which are more obvious at times of transition (eg change of school, leaving school)
- significant discrepancy between academic ability and 'social' intelligence, most difficulties in unstructured social situations, eg in school or work breaks
- socially 'naïve', lack common sense, not as independent as peers.

**Language, non-verbal skills and social communication:**

- problems with communication, even if wide vocabulary and normal use of grammar. May be unduly quiet, may talk at others rather than hold a to and fro conversation, or may provide excessive information on topics of own interest
- unable to adapt style of communication to social situations eg may sound like 'a little professor' (overly formal), or be inappropriately familiar
- may have speech peculiarities including 'flat', unmodulated speech, repetitiveness, use of stereotyped phrases
- may take things literally and fail to understand sarcasm or metaphor
- unusual use and timing of non-verbal interaction (eg eye contact, gesture and facial expression).

**Social problems:**

- difficulty making and maintaining peer friendships, though may find it easier with adults or younger children
- can appear unaware or uninterested in peer group 'norms', may alienate by behaviours which transgress 'unwritten rules'
- may lack awareness of personal space, or be intolerant of intrusions on own space.

**Rigidity in thinking and behaviour:**

- preference for highly specific, narrow interests or hobbies, or may enjoy collecting, numbering or listing
- strong preferences for familiar routines, may have repetitive behaviours or intrusive rituals
- problems using imagination eg in writing, future planning
- may have unusual reactions to sensory stimuli eg sounds, tastes, smell, touch, hot or cold.

*Based on the expert opinion of the guideline development group

**Adults**[13]

- persistent difficulty in social interaction
- persistent difficulty in social communication
- stereotypic (rigid/repetitive) behaviours, resistance to change
- restricted interests
- problems with obtaining/sustaining employment/education
- difficulty in initiating or sustaining social relationships
- history of neurodevelopmental condition (including intellectual disability and ADHD) or mental disorder
- gender dysphoria
- diagnosis of an eating disorder.

**Adults who have a moderate or severe intellectual disability[13]**

If necessary use information from a family member, partner or carer.

Presence of two or more of the following:

- difficulties in reciprocal social interaction including:
  - limited interaction with others (eg being aloof, indifferent or unusual)
  - interaction to fulfil needs only
  - interaction that is naive or one sided
- lack of responsiveness to others
- little or no change in behaviour in response to different social situations
- limited social demonstration of empathy
- rigid routines and resistance to change
- marked repetitive activities (eg rocking and hand or finger flapping), especially when under stress or expressing emotion.

*Individuals with severe intellectual disability without ASD may present with rigid routines, repetitive activities and limited empathy. Those with this level of intellectual disability and ASD will present with a more significant level of such difficulties with a qualitative autistic difference.*

# Annex 3

## Risk factors for autism and ASD

Adjusted relative risk or odds ratios for factors for autism[5]

| Factors | Studies | Quality | Number of participants | | Adjusted OR/RR (95%CI) |
|---|---|---|---|---|---|
| | | | ASD | Non-ASD | |
| **Familiar or parental factors** | | | | | |
| Maternal age over 40 years | 1 | Low | 12,159 | 4,935,776 | Adj OR 1.51 (1.35 to 1.70) |
| Mother's race(black) | 2 | Low | 4,957 | 3,498,470 | Adj OR 1.66 (1.48 to 1.85) |
| Paternal age over 40 years | 1 | Low | 12,159 | 4,935,776 | Adj OR 1.36 (1.26 to 1.47) |
| **Perinatal or neonatal factors** | | | | | |
| Birthweight under 2500 g | 2 | Low | 655 | 90,358 | Adj OR 2.15 (1.47 to 3.15) |
| Prematurity (under 37 weeks) | 1 | Low | 182 | 85,628 | Adj OR 2.3 (1.5 to 3.7) |
| Admission to neonatal intensive care unit | 1 | Low | 461 | 461 | Adj OR 1.8 (1.3 to 2.7) |
| Male gender | 3 | Low | 5,439 | 3,584,098 | Adj OR 4.28 (4.02 to 4.57) |
| Serum bilirubin test undertaken | 1 | Low | 461 | 461 | Adj OR 3.7 (1.3 to 10.5) |
| Hypertonic/hyper-reflexive/ jittery | 1 | Low | 461 | 461 | Adj OR 6.7 (1.5 to 29.7) |
| **Pregnancy-related factors** | | | | | |
| No studies found for this analysis | | | | | |
| **Environmental factors** | | | | | |
| No studies found for this analysis | | | | | |
| Reproduced with permission from National Institute for Health and Clinical Excellence (2011) *CG 128: Autism: recognition, referral and diagnosis of children and young people on the autism spectrum*. London: NICE. Available from www.nice.org.uk/CG128 | | | | | |

Adjusted relative risk or odds ratios for factors for ASD[5]

| Factors | Studies | Quality | Number of participants | | Adjusted OR/RR (95%CI) |
|---|---|---|---|---|---|
| | | | ASD | Non-ASD | |
| **Familiar or parental factors** | | | | | |
| Sibling history of autism | 1 | Low | 818 | 942,836 | Adj RR 22.27 (13.09 to 37.90) |
| Sibling history of ASD | 1 | Low | 818 | 942,836 | Adj RR 13.40 (6.93 to 25.92) |
| Parental history of schizophrenia-like psychosis | 1 | Low | 698 | 17,450 | Adj RR 3.44 (1.48 to 7.95) |
| Parental affective disorder | 1 | Low | 698 | 17,450 | Adj RR 2.91 (1.65 to 5.14) |
| Parental history of other mental and behavioural disorder diagnosis | 1 | Low | 698 | 17,450 | Adj RR 2.85 (2.20 to 3.69) |
| Paternal age 40–49 years | 1 | Low | 110 | 132,161 | Adj OR 5.75 (2.65 to 12.46)[a] |
| Paternal age 31–35 years | 1 | Low | 1,227 | 30,693 | Adj OR 1.7 (1.3 to 2.1)[b] |
| Paternal age 36–40 years | 1 | Low | 1,227 | 30,693 | Adj OR 1.8 (1.4 to 2.4)[b] |
| Paternal age 41–50 years | 1 | Low | 1,227 | 30,693 | Adj OR 1.9 (1.4 to 2.5)[b] |
| Paternal age 50 years or older | 1 | Low | 1,227 | 30,693 | Adj OR 2.7 (1.5 to 4.8)[b] |
| Maternal history of neurotic/ personality disorders | 1 | Low | 1,227 | 30,693 | Adj OR 1.7 (1.3 to 2.2) |
| Parental mental and behavioural disorder diagnosis | 1 | Low | 1,227 | 30,693 | Adj OR 1.7 (1.5 to 2.0) |
| **Perinatal or neonatal factors** | | | | | |
| Multiple birth defects | 2 | Low | 882 | 2,548 | Adj OR 2.73 (1.37 to 5.42) |
| Prematurity (under 28 weeks) | 1 | Low | 1,251 | 253,347 | Adj OR 2.5 (1.6 to 3.9) |
| Prematurity (under 35 weeks) | 1 | Low | 595 | 14,875 | Adj OR 2.45 (1.55 to 3.86) |
| Any birth defects | 2 | Low | 882 | 6,380 | Adj OR 1.7 (1.31 to 52.20) |
| Male gender | 1 | Low | 1,251 | 253,347 | Adj OR 4.2 (3.7 to 4.9) |
| **Pregnancy-related factors** | | | | | |
| Threatened abortion at before 20 weeks | 1 | Low | 465 | 1,313 | Adj OR 2.09 (1.32 to 3.32) |
| Elective caesarean | 1 | Low | 465 | 1,313 | Adj OR 1.83 (1.32 to 2.54) |
| Residing in capital city | 1 | Low | 818 | 942,836 | Adj RR 2.05 (1.67 to 2.51) |
| Residing in capital city suburb | 1 | Low | 818 | 942,836 | Adj RR 1.67 (1.35 to 2.06) |

a. reference group 15–29 years

b. reference group 25 years or younger

# Annex 4

## Structured instruments for use in screening high risk groups

| Instrument | Format | Description | Target Age Range |
|---|---|---|---|
| Pervasive Developmental Disorders Rating Scale[229] | Completed by a professional | Adequate reliability | 1–18 years old |
| Modified-Checklist for Autism in Toddlers (**M-CHAT**) [30] | Parent questionnaire | Developed from the CHAT, accurately discriminates autism from other developmental disorders | 18–30 months old |
| The Childhood Autism Rating Scale (**CARS and CARS-2**) [53] | Completed by professionals after taking a clinical history and observing the child | | Over 2 years old |
| The Screening Tool for Autism in Two Year Olds (**STAT**) [34] | Completed by a professional after interacting with the child in a structured play context | High sensitivity, specificity and acceptable reliability | 24–35 months old |
| Checklist for Autism in Toddlers (**CHAT**) [37] | Completed by a professional after a brief interview with parents and a semi-structured observation period with the child | Accurately discriminates autism from other developmental disorders | 2–3 years old |
| The Social Communication Disorders Checklist[230] | Parent self report | Good reliability and validity | 3–18 years old |
| Social Communication Questionnaire[36] | Parent or primary care giver report | Based on ADI-R, able to discriminate between children with a diagnosis of an ASD and children who do not have an ASD | Over 4 years old |
| Social Responsiveness Scale[231] | Parent or teacher report | Measures the severity of social impairment. Correlates with ADI-R scores | 4–18 years old |
| Childhood Asperger Syndrome Test (**CAST**) [33, 232] | Parent questionnaire | Good sensitivity and specificity | 5–11 years old |
| Autism Spectrum Screening Questionnaire (ASSQ)[245] | 27 point questionnaire to be completed by parent, carer or teacher | | Children and adolescents |

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