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ARTICLE

Pharmacological management of psychopathology in people with intellectual disabilities and/or autism spectrum disorder

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SUMMARY

On average, 49–63% of people with intellectual disabilities and/or autism spectrum disorder (ASD) are prescribed psychotropic medications to treat psychopathology, including psychiatric illness, behaviours that challenge and the core symptoms and associated behaviours of these developmental disorders. In many cases, psychotropics, particularly antipsychotics, are used off-label without a proper indication, particularly to manage behaviours that challenge. The RCTs show moderate evidence supporting the efficacy of low-dose risperidone and some preliminary evidence for aripiprazole in treating behaviours that challenge among children with ASD and/or intellectual disabilities. The RCT-based evidence for the other psychotropics is equivocal, so no definitive conclusions can be made on their efficacy. Polypharmacy and the use of high doses of antipsychotics are prevalent in this population, leading to the risk of adverse events and drug–drug interactions. Despite various national and international guidelines, and government initiatives encouraging reduced psychotropic use, there is little evidence of this happening; on the contrary, the use of antidepressants, mood stabilisers and benzodiazepines may be increasing. A concerted multi-agency effort is urgently needed to address this significant public health concern of the overmedication of people with intellectual disabilities and/or ASD.

LEARNING OBJECTIVES

After reading this article, you will be able to:

- identify the extent of use of psychotropic medication among people with intellectual disabilities and autism
- acknowledge the evidence for the efficacy of different psychotropic medications for the management of psychopathology in people with intellectual disabilities and autism
- recognise the medication-related adverse effects and effects of the withdrawal of these medications.

KEYWORDS

Intellectual disabilities; autism spectrum disorder; behaviours that challenge; psychotropic medications; evidence base.

A high proportion of individuals with intellectual disabilities (18–60%) display behaviours that challenge, such as aggressive, disruptive, destructive and self-injurious behaviour (Deb 2016a, 2022a). These behaviours pose a complex management problem, may cause obstacles to social integration and may lead to carer stress, community placement breakdown, hospital admission and restrictive practices such as physical restraint and medication use without appropriate indications (Box 1). However, behaviours that challenge are often a means of communication for people with intellectual disabilities who cannot express their feelings through speech. So, for example, if an individual is in pain or distressed, they may shout and scream because they cannot communicate their needs to others (Box 2). To address these behaviours, it is essential to understand the reasons behind them rather than use psychotropic medications without appropriate indications. Therefore, a thorough person-centred assessment with multidisciplinary input is vital for a proper biopsychosocial formulation leading to successful interventions (Box 3). For further information on assessment and formulation see: Deb et al (2016a, 2022a); the SPECTROM website (https://spectrom.wixsite.com/project); and supplementary Appendix 1, available at https://doi.org/10.1192/bja.2022.61.

Current treatment practices

Both pharmacological (Deb 2022b) and non-pharmacological psychosocial interventions (such as positive behaviour support; Gore 2022) are used to address behaviours that challenge. Positive behaviour support is a way of understanding such behaviours using a person-centred approach,

BOX 1 Indications for antipsychotic use to manage behaviour that challenges

The National Institute for Health and Care Excellence advises that antipsychotic medication to manage behaviour that challenges should be considered only if:

- psychological or other interventions alone do not produce change within an agreed time, or
- treatment of any coexisting mental or physical health problem has not led to a reduction in the behaviour, or
- the risk to the person or others is very severe (for example, because of violence, aggression or self-injury).

Antipsychotic medication should be offered only in combination with psychological or other interventions.

(NG11: NICE, May 2015)

assessing the broad social and physical context in which they occur, and planning and implementing ways of supporting the person, thus enhancing their quality of life and that of their caregivers (www.pbsacademy.org.uk). A recent meta-analysis (Bruinsma 2020) found a significant moderate overall long-lasting effect of non-pharmacological interventions on behaviours that challenge (d = 0.573). In contrast, the evidence for the effectiveness of medication in improving such behaviour is at best equivocal (Deb 2016b).

BOX 2 Examples of physical problems leading to behaviours that challenge

Frustration due to spasticity

A 65-year-old woman with severe intellectual disabilities suffered a stroke that caused paralysis of the right side of her body. She started screaming and shouting regularly, and the care staff asked the doctor for psychotropic medication to manage her behaviour. However, close examination revealed that she had developed spasticity in her right hand and she was constantly frustrated by not being able to stretch the fingers of that hand, which led to screaming. Instead of psychotropic medication, baclofen was prescribed as a muscle relaxant and the woman's behaviour improved.

Pain

A 75-year-old man with moderate intellectual disabilities and limited communication skills developed symptoms of dementia. He started screaming and headbanging. His sister, who was his primary carer, asked for psychotropic medication, but the clinician prescribed paracetamol regularly, assuming that headaches may have precipitated the behaviour. This produced a good result and the man stopped screaming and headbanging.

BOX 3 The importance of person-centred assessment with multidisciplinary input

The following examples show how input from a speech and language therapist may help improve behaviours that challenge and reduce overmedication by using different methods to communicate with the person.

Care staff in a community group home wanted psychotropic medication to manage the behaviour of a 27-year-old man with severe intellectual disabilities who was not able to communicate through speech. Further investigation revealed that he became agitated if he was not allowed to go out for car rides, which he enjoyed. A speech and language therapy assessment revealed that when the care staff said to him 'You can't go out in a car today' he heard the word 'car' and thought he was going out, so he became very frustrated and disturbed when this did not happen. The speech therapist devised a picture board with a picture of a car crossed out, which care staff showed the man when he was not allowed to go out, engaging him instead in indoor activities that he enjoyed. This strategy was successful, and his behaviour improved without any psychotropic medication.

In another group home, care staff asked for medication to control the behaviour of a 36-year-old woman with moderate intellectual disabilities who had no speech. Further assessment by a speech therapist revealed that the care staff usually asked her what she wanted for her dinner and gave her two or three choices. She always opted for the last option, but when the food was served, she refused to eat it and became disturbed. The speech therapist suggested that instead of giving her choices verbally, the care staff should show pictures of the different meals and also involve her in the preparation of her meals. This strategy was successful, and her behaviour improved without any psychotropic medication.

Intellectual disabilities

Regardless of the evidence, psychotropic medications are used widely among, on average, 49–63% of people with intellectual disabilities (Sheehan 2015). This rate has not changed much since a review on the subject published almost three decades ago (Deb 1994). Most widely used among psychotropics are the antipsychotics, which are prescribed to around 24–32% of adults with intellectual disabilities (de Kuijper 2010; Sheehan 2015), compared with <1% in the general population who do not have intellectual disabilities (Marston 2014). In a study conducted on a Dutch population (de Kuijper 2010), 17% of people with intellectual disabilities also received antidepressants and 20% received benzodiazepines. Of those who received antipsychotics, 78% either did not have a diagnosis of psychosis or the indication was not reported: 58% had behaviours that challenge and 22% psychosis, and in 20% of cases the indication was not

known. In a study conducted on an English population (Sheehan 2015), a similar proportion (71%) of those who received antipsychotics did not have a severe mental illness. In the same study, 47% of those who had a record of behaviours that challenge received antipsychotics. Therefore, it seems that psychotropics in general and antipsychotics in particular are used in a high proportion of people with intellectual disabilities without a proper indication. This assumption was supported by a Public Health England document which estimated that 30 000–35 000 adults with intellectual disabilities might be receiving antipsychotics and antidepressants in England in the absence of the conditions for which they are indicated (Glover 2015).

Autism spectrum disorder

Autism spectrum disorder (ASD) is frequently associated with comorbid disorders (55–70%) such as intellectual disabilities (38%), anxiety disorder (18–20%), attention-deficit hyperactivity disorder (ADHD) (25–28%), psychosis (4–12%), depression (11–19%) and obsessive–compulsive disorder (7–10%) (Simonoff 2008; Bertelli 2015; Lai 2019; Lugo-Marína 2019; Bertelli 2022). Behaviours that challenge, which may or may not be due to underlying anxiety, are also common in ASD (10–15%) (Lai 2019). The use of pharmacological treatment for people with ASD has increased significantly over the years, from 57% in 1998 to 64% in 2014 ($P < 0.05$) (Murray 2014) and it is also common in children as young as 2 years of age (Mandell 2008). The rate increases with increasing age (11% among children aged 3–5 years, 46% among those aged 6–11 years and 66% among those aged 12–17 years) (Coury 2012). A German study reported that the most frequently used psychotropics in ASD were psychostimulants (13%), followed by antipsychotics (particularly risperidone) (12%) and mood stabilisers/anti-epileptics such as sodium valproate (9%), antidepressants (4%) and benzodiazepines (7%) (Bachmann 2013).

Off-label and long-term prescribing and polypharmacy

The off-label prescribing of psychotropics in people with intellectual disabilities and/or ASD, particularly for behaviours that challenge, in the absence of a psychiatric disorder is a significant public health concern (Glover 2015) (Box 4). Furthermore, the long-term use of antipsychotics carries an increased risk of medication-related adverse events such as sedation, constipation, obesity, diabetes and metabolic syndrome, which can impair a person's quality of life (Ramerman 2018a). Other reasons for concern include (a) the use of psychotropics in addition to the existing high use of medication for physical problems, thus increasing the risk of drug–drug interactions and adverse events, (b) an overall lack of evidence on the effectiveness of psychotropics for behaviours that challenge, (c) use of antipsychotics at a higher than the recommended dose, as well as polypharmacy of psychotropics, which again increase the risk of drug–drug interactions and adverse effects (Box 5), (d) long-term use without reviews and (e) difficulty in detecting drug-related adverse events and carrying out necessary investigations in this population (Unwin 2008a).

Because of these concerns, NHS England has embarked on a major campaign called 'Stopping over-medication of people with learning disabilities, autism or both' (STOMP) (Branford 2019), to which 'Supporting treatment and appropriate medication in paediatrics' (STAMP) was recently added. The Royal College of Psychiatrists has also published a position statement to support the STOMP-STAMP initiative (PS05/21) (Biswas 2021). The National Institute for Health and Care Excellence (NICE) in the UK (2015) and the World Psychiatric Association (Deb 2009) have developed guidelines for the use of psychotropics to address behaviours that challenge among people with intellectual disabilities, including recommendations for initiation, monitoring and potential withdrawal of psychotropic medications (supplementary Appendix 2). Despite these initiatives, a recent Scottish survey has shown an increased rate of use of both antipsychotics and antidepressants among school children with and without intellectual disabilities between 2010 and 2013, and a significantly higher proportion of children with intellectual disabilities received antipsychotics and antidepressants than the other children (Henderson 2021).

BOX 4 Inappropriate use of psychotropic medication

The proprietor of a group home brought a 63-year-old man with moderate intellectual disabilities to a psychiatric clinic asking for medication to control his non-cooperative and anxious behaviour. Further assessment revealed that the man did not want to go to the day centre and became disturbed when forced to do so. When asked, the proprietor of the group home told the clinician that they did not have a contract with the social services department for payment of this man's day care within the group home. Therefore, they had no choice but to send him to the day centre. The clinician refused to prescribe psychotropic medication and asked the proprietor to resolve the contract issue with the social services department.

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The same group of authors reported, using a linkage study in Scotland, an increased rate of psychotropics (47% *v.* 58%; $P<0.001$), antipsychotics (23.5% *v.* 26%; $P=0.099$), antidepressants (9.9% *v.* 22%; $P<0.001$), anti-epileptics (24.8% *v.* 31%; $P<0.001$), lithium (1.3% *v.* 1.8%; $P=0.18$) and hypnotic/anti-anxiety medications (4.6 *v.* 9.4%; $P<0.001$) use over 10 years (2004–2014) in a cohort of adults with intellectual disabilities (Henderson 2020). Other sources of information also support an increasing use over the last five years of antidepressants and antiepileptic medications for behaviours that challenge in adults with intellectual disabilities (Branford 2022; NHS Digital 2022).

Our recent questionnaire survey has shown that although UK psychiatrists are initiating antipsychotics less often than before to manage behaviours that challenge, they have not had much success in withdrawing existing psychotropics/antipsychotics (Deb 2020). Reasons given were the lack of a nationally recommended structured withdrawal framework, unavailability of non-medication-based interventions/resources to manage challenging behaviours and caregivers' anxiety about the withdrawal of psychotropics (details available from the first author, S.D., on request). To address the caregiver issue, we have recently developed free online training resources delivered through face-to-face workshops to help reduce the overmedication of people with intellectual disabilities (Deb 2021a). The project, called 'Short-term psycho-education for caregivers to reduce overmedication of people with intellectual disabilities' (SPECTROM) can be found at https://spectrom.wixsite.com/project.

BOX 5 A real-life example of polypharmacy with the potential for drug–drug interactions

The following is an example of a prescription for an adult with intellectual disabilities:

- risperidone 2.5 mg/day
- carbamazepine 2000 mg/day
- sodium valproate 2700 mg/day
- lamotrigine 400 mg/day
- lithium carbonate 1200 mg/day
- methylphenidate 5 mg/day
- procyclidine 15 mg/day
- ferrous fumarate + vitamins + lactulose + cod liver oil + various skin ointments
- as required medication (PRN): clobazam + lorazepam
- rectal diazepam + buccal midazolam as rescue medication for status epilepticus.

Examples of drug–drug interactions (from the British National Formulary, accessed on 1 August 2022):

- carbamazepine reduces serum levels of sodium valproate, methylphenidate, midazolam and risperidone
- lithium in combination with carbamazepine increases the risk of neurotoxicity
- lamotrigine may increase the serum level of carbamazepine
- sodium valproate increases the serum level of lamotrigine, so lamotrigine should be prescribed at a lower dose – a maximum of 200 mg/day – but carbamazepine reduces the serum level of lamotrigine, thus complicating the three-way interactions between sodium valproate, lamotrigine and carbamazepine
- a higher dose of risperidone could make epilepsy worse.

The evidence base

The gold standard of evidence is based on randomised controlled trials (RCTs), as case studies may produce bias. However, RCTs involving people with intellectual disabilities and/or ASD are rare because of practical difficulties, including the difficulty of obtaining informed consent to participate as well as caregivers' anxiety about the unknown effect of the placebo (Oliver-Africano 2010; Scheifes 2011; Mulhall 2018). We have summarised here the RCT-based evidence on the effectiveness of different classes of psychotropic in ASD and intellectual disabilities.

Antipsychotics

Although there are a few old small-scale RCTs on haloperidol and chlorpromazine showing equivocal results, most RCT-based evidence is on the second-generation antipsychotics, particularly risperidone, which is the most widely used medication among people with intellectual disabilities and the second most widely used among people with ASD, particularly for the management of behaviours that challenge (Unwin 2008b; Coury 2012; Deb 2015; Sheehan 2015). None of the RCTs on antipsychotics assessed their efficacy for treating psychosis or bipolar disorder in people with intellectual disabilities and/or ASD.

Risperidone

Children and adults with ASD and/or intellectual disabilities

There are four RCTs on risperidone involving children (Buitelaar 2001; van Bellinghen 2001; Aman 2002; Snyder 2002) and three involving adults with intellectual disabilities (van Den Borre 1993; Gagiano 2005; Tyrer 2008).

There are nine RCTs on risperidone involving children (McCracken 2002; Shea 2004; Hellings 2006; Luby 2006; Nagraj 2006; Aman 2009; Kent 2013; Kouhbanani 2021; NCT 01624675 2015) and one involving adults with ASD (McDougle 1998). One of these RCTs, involving children (Aman 2009), compared risperidone with a combination of risperidone and parent training and found the latter more effective. Another (Kouhbanani 2021) compared risperidone with placebo and with a combination of risperidone and behavioural intervention using virtual reality and found the last to be significantly better. The rest of the RCTs compared risperidone at a low dose of around 1.5 mg/day with

a placebo (Unwin 2011; Deb 2016b; Alfageh 2019; D'Alò 2021; Deb 2022b). One study compared baseline placebo conditions with two doses of risperidone and showed the efficacy of the medication in children with ASD (Hellings 2006).

All placebo-controlled studies of risperidone involving children with ASD ($n = 9$) (some of whom also had comorbid intellectual disabilities) and also intellectual disabilities ($n = 4$) (some had comorbid ASD) have shown significant improvement of symptoms in the risperidone groups compared with the placebo groups using measures such as the Nisonger Child Behavior Rating Form (NCBRF) (Tassé 1996), Aberrant Behavior Checklist, Irritability subscale (ABC-I) and Clinical Global Impression-Improvement (CGI-I) (Deb 2016b, 2022b). According to these studies, the mean number needed to treat (NNT) was around 3 (Unwin 2011). Most studies were from the USA and were supported by pharmaceutical companies. Because intellectual disabilities and ASD commonly coexist (Bertelli 2022; Deb 2022c), most studies included participants with a mixture of these two neurodevelopmental disorders. For example, many participants in studies primarily on ASD also had intellectual disabilities and vice versa.

One RCT involving adults with ASD (McDougle 1998) and two RCTs involving adults with intellectual disabilities (van Den Borre 1993; Gagiano 2005) have shown a significantly better outcome of risperidone compared with the placebo. On the other hand, a study by Tyrer et al (2008) did not find any significant intergroup difference in aggressive behaviour among risperidone-, haloperidol- and placebo-treated groups at 4-week follow-up. All three groups showed improvement at follow-up, but the placebo group showed the greatest score change. These studies used outcome measures such as the Modified Overt Aggression Scale (MOAS) (Ratey 1991), ABC-I (Aman 1995) and CGI-I (NIMH 1985). These studies are underpowered and risk type II errors because of small sample sizes.

After the RCT phase, five studies (two included children with intellectual disabilities only and three included children with ASD with and without intellectual disabilities) (Turgay 2002; Findling 2004; Research Units on Pediatric Psychopharmacology Autism Network 2005; Troost 2005; Kent 2013) continued with risperidone in open-label trials for 48–52 weeks, showing continuing efficacy of risperidone over time, with reasonable tolerance of adverse effects. Another open-label 1-year follow-up study of 504 children with intellectual disabilities reported similar findings (Croonenberghs 2005). The most common adverse events were sedation and weight gain, but some studies reported hypersalivation and hyperprolactinaemia with or without breast milk discharge. Most studies, but not all, have shown these adverse events to improve over weeks and months, although weight gain remained a long-term problem. Three placebo-controlled withdrawal studies of risperidone following the primary RCTs among children with intellectual disabilities showed a significantly higher rate and earlier relapse of behaviours that challenge in the placebo group compared with the group that continued to take risperidone (in one study, 63% in the placebo group, versus 13% in the risperidone group). More recent double-blind placebo-controlled antipsychotic withdrawal studies in the UK (McNamara 2017) and The Netherlands (Ramerman 2019) had difficulty recruiting participants.

Additionally, there are two head-to-head comparisons of risperidone's efficacy. Miral et al (2008) found that risperidone was significantly better than haloperidol in improving behavioural symptoms in children with ASD. On the other hand, Nikvarz et al (2016) did not find any significant intergroup difference in outcome, although both memantine and risperidone significantly improved behaviour in children with ASD.

In summary, there is some moderate-quality evidence on the efficacy of low-dose risperidone in improving behaviours that challenge in children with ASD and/or intellectual disabilities. The RCTs also show a strong placebo effect. The effect of placebo and risperidone is evident within the first week or two but then tends to plateau, often leading to a dose increase. The main concerns are adverse effects such as weight gain and sedation. Although the sedative effect tends to diminish over time, weight gain remains a long-term problem. The evidence to support the use of risperidone for treating behaviours that challenge in adults with intellectual disabilities and/or ASD is at present equivocal.

Aripiprazole

Children with ASD

There are four RCTs on aripiprazole versus placebo in children with ASD (Marcus 2009; Owen 2009; Ichikawa 2017; NCT00198107 2019) (see Deb 2014; Alfageh 2019; D'Alò 2021). The two large-scale studies (Marcus 2009; Owen 2009) were conducted by the pharmaceutical company that produces aripiprazole, and the overlap among participants in these two studies is unclear. All four RCTs showed the superiority of aripiprazole over placebo using outcome measures such as the ABC-I, CGI-I and NCBRF. Following the RCT phase, two of these studies continued

with open-label administration of aripiprazole for 48–52 months, showing continuing efficacy over time, with reasonable tolerance of the adverse events (Marcus 2011; Findling 2014). Adverse events included weight gain, increased appetite, sedation, tiredness, drooling and tremor. However, aripiprazole improved serum prolactin levels in some participants and overall did not show any adverse effect on QTc interval (Deb 2014, 2016b).

Additionally, there are two head-to-head comparisons of aripiprazole's efficacy. One RCT (Ghanizade 2014) showed a significant treatment effect of both aripiprazole and risperidone on behaviours that challenge in children with ASD but no significant intergroup difference in the efficacy or the adverse events profile. Another RCT (DeVane 2019) found that both risperidone and aripiprazole significantly improved behaviour in children with ASD; risperidone showed better efficacy than aripiprazole, which was significant at some follow-up points, but there was a higher rate of weight gain than in the aripiprazole group, which became significant at some follow-up points.

In summary, there is some preliminary evidence to show the efficacy of aripiprazole in improving aggression, agitation and irritability in children with ASD. However, most of the evidence comes from research conducted by pharmaceutical companies. Therefore, more independent research is needed to draw any definitive conclusion.

Other second-generation antipsychotics

Children with ASD

Although several case studies have been published on other second-generation antipsychotics, apart from risperidone and aripiprazole, only two RCTs have been published; these are on olanzapine and lurasidone respectively. The olanzapine study (Hollander 2006) included only 11 children with ASD, who showed a significant improvement in CGI-I scores in the intervention group compared with the placebo group, but the treatment was associated with substantial weight gain. The multicentre lurasidone study (Loebel 2016) randomised 50 children with ASD (aged 6–17 years) to receive 20 mg/day lurasidone, 49 to receive 60 mg/day lurasidone and 51 to receive placebo. The 6-week double-blind trial did not show any significant intergroup difference in the primary outcome measure, the ABC-I score change. However, CGI-I scores showed a significant improvement at follow-up in the 20 mg/day dose group compared with the placebo group but not the other group. Adverse events included vomiting, drowsiness, modest weight gain and modest changes in the selected metabolic parameters. The rate of adverse events was non-significantly higher in the placebo group (Ji 2015, 2016; Alfageh 2019; D'Alò 2021).

There are no published RCTs on quetiapine, ziprasidone, paliperidone, iloperidone, brexpiprazole and asenapine involving people with intellectual disabilities or ASD.

There is not enough evidence to draw any definitive conclusion about the efficacy of any other antipsychotics apart from risperidone and aripiprazole for improving behaviours that challenge in children or adults with ASD and/or intellectual disabilities.

Antidepressants

Children with ASD

A recent systematic review and meta-analysis (Deb 2021b) found 13 RCTs on antidepressants (four on fluoxetine, two each on clomipramine, fluvoxamine, venlafaxine, and one each on citalopram, sertraline and agomelatine), involving a total of 782 primarily children with ASD (some of whom also had comorbid intellectual disabilities and a very small number were adults), which mainly assessed the effect of these medications on core ASD symptoms such as restricted and repetitive behaviour and language and communication impairment but also associated behaviours such as aggression, agitation, hyperactivity and irritability using measures such as the Children's Yale–Brown Obsessive–Compulsive Scale (Scahill 2006), CGI-I, Autism Diagnostic Observation Schedule (ADOS) (Lord 1999) and ABC-I. No RCT assessed the efficacy of antidepressants on depression or anxiety symptoms in children with ASD. The RCTs showed mixed results, and the meta-analysis of pooled data did not reveal any statistically significant intergroup difference in efficacy. The reported adverse events were mild and showed no significant intergroup difference in most studies. The overall quality of the included studies was poor, with 47% showing high risk of at least one bias according to the Cochrane Risk of Bias tool (Higgins 2020) and 67% scoring less than the maximum achievable score of 5 on the Jadad scale (Jadad 1996).

Adults with intellectual disabilities

A previous systematic review (Sohanpal 2007) found only one very small RCT on clomipramine involving ten adults with intellectual disabilities, showing some improvement in stereotypies and repetitive behaviours in the intervention group compared with the placebo group. Additionally, two very small RCTs involving clomipramine and imipramine did not show any superiority of

antidepressants over placebo in people with intellectual disabilities but produced significant adverse events (Ji 2016). The rest were case studies or retrospective chart reviews that showed improvement in behaviours that challenge, including self-injurious behaviour, in less than half of the individuals concerned. The effect was more pronounced in the presence of background depressive and anxiety symptoms, but a high proportion showed medication-related adverse events. First-generation antidepressants are no longer recommended, owing to their significant adverse effects and potential for overdose-related death.

There is not enough evidence currently to draw any definitive conclusion on the efficacy of antidepressants in treating core ASD symptoms or behaviours that challenge in children or adults with ASD and/or intellectual disabilities.

Anti-anxiety medication

Children and adults with ASD

A recent systematic review and meta-analysis found, apart from a few small single-dose studies of the beta-blocker propranolol, only two RCTs on anti-anxiety medication. The RCTs were both on buspirone, involved a total of 176 people with ASD and showed contradictory findings. It was impossible to pool data on the two buspirone studies to conduct a meta-analysis (Deb 2021b, 2022d). A literature review in 2016 found no RCT on anti-anxiety medications involving people with intellectual disabilities (Deb 2016b). The long-term use of benzodiazepines is not recommended because of the potential for addiction, tolerance and withdrawal symptoms and their effect on cognition, particularly affecting children's development and, in some cases, the emergence of paradoxical aggression (Kalachnik 2002).

There is currently not enough evidence to draw a definitive conclusion on the efficacy of anti-anxiety medication in treating core ASD symptoms and associated behaviours, such as behaviours that challenge, in children or adults with ASD and/or intellectual disabilities.

Mood stabilisers

Children with ASD

A recent systematic review and meta-analysis (Limbu 2022) found eight RCTs (four on valproate, two on levetiracetam and one each on lamotrigine and topiramate) involving 310 people with ASD, primarily children, that assessed the efficacy of mood stabilisers on core ASD symptoms and associated behaviours, including irritability and aggression but not bipolar disorder. Only two small studies (25%) from the same research group (Hollander 2006, 2010) showed superiority of divalproex sodium over placebo. Another study showed superiority of combined treatment with levetiracetam and psychoeducation over psychoeducation alone (Wang 2017). Meta-analysis of pooled data on scores on the ABC-I, CGI-I and Overt Aggression Scale (OAS)/OAS-modified (OAS-M) (Coccaro 2020) did not show any significant intergroup difference in the efficacy of mood stabilisers and the rate of adverse events.

Children and adults with intellectual disabilities

There are four RCTs (two cross-over and two parallel-design) on add-on lithium therapy involving a small number of (n = 14–52) in-patient adults or outpatient children with intellectual disabilities (Ji 2015 and Deb 2008). Three were published in peer-reviewed journals and one in a book chapter. The outcome measures used in these studies were not standardised. The findings were equivocal as in the same studies there were improvements according to some outcome measures but not others. As for other mood stabilisers, there is only one small RCT involving ten adults with intellectual disabilities that compared add-on carbamazepine with placebo in a cross-over trial that showed no significant intergroup difference in behaviours that challenge (Reid 1981). It may be challenging to conduct the necessary investigations required for lithium therapy in many people with intellectual disabilities. Once the drug is started, it becomes difficult to withdraw it. Any imbalance in the body's homeostasis, such as dehydration, can cause toxicity. Therefore, lithium should only be considered after a careful multidisciplinary discussion.

There is not enough evidence to conclude on the efficacy of mood stabilisers in treating core ASD symptoms or associated behaviours, such as behaviours that challenge, in children or adults with ASD and/or intellectual disabilities.

Opioid antagonists

A systematic review of the use of naltrexone in children with ASD and/or intellectual disabilities found ten RCTs, primarily cross-over trials; these showed some efficacy of this medication on symptoms such as irritability, hyperactivity and self-injurious behaviour (Roy 2015a). Another systematic review of naltrexone in adults with ASD and/or intellectual disabilities found a further ten cross-over trials and these showed some efficacy primarily on self-injurious behaviour (Roy 2015b). Adverse events were mild and included sedation, loss of appetite, weight loss, sleep problems, stereotypies and paradoxical increase in aggression.

There is therefore some weak evidence that is insufficient to draw any definitive conclusion about the efficacy of opioid antagonists in treating behaviours that challenge in children or adults with ASD and/or intellectual disabilities.

Psychostimulants

Children with intellectual disabilities

A recent systematic review of methylphenidate for ADHD found 13 RCTs involving 315 children with intellectual disabilities but no study on adults (Tarrant 2018). The mean response rate to methylphenidate of 40–50% (effect size: 0.5) is lower than that reported in the general population (average: 70–80%; effect size: 0.8–1.3). Significant adverse events included sleep difficulties, poor appetite and weight loss. Other important adverse events included irritability, social withdrawal and increased motor activities, including tic. The types and rates of adverse events (average: 12–24%) are similar in the intervention and the placebo groups and in typically developing children (average: 12.5%). Methylphenidate effectively improves aggression associated with ADHD in typically developing children, but there is no definte evidence for this effect among children with intellectual disabilities. In practice, it is not always easy to diagnose aggression or other behaviours that challenge in people with ADHD, particularly in the presence of intellectual disabilities, because of symptom overlap among these conditions (Deb 2022e).

Children with ASD

There have not been many RCTs on methylphenidate involving individuals with ASD. This is for two reasons. First, before the publication of DSM-5 (American Psychiatric Association 2013) it was not possible to make an ADHD diagnosis in the presence of ASD. Second, there was concern that methylphenidate might make ASD symptoms worse. In contrast, some studies have reported improvement in core ASD symptoms, such as social communication and self-regulation, in children treated with methylphenidate (Jahromi 2009; Pearson 2013). Studies have shown a moderate effect size for methylphenidate (about 0.5) in improving ASD symptoms (Research Units on Pediatric Psychopharmacology Autism Network 2005; Pearson 2013 cited in Tarrant 2018). Overall, methylphenidate was reasonably tolerated, although a proportion showed adverse events, and about 18% discontinued the RUPP trial because of either definite or possible adverse events (Research Units on Pediatric Psychopharmacology Autism Network 2005). The adverse effects reported in the small sample in Pearson et al's study (2013) were mild. In Simonoff et al's study (2013), the presence of ASD in children with intellectual disabilities did not affect the overall outcome.

There is evidence for the efficacy of methylphenidate in treating ADHD symptoms in children with intellectual disabilities. However, evidence for children with ASD is in its early stages, and there is not enough evidence to draw any definitive conclusion about the efficacy of methylphenidate for treating ADHD symptoms in adults with intellectual disabilities and/or ASD.

Other pharmacological interventions

Several RCTs have been published involving ampakine, mavoglurant, basimglurant, piracetam, memantine, arbaclofen, anti-dementia medications, L-carnitine, L-acetylcarnitine, oxytocin, growth hormones, melatonin, thyroxine, minocycline, creatin, folate, betaine, Metafolin® (L-methylfolate), creatine, vitamin B_{12} and folinic acid for core symptoms and associated behaviours in intellectual disabilities, for specific syndromes such as fragile-X or Rett or for dementia symptoms; these primarily showed no effect of these interventions (see review by Ji & Findling, 2016).

RCTs have also been published involving known and novel pharmaceutical interventions such as rivastigmine, galantamine, donepezil, D-cycloserine, N-acetylcysteine, amantadine, memantine, riluzole, acamprosate, arbaclofen, bumetanide, oxytocin, vasopressin, balovaptan, sulforaphane, tetrahydrobiopterin, L-carnitine, methyl B_{12}, omega-3 fatty acids, folinic acid, intranasal ketamine, prednisolone, cannabinoid, dextromethorphan/quinine, naltrexone, melatonin and secretin to treat core ASD symptoms and associated behaviours; these have shown very mixed results so far. A detailed description of these studies is outside the scope of this article, but further information is available from reviews by Ji & Findling (2015), Deb et al (2022b) and Baribeau et al (2022).

Evidence summary

- There is moderate-quality evidence to show that short-term low-dose risperidone is probably effective in improving irritability, agitation and aggression in children with ASD and/or intellectual disabilities.
- However, the evidence shows a pronounced placebo effect and also, after initial improvement within a week or two, the effect tends to plateau, sometimes leading to further dose increase.
- The evidence on the efficacy of risperidone in adults with intellectual disabilities and/or ASD is equivocal.

BOX 6 Common and serious adverse events associated with psychotropic medications

Both treatment with and withdrawal of selective serotonin reuptake inhibitors (SSRIs) and benzodiazepines can cause hyperactivity, restlessness, irritability and aggression. Therefore, starting treatment with a low dose and increasing the dose gradually is necessary. Withdrawal of the medications should be cautious, with gradual dose reduction. If necessary, restart slowly or use a different SSRI.

Long-term use of benzodiazepines is contraindicated because of their propensity to result in tolerance over time, leading to the potential for addiction and difficulty with withdrawal. Their effect on cognition is likely to impair the development of children. Benzodiazepines can also paradoxically increase aggression in some people.

Serotonin syndrome is a rare but serious adverse event usually associated with SSRIs (particularly with the polypharmacy of SSRIs). Symptoms include tachycardia, sweating, raised blood pressure and body temperature, dilated pupils and myoclonus leading to shock. Treatment is symptomatic, with the immediate discontinuation of the SSRIs and the use of serotonin antagonists such as cyproheptadine.

Obesity, metabolic syndrome and diabetes, the common adverse effects of antipsychotics, may significantly increase premature death if not treated promptly.

Sedation, weight gain and hyperprolactinaemia with or without breast milk discharge are common adverse effects of risperidone and other second-generation antipsychotics. In many cases, these symptoms tend to improve over time.

Extrapyramidal symptoms such as akathisia (often confused with agitation and improperly treated), dystonia, oculogyric crises and Parkinsonism are associated primarily with first-generation antipsychotics but may also occur with risperidone and other second-generation antipsychotics. These symptoms may be misinterpreted as part of intellectual disabilities or autism spectrum disorder phenotypes because of diagnostic overshadowing (Reiss 1993) (Box 7).

Neuroleptic malignant syndrome associated with antipsychotic treatment is rare but can be life-threatening. Symptoms include raised body temperature, fluctuating blood pressure, muscle stiffness, sweating and other evidence of autonomic dysregulation. Muscle creatine phosphokinase is raised, treatment should be symptomatic and immediate discontinuation of antipsychotics is necessary.

Constipation is primarily associated with tricyclic antidepressants and some antipsychotics. If neglected, it can lead to severe distress due to headache, depression and/or abdominal pain, which may be expressed as sleep disorders, loss of appetite, agitation and aggression in people with neurodevelopmental disorders.

Anticholinergic syndrome, associated with tricyclic antidepressants and some antipsychotics, may lead to agitation, motor restlessness, dysarthria, disorientation, hallucinations and convulsions. More severe symptoms include constipation, urinary retention, dry mouth, fever and tachycardia.

- Weight gain and sedation remain two main worrying adverse events, among others. Whereas sedation tends to reduce over time, weight gain remains a long-term problem.
- There is some preliminary evidence that aripiprazole may be effective in improving agitation and aggression in children with ASD.
- More independent research is needed without the involvement of pharmaceutical companies to reach a definitive conclusion.
- Based on the current evidence, the US Food and Drug Administration (FDA) has licensed the short-term use of low-dose risperidone and aripiprazole to treat agitation, irritation and aggression in children with ASD.
- Currently, there is not enough evidence to draw any definitive conclusion about the efficacy of any other medication for treating behaviours that challenge in people with intellectual disabilities and/or ASD.

Adverse events

Many people with intellectual disabilities and/or ASD receive psychotropic polypharmacy and high-dose antipsychotics (Deb 2015; Sheehan 2015; Bertelli 2022), which as we have mentioned increases the chance of drug–drug interactions and medication-related adverse events. Extrapyramidal adverse events may be more pronounced in this population than in the general population (Sheehan 2017). The metabolic syndrome usually associated with second-generation antipsychotics may or may not be more prevalent in people with intellectual disabilities than in the general population (Frighi 2011). However, weight gain and sedation remain two main adverse events that may impair the person's quality of life. Agitation associated with some selective serotonin reuptake inhibitors (SSRIs) and constipation from the use of antipsychotics may also cause significant problems in this vulnerable group, and cholinergic overload with these medications brings the risk of cognitive impairment, particularly in children (Box 6) (Deb 2022b). In people with schizophrenia in the general population, the number needed to harm (NNH) for risperidone varies from 15 for akathisia to 13 for sedation; for aripiprazole the NNH varies from 31 for akathisia to 34 for somnolence (Citrome 2017). No equivalent data on NNH are

BJPsych Advances (2023), vol. 29, 322–333 doi: 10.1192/bja.2022.61

available for people with ASD and/or intellectual disabilities.

Withdrawal of psychotropics

One way of reducing the overmedication of people with intellectual disabilities and/or ASD is to discontinue psychotropic medications used to manage their behaviour. Studies have shown that withdrawal of psychotropic medications even after long-term use improves the person's quality of life (Ramerman 2018b). Studies in the UK and The Netherlands have shown that even after long-term use, it is possible to discontinue antipsychotic medication in 25–61% of adults with intellectual disabilities and to achieve a 50% or more dose reduction in another 11–19%, although in up to 20% of cases antipsychotics were reinstated within 3–4 years, primarily due to resurgence of behaviours that challenge (Sheehan 2017; Shankar 2019).

However, the resurgence of challenging behaviour may not be related to the withdrawal of medication, and the clinician will need to make a full assessment of the causes and effects of such behaviour using standard methodology (Deb 2016a, 2022a; https://spectrom.wixsite.com/project; supplementary Appendix 1). The withdrawal of psychotropic medications might unmask a previously undiagnosed psychiatric disorder or lead to a relapse of behaviours that challenge (Box 8, example (a)). Discontinuation or dose reduction may lead to withdrawal or rebound syndromes such as insomnia, anxiety and panic, which have been associated with the withdrawal of benzodiazepines and SSRIs. A supersensitivity syndrome consisting of extrapyramidal symptoms such as akathisia, Parkinsonism and dyskinesia has been associated with antipsychotic withdrawal (Box 8, example (b)) (Cerovecki 2013). Supersensitivity psychosis may emerge within 6 to 12 weeks of antipsychotic discontinuation or dose reduction (Chouinard 2008). These discontinuation syndromes all produce psychiatric symptoms that can be confounded with true relapse of psychosis or behaviours that challenge. Alternatively, these symptoms may manifest as behaviours that challenge in people with intellectual disabilities and/or ASD. An important message for the clinicians is that most of these symptoms are treatable and resolve within weeks or months. Clinicians should also consider the nocebo effect (Planès 2016). For example, in some cases, caregiver's anxiety may exacerbate an individual's challenging behaviour or its perception, leading to greater reporting of such behaviour. Therefore, clinicians need to develop a detailed withdrawal plan considering all the factors that might affect withdrawal and have a contingency plan after a full multidisciplinary discussion involving the family and the individual concerned.

BOX 7 The influence of carers on psychotropic prescribing and an example of diagnostic overshadowing

The proprietor of a community group home brought a 32-year-old man with moderate intellectual disabilities to the psychiatric clinic who did not speak. He had been on multiple psychotropic medications for several years, including several antipsychotics at a high dose and a regular dose of procyclidine. Examination revealed that he had severe tremors and dyskinetic body movements, including abnormal movements in his facial muscles. When the clinician proposed a reduction in psychotropic medications, the proprietor became very anxious, suggesting that the man had a long history of challenging behaviour and needed all his medication. Otherwise, he would become very aggressive. The proprietor commented that the movement disorders were nothing new, indirectly implying that they could not be harmful and were part of the phenotype of the man's intellectual disabilities.

BOX 8 Withdrawal of antipsychotic medication

(a) An example of a failed antipsychotic withdrawal attempt

A 68-year-old man with mild intellectual disability who developed dementia was treated with risperidone for many years because of a history of aggressive behaviour. After 3 months of gradual withdrawal of risperidone, the man became physically aggressive on one occasion in an evening club. The care staff panicked, and local police were called out, which led to the reinstating of risperidone by an emergency doctor.

(b) Withdrawal-related dyskinesia

A 54-year-old woman with mild intellectual disability with a long history of paranoid ideas and crying became confused and developed orofacial dyskinesia after withdrawal of long-standing risperidone. These symptoms improved after reinstating risperidone.

Conclusions

Despite significant public health concerns and the NHS England STOMP-STAMP initiative, and in general the lack of evidence of the efficacy of psychotropic medications, their rate of use (particularly off-label) to treat behaviours that challenge in children and adults with intellectual disabilities and/or autism does not seem to have changed much in the past three decades, even after the resettlement of these people from long-stay institutions into community settings. Despite the publication of national and international guidelines, good clinical practice has not been implemented. Although free online training introduced through face-to-face workshops has recently been developed for care/support staff to help with the implementation of STOMP-STAMP, there is an urgent need to establish a national/

MCQ answers
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international structure backed up by training to guide clinicians to embark on good clinical practice to help reduce the overmedication of this population.

Supplementary material

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Author contributions

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Declaration of interest

None.

References[a]

Bachmann CJ, Manthey T, Kamp-Becker I, et al (2013) Psychopharmacological treatment in children and adolescents with autism spectrum disorders in Germany. *Research in Developmental Disabilities*, **34**: 2551–63.

Bertelli MO, Azeem MW, Underwood L, et al (2022) Autism spectrum disorder. In *Textbook of Psychiatry for Intellectual Disability and Autism Spectrum Disorder* (eds MO Bertelli, S Deb, K Munir, et al): 369–455. Springer Nature.

Coury DL, Anagnostou E, Manning-Courtney P, et al (2012) Use of psychotropic medication in children and adolescents with autism spectrum disorders. *Pediatrics*, **130** (suppl 2): s69–76.

D'Alò GL, Crescenzo FD, Amato L, et al (2021) Impact of antipsychotics in children in children and adolescents with autism spectrum disorder: a systematic review and meta-analysis. *Health and Quality of Life Outcomes*, **19**: 33.

Deb S, Fraser WI (1994) The use of psychotropic medication in people with learning disability: towards rational prescribing. *Human Psychopharmacology*, **9**: 259–72.

Deb S, Chaplin R, Sohanpal S, et al (2008) The effectiveness of mood stabilisers and antiepileptic medication for the management of behaviour problems in adults with intellectual disability: a systematic review. *Journal of Intellectual Disability Research*, **52**: 107–13.

Deb S, Kwok H, Bertelli M, et al (2009) International guide to prescribing psychotropic medication for the management of problem behaviours in adults with intellectual disabilities. *World Psychiatry*, **8**: 181–6.

Deb S, Farmah BK, Arshad E, et al (2014) The effectiveness of aripiprazole in the management of problem behaviour in people with intellectual disabilities, developmental disabilities and/or autistic spectrum disorder: a systematic review. *Research in Developmental Disabilities*, **35**: 711–25.

Deb S, Unwin G, Deb T (2015) Characteristics and the trajectory of psychotropic medication use in general and antipsychotics in particular among adults with an intellectual disability who exhibit aggressive behaviour. *Journal of Intellectual Disability Research*, **59**: 11–25.

Deb S, Bethea T, Havercamp S, et al (2016a) Disruptive, impulse-control, and conduct disorders. In *Diagnostic Manual – Intellectual Disability: A Textbook of Diagnosis of Mental Disorders in Persons with Intellectual Disability. DM-ID-2* (2nd edn) (eds R Fletcher, J Barnhill, S-A Cooper): 521–60. NADD Press.

Deb S (2016b) Psychopharmacology. In *Handbook of Evidence-Based Practices in Intellectual and Developmental Disabilities* (ed NN Singh): 347–81. Springer International Publishing.

Deb S, Nancarrow T, Limbu B, et al (2020) UK Psychiatrists' experience of withdrawal of antipsychotics prescribed for behaviours that challenge in adults with intellectual disabilities and/or autism. *BJPsych Open*, **6**(5): e112.

Deb S, Limbu B, Unwin G, et al (2021a) Short-term Psycho-Education for Caregivers to Reduce Overmedication of People with Intellectual Disabilities (SPECTROM): development and field testing. *International Journal of Environmental Research and Public Health*, **18**: 13161.

Deb S, Roy M, Lee R, et al (2021b) Randomised controlled trials of antidepressant and anti-anxiety medications for people with autism spectrum disorder: systematic review and meta-analysis. *BJPsych Open*, **7**(6): e179.

Deb S, Unwin G, Cooper S-A, et al (2022a) Problem behaviours. In *Textbook of Psychiatry for Intellectual Disability and Autism Spectrum Disorder* (eds MO Bertelli, S Deb, K Munir, et al): 145–86. Springer Nature.

Deb S, Bertelli MO, Rossi M (2022b) Psychopharmacology. In *Textbook of Psychiatry for Intellectual Disability and Autism Spectrum Disorder* (eds MO Bertelli, S Deb, K Munir, et al): 247–2. Springer Nature.

Deb S, Perera B, Krysta K, et al (2022c) The European guideline on the assessment and diagnosis of psychiatric disorders in adults with intellectual disabilities. *European Journal of Psychiatry*, **36**: 11–25.

Deb S, Roy M, Limbu B, et al (2022d) Anti-anxiety medications and novel treatments for autism. In *Handbook of Autism and Pervasive Developmental Disorder: Assessment, Diagnosis, and Treatment* (eds JL Matson, P Sturmey): 1157–72. Springer Nature.

Deb S, Perera B, Bertelli MO (2022e) Attention deficit hyperactivity disorder. In *Textbook of Psychiatry for Intellectual Disability and Autism Spectrum Disorder* (eds MO Bertelli, S Deb, K Munir, et al): 457–82. Springer Nature.

de Kuijper G, Hoekstra P, Visser F, et al (2010) Use of antipsychotic drugs in individuals with intellectual disability (ID) in the Netherlands: prevalence and reasons for prescription. *Journal of Intellectual Disability Research*, **54**: 659–67.

Gore NJ, Sapiets SJ, Denne LD, et al (2022) Positive behavioural support in the UK: a state of the nation report. *International Journal of Positive Behavioural Support*, **12** (suppl 1): 4–39.

Ji NY, Findling RL (2015) An update on pharmacotherapy for autism spectrum disorder in children and adolescents. *Current Opinion in Psychiatry*, **28**: 91–101.

Ji NY, Findling RL (2016) Pharmacotherapy for mental health problems in people with intellectual disability. *Current Opinion in Psychiatry*, **29**: 103–25.

Lai M-C, Kassee C, Besney R, et al (2019) Prevalence of co-occurring mental health diagnoses in the autism population: a systematic review and meta-analysis. *Lancet Psychiatry*, **6**: 819–29.

Limbu B, Deb S, Roy M, et al (2022) Randomised controlled trials of mood stabilisers for people with autism spectrum disorder: a systematic review and a meta-analysis. *BJPsych Open*, **8**(2): e52.

Lugo-Marína J, Magán-Magantob M, Rivero-Santanac A, et al (2019) Prevalence of psychiatric disorders in adults with autism spectrum

a. This list of references has been truncated owing to space restrictions. The full list is available in the supplementary material.

disorder: a systematic review and meta-analysis. *Research in Autism Spectrum Disorders*, **59**: 22–33.

Oliver-Africano PC, Dickens S, Ahmed Z, et al (2010) Overcoming the barriers experienced in conducting a medication trial in adults with aggressive challenging behaviour and intellectual disabilities. *Journal of Intellectual Disability Research*, **54**: 17–25.

Research Units on Pediatric Psychopharmacology Autism Network (2005) Randomized, controlled, crossover trial of methylphenidate in pervasive developmental disorders with hyperactivity. *Archives of General Psychiatry*, **62**: 1266–74.

Roy A, Roy M, Deb S, et al (2015a) Are opioid antagonists effective in attenuating the core symptoms of autism spectrum conditions in children? A systematic review. *Journal of Intellectual Disability Research*, **59**: 293–306.

Roy A, Roy M, Deb S, et al (2015b) Are opioid antagonists effective in adults with intellectual disability? A systematic review. *Journal of Intellectual Disability Research*, **59**: 55–67.

Scahill L, McDougle CJ, Williams SK, et al (2006) Children's Yale-Brown Obsessive Compulsive Scale modified for pervasive developmental disorders. *Journal of the American Academy of Child & Adolescent Psychiatry*, **45**: 1114–23.

Scheifes A, Stolker JJ, Egberts ACG, et al (2011) Representation of people with intellectual disabilities in randomized controlled trials of antipsychotic treatment for behavioural problems. *Journal of Intellectual Disability Research*, **55**: 650–64.

Shankar R, Wilcock M, Deb S, et al (2019) A structured programme to withdraw antipsychotics among adults with intellectual disabilities: the Cornwall experience. *Journal of Applied Research in Intellectual Disability*, **32**: 1389–400.

Sheehan R, Hassiotis A, Walters K, et al (2015) Mental illness, challenging behaviour, and psychotropic drug prescribing in people with intellectual disability: UK population-based cohort study. *BMJ*, **351**: h4326.

Simonoff E, Pickles A, Charman T, et al (2008) Psychiatric disorders in children with autism spectrum disorders: prevalence, comorbidity, and associated factors in a population-derived sample. *Journal of the American Academy of Child & Adolescent Psychiatry*, **47**: 921–9.

Simonoff E, Taylor E, Baird G, et al (2013) Randomized controlled double-blind trial of optimal dose methylphenidate in children and adolescents with severe attention deficit hyperactivity disorder and intellectual disability. *Journal of Child Psychology and Psychiatry*, **54**: 527–35.

Sohanpal SK, Deb S, Thomas C, et al (2007) The effectiveness of antidepressant medication in the management of behaviour problems in adults with intellectual disabilities: a systematic review. *Journal of Intellectual Disability Research*, **51**: 750–65.

Tarrant N, Roy M, Deb S, et al (2018) The effectiveness of methylphenidate in the management of attention deficit hyperactivity disorder (ADHD) in people with intellectual disabilities: a systematic review. *Research in Developmental Disabilities*, **83**: 217–32.

Tyrer P, Oliver-Africano PC, Ahmed Z, et al (2008) Risperidone, haloperidol, and placebo in the treatment of aggressive challenging behaviour in patients with intellectual disability: a randomised controlled trial. *Lancet*, **371**: 57–63.

Unwin G, Deb S (2008a) A multi-centre audit of practice of prescribing psychotropic medication among adults with intellectual disabilities. *British Journal of Learning Disability*, **36**: 140–3.

Unwin G, Deb S (2008b) Use of medication for the management of behaviour problems among adults with intellectual disabilities: a clinicians' consensus survey. *American Journal on Mental Retardation*, **113**: 19–31.

Unwin GL, Deb S (2011) Efficacy of atypical antipsychotic medication in the management of behaviour problems in children with intellectual disabilities and borderline intelligence: a systematic review. *Research in Developmental Disabilities*, **32**: 2121–33.

MCQs

Select the single best option for each question stem

1 How many RCTs have assessed the efficacy of risperidone as a treatment for challenging behaviour in adults with intellectual disabilities and/or autism?
a 20
b 3
c 4
d 15
e 35.

2 How many RCTs have assessed the efficacy of risperidone for challenging behaviour in children with autism and/or intellectual disabilities?
a 13
b 10
c 20
d 30
e 4.

3 How many RCTs have assessed the efficacy of antidepressants for challenging behaviour in people with autism?
a 10
b 15
c 12
d 14
e 13.

4 How many RCTs have assessed the efficacy of mood stabilisers for challenging behaviour in people with autism?
a 2
b 4
c 6
d 8
e 5.

5 The mean number needed to treat to show effectiveness of risperidone for challenging behaviour in children with intellectual disabilities and/or ASD is:
a 1
b 3
c 8
d 9
e 10.