

Autism in adults

Evidence Update May 2014

A summary of selected new evidence relevant to NICE clinical guideline 142 'Autism: recognition, referral, diagnosis and management of adults on the autism spectrum' (2012)

Evidence Update 59



Contents

Introduction	3
Key points	5
1.1 General principles of care.....	6
1.2 Identification and assessment	8
1.3 Identifying the correct interventions and monitoring their use	10
1.4 Interventions for autism	11
1.5 Interventions for challenging behaviour.....	13
1.6 Interventions for coexisting mental disorders	13
1.7 Assessment and interventions for families, partners and carers.....	13
1.8 Organisation and delivery of care.....	14
Areas not covered by NICE CG142	14
Appendix A: Methodology.....	16
Appendix B: The Evidence Update Advisory Group and Evidence Update project team	18

Introduction

Evidence Updates are intended to increase awareness of new evidence – they do not replace current NICE guidance and do not provide formal practice recommendations.

Evidence Updates reduce the need for individuals, managers and commissioners to search for new evidence. For contextual information, this Evidence Update should be read in conjunction with the relevant clinical guideline, available from the [NICE Evidence Services](#) topic page for [autism](#).

This Evidence Update provides a summary of selected new evidence published since the literature search was last conducted for the following NICE guidance:

¹  [Autism in adults](#). NICE clinical guideline 142 (2012)

A search was conducted for new evidence from 9 September 2011 to 27 November 2013. A total of 4799 pieces of evidence were initially identified. After removal of duplicates, a series of automated and manual sifts were conducted to produce a list of the most relevant references. The remaining 29 references underwent a rapid critical appraisal process and then were reviewed by an [Evidence Update Advisory Group](#), which advised on the final list of 10 items selected for the Evidence Update. See [Appendix A](#) for details of the evidence search and selection process.

Evidence selected for inclusion in this Evidence Update may highlight a potential impact on guidance: that is, a high-quality study, systematic review or meta-analysis with results that suggest a change in practice. Evidence that has no impact on guidance may be a key read, or may substantially strengthen the evidence base underpinning a recommendation in the NICE guidance.


The Evidence Update gives a preliminary assessment of changes in the evidence base and a final decision on whether the guidance should be updated will be made by NICE according to its published processes and methods.

This Evidence Update was developed to help inform the review proposal on whether or not to update NICE clinical guideline 142 ([NICE CG142](#)). The process of updating NICE guidance is separate from both the process of an Evidence Update and the review proposal.

See the [NICE clinical guideline development methods guides](#) for information about updating clinical guidelines.

Other relevant NICE guidance

The focus of the Evidence Update is on the guidance stated above. However, overlap with other NICE guidance has been outlined as part of the Evidence Update process. Where relevant, this Evidence Update therefore makes reference to the following guidance:

¹  [Autism – recognition, referral and diagnosis of children and young people on the autism spectrum](#). NICE clinical guideline 128 (2011).

¹ [NICE-accredited guidance](#)

NICE Pathways

NICE pathways bring together all related NICE guidance and associated products on the condition in a set of interactive topic-based diagrams. The following NICE Pathways cover advice and recommendations related to this Evidence Update:

- [Autism](#). NICE Pathway

Quality standards

- [Autism](#). NICE quality standard 51

Feedback

If you would like to comment on this Evidence Update, please email contactus@evidence.nhs.uk

Key points

The following table summarises the key points for this Evidence Update and indicates whether the new evidence may have a potential impact on [NICE CG142](#). Please see the full commentaries for details of the evidence informing these key points.

The section headings used in the table below are taken from [NICE CG142](#).

Evidence Updates do not replace current NICE guidance and do not provide formal practice recommendations.

Key point	Potential impact on guidance	
	Yes	No
General principles of care <ul style="list-style-type: none"> Adults with autism and intellectual disability may need higher levels of support for behavioural problems than adults with intellectual disability alone. Mortality risk may be increased in adults with autism, which may be related to the presence of intellectual disability and comorbid medical conditions (particularly epilepsy). 		<ul style="list-style-type: none"> ✓ ✓
Identification and assessment <ul style="list-style-type: none"> The Autism Diagnostic Observation Schedule (ADOS) and Autism Diagnostic Interview – Revised (ADI-R) seem to be valid diagnostic tools for suspected autism in patients with intellectual disability, although it may be advisable not to rely on any autism-specific diagnostic tool alone to diagnose autism in adults. Psychiatric comorbidity is higher in adults with autism, particularly major depressive disorder, anxiety disorders, agoraphobia, obsessive–compulsive disorder and social phobia. 		<ul style="list-style-type: none"> ✓ ✓
Identifying the correct interventions and monitoring their use <ul style="list-style-type: none"> Adults with autism may be receiving psychotropic medication, despite not having a relevant psychiatric diagnosis. 		<ul style="list-style-type: none"> ✓
Interventions for autism <ul style="list-style-type: none"> An individualised supported employment programme of workplace-based education and training for people with autism during their final year of education may result in higher rates of employment compared with similar students who continued with usual education. Fluoxetine may reduce repetitive behaviour in people with autism, who also have symptoms of obsessive-compulsive disorder. 		<ul style="list-style-type: none"> ✓ ✓
Assessment and interventions for families, partners and carers <ul style="list-style-type: none"> Parents caring for young people with autism as they reach adulthood may have a high level of caregiver burden, which seems to be correlated with a perception that the young person's needs are not being met. 		<ul style="list-style-type: none"> ✓
Areas not covered by NICE CG142 <ul style="list-style-type: none"> There is currently insufficient evidence on the use of new technological approaches (for example, smartphones and social media) to address core symptoms of autism. 		<ul style="list-style-type: none"> ✓

1 Commentary on new evidence

These commentaries focus on the 'key references' identified through the search process and prioritised by the EUAG for inclusion in the Evidence Update, which are shown in bold text. Supporting references provide context or additional information to the commentary. Section headings are taken from [NICE CG142](#).

1.1 [General principles of care](#)

Autism and coexisting conditions

[NICE CG142](#) recommends that all health and social care professionals providing care and support for adults with autism should have a broad understanding of the:

- nature, development and course of autism
- impact on personal, social, educational and occupational functioning
- impact of and interaction with the social and physical environment
- impact on and interaction with other coexisting mental and physical disorders and their management
- potential discrepancy between intellectual functioning as measured by intelligence quotient (IQ) and adaptive functioning as reflected, for example, by difficulties in planning and performing activities of daily living including education or employment.

Autism and intellectual disability in an ageing population

[Kats et al. \(2013\)](#) analysed a US database that, for each participating state, collects data annually from a random sample of 400 people who have an intellectual disability and have used at least 1 state service in the previous year. This study evaluated data from 18 states that participated in 2009–10 and 15 states that participated in 2010–11.

Data for adults (30–59 years) with intellectual disability and a diagnosis of autism were compared with those for people with intellectual disability alone. People with mild, moderate or severe intellectual disability were included; those whose intellectual disability was 'profound' or unspecified were excluded from both groups because of concerns about the validity of a diagnosis of autism. Data for the years 2009–10 (438 adults with autism and 4551 in the comparator group), and 2010–2011 (n=298 and n=3963, respectively) were analysed separately.

For the years 2009–10, the mean age of people with autism was 42 years (standard deviation [SD] 8 years), and of comparator was 45 years (SD 8 years). The group with autism consisted of 75% men whereas just over half of comparators were men. Intellectual disability was classed as: mild in 27% of people with autism and in 47% of comparators; moderate in 37% and 33% respectively; and severe in 36% and 19% respectively.

Medication for behavioural problems was more widely used among adults with autism (42%) than those without this diagnosis (25%; prevalence ratio [PR]=1.11, 95% confidence interval [CI] 1.07 to 1.15). There was also a greater need for support to manage behavioural problems among the adults with autism and intellectual disability than among those with intellectual disability alone for all types of behaviour examined:

- self-injury behaviour
 - 11% of people with autism needed 'extensive' support compared with 4% of comparators
 - 28% of people with autism needed 'some' support compared with 14% of comparators
 - overall PR=1.87, 95% CI 1.62 to 2.17

- disruptive behaviour
 - 12% of people with autism needed ‘extensive’ support compared with 8% of comparators
 - 38% of people with autism needed ‘some’ support compared with 31% of comparators
 - overall PR=1.25, 95% CI 1.12 to 1.39
- destructive behaviour
 - 10% of people with autism needed ‘extensive’ support compared with 5% of comparators
 - 27% of people with autism needed ‘some’ support compared with 19% of comparators
 - overall PR=1.38, 95% CI 1.19 to 1.59.

Adjustment for age, gender and severity of intellectual disability did not significantly affect the results. Results for the 2010–11 sample were described as similar, although statistical comparisons between years were not reported.

Limitations of the study included the potential overlap of participants in annual samples and the lack of standardisation across US states and in rating data. Furthermore, autism may be under-diagnosed in older populations, which may have resulted in inclusion of people with autism in the comparator group. Although the primary aim of the study was to provide insight into potential age effects, the small number of adults with autism aged over 60 years meant that the target population was limited to those aged up to 59 years. Additionally, the population studied included relatively few participants with autism in the age range 50–59 years in both the sample of 2009–10 (21%) and 2010–11 (17%).

This evidence suggests that adults with autism and intellectual disability may need higher levels of support for behavioural problems than adults with intellectual disability alone. This study adds to the evidence base on adults aged 30–59 years with autism and reinforces the recommendation in [NICE CG142](#) for staff to understand the course of autism and its impact on, and interaction with, other conditions. Data for people with autism aged 60 years and older is needed to help assess the potential challenges that this population may present for services caring for older people.

Key reference

Kats D, Payne L, Parlier M et al. (2013) [Prevalence of selected clinical problems in older adults with autism and intellectual disability](#). *Journal of Neurodevelopmental Disorders* 5: 27

Epilepsy and mortality in adults with autism

[Woolfenden et al. \(2012\)](#) undertook a systematic review of observational studies to determine a pooled estimate for the epilepsy and mortality rates in people with autism compared with the general population. Studies were included if they consisted of least 30 children who received a diagnosis of autism, Asperger’s disorder or pervasive developmental disorder using a standardised diagnostic instrument or criteria. The observational period for outcomes of epilepsy or mortality was at least 12 months. A total of 21 studies were included in the analysis.

Epilepsy outcomes were reported in 16 studies (n=15,418) during a follow-up of 2 to 24 years. Separate analyses were undertaken for studies with the age of participants at follow-up less than or at least 12 years. For studies with participants aged at least 12 years and with the majority having autism but not intellectual disability, the pooled estimate for the prevalence of epilepsy was 8.9% (95% CI 3.7 to 15.7%, 4 studies). For studies with participants aged at least 12 years and with the majority having autism and intellectual disability, the pooled estimate for the prevalence of epilepsy was 23.7% (95% CI 17.5 to 30.5%, 9 studies).

Standardised mortality rate (SMR) was reported in 5 population-based studies of between 120 and 13,111 participants and mean follow-up of 14 to 36 years. Studies were conducted in

the USA (2 studies with an overlapping population), Sweden (2 studies with the same population) and Denmark (1 study). Pooled analysis of studies with mutually exclusive populations (that is, the most recent studies from the USA and Sweden together with the Danish study) gave SMR=2.8% (95% CI 1.8 to 4.2%). Across all studies, epilepsy was associated with 7–30% of deaths.

Limitations of the analysis included inadequate reporting in the included studies of factors that could affect outcomes other than sex, age and intellectual disability.

[Bilder et al. \(2013\)](#) reported a follow-up (after 20–29 years) of 305 people with autism originally included in an epidemiological study conducted in Utah, USA, in the 1980s. The study aimed to estimate the mortality hazard rate ratio (HRR), compared with 3 different control populations: siblings, first cousins, and an age- and gender-matched general population. The study also aimed to identify mortality risk factors and examine patterns in the causes of deaths.

Living participants (n=276) were aged 27–54 years. Since the original study, 29 people had died, including 20 men (8.8% of all men, 100% of men with IQ below 70) and 9 women (11.6% of all women, 78% of women with IQ below 70). The mortality rate was significantly higher, and by a similar extent, compared with all 3 control groups. After adjusting for confounders and compared with a general population, women had an HRR of 20.7 (95% CI 6.2 to 69.2) and men had an HRR of 7.9 (95% CI 4.2 to 15.0). A history of seizures was noted in 13 of the people with autism who died, and 2 more patients had epileptiform or spike wave discharges (total of 52% of people who died). The most common causes of death were respiratory events (n=9, including pneumonia, sleep apnoea and respiratory arrest associated with status epilepticus), epilepsy (n=6) and cardiovascular events (n=5, including myocarditis, arrhythmia, congestive heart failure and congenital heart disease); collectively, these causes were reported in 12 of the deaths. Limitations of the study included reliance on death certificates for information about the cause of death.

Taken together, these studies demonstrate the increased mortality risk for adults with autism, which may be related to the presence of intellectual disability and comorbid medical conditions (particularly epilepsy). These studies add to the evidence base for [NICE CG142](#) and emphasise the need for appropriate monitoring and management of coexisting conditions in adults with autism, particularly in those with epilepsy.

Key references

Bilder D, Botts EL, Smith KR et al. (2013) [Excess mortality and causes of death in autism spectrum disorders: a follow-up of the 1980s Utah/UCLA autism epidemiologic study](#). *Journal of Autism and Developmental Disorders* 43: 1196–204

Woolfenden S, Sarkozy V, Ridley G et al. (2012) [A systematic review of two outcomes in autism spectrum disorder – epilepsy and mortality](#). *Developmental Medicine and Child Neurology* 54: 306–12

1.2 [Identification and assessment](#)

Assessment tools for suspected autism in adults with intellectual disabilities

[NICE CG142](#) recommends that to aid more complex diagnosis and assessment for adults, professionals should consider using a formal assessment tool, such as:

- the following tools for people who do not have a learning disability:
 - Adult Asperger Assessment (AAA; includes the Autism-Spectrum Quotient [AQ] and the Empathy Quotient [EQ])
 - Autism Diagnostic Interview – Revised (ADI-R)
 - Autism Diagnostic Observation Schedule – Generic (ADOS-G)
 - Asperger Syndrome (and high-functioning autism) Diagnostic Interview (ASDI)

- Ritvo Autism Asperger Diagnostic Scale – Revised (RAADS-R)
- the following tools in particular for people with a learning disability:
 - ADOS-G
 - ADI-R.

[Sappok et al. \(2013\)](#) evaluated the psychometric properties of the ADOS and ADI-R in adults (over 18 years) with intellectual disabilities (diagnosed using International Classification of Diseases [ICD-10] criteria) and suspected autism who attended a psychiatric department in a German hospital. Of the 79 patients (mean age 36 years, 20 women), 55 received a clinical diagnosis of autism and 24 patients were diagnosed with other psychiatric conditions including schizophrenia, seizure disorders and mood disorders. The ADOS and ADI-R results were compared for the two groups of patients.

The validated German version of ADOS was completed by 54 people (68%; n=34 with autism); 10 patients receiving institutional care could not be evaluated and patient characteristics (for example, blindness, irritability, severe movement disorders) precluded use in a further 15 patients. The ADI-R was completed by 29 patients (37%; n=24 with autism); lack of parental input precluded use of this tool in other patients.

The total ADOS score was significantly higher in the group diagnosed with autism (mean=16, SD=4) than in those without this diagnosis (mean=10, SD=6; p=0.002). The sensitivity of the ADOS was 100% and specificity was 45%. All patients who were negative for autism on the ADOS were also negative for autism on clinical consensus. The ADI-R score did not differ significantly between patients diagnosed with autism (mean=41, SD=10) and other patients (mean=34, SD=10; p=0.181). The sensitivity of the ADI-R was 88% and specificity was 80%. Correlation between the ADOS and ADI-R in the 17 patients who completed both assessment tools was low (Spearman's r=0.147) and non-significant (p=0.572).

Limitations of the study included the small number of participants initially recruited, with a further reduction in number as not all participants were able to complete the assessment tools. The severity of intellectual disability was significantly greater among the group with autism than in the comparator group (although this did not appear to influence the ADOS or ADI-R performance).

This study strengthens the evidence base on assessment of suspected autism in patients with learning disabilities. The findings that ADOS and ADI-R may be valid diagnostic tools for suspected autism in such patients are consistent with the recommendations of [NICE CG142](#). However, the high sensitivity and low specificity of ADOS suggest that if used alone, it may result in over-diagnosis of autism. The more balanced psychometric properties of ADI-R suggest that developmental history is key to a diagnosis of autism in adults, although this information may not always be available. As with the diagnosis of autism in children (see [NICE clinical guideline 128](#)), it may be advisable not to rely on any autism-specific diagnostic tool alone to diagnose autism in adults.

Key reference

[Sappok T, Diefenbacher A, Budczies J et al. \(2013\) Diagnosing autism in a clinical sample of adults with intellectual disabilities: how useful are the ADOS and the ADI-R? Research in Developmental Disabilities 34: 1642–55](#)

Psychiatric comorbidity in adults with autism

[NICE CG142](#) recommends that during a comprehensive assessment, professionals should take into account and assess for possible differential diagnoses and coexisting disorders or conditions, such as:

- other neurodevelopmental conditions (using formal assessment tools for learning disabilities)

- mental disorders (for example, schizophrenia, depression or other mood disorders, and anxiety disorders, in particular, social anxiety disorder and obsessive–compulsive disorder)
- neurological disorders (for example, epilepsy)
- physical disorders
- communication difficulties (for example, speech and language problems, and selective mutism)
- hyper- and/or hypo-sensory sensitivities.

[Joshi et al. \(2013\)](#) evaluated psychiatric comorbidity and functioning in 63 adults (97% with IQ over 70) with behavioural and emotional difficulties referred to a specialist autism clinic compared with age- and sex-matched adults referred to a general psychopharmacology programme at a major academic centre in the USA. Participants received a neuropsychological assessment and structured clinical interview for autism using the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV), with interviewers blind to information regarding the specific complaints, clinical diagnosis and referral status. Psychiatric diagnoses and functional ability (assessed using the global assessment of functioning scale) were compared in patients with and without a diagnosis of autism.

Compared with people without autism, the group of patients with a diagnosis of autism had significantly more lifetime comorbidities (mean=6, SD=3.4 versus mean=3.5, SD=2.7, $p<0.001$) and current comorbidities (mean=3, SD=2.3 versus mean=1.5, SD=1.6, $p<0.001$). Lifetime psychiatric comorbidities that were significantly increased ($p<0.0001$) in the group with autism included major depressive disorder, 2 or more anxiety disorders, agoraphobia, obsessive–compulsive disorder and social phobia. Global assessment of functioning was significantly lower in the group with autism (mean=43.0, SD=6.0) compared with the matched patients (mean=51.8, SD=9.2, $p<0.0001$).

Limitations of the study included the potential lack of generalisability from the specialist clinic sample to community populations and lack of validated instruments to measure psychiatric morbidity in this population.

This study demonstrating the higher psychiatric comorbidity (particularly major depressive disorder, anxiety disorders, agoraphobia, obsessive–compulsive disorder and social phobia) in adults with autism is consistent with [NICE CG142](#) and strengthens the evidence supporting the need for psychiatric evaluation in this population as part of a comprehensive diagnostic assessment.

Key reference

Joshi G, Wozniak J, Petty C et al. (2013) [Psychiatric comorbidity and functioning in a clinically referred population of adults with autism spectrum disorders: a comparative study](#). *Journal of Autism and Developmental Disorders* 43: 1314–25

1.3 [Identifying the correct interventions and monitoring their use](#)

Use of psychotropic medication in adults with autism

[NICE CG142](#) recommends that for any intervention used in adults with autism, there should be a regular review of:

- the benefits of the intervention, where feasible using a formal rating of the target behaviour(s)
- any adverse events
- specific monitoring requirements of pharmacological interventions as highlighted by the summary of product characteristics
- adherence to the intervention.

[Lake et al. \(2012\)](#) examined the medication profiles and predictors of polypharmacy in 142 adults (21–61 years, mean age 35 years, 76% men) with autism in Ontario, Canada. All participants had experienced a psychiatric crisis (defined as an acute disturbance of thought, mood, behaviour or social relationship that needed immediate attention) during a 2-year period. Staff from participating social service or mental health agencies provided medication and demographic information. Association between demographic characteristics and use of psychotropic medication was analysed.

At the time of the psychiatric crisis, 64% of the participants were taking at least 1 psychotropic medication, with 29% prescribed 3 or more such treatments. Of the patients prescribed at least 1 psychotropic medication, 62% had no psychiatric diagnosis other than autism and 22% were not being followed up by a psychiatrist. More than half the patients receiving the most commonly prescribed treatments did not have an associated psychiatric diagnosis:

- 80 patients (56%) prescribed antipsychotics (62% of whom had no relevant psychiatric diagnosis)
- 43 patients (30%) prescribed anxiolytics (61% with no relevant diagnosis)
- 35 patients (25%) prescribed antidepressants (56% with no relevant diagnosis)
- 26 patients (18%) prescribed mood stabilisers (58% with no relevant diagnosis).

Patients taking multiple psychotropic medications were significantly more likely to live in a group home (odds ratio [OR]=3.33, 95% CI 1.51 to 7.38), have a history of aggression (OR=3.73, 95% CI 1.72 to 8.09) and have a history of psychiatric support (OR=3.68, 95% CI 1.72 to 7.89) compared with those with no polypharmacy.

Limitations of the study included its retrospective nature with reliance on staff reports and lack of validation of clinical records. It was not a population-based study as it included only adults with autism who had experienced a crisis, so although this population was highly medicated, the findings may not be generalisable to the general population of adults with autism.

The study indicates that adults with autism may be receiving psychotropic medication, despite not having a relevant psychiatric diagnosis, underlining the importance of the [NICE CG142](#) recommendation to review medication regularly.

Key reference

[Lake JK, Balogh R, Lunsky Y \(2012\) Polypharmacy profiles and predictors among adults with autism spectrum disorders. Research in Autism Spectrum Disorders 6: 1142–9](#)

1.4 [Interventions for autism](#)

Psychosocial interventions focused on life skills

[NICE CG142](#) recommends that adults with autism without a learning disability or with a mild learning disability who are having difficulty obtaining or maintaining employment should consider an individual supported employment programme. This should typically include:

- help with writing CVs and job applications and preparing for interviews
- training for the identified work role and work-related behaviours
- carefully matching the person with autism to the job
- advice to the employers about making reasonable adjustments to the workplace
- support for the person with autism after they start work
- support for the employer before and after the job starts, including autism awareness training.

[Wehman et al. \(2014\)](#) conducted a randomised controlled trial (RCT) to evaluate the impact on employment of a psychosocial intervention carried out before job searches were started by students in two public special education programmes in Virginia, USA. Students applying for inclusion in the study were accepted if they were aged 18–21 years, had a diagnosis of autism, and were independent and responsible for their daily personal hygiene, dressing and eating. Students with comorbid medical, development or psychiatric diagnoses and challenging behaviour were accepted into the study but those with a history of drug misuse or setting fires were excluded.

The 24 students (75% men) randomised to receive the intervention ([Project SEARCH](#) plus ASD specific elements) were embedded in two suburban hospitals for 9 months during their final year of education. Students spent the beginning and end of each school day in a classroom, located within the hospital site, learning job skills and social communication behaviours (total of about 180 hours). For the rest of the day, students rotated through 3 placements within the hospital, each of 10–12 weeks duration (about 720 hours). Specific and individualised support was provided by a team at each site that included a special education teacher, an assistant and 2 employment specialists. The 16 students (68% male) in the control group continued to attend their assigned high school and received services as stipulated in their individual education plans.

In the group receiving the intervention, 21 young people (87.5%) obtained employment in competitive jobs (earning up to 24% above the state minimum wage), with 78% remaining employed and earning higher wages after 2 years. In comparison, 1 person (6.25%) who received usual education obtained employment after leaving high school.

Limitations of the study included the lack of interaction with the control group who may have received diverse services, and exclusion of students with high personal care support needs. The study was also conducted in the USA and included person-specific support so it may not be possible to generalise the findings to other settings.

This study suggests that an individualised supported employment programme of workplace-based education and training for people with autism during their final year of education may result in higher rates of employment compared with similar students who continued with usual education. These findings are consistent with [NICE CG142](#) and strengthen the evidence base demonstrating the value of an individualised supported employment programme of workplace-based education and training for young people with autism, before they start seeking a job.

Key reference

[Wehman PH, Schall CM, McDonough J et al. \(2014\) Competitive employment for youth with autism spectrum disorders: early results from a randomized clinical trial. *Journal of Autism and Developmental Disorders* 44: 487–500](#)

Antidepressant medication for management of repetitive behaviour

[NICE CG142](#) states: do not use antidepressant medication for the routine management of core symptoms of autism in adults.

[Hollander et al. \(2012\)](#) conducted a 12-week RCT to compare the effects of fluoxetine versus placebo on repetitive behaviours and global symptoms in 37 adults (18–60 years) with autism. The clinical diagnosis was supported by evaluation with ADOS-G, and ADI-R if development history was available. Participants had a score of 4 or more on the Clinical Global Impression (CGI) but severity of repetitive behaviours (which were evaluated using the compulsion subscale of the Yale-Brown Obsessive Compulsive Scale) was not an inclusion criterion. Exclusion criteria included schizophrenia, schizoaffective disorder, bipolar disorder and active seizure disorder. Most participants (92%) were high functioning (IQ of 70 or above). The primary efficacy measures were the change in score for repetitive behaviour and improvement in CGI rating.

In the 21 patients receiving fluoxetine, the mean repetitive behaviour score at baseline was 12.48 (SD=2.71, range 7–18), which reduced by 2 points at the endpoint (mean=10.48, SD=3.92). In the 13 patients receiving placebo the mean repetitive behaviour score at baseline was 11.92 (SD=2.02, range 9–16), which reduced by 0.77 points at the endpoint (mean=11.15, SD=3.05). No statistical comparison between groups was reported.

In a mixed-effects regression analysis, the treatment-by-time interaction indicated a significantly greater reduction in compulsion score with fluoxetine than placebo (0.31 points/week, $p=0.005$). CGI score showed significantly greater improvement with fluoxetine than placebo for clinician assessments (risk ratio [RR]=1.5, $p=0.03$) but not for those carried out by independent assessors ($p=0.07$). Analyses did not account for 1 person who dropped out of the fluoxetine group and 3 people who dropped out of the placebo group. Fluoxetine was associated with higher levels of adverse events: 1.4 events per person compared with 0.6 events per person with placebo.

Limitations of the study included the small size and short duration. There were unequal numbers of participants in the two treatment arms, with baseline characteristics differing between groups. The analysis was based on the per-protocol population, reducing the number of patients included in the analysis. The level of repetitive behaviour showed considerable variation, and although the predicted difference in score between groups reached statistical significance, it is unclear whether this was clinically meaningful. Independent assessors did not find a statistical significance in CGI score.

The study did not evaluate core symptoms of autism other than repetitive behaviour, so is unlikely to affect the recommendation in [NICE CG142](#) not to use antidepressant medication for routine management of core symptoms of autism. However this study indicates that fluoxetine may reduce repetitive behaviour in people with autism who also have symptoms of obsessive-compulsive disorder.

Key reference

Hollander E, Soorya L, Chaplin W et al. (2012) [A double-blind placebo-controlled trial of fluoxetine for repetitive behaviors and global severity in adult autism spectrum disorders](#). *American Journal of Psychiatry* 169: 292–9

1.5 [Interventions for challenging behaviour](#)

No new key evidence for this section was selected for inclusion in this Evidence Update.

1.6 [Interventions for coexisting mental disorders](#)

No new key evidence for this section was selected for inclusion in this Evidence Update.

1.7 [Assessment and interventions for families, partners and carers](#)

Caregiver burden

[NICE CG142](#) recommends offering families, partners and carers of adults with autism an assessment of their own needs including:

- personal, social and emotional support
- support in their caring role, including respite care and emergency plans
- advice on and support in obtaining practical support
- planning of future care for the person with autism.

[Cadman et al. \(2012\)](#) conducted an observational study to assess the burden on caregivers of young people with autism (14–24 years). The clinical diagnosis of autism was confirmed for all patients using the ADI-R. Caregiver burden in 89 families was measured using the Zarit Burden Interview (ZBI), which includes 12 items and gives a total score of 0 (no impact) to 48 (high impact).

Patients and caregivers were interviewed to identify factors associated with caregiver burden, using a stress appraisal model that incorporated family background, the young person's level of symptoms and psychological comorbidities, and parental perceptions about care and resource needs. Correlation between these factors and score on the ZBI were explored using sequential multiple regression models. Results were compared with findings using the same questionnaires, interviews and analyses conducted with 81 families where the young person (14–24 years) had attention deficit hyperactivity disorder (ADHD); people with a diagnosis of autism, epilepsy or general learning difficulties were excluded from this group.

Caregiver burden was high in both groups but significantly higher in the families of young people with autism (mean=22.66, SD=8.84) than for ADHD (mean=17.80, SD=9.18, $p=0.001$). In both groups, caregiver burden was mainly explained by perceptions that the young person's needs were not being met. Caregiver burden for both young people with autism and the group with ADHD was significantly correlated with unmet needs relating to depression, anxiety, inappropriate behaviour, risk of exploitation, and daytime activities (all $p<0.05$). In addition, the burden on caregivers for people with autism was significantly correlated with unmet needs relating to social relationships, mental health problems, safety of self, and communication (all $p<0.01$).

Limitations of the study included analysis of caregiver burden at a single time-point and lack of a direct measure of maladaptive behaviour. Generalisability of the findings may be limited because the sample group of patients with autism differed from the general population of adults with autism. Around 15% of the sample had a learning disability, which was substantially lower than the 56% previously reported in a population cohort. Other factors potentially reducing generalisability were that the study included 92% male participants and almost all caregivers in the study were mothers.

This study demonstrates that parents caring for young people with autism as they reach adulthood may have a high level of caregiver burden, and that burden seems to be correlated with a perception that the young person's needs are not being met. This evidence reinforces the importance of [NICE CG142](#) recommendations to assess caregiver needs.

Key reference

[Cadman T, Eklund H, Howley D et al. \(2012\) Caregiver burden as people with autism spectrum disorder and attention-deficit/hyperactivity disorder transition into adolescence and adulthood in the United Kingdom. Journal of the American Academy of Child and Adolescent Psychiatry 51: 879–88](#)

1.8 Organisation and delivery of care

No new key evidence for this section was selected for inclusion in this Evidence Update.

Areas not covered by NICE CG142

Using technological approaches for core symptoms of autism

[NICE CG142](#) contained a [research recommendation](#) to determine the clinical and cost effectiveness of augmentative communication (that is, alternative ways of helping people with communication difficulties by using assistive technology such as computers or other devices, such as a speech output device). This was considered important to address core symptoms of autism including communication problems (for example, the absence of spoken language

or significant deficits in interpersonal skills) that have a profound effect on the ability to lead a full and rewarding life. The guideline noted that although a number of communication devices have been developed for autism, few, if any, have been subjected to a proper evaluation in adults. The suggested programme of research would need to identify current devices for which there is:

- some evidence of benefit (for example, case series and small-scale pilot studies)
- some evidence that it meets a key communication need for people with autism (based on reviews of people's need in this area)
- indication that the device is feasible for routine use, with formal evaluation in a large-scale randomised trial.

[Kagohara et al. \(2013\)](#) conducted a systematic review of studies that involved iPods, iPads and related devices (for example, iPhones) for teaching skills to at least 1 person with a developmental disability (including autism, intellectual disability, Down's syndrome and cerebral palsy). A total of 15 studies were included in the review, involving a total of 47 people (range 1–6 people). Most studies were of children; 3 studies each of 3 people included children and adults (with 2 studies involving the same 3 participants), and 1 study included 6 adults (18–27 years). Target behaviour was assessed within categories of communication, employment, leisure and transitioning skills. The review gave narrative reports of the findings from individual studies; there was no consistent pattern in the results obtained.

A key limitation of the review was the paucity of studies to evaluate, and small sample sizes in each study. The research recommendations from [NICE CG142](#) have yet to be fulfilled. The EU-funded [HANDS project](#) (reported by [Mintz et al. 2013](#)) made some progress towards meeting these research needs for a smartphone-based cognitive support system, but further work has been hampered by technological changes. Future research into the use of new technology (including the use of social media and specific phone apps developed for use by people with autism) needs to assess the impact on core symptoms using validated measures in studies of appropriate design and sufficient size to allow meaningful statistical evaluation.

Key reference

[Kagohara DM, van der Meer L, Ramdoss S et al. \(2013\) Using iPods® and iPads® in teaching programs for individuals with developmental disabilities: a systematic review. Research in Developmental Disabilities 34: 147–56](#)

Supporting reference

[Mintz J, Gyori M, Aagaard M \(2012\) Touching the future technology for autism? Lessons from the HANDS project. Amsterdam: IOS Press](#)

2 New evidence uncertainties

During the development of the Evidence Update, the following evidence uncertainties were identified for the UK Database of Uncertainties about the Effects of Treatments (UK DUETs).

Areas not covered by NICE CG142

- [Information technology and electronic devices for people with autism spectrum conditions to improve social skills and other outcomes](#)

Further evidence uncertainties for autism can be found in the [UK DUETs database](#) and in the [NICE research recommendations database](#).

UK DUETs was established to publish uncertainties about the effects of treatments that cannot currently be answered by referring to reliable up-to-date systematic reviews of existing research evidence.

Appendix A: Methodology

Scope

The scope of this Evidence Update is taken from the scope of the reference guidance:

- [Autism in adults](#). NICE clinical guideline 142 (2012)

[NICE CG142](#) included case series; however this type of evidence was omitted from the scope of the Evidence Update to focus on stronger types of evidence.

Searches

The literature was searched to identify studies and reviews relevant to the scope. Searches were conducted of the following databases, covering the dates 9 September 2011 (the end of the search period of NICE CG142) to 27 November 2013:

- ASSIA (Applied Social Services Index and Abstracts)
- CDSR (Cochrane Database of Systematic Reviews)
- CENTRAL (Cochrane Central Register of Controlled Trials)
- CINAHL (Cumulative Index to Nursing and Allied Health Literature)
- DARE (Database of Abstracts of Reviews of Effects)
- EMBASE (Excerpta Medica database)
- ERIC (Education Resources in Curriculum)
- HTA (Health Technology Assessment) database
- MEDLINE (Medical Literature Analysis and Retrieval System Online)
- MEDLINE In-Process
- NHS EED (Economic Evaluation Database)
- PsycINFO

The Evidence Update search strategy replicates the strategy used by [NICE CG142](#) (for key words, index terms and combining concepts) as far as possible. Where necessary, the strategy is adapted to take account of changes in search platforms and updated indexing language.

Table 1 provides details of the MEDLINE search strategy used, which was adapted to search the other databases listed above. The search strategy was used in conjunction with validated Scottish Intercollegiate Guidelines Network [search filters](#) for systematic reviews and observational studies and an adaptation of the RCT filter to retrieve controlled, non-randomised trials.

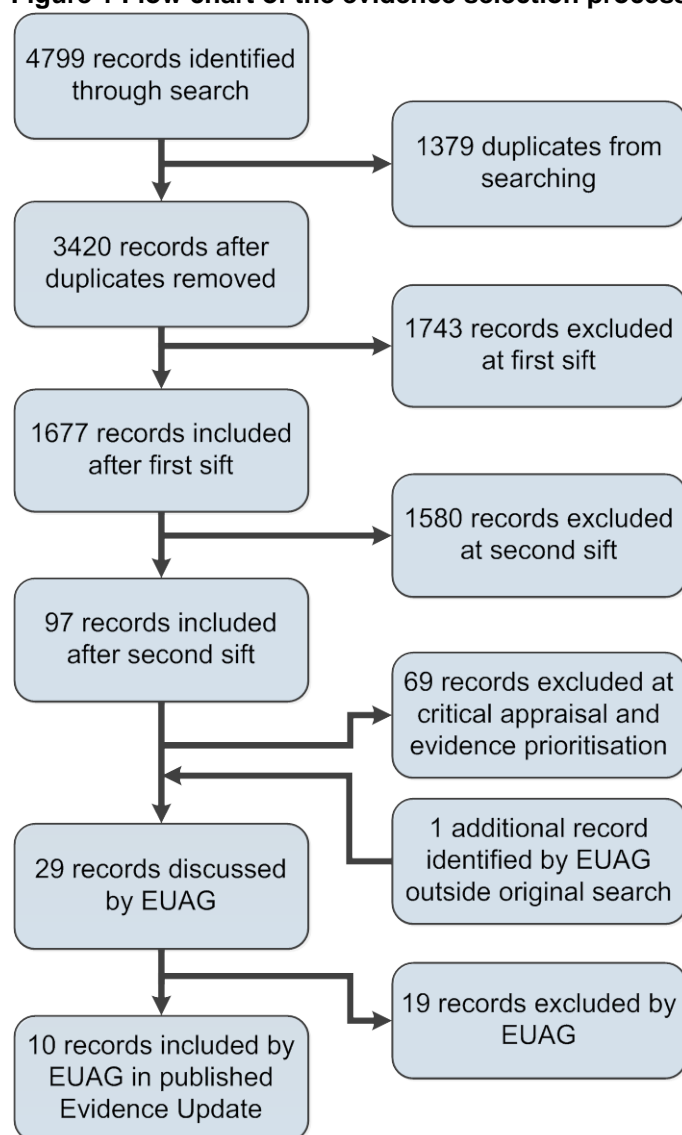
Additionally, 1 study (Wehman et al. 2014) was identified outside of the literature search. Figure 1 provides details of the evidence selection process. The list of evidence excluded after review by the Chair of the EUAG, and the full search strategies, are available on request from contactus@evidence.nhs.uk

See the [NICE Evidence Services](#) website for more information about [how NICE Evidence Updates are developed](#).

Table 1 MEDLINE search strategy (adapted for individual databases)

1	child development disorders, pervasive/ or asperger syndrome/ or autistic disorder/	(pervasive\$ adj2 (development\$ or neurodevelopment\$)).ti,ab.
2	Rett Syndrome/	
3	(asperger\$ or autis\$ or cerebroatrophic hyperammonemia\$ or (kanner\$ adj (disorder\$ or syndrome\$)) or	
4		(pddnos or pdd?nos or (rett\$ adj (disorder\$ or syndrome\$)).ti,ab
5		Or/1-5

Figure 1 Flow chart of the evidence selection process



EUAG – Evidence Update Advisory Group

Appendix B: The Evidence Update Advisory Group and Evidence Update project team

Evidence Update Advisory Group

The Evidence Update Advisory Group is a group of topic experts who reviewed the prioritised evidence from the literature search and advised on the development of the Evidence Update.

Professor Simon Baron-Cohen – Chair

Director, Autism Research Centre, Psychiatry Department, Cambridge University

Professor Gillian Baird

Consultant Paediatrician and Professor of Paediatric Neurodisability, Guy's and St Thomas' NHS Foundation Trust and King's Health Partners

Dr Carole Buckley

General Practitioner, The Old School Surgery, Bristol

Dr Juli Crocombe

Consultant Psychiatrist and Clinical Director, St Andrew's Healthcare, Birmingham

Ms Annie Foster-Jones

Challenging Behaviour/Autism Specialist Nurse, Cheshire and Wirral Partnership NHS Foundation Trust

Dr Marga Hogenboom

General Practitioner, Camphill Medical Practice, Bielside, Aberdeen

Professor Patricia Howlin

Emeritus Professor of Clinical Child Psychology, King's College London

Ms Melissa McAuliffe

Asperger's Specialist Social Worker, East London NHS Foundation Trust/London Borough of Newham

Mr Richard Mills

Research Director, Research Autism, and Lecturer and Associate, University of Kent, Canterbury

Evidence Update project team

Marion Spring

Associate Director

Chris Weiner

Consultant Clinical and Public Health Adviser

Cath White

Programme Manager

Fran Wilkie

Project Manager

Diane Storey

Medical Writer

Bazian

Information Specialist support

© National Institute for Health and Care Excellence, 2014. All rights reserved. NICE copyright material can be downloaded for private research and study, and may be reproduced for educational and not-for-profit purposes. No reproduction by or for commercial organisations, or for commercial purposes, is allowed without the written permission of NICE.