Pharmacological Treatment of Autism Spectrum Disorder: A Systematic Review of Treatment Guidelines

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ABSTRACT

Introduction Currently available systematic reviews on the pharmacological treatment of autism spectrum disorder (ASD) do not encompass all the evidence, as they exclude guidelines issued by national or local authorities that are not indexed in search engines such as PubMed.

Methods A systematic literature search was conducted to identify clinical guidelines on this topic using EMBASE, Medline, and PsycINFO. A manual search was also performed to identify guidelines by national or local authorities not included in the aforementioned databases.

Results Thirty-eight guidelines were identified through manual search, including 27 items through search engines, 2 general guidelines, and 9 government agency guidelines. Many guidelines recommended risperidone (N = 16) for the characteristic behaviors of ASD core features. For attention-deficit/hyperactivity disorder (ADHD) features, methylphenidate was most frequently recommended (N = 23) for both inattention (N = 6) and hyperactivity/impulsivity (N = 16). Risperidone was also frequently recommended for maladaptive behaviors (N = 33).

Discussion A comprehensive literature search identified treatment guidelines for ASD issued by local or national administrative bodies that were not captured through search engines alone. There was some consensus among the guidelines on the use of psychotropics in alleviating specific features of ASD. However, physicians need to be aware of the lack of high-quality evidence supporting these recommendations.

Introduction

Autism spectrum disorder (ASD) is a prevalent neurodevelopmental disorder. According to the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5), the essential features of ASD include persistent impairments in reciprocal social communication and social interaction, as well as restricted repetitive patterns of behavior, interests, or activities [1]. Additionally, many individuals with ASD exhibit psychiatric symptoms that are not part of the diagnostic criteria for the disorder [1]. The management of difficulties associated with ASD often includes psychosocial and behavioral interventions, because the evidence base for pharmacotherapy remains weak. Only two antipsychotics, risperidone and aripiprazole, have been approved by the U.S. Food and Drug Administration (FDA) for the treatment of severe irritability and aggression in children with ASD [2]. To guide physicians in selecting appropriate pharmacological treatments for individuals with ASD, several guidelines and consensus statements have been published. A previous systematic review of clinical practice guidelines did not

include many guidelines issued by national or local authorities that were not indexed in databases such as PubMed [3]. It is important to review a broader range of available treatment guidelines to examine the currently recommended treatment options for ASD comprehensively. Therefore, we systematically reviewed the treatment guidelines and consensus statements regarding pharmacotherapy for ASD, including those that were not identified in previous meta-guidelines.

Methods

Literature search

This review adhered to the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [4]. A study protocol was prepared before commencing data collection and was registered in the International Prospective Register of Systematic Reviews (registration number CRD42023418829). The literature search was conducted using EMBASE, Medline, and PsycINFO with the following keywords: (autism OR autistic OR ASD) AND (treatment* OR therap* OR intervention) AND (guideline* OR algorithm* OR consensus* OR recommendation*). The final search was conducted on March 21, 2024. The search was limited to publications from the year 2000 onwards, focusing on studies involving humans and published in English. Additionally, a manual search was performed to identify guidelines from national or local authorities not included in the aforementioned databases. Additionally, a manual search was performed, which included Google searches for government agency documents and updated guidelines, as well as citation chaining for other relevant sources. This search aimed to identify guidelines from national or local authorities not included in the aforementioned databases. Our review did not set specific age criteria in the initial search to ensure comprehensive coverage across all age groups. However, in this analysis, we categorized recommendations for children (under 18 years) and adults (18 years and older) to capture age-specific guidance.

Data extraction

Two researchers (ST and HU) independently searched for and identified treatment guidelines or consensus statements that met the inclusion criteria. We included literature describing (1) pharmacotherapy for ASD, Asperger syndrome, or pervasive developmental disorder (PDD), and (2) the type or name of drugs recommended for the treatment of core features and common co-occurring conditions in these disorders. Literature focusing on diagnosis, assessment or non-pharmacological treatment were excluded. Reviews that did not include any treatment recommendations were also excluded. Any disagreements regarding the inclusion or exclusion of studies were resolved through discussion with a third researcher.

Features

This review categorized the target features of ASD into three major groups: ASD core features, Attention-Deficit/Hyperactivity Disorder (ADHD) features, and comorbidities with further sub-features within each category. Based on the DSM-5 criteria [1], ASD core features were broadly classified into social communication and interaction, including impairment in social interaction/relationship/skill, communication difficulties, and social withdrawal; and characteristic behaviors, including stereotypy, and restricted repetitive behaviors. ADHD symptoms, frequently comorbid with ASD, are defined by impairing levels of inattention, disorganization, and/or hyperactivity-impulsivity [1]. In this review, ADHD features were classified into attention disorder features, including inattention; and hyperactive disorder features, including hyperactivity and impulsivity. Individuals with ASD, including children and adults, often have comorbid conditions such as ADHD, anxiety disorders, sleep-wake disorders, disruptive impulse-control and conduct disorders, depressive disorders, and obsessive-compulsive disorder (OCD) [5, 6]. In this review, comorbid features were broadly classified into maladaptive behaviors, including self-injury, behavioral problems such as disruptive behavior, tantrums, and irritability/aggression; anxiety and OCD features; mood disorder features; sleep problems; catatonia; and Tourette/tic features.

Results

The literature search process is illustrated in ▶ **Fig. 1**. A total of 38 treatment guidelines and algorithms were identified [7–54] (▶ **Table 1**). The recommendations are categorized as "children" under 18 years and 'adults' over 18 years. They are listed together with the recommendations in ▶ **Table 1–4**.

Core features

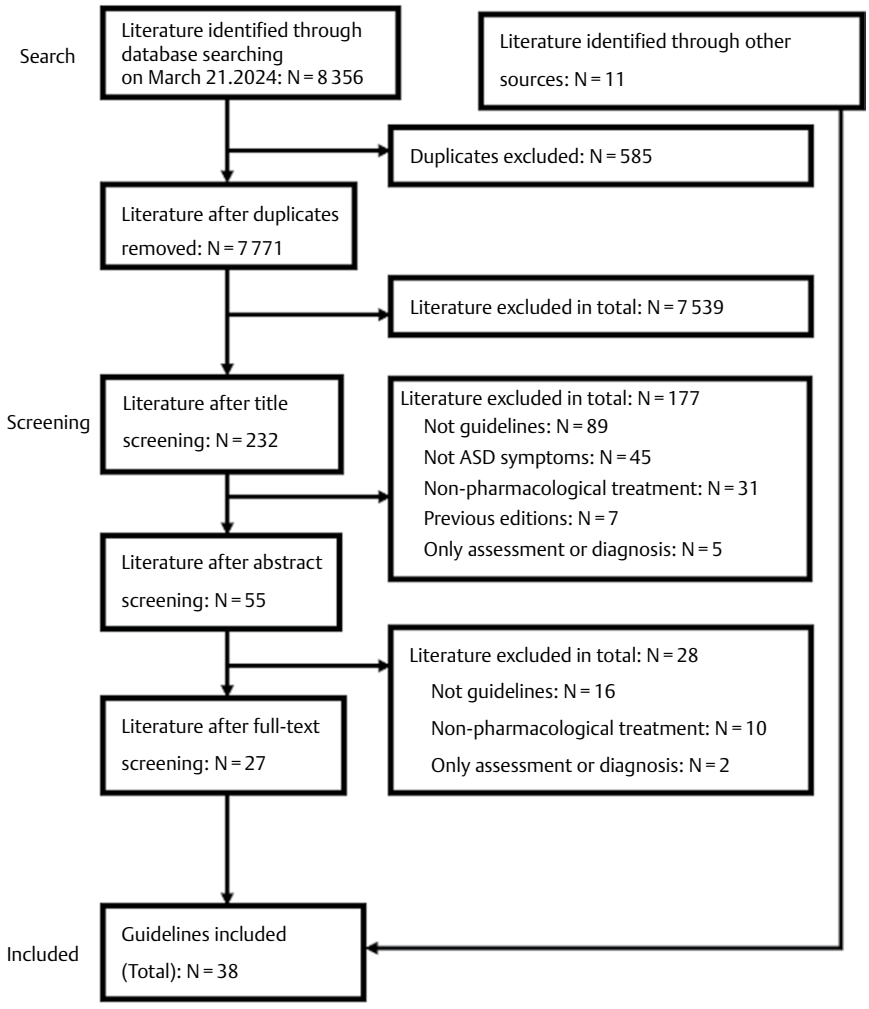
Of the 38 guidelines, 30 medications or medication classes were recommended for the core features of ASD (▶ **Table 2**). Risperidone was recommended by the highest number of guidelines (N = 17). This was followed by aripiprazole (N = 5), fluoxetine (N = 5), and haloperidol (N = 3). However, haloperidol was not recommended in guidelines published after 2016.

Twenty drugs were recommended for the characteristics of social communication and interaction according to eight guidelines. Of these, risperidone was the most frequently recommended drug (N = 3), followed by fluvoxamine (N = 2) and galantamine (N = 2).

Twenty-three drugs were recommended for alleviating the behavioral characteristics of autism, including stereotype behavior, restricted behavior, repetitive behavior, and the features described as "autistic behavior", according to the 21 guidelines. Risperidone was the most frequently recommended drug (N = 16), followed by aripiprazole (N = 11), fluoxetine (N = 5), haloperidol (N = 3), fluvoxamine (N = 3), citalopram (N = 2), valproic acid (N = 2), and an unspecified "antidepressant" (N = 2). Two guidelines referred to "core features (or autistic features)" without further specification. Donepezil (N = 1) and tetrahydrobiopterin (N = 1) were recommended to treat these "core features." The guideline by Choueiri and Zimmerman [35] extends its recommendations beyond galantamine to include buspirone, donepezil, rivastigmine, and tetrahydrobiopterin for managing behavioral characteristics in ASD. These recommendations are based on credible postulated mechanisms of action for each compound. However, the guideline emphasizes that the safety and efficacy of these medications are supported by limited evidence.

ADHD features

Of the 38 guidelines, 27 medications or medication classes were recommended for ADHD features in individuals with ASD (▶ **Table 3**).



▶ **Fig. 1** PRISMA flow diagram of the literature search.

Methylphenidate was recommended by the highest number of guidelines (N = 23). This was followed by atomoxetine (N = 16), aripiprazole (N = 12), guanfacine (N = 13), risperidone (N = 11), clonidine (N = 10), naltrexone (N = 3), α2 agonists (N = 3), "stimulants" (N = 2), amphetamine (N = 2), lofexidine (N = 2), and dextroamphetamine (N = 2).

In total, 21 drugs were recommended for attention disorder features, one of the ADHD features, in 11 guidelines. Among them, methylphenidate was the most frequently recommended (N = 6), followed by atomoxetine (N = 4), guanfacine (N = 4), amphetamine (N = 2), dextroamphetamine (N = 2), and clonidine (N = 2). Recommendations for 24 drugs for hyperactive disorder and other ADHD features were included in the 24 guidelines. Methylphenidate was the most frequently recommended drug (N = 16), followed by risperidone (N = 11), atomoxetine (N = 7), clonidine (N = 4), naltrexone (N = 3), haloperidol (N = 2), unspecified "stimulants" (N = 2), amphetamine (N = 2), and dextroamphetamine (N = 2).

Twenty guidelines referred to "ADHD features" without further specification. For these "ADHD features," seven medications were recommended. Of these, methylphenidate (N = 9) and atomoxetine (N = 9) were the most frequently recommended, followed by clonidine (N = 6), guanfacine (N = 6), and lofexidine (N = 2).

Comorbid features

Of the 38 guidelines, 49 medications or medication classes were recommended for maladaptive behaviors in individuals with ASD (▶ **Table 4**). Risperidone was recommended by the highest number of guidelines (N = 33). This was followed by aripiprazole (N = 26), haloperidol (N = 8), clonidine (N = 5), olanzapine (N = 3), fluvoxamine (N = 3), guanfacine (N = 3), valproic acid (N = 3), and propranolol (N = 3). Other medications recommended included "antipsychotics" (N = 2), "selective serotonin reuptake inhibitors (SSRIs)" (N = 2), sertraline (N = 2), divalproex sodium (N = 2), citalopram (N = 2), escitalopram (N = 2), pentoxifylline (N = 2), and galantamine (N = 2). The guideline by Choueiri and Zimmerman [35] extends its recommendations beyond galantamine to include buspirone and luteolin for managing maladaptive behaviors in ASD. These recommendations are based on credible postulated mechanisms of action

▶ **Table 1** List of identified guidelines/consensus.

First author, editor, or organization	Year	Title	Entity authorizing the guideline/ consensus	Source
Wiener JM [7]	2004	The American psychiatric publishing textbook of child and adolescent psychiatry, 3rd ed	N.A.	S.E.
Filipek PA [8]	2006	Intervention for autistic spectrum disorders	N.A.	S.E.
Carr JE [9]	2007	Autism spectrum disorders in early childhood: An overview for practicing physicians	N.A.	S.E.
Gleason MM [10]	2007	Psychopharmacological treatment for very young children: Contexts and guidelines	N.A.	S.E.
Hollander E [11–15]	2007	Clinical manual for the treatment of autism	N.A.	S.E.
Myers SM [16]	2007	Management of children with autism spectrum disorders	American Academy of Pediatrics	H.S.
Tsai LY [17]	2007	Asperger syndrome and medication treatment	N.A.	S.E.
Dryden-Edwards RC [18]	2010	Developmental disabilities from childhood to adulthood: What works for psychiatrists in community and institutional settings	N.A.	H.S.
Matson JL [19–21]	2011	International handbook of autism and pervasive developmental disorders	N.A.	S.E.
Brian R [22]	2011	Evidence-based practices and treatments for children with autism	N.A.	S.E.
Missouri Autism Guidelines Initiative [23]	2012	Autism spectrum disorders: Guide to evidence-based intervention	Missouri Autism Guidelines Initiative	H.S.
National Institute for Health and Care Excellence [24]	2012	Autism spectrum disorder in adults: Diagnosis and management	National Institute for Health and Care Excellence	H.S.
Siegel M [25]	2012	Psychopharmacology of autism spectrum disorder: Evidence and practice	N.A.	S.E.
Manning-Courtney P [26]	2013	Autism spectrum disorders	N.A.	S.E.
National Institute for Health and Care Excellence [27]	2013	Autism spectrum disorder in under 19 s: Support and management	National Institute for Health and Care Excellence	H.S.
Swedish Agency for Health Technology Assessment of Social Services [28]	2013	Autism spectrum disorders diagnosis and interventions, organization of care and patient involvement	Swedish Agency for Health Technology Assessment and Assessment of Social Services	H.S.
McPartland JC [29]	2014	Asperger syndrome: Assessing and treating high-functioning autism spectrum disorders, 2nd ed	N.A.	S.E.
Veereman G [30]	2014	Management of autism in children and young people: A good clinical practice guideline	Belgian Health Care Knowledge Centre	H.S.
Volkmar, F [31]	2014	Practice parameter for the assessment and treatment of children and adolescents with autism spectrum disorder	The American Academy of Child and Adolescent Psychiatry	S.E.
Ministries of Health and Education [32]	2016	New Zealand autism spectrum disorder guideline, 2nd ed	New Zealand Ministries of Health and Education	H.S.
Scottish Intercollegiate Guidelines Network [33–34]	2016	Assessment, diagnosis and interventions for autism spectrum disorders	Scottish Intercollegiate Guidelines Network	H.S.
Choueiri RN [35]	2017	New assessments and treatments in ASD	N.A.	S.E.
National Consultation Meeting for Developing IAP Guidelines on Neuro Developmental Disorders under the aegis of IAP Childhood Disability Group and the Committee on Child Development and Neurodevelopmental Disorders [36]	2017	Consensus statement of the Indian academy of pediatrics on evaluation and management of autism spectrum disorder	Indian Academy of Pediatrics	S.E.
Schroeder CS [37]	2017	Assessment and treatment of childhood problems: A clinician's guide, 3rd ed	N.A.	S.E.

▶ **Table 1** Continued.

First author, editor, or organization	Year	Title	Entity authorizing the guideline/ consensus	Source
Baumer N [38]	2018	Evaluation and Management of the Child with Autism Spectrum Disorder	N.A.	S.E.
Chaplin S [39]	2018	BAP consensus guidelines on autism spectrum disorder	The British Association for Psychopharmacology	S.E.
Howes OD [40]	2018	Autism spectrum disorder: Consensus guidelines on assessment, treatment and research from the British association for psychopharmacology	The British Association for Psychopharmacology	S.E.
Ip A [41]	2019	Post-diagnostic management and follow-up care for autism spectrum disorder	Canadian Paediatric Society	S.E.
Subramanyam AA [42]	2019	Clinical practice guidelines for autism spectrum disorders	N.A.	S.E.
Hyman SL [43]	2020	Identification, evaluation, and management of children with autism spectrum disorder	The American Academy of Pediatrics	S.E.
Young S [44]	2020	Guidance for identification and treatment of individuals with attention deficit/hyperactivity disorder and autism spectrum disorder based upon expert consensus	N.A.	S.E.
Dubai Health Authority [45]	2021	Dubai clinical practice guidelines for autism spectrum disorder (ASD) in children and adolescents (from birth to 18 years of age) version 1	Dubai Health Authority	H.S.
Fuentes J [46]	2021	ESCAP practice guidance for autism: A summary of evidence-based recommendations for diagnosis and treatment	European Child & Adolescent Psychiatry ASD Working Party	S.E.
Long M [47]	2021	Autism Spectrum Disorder	N.A.	S.E.
National Collaborating Centre for Mental Health [48]	2021	Autism – management of autism in children and young people	National Institute for Health and Care Excellence	H.S.
Lord C [49]	2022	The Lancet commission on the future of care and clinical research in autism	The Lancet	S.E.
Matson JL [50–53]	2022	Handbook of autism and pervasive developmental disorder: Assessment diagnosis and treatment	N.A.	S.E.
Spain D [54]	2022	Psychological therapies for adults with autism	N.A.	S.E.

Abbreviations: N.A., not applicable; S.E., search engine; H.S., hand search.

for each compound. However, the guideline emphasizes that the safety and efficacy of these medications are supported by limited evidence.

Fifteen of the 38 guidelines recommended 23 medications or medication classes for anxiety and OCD features in individuals with ASD (▶ **Table 4**). Fluoxetine (N = 6) and sertraline (N = 6) were the most frequently recommended drugs, followed by "SSRIs" (N = 5), buspirone (N = 3), fluvoxamine (N = 3), risperidone (N = 3), and citalopram (N = 3). Other medications recommended included clomipramine (N = 2), escitalopram (N = 2), paroxetine (N = 2), propranolol (N = 2), and clonidine (N = 2).

Nine of the 38 guidelines recommended 23 medications or medication classes for mood disorders in individuals with ASD (▶ **Table 4**). Six guidelines referred to depression; one mentioned depression, bipolar depression, and manic episodes, and the other two did not specify depression or bipolar disorder. In this meta-guideline, we decided not to address the recommended content on mood disorders in these two references. According to the seven guidelines referring to depression, "SSRIs" were the most frequently recommended (N = 3), followed by risperidone (N = 2), mirtazapine (N = 2), fluvoxamine (N = 2), and fluoxetine (N = 2). For bipolar disorder, antidepressants combined with mood stabilizers are recommended as the first-line treatment for bipolar depression. Valproic acid and lithium are recommended for mild-to-moderate manic features, and benzodiazepines for moderate-to-severe manic features.

Of the 38 guidelines, 22 medications or medication classes were recommended for sleep problems in individuals with ASD (▶ **Table 4**). Melatonin was the most frequently recommended drug (N = 24), followed by clonidine (N = 6), hydroxyzine (N = 2), risperidone (N = 2), guanfacine (N = 2), and clonazepam (N = 2).

Two of the 38 guidelines recommended 13 medications or medication classes for catatonia. Four of the 38 guidelines addressed Tourette or tic in individuals with ASD (▶ **Table 4**), and haloperidol (N = 2) and pimozide (N = 2) were recommended as treatments. Haloperidol and pimozide were recommended in guidelines released before 2014.

Discussion

This study aimed to review pharmacological guidelines for ASD by incorporating literature from both search engines and national

▶ **Table 2** Recommended medications for ASD core features.

			Characteristics of Social Communication and Interaction			Characteristics of Behaviors				Autistic features*
First author, editor, or organization	**Year**	**Target**	**Impairment in social interaction/ relationship/ skill**	**Communication difficulties**	**Social withdrawal**	**Stereotype behavior**	**Restricted behavior**	**Repetitive behavior**	**Autistic behavior**	
Wiener JM [7]	2004	Children	Fluvoxamine, Clonidine	Venlafaxine			Venlafaxine	Venlafaxine, Fluvoxamine, Risperidone		
Hollander E, ed [11–15]	2007	N/A				"antidepressants"	"antidepressants"			
Myers SM [16]	2007	Children			"SSRI" (Fluoxetine, Fluvoxamine, Citalopram, Escitalopram, Paroxetine, Sertraline), Mirtazapine			"SSRI" (Fluoxetine, Fluvoxamine, Citalopram, Escitalopram, Paroxetine, Sertraline) antipsychotics (Risperidone, Aripiprazole, Olanzapine, Quetiapine, Ziprasidone)		
Dryden-Edwards RC [18]	2010	Children and Adults						Risperidone (C)*[2], Fluvoxamine (A)*[3], Fluoxetine (A), Oxytocin (A)		
Missouri Autism Guidelines Initiative [23]	2012	Children						Risperidone		
Siegel M [25]	2012	Children				Risperidone, Haloperidol, Aripiprazole		Risperidone, Haloperidol, Aripiprazole		
Swedish Agency for Health Technology Assessment of Social Services [28]	2013	Children			Risperidone	Risperidone				
McPartland JC [29]	2014	Children and Adults						"SSRI" (A), Valproic acid		
Volkmar, F [31]	2014	Children			Pentoxifylline (+ Risperidone)	Aripiprazole, Risperidone		Risperidone, Valproic acid, Citalopram, Fluoxetine, Clomipramine		Donepezil
Ministries of Health and Education [32]	2016	Children and Adults	Typical antipsychotics (Haloperidol, Thioridazine)			Typical antipsychotics (Haloperidol, Thioridazine)	Risperidone			
Scottish Intercollegiate Guidelines Network [33–34]	2016	Children and Adults			Risperidone (C), Galantamine (C), Celecoxib (C)	Memantine (C), Riluzole (C)				
Choueiri RN [35]	2017	Children		Folinic acid, Propranolol, Rivastigmine[2]	Galantamine (+ Risperidone)		Buspirone	Buspirone	Donepezil, Rivastigmine	Tetrahydrobiopterin

▶ **Table 2** Continued.

			Characteristics of Social Communication and Interaction			Characteristics of Behaviors				Autistic features*
First author, editor, or organization	**Year**	**Target**	**Impairment in social interaction/ relationship/ skill**	**Communication difficulties**	**Social withdrawal**	**Stereotype behavior**	**Restricted behavior**	**Repetitive behavior**	**Autistic behavior**	
National Consultation Meeting for Developing IAP Guidelines on Neuro Developmental Disorders under the aegis of IAP Childhood Disability Group and the Committee on Child Development and Neurodevelopmental Disorders [36]	2017	Children						"SSRI" (Fluoxetine)		
Schroeder CS [37]	2017	Children				Risperidone, Aripiprazole				
Chaplin S [39]	2018	Children and Adults						Risperidone, Aripiprazole		
Howes OD [40]	2018	Children and Adults	Oxytocin		Risperidone	Risperidone, Aripiprazole		Fluoxetine, Risperidone, Aripiprazole		
Subramanyam AA [42]	2019	N/A				Risperidone, Aripiprazole				
Hyman SL [43]	2020	Children				"antipsychotics" (Aripiprazole, Risperidone)		"antipsychotics" (Aripiprazole, Risperidone), Anticonvulsants (valproic acid and divalproex sodium)		
Dubai Health Authority [45]	2021	Children				Aripiprazole	Risperidone	Risperidone		
National Collaborating Centre for Mental Health [48]	2021	Children				Risperidone, Aripiprazole	"antidepressants"		Haloperidol	
Lord C [49]	2022	N/A						Risperidone, Aripiprazole		

*No specific symptoms are described in the guidelines; *2 For children; *3 For Adults; Abbreviations: ASD, autism spectrum disorder; SSRI, selective serotonin reuptake inhibitor.; Definitions: Autistic behavior; No explanation beyond autistic behavior in the guidelines, or a combination of various factors manifesting in behaviors, Children: birth to 20, or descriptions as "child(children)," "adolescent(s)," or "young adult(s)"; Adults: over 20 years old or descriptions as "adult(s)".

▶ **Table 3** Recommended medications for ADHD features in individuals with ASD.

			Attention disorder features	Hyperactive disorder features		ADHD features*
First author or editor or organization	**Year**	**Target**	**Inattention**	**Hyperactivity**	**Impulsivity**	
Wiener JM [7]	2004	Children	Venlafaxine	Methylphenidate, Venlafaxine, Niaprazine		
Filipek PA [8]	2006	Children	Atomoxetine, “Atypical neuroleptics”, “SSRI”	“stimulants”, “antipsychotics”		
Gleason MM [10]	2007	Children		Methylphenidate		
Myers SM [16]	2007	Children	“stimulants” (Methylphenidate, Dextroamphetamine, mixed Amphetamine salts), “α2-agonists” (Clonidine, Guanfacine), Atomoxetine, "atypical antipsychotics” (Risperidone, Aripiprazole, Olanzapine, Quetiapine, Ziprasidone)	“stimulants” (Methylphenidate, Dextroamphetamine, mixed Amphetamine salts), “α2-agonists” (Clonidine, Guanfacine), Atomoxetine, “antipsychotics” (Risperidone, Aripiprazole, Olanzapine, Quetiapine, Ziprasidone)"	“stimulants” (Methylphenidate, Dextroamphetamine, mixed Amphetamine salts), “α2-agonists” (Clonidine, Guanfacine), Atomoxetine, “antipsychotics” (Risperidone, Aripiprazole, Olanzapine, Quetiapine, Ziprasidone)	
Dryden-Edwards RC [18]	2010	Children and Adults	Methylphenidate (C)**	Methylphenidate (C), Aripiprazole	Methylphenidate (C)	
Matson JL [19–21]	2011	N/A			Risperidone, Aripiprazole, Methylphenidate	Methylphenidate, Atomoxetine, “α2-agonists” (Clonidine)
Brian R [22]	2011	Children		Methylphenidate, Guanfacine		
Missouri Autism Guidelines Initiative [23]	2012	Children	Methylphenidate	Aripiprazole, Methylphenidate		
Siegel M [25]	2012	Children		Methylphenidate, Aripiprazole, Risperidone, Haloperidol, Atomoxetine HCI, Naltrexone		
Manning-Courtney P [26]	2013	Children (under 22 years old)		Methylphenidate, Atomoxetine		Clonidine, Guanfacine
Swedish Agency for Health Technology Assessment of Social Services [28]	2013	Children			Risperidone	
McPartland JC [29]	2014	Children and Adults	“stimulants” (Methylphenidate), “α2-agonists” (Guanfacine), Atomoxetine, “Antidepressants” (Bupropion), Haloperidol, Risperidone, Naltrexone	“stimulants” (Methylphenidate), “α2-agonists” (Guanfacine), Atomoxetine, “Antidepressants” (Bupropion), Haloperidol, Risperidone, Naltrexone		
Volkmar F [31]	2014	Children		Guanfacine, Aripiprazole, Risperidone, Atomoxetine, Methylphenidate, Amantadine, Naltrexone		Atomoxetine
Ministries of Health and Education [32]	2016	Children and Adults				Methylphenidate
Scottish Intercollegiate Guidelines Network [33–34]	2016	Children and Adults		Aripiprazole (C), Riluzole (C), Methylphenidate (C)		Atomoxetine (C)
Choueiri RN [35]	2017	Children				Methylphenidate, Guanfacine, Clonidine, Atomoxetine, “NRI”

▶ **Table 3** Continued.

			Attention disorder features	Hyperactive disorder features		ADHD features*
First author or editor or organization	**Year**	**Target**	**Inattention**	**Hyperactivity**	**Impulsivity**	
National Consultation Meeting for Developing IAP Guidelines on Neuro Developmental Disorders under the aegis of IAP Childhood Disability Group and the Committee on Child Development and Neurodevelopmental Disorders [36]	2017	Children	Methylphenidate	Methylphenidate		
Schroeder CS [37]	2017	Children		Risperidone, Aripiprazole		
Baumer N [38]	2018	Children	"α2-agonists", "stimulants"	"α2-agonists", "stimulants"	"α2-agonists", "stimulants"	
Chaplin S [39]	2018	Children and Adults				Methylphenidate, Atomoxetine, Clonidine, Guanfacine, Lofexidine
Howes OD [40]	2018	Children and Adults		Risperidone, Atomoxetine (C), Clonidine (C)	Methylphenidate (C)	Methylphenidate, (C) Clonidine (C), Guanfacine (C), Lofexidine (C)
Ip A [41]	2018	Children				Methylphenidate, Atomoxetine, "α2-agonists" (Clonidine, Guanfacine)
Subramanyam AA [42]	2019	N/A		Risperidone, Aripiprazole		Methylphenidate, Atomoxetine, "α2-agonists"
Hyman SL [43]	2020	Children	"stimulants" (Methylphenidate, Dexmethylphenidate, mixed amphetamine salts, Lisdexamfetamine, Dextroamphetamine), "NRI" (Atomoxetine), "α2-agonists" (Clonidine, Guanfacine)	"antipsychotics" (Aripiprazole, Risperidone), "stimulants" (Methylphenidate, Dexmethylphenidate, mixed amphetamine salts, Lisdexamfetamine, Dextroamphetamine), "NRI" (Atomoxetine), "α2-agonists" (Clonidine, Guanfacine)	"stimulants" (Methylphenidate, Dexmethylphenidate, mixed amphetamine salts, Lisdexamfetamine, Dextroamphetamine), "NRI" (Atomoxetine), "α2-agonists" (Clonidine, Guanfacine)	
Young S [44]	2020	Children and Adults	ADHD medications	ADHD medications	ADHD medications	
Dubai Health Authority [45]	2021	Children	Guanfacine	Aripiprazole, Guanfacine	Guanfacine, Clonidine	"stimulants" (Methylphenidate), Atomoxetine
Fuentes J [46]	2021	Children and Adults		Methylphenidate, Guanfacine		
National Collaborating Centre for Mental Health [48]	2021	Children		Risperidone, Aripiprazole		
Lord C [49]	2022	N/A				Methylphenidate, Atomoxetine, Guanfacine

*No specific symptoms are described in the guidelines; **For children. Abbreviations: ADHD, attention deficit hyperactivity disorder; ASD, autism spectrum disorder; NRI, noradrenaline reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor; Definitions: Children: birth to 20, or descriptions as "child(children)," "adolescent(s)," or "young adult(s)"; Adults: over 20 years old or descriptions as "adult(s)".

▶ **Table 4** Recommended medications for comorbid features in individuals with ASD.

			Maladaptive behaviors			Anxiety/ OCD	Mood disorders	Sleep problems	Catatonia	Tourette /Tic
First author or editor or organization	**Year**	**Target**	**Self-injury**	**Behavior problems**	**Irritability/ Aggression**					
Wiener JM [7]	2004	Children	Sertraline, Risperidone	Fluvoxamine, Clonidine	Fluvoxamine, Sertraline, Risperidone, Niaprazine	Sertraline, Risperidone, Niaprazine	Risperidone	Niaprazine		
Filipek PA [8]	2006	Children				Atomoxetine, "SSRI"				
Carr JE [9]	2007	Children		Risperidone			Divalproex sodium			
Gleason MM [10]	2007	Children		Risperidone						
Hollander E [11–15]	2007	N/A		Risperidone, Haloperidol	Sodium Valproate			Melatonin		
Myers SM [16]	2007	Children	Risperidone, Aripiprazole, Olanzapine, Quetiapine, Ziprasidone, Clonidine, Guanfacine, Levetiracetam, Topiramate, Valproic acid, Fluoxetine, Fluvoxamine, Citalopram, Escitalopram, Paroxetine, Sertraline, Propranolol, Nadolol, Metoprolol, Pindolol		Risperidone, Aripiprazole, Olanzapine, Quetiapine, Ziprasidone, Clonidine, Guanfacine, Levetiracetam, Topiramate, Valproic acid, Fluoxetine, Fluvoxamine, Citalopram, Escitalopram, Paroxetine, Sertraline, Propranolol, Nadolol, Metoprolol, Pindolol	Fluoxetine, Fluvoxamine, Citalopram, Escitalopram, Paroxetine, Sertraline, Buspirone, Mirtazapine	Fluoxetine, Fluvoxamine, Citalopram, Escitalopram, Paroxetine, Sertraline, Mirtazapine	Melatonin, Ramelteon, Diphenhydramine, Hydroxyzine, Clonidine, Guanfacine, Mirtazapine		
Tsai LY [17]	2007	N/A			Catapres, Prozac, Paxil, "SSRI", Risperidone, Divalproex sodium, lithium, Benzodiazepine, Haloperidol, Desyrel, Propranolol	Benzodiazepine, Buspirone, "TCA", Clomipramine, Fluoxetine, Fluvoxamine, Sertraline, Paroxetine, Alprazolam, Clonidine, Propranolol	"SSRI", Venlafaxine, Nefazodone, Mirtazapine, "antidepressants", "TCA", Benzodiazepine, mood stabilizer, Haloperidol, Risperidone, lithium, Pindolol, Haloperidol, Risperidone	Melatonin, antihistamines, Hydroxyzine, Catapres, Imipramine, Trazodone		Haloperidol, Pimozide, Catapres, "SSRI", Risperidone, Verapamil, Nifedipine
Dryden-Edwards RC [18]	2010	Children and Adults	Clonidine (C)*, Guanfacine (C), Methylphenidate (C), Aripiprazole, Risperidone (C)		Clonidine (C), Guanfacine (C), Methylphenidate (C), Aripiprazole, Risperidone (C)			Melatonin		
Matson JL [19–21]	2011	N/A	Naltrexone		Risperidone, Olanzapine, Aripiprazole				Benzodiazepine	
Brian R [22]	2011	Children	Risperidone	Risperidone	Risperidone	"SSRI"				

▶ **Table 4** Continued.

			Maladaptive behaviors			Anxiety/ OCD	Mood disorders	Sleep problems	Catatonia	Tourette /Tic
First author or editor or organization	**Year**	**Target**	**Self-injury**	**Behavior problems**	**Irritability/ Aggression**					
Missouri Autism Guidelines Initiative [23]	2012	Children	Risperidone, Aripiprazole		Risperidone, Aripiprazole			Melatonin, Clonidine, Risperidone, Aripiprazole		
National Institute for Health and Care Excellence [24]	2013	Children		"antipsychotics"						
Siegel M [25]	2012	Children			Aripiprazole, Risperidone, Haloperidol			Melatonin		
Swedish Agency for Health Technology Assessment of Social Services [28]	2013	Children	Risperidone							
McPartland JC [29]	2014	Children and Adults			Haloperidol, Risperidone, Olanzapine, Aripiprazole (C), Valproic acid	"SSRI" (A)**, Aripiprazole	Fluvoxamine (C), Fluoxetine (C)	Melatonin		Haloperidol, Pimozide, atypical "antipsychotics", "α2-agonists"s
Veereman G [30]	2014	Children		Haloperidol, Risperidone, Aripiprazole				Melatonin		
Volkmar, F [31]	2014	Children		Haloperidol, Amantadine	Clonidine, Aripiprazole, Valproic acid, Pentoxifylline					
Ministries of Health and Education [32]	2016	Children and Adults	Risperidone (C)	Haloperidol, Thioridazine	Risperidone (C), Aripiprazole (C)	Fluoxetine (C), Citalopram (C)		Melatonin (C)		
Scottish Intercollegiate Guidelines Network [33–34]	2016	Children and Adults		"antipsychotics" (A)	Aripiprazole (C), Risperidone (C), Galantamine (C), Celecoxib (C), Memantine (C), Riluzole (C)			Melatonin (C)		
Choueiri RN [35]	2017	Children		Luteolin	Risperidone, Aripiprazole, Buspirone, Galantamine			Melatonin, Clonidine		

▶ **Table 4** Continued.

			Maladaptive behaviors			Anxiety/ OCD	Mood disorders	Sleep problems	Catatonia	Tourette /Tic
First author or editor or organization	**Year**	**Target**	**Self-injury**	**Behavior problems**	**Irritability/ Aggression**					
National Consultation Meeting for Developing IAP Guidelines on Neuro Developmental Disorders under the aegis of IAP Childhood Disability Group and the Committee on Child Development and Neurodevelopmental Disorders. [36]	2017	Children		"Stimulants", Risperidone		Buspirone	"SSRI", "SNRI"	Melatonin		
Schroeder CS [37]	2017	Children	Risperidone, Aripiprazole	Risperidone, Aripiprazole	Risperidone, Aripiprazole			Benadryl, Melatonin		
Baumer N [38]	2018	Children			Risperidone, Aripiprazole	"SSRI"		Melatonin, sedatives		
Chaplin S [39]	2018	Children and Adults			Risperidone (C), Aripiprazole (A), "SSRI" (A)	Risperidone (C), "SSRI" (C)		Melatonin		
Howes OD [40]	2018	Children and Adults			Risperidone, Aripiprazole, Fluvoxamine (A), Pregnenolone (A)	Risperidone (C), Clomipramine (C), Fluoxetine (A), Fluvoxamine (A)		Melatonin (C)		Clonidine (A), Guanfacine (A)
Ip A [41]	2018	Children		Risperidone, Aripiprazole		Fluoxetine, Sertraline	Antidepressants, "SSRI"	Melatonin		
Subramanyam AA [42]	2019	N/A			Risperidone, Aripiprazole, "α2-agonists"			Melatonin, Risperidone, Clonazepam, Clonidine		
Hyman SL [43]	2020	Children	Aripiprazole, Risperidone		Aripiprazole, Risperidone, Clonidine, Guanfacine, valproic acid, divalproex sodium	Sertraline, Fluoxetine, Citalopram, Escitalopram, Guanfacine, Clonidine, Propranolol, Lorazepam				
Young S [44]	2020	Children and Adults			Risperidone (C), Aripiprazole (C)			Melatonin		

▶ **Table 4** Continued.

			Maladaptive behaviors			Anxiety/ OCD	Mood disorders	Sleep problems	Catatonia	Tourette /Tic
First author or editor or organization	**Year**	**Target**	**Self-injury**	**Behavior problems**	**Irritability/ Aggression**					
Dubai Health Authority [45]	2021	Children	Risperidone	Risperidone, Aripiprazole	Risperidone, Aripiprazole, Citalopram, Escitalopram	Sertraline		Melatonin, Clonidine, Guanfacine		Guanfacine
Fuentes J [46]	2021	Children and Adults			Risperidone, Aripiprazole, Haloperidol (C)			Melatonin		
Long M [47]	2021	N/A			Risperidone, Aripiprazole			Melatonin		
National Collaborating Centre for Mental Health [48]	2021	Children		Risperidone, Aripiprazole, Cyproheptadine, Piracetam, Pentoxifylline	Risperidone, Aripiprazole					
Lord C [49]	2022	N/A		Risperidone, Aripiprazole	Risperidone, Aripiprazole			Melatonin		
Matson JL [50–53]	2022	Children and Adults			Risperidone (C), Aripiprazole (C)			Melatonin (C), Ubiquinol (C), Carnosine (C), Cannabidiol (C), Quetiapine (C), Agomelatine (C), Clonazepam, Clonidine (C),		
Spain D [54]	2022	Adults		Propranolol		Benzodiazepine			Lorazepam	

*For children; **For Adults; Abbreviations: ASD, autism spectrum disorder; OCD, obsessive-compulsive disorder; SNRI, selective noradrenaline reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor; TCA, Tricyclic antidepressant.; Definitions: Children: birth to 20, or descriptions as “child(children),” “adolescent(s),” or “young adult(s)”; Adults: over 20 years old or descriptions as “adult(s)”.

guidelines, which were often not included in previous reviews or meta-analyses. In addition to the 27 guidelines identified by search engines, this review included 2 general guidelines and 9 guidelines from governmental agencies. For ASD core features, risperidone was frequently recommended (N = 17), especially for characteristic behaviors (N = 16). For ADHD features, methylphenidate was the most recommended (N = 23), addressing both inattention (N = 6) and hyperactivity/impulsivity (N = 16). Risperidone was also often recommended for comorbid maladaptive behaviors, including self-injury, behavioral problems, and irritability/aggression (N = 33).

The review identified 38 guidelines and algorithms: 27 through search engines, 9 from government agency websites, 1 from a manual search, and 1 updated version of a previously identified guideline. The 27 guidelines from search engines were all issued by privately owned publishers or journals, while only 2 of the 11 guidelines from other sources were similarly published. The remaining 9 were from administrative agencies. This indicates that relying solely on search engines is insufficient for identifying all relevant treatment guidelines, particularly those issued by local or national bodies, which are typically available only on government websites. Risperidone was the most frequently recommended drug for the characteristic behaviors of patients with ASD (N = 16), particularly for repetitive behaviors (N = 11). Of these recommendations, five guidelines were based on the results of a clinical trial [55], two were based on randomized controlled trials [56], one was based on a meta-analysis [57], and the remaining three provided no rationale. McDougle et al. used the Y-BOCS to assess repetitive behaviors in individuals with ASD [55]. However, it should be noted that the Y-BOCS may be insufficient for assessing the repetitive behaviors of individuals with ASD due to the heterogeneity of this phenomenon in this population [60]. The Research Unit on Pediatric Psychopharmacology (RUPP) (2002) used all subscales of the Aberrant Behavior Checklist (ABC), including irritability, social withdrawal, stereotypy, hyperactivity, and inappropriate speech, to assess characteristic behaviors in individuals with ASD [56]. In contrast, Fung et al. used only the irritability subscale of the ABC [57]. Therefore, evidence supporting the use of risperidone for repetitive behaviors remains insufficient, underscoring the need for further investigation in this area.

Galantamine was recommended specifically for addressing social withdrawal, a core symptom of ASD, in two guidelines [33–35], both cited the study by Ghaleiha et al. (2014) [58] to support this recommendation. However, a recent review by Ure et al. (2023) [59] highlighted that this study remains the sole comparative investigation of galantamine in ASD and concluded that the efficacy of acetylcholinesterase inhibitors, including galantamine, in ASD treatment lacks robust evidence and remains uncertain.

The most frequently recommended drug for treating ADHD features in individuals with ASD is methylphenidate, which is endorsed in 23 guidelines. According to these guidelines, methylphenidate is effective in children with ASD. However, it has a lower response rate and more frequent adverse effects compared to its use in children with ADHD who do not have autism [16, 18, 22, 23, 46]. This conclusion is supported by a randomized controlled crossover trial conducted by the RUPP group (2005) [61], which included 72 individuals aged 5–14 years diagnosed with autistic disorder, Asperger's disorder, or PDD not otherwise specified. The study reported a response rate of 49 % and an 18 % discontinuation rate due to adverse effects. Although the study did not include individuals with ADHD, it concluded that methylphenidate was less effective and had more frequent adverse effects in children with PDD than in those with ADHD, based on comparisons with previous studies [62, 63]. Therefore, the lack of clinical trial data highlights the need for further investigation to develop effective treatment approaches for ADHD in individuals with ASD.

Risperidone is also frequently recommended for alleviating maladaptive behaviors in patients with ASD. Specifically, risperidone is recommended for treating irritability and/or aggression in 32 guidelines, leading to a consensus on its use for these features. Risperidone has been approved by the FDA and the European Medicines Agency for treating these symptoms [64]. One of the earliest trials supporting the FDA approval of risperidone was an 8-week, multicenter, randomized, double-blind, placebo-controlled trial of flexible-dose risperidone (0.25–3.5 mg per day) conducted from 1999 to 2001 [65]. A recent systematic review by Mano-Sousa et al. reported that both long- and short-term use of risperidone was effective in improving irritability in children and adolescents [66]. Therefore, risperidone may be effective in managing irritability and aggression in patients with ASD.

However, the risperidone product monograph warns of Parkinsonism, akathisia, dystonia, tremors, and sedation as common adverse effects [67]. The treatment guidelines identified in this review also refer to various adverse effects of risperidone, including weight gain, prolactin elevation, sedation, and extrapyramidal symptoms [16, 22, 23, 26, 39, 41, 48]. Considering the risk of these adverse effects, guidelines recommend titration (i. e., starting with a low dose and slowly increasing it) [45, 49]. This approach may be especially important for individuals with ASD since previous studies have reported a higher incidence of adverse effects in this population [38, 44]. Moreover, it is possible that risperidone might not directly address the maladaptive behaviors themselves, but rather may alleviate underlying conditions such as anxiety or irritability that can trigger or worsen these behaviors. This distinction is important because it implies that pharmacological intervention alone may not be sufficient for long-term behavioral management. Without accompanying behavioral interventions, challenging behaviors may recur over time and may not respond even to an increased dose of risperidone. This highlights the need for a comprehensive approach that combines pharmacological and behavioral strategies for effective long-term management of ASD-related challenging behaviors.

Among the literature identified in our review, although several guidelines discussed individuals with ASD and intellectual disability (ID), none provided specific pharmacological recommendations for this population. For example, some guidelines simply noted increased medication use in this population [25, 43]. While both risperidone and aripiprazole have FDA approval for managing aggression in ASD or ID, and a meta-analysis has shown their similar short-term efficacy (6–10 weeks) in reducing behavioral problems regardless of ID status [68], these findings were not translated into specific recommendations for individuals with ASD and ID. The guidelines only emphasized that these medications should be

prescribed by appropriately trained clinicians due to their potentially serious or fatal side effects [37].

This study has several limitations. First, because the literature search was limited to English, some local non-English items may have been missed. Second, nonpharmacological treatment options were not the focus of this review. However, it should be noted that some guidelines recommend the use of pharmacotherapy when individuals with ASD fail to respond to nonpharmacological treatments (e. g., behavioral interventions and environmental modifications) [24, 44]. Third, this study did not specifically address differences in pharmacological interventions for problem behaviors based on the presence or absence of ID in individuals with ASD. While many of the guidelines cited in this study acknowledged the frequent co-occurrence of ASD and ID, they did not provide distinct recommendations for pharmacotherapy based on ID status. Fourth, some references included in this study used general terms like "stimulants" or "alpha-2 agonists" without specifying examples, therefore some recommendations were unclear. For example, the term "stimulants" in our review does not necessarily include specific mentions of methylphenidate or amphetamine, and "alpha-2 agonists" does not necessarily include specific mentions of clonidine or guanfacine.

Conclusion

There appears to be a consensus among various guidelines on the use of certain medications for individuals with ASD, particularly risperidone, for treating irritability and/or aggression. Additionally, some guidelines recommend risperidone for repetitive behavior and methylphenidate for ADHD features in individuals with ASD, though they do not provide sufficient evidence to support these recommendations. This review indicates that relying solely on search engines for a literature search cannot effectively identify all treatment guidelines for ASD, especially those issued by local or national administrative bodies. Researchers and physicians must recognize that search engines do not cover all relevant treatment guidelines for ASD. Therefore, administrative bodies need to improve the dissemination of their guidelines to reach a broader audience of researchers and physicians. Furthermore, it should be noted that the recommendations in treatment guidelines are not always based on robust evidence, highlighting the urgent need for further research in this population.

Conflict of Interest

The authors declare that they have no conflict of interest.

References

[1] American Psychiatric Association. Diagnostic and statistical manual of mental disorders: DSM-5. 5th ed. Arlington, VA: American Psychiatric Association; 2013

[2] Salpekar JA, Scahill L. Psychopharmacology management in autism spectrum disorder. Pediatr Clin North Am 2024; 71: 283–299. DOI: 10.1016/j.pcl.2023.12.001

[3] Wickstrom J, Dell'Armo K, Salzman E et al. Systematic review: Recommendations for rehabilitation in ASD and ID from clinical practice guidelines. Arch Rehabil Res Clin Transl 2021; 3: 10014. DOI: 10.1016/j.arrct.2021.100140

[4] Page MJ, McKenzie JE, Bossuyt PM et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. BMJ 2021; 372: n71. DOI: 10.1136/bmj.n71

[5] Croen LA, Zerbo O, Qian Y et al. The health status of adults on the autism spectrum. Autism 2015; 19: 814–823. DOI: 10.1177/1362361315577517

[6] Lai MC, Kassee C, Besney R et al. Prevalence of co-occurring mental health diagnoses in the autism population: A systematic review and meta-analysis. The Lancet Psychiatry 2019; 6: 819–829. DOI: 10.1016/S2215-0366(19)30289-5

[7] Tsai LY. Autistic Disorder. In: Wiener JM, Dulcan MK, eds. The American Psychiatric Publishing textbook of child and adolescent psychiatry, 3rd ed. American Psychiatric Publishing Inc; 2004: 261–316

[8] Filipek PA, Steinberg-Epstein R, Book TM. Intervention for autistic spectrum disorders. NeuroRx 2006; 3: 207–216. DOI: 10.1016/j.nurx.2006.01.014

[9] Carr JE, LeBlanc LA. Autism spectrum disorders in early childhood: An overview for practicing physicians. Prim Care 2007; 34: 343–359. DOI: 10.1016/j.pop.2007.04.009

[10] Gleason MM, Egger HL, Emslie GJ et al. Psychopharmacological treatment for very young children: Contexts and guidelines. J Am Acad Child Adolesc Psychiatry 2007; 46: 1532–1572. DOI: 10.1097/chi.0b013e3181570d9e

[11] Schapiro ML, Wasserman S, Hollander E. Treatment of Autism With Selective Serotonin Reuptake Inhibitors and Other Antidepressant. In: Hollander E, Anagnostou, E., eds. Clinical manual for the treatment of autism. American Psychiatric Publishing; 2007: 51–80

[12] Anagnostou E, Fisher AJ, Hollamder E. Treatment of Autism With Anticonvulsants and Mood Stabilizers. In: Hollander E, Anagnostou E, eds. Clinical manual for the treatment of autism. American Psychiatric Publishing; 2007: 81–98

[13] Posey D, Stigler KA, Erickson CA et al Treatment of Autism With Antipsychotics. In: Hollander E, Anagnostou E, eds. Clinical manual for the treatment of autism. American Psychiatric Publishing; 2007: 99–120

[14] Chez MG, Coughlin C, Kominsky M. Cholinesterase Inhibitor Therapy in Patients With Autism Spectrum Disorders. In: Hollander E, Anagnostou E, eds. Clinical manual for the treatment of autism. American Psychiatric Publishing; 2007: 121–130

[15] Poncin Y, Scahill L. Stimulants and Nonstimulants in the Treatment of Hyperactivity in Autism. In: Hollander E, Anagnostou E, eds. Clinical manual for the treatment of autism. American Psychiatric Publishing; 2007: 131–152

[16] the Council on Children With DisabilitiesMyers SC, Johnson CP. Management of children with autism spectrum disorders. Pediatrics 2007; 120: 1162–1182. DOI: 10.1542/peds.2007-2362

[17] Tsai LY. Asperger syndrome and medication treatment. Focus on autism and other developmental disabilities 2007; 22: 138–148. DOI: 10.1177/10883576070220030101

[18] Golombek AA, King B. Pharmacotherapy. In: Dryden-Edwards RC, Combrinck-Graham, L, eds. Developmental disabilities from childhood to adulthood: What works for psychiatrists in community and institutional settings. Johns Hopkins University Press; 2010: 271–295

[19] Singh NN, Lancioni GE, Winton ASW et al. Aggression, Tantrums, and Other Externally Driven Challenging Behaviors. In: Matson JL, Sturmey P, eds. International handbook of autism and pervasive developmental disorders. New York: Springer; 2011: 413–435

[20] Furniss F, Biswas AB, Bezilla B et al. Self-Injurious Behavior: II. Pharmacological and Integrated Treatments. In: Matson JL, Sturmey P, eds. International handbook of autism and pervasive developmental disorders. New York: Springer; 2011: 453–462

[21] Mohiuddin S, Bobak S, Gih D et al. Autism Spectrum Disorders: Comorbid Psychopathology and Treatment. In: Matson JL, Sturmey P, eds. International handbook of autism and pervasive developmental disorders. New York: Springer; 2011: 463–478

[22] Scahill L, Boorin GS. Psychopharmacology in Children with PDD: Review of Current Evidence. In: Brian R, Peter D, Domenic VC, Fred RV, eds. Evidence-based practices and treatments for children with autism. New York: Springer; 2011: 231–244

[23] Missouri Autism Guidelines Initiative. Autism spectrum disorders: Guide to evidence-based intervention. 2012

[24] National Institute for Health and Care Excellence. Autism spectrum disorder in adults: Diagnosis and management. 2012

[25] Siegel M. Psychopharmacology of autism spectrum disorder: Evidence and practice. Child Adolesc Psychiatr Clin N Am 2012; 21: 957–973. DOI: 10.1016/j.chc.2012.07.006

[26] Manning-Courtney P, Murray D, Currans K et al. Autism spectrum disorders. Curr Probl Pediatr Adolesc Health Care 2013; 43: 2–11. DOI: 10.1016/j.cppeds.2012.08.001

[27] National Institute for Health and Care Excellence. Autism spectrum disorder in under 19s: Support and management. 2013

[28] Swedish agency for health technology assessment of social services. Autism spectrum disorders diagnosis and interventions, organization of care and patient involvement. 2013

[29] Volkmar F, Siegel M, Woodbury-Smith M et al. Psychopharmacological Treatment of Asperger Syndrome In: McPartland JC, Klin A, Volkmar FR, eds. Asperger syndrome: Assessing and treating high-functioning autism spectrum disorders, 2nd ed. The Guilford Press; 2014: 280–310

[30] Veereman G, Henningsen KH, Eyssen M et al. Management of autism in children and young people: A good clinical practice guideline. 2014

[31] Volkmar F, Siegel M, Woodbury-Smith M et al. Practice parameter for the assessment and treatment of children and adolescents with autism spectrum disorder. J Am Acad Child Adolesc Psychiatry 2014; 53: 237–257. DOI: 10.1016/j.jaac.2013.10.013

[32] Ministries of Health and Education. New Zealand autism spectrum disorder guideline (2nd ed) 2016; 132–161

[33] Pharmacological interventions for children and young people. In: Scottish Intercollegiate Guidelines Network., ed. SIGN 145 Assessment, diagnosis and interventions for autism spectrum disorders.2016: 32–36. Available at https://www.sign.ac.uk/assets/sign145.pdf

[34] Pharmacological interventions for adults In: Scottish Intercollegiate Guidelines Network., ed. SIGN 145 Assessment, diagnosis and interventions for autism spectrum disorders. 2016: 37–39. Available at https://www.sign.ac.uk/assets/sign145.pdf

[35] Choueiri RN, Zimmerman AW. New Assessments and Treatments in ASD. Curr Treat Options Neurol 2017; 19. DOI: 10.1007/s11940-017-0443-8

[36] National Consultation Meeting for Developing IAP Guidelines on Neuro Developmental Disorders under the aegis of IAP Childhood Disability Group and the Committee on Child Development and Neurodevelopmental Disorders. Consensus statement of the Indian Academy of Pediatrics on evaluation and management of autism spectrum disorder. Indian Pediatr 2017; 54: 385–393. DOI: 10.1007/s13312-017-1112-4

[37] Developmental Disabilities: Intellectual Disability and Autism. In: Schroeder CS, Smith-Boydston JM, eds. Assessment and treatment of childhood problems: A clinician's guide, 3rd ed. 2017: 389–414

[38] Baumer N, Spence SJ. Evaluation and management of the child with autism spectrum disorder. Continuum (Minneap Minn) 2018; 24: 248–275. DOI: 10.1212/CON.0000000000000578

[39] Chaplin S. BAP consensus guidelines on autism spectrum disorder. Prescriber 2018; 29: 13–17. DOI: 10.1002/psb.1670

[40] Howes OD, Rogdaki M, Findon JL et al. Autism spectrum disorder: Consensus guidelines on assessment, treatment and research from the British Association for Psychopharmacology. J Psychopharmacol 2018; 32: 3–29. DOI: 10.1177/0269881117741766

[41] Ip A, Zwaigenbaum L, Brian JA. Post-diagnostic management and follow-up care for autism spectrum disorder. Paediatr Child Health 2019; 24: 461–477. DOI: 10.1093/pch/pxz121

[42] Subramanyam AA, Mukherjee A, Dave M et al. Clinical practice guidelines for autism spectrum disorders. Indian J Psychiatry 2019; 61: 254–269. DOI: 10.4103/psychiatry.IndianJPsychiatry_542_18

[43] Hyman SL, Levy SE, Myers SM et al. Identification, evaluation, and management of children with autism spectrum disorder. Pediatrics 2020; DOI: 10.1542/peds.2019-3447

[44] Young S, Hollingdale J, Absoud M et al. Guidance for identification and treatment of individuals with attention deficit/hyperactivity disorder and autism spectrum disorder based upon expert consensus. BMC Med 2020; 18. DOI: 10.1186/s12916-020-01585-y

[45] Dubai Health Authority. Dubai clinical practice guidelines for autism spectrum disorder (ASD) in children and adolescents (from birth to 18 years of age) version 1. 2021

[46] Fuentes J, Hervas A, Howlin P. ESCAP practice guidance for autism: A summary of evidence-based recommendations for diagnosis and treatment. Eur Child Adolesc Psychiatry 2021; 30: 961–984. DOI: 10.1007/s00787-020-01587-4

[47] Long M, Register-Brown K. Autism spectrum disorder. Pediatr Rev 2021; 42: 360–374. DOI: 10.1542/pir.2020-000547

[48] National Collaborating Centre for Mental Health. Autism – management of autism in children and young people. The British Psychological Society and The Royal College of Psychiatrists. 2021

[49] Lord C, Charman T, Havdahl A et al. The Lancet Commission on the future of care and clinical research in autism. Lancet 2022; 399: 271–334. DOI: 10.1016/s0140-6736(21)01541-5

[50] Deb SS, Roy M, Limbu B et al. Antidepressants. In: Matson JL, Sturmey P, eds. Handbook of autism and pervasive developmental disorder: Assessment, diagnosis, and treatment. Springer Nature Switzerland AG; 2022: 1139–1156

[51] Deb SS, Roy M, Limbu B et al. Anti-Anxiety Medications and Novel Treatments for Autism. In: Matson JL, Sturmey P, eds. Handbook of autism and pervasive developmental disorder: Assessment, diagnosis, and treatment. Switzerland, AG: Springer Nature; 2022: 1157–1172

[52] Shaw SR, Wang J. Antipsychotic Medications. In: Matson JL, Sturmey P, eds. Handbook of autism and pervasive developmental disorder: Assessment, diagnosis, and treatment. Switzerland: AG: Springer Nature; 2022: 1173–1190

[53] Rossignol DA, Frye RE. Psychotropic Medications for Sleep Disorders in Autism Spectrum Disorders. In: Matson JL, Sturmey P, eds. Handbook of autism and pervasive developmental disorder: Assessment, diagnosis, and treatment. Switzerland: AG: Springer Nature; 2022: 1191–1217

[54] Hirota T, King BH. Pharmacological Interventions. In: Spain D, Musich FM, White SW, eds. Psychological therapies for adults with autism. Oxford Academic. 2022: 234–252

[55] McDougle CJ, Scahill L, Aman MG et al. Risperidone for the core symptom domains of autism: Results from the study by the autism network of the research units on pediatric psychopharmacology. Am J Psychiatry 2005; 162: 1142–1148. DOI: 10.1176/appi.ajp.162.6.1142

[56] McCracken JT, McGough J, Shah B et al. Research unit on pediatric psychopharmacology autism network. Risperidone in children with autism and serious behavioral problems. N Engl J Med 2002; 347: 314–321. DOI: 10.1056/NEJMoa013171

[57] Fung LK, Mahajan R, Nozzolillo A et al. Pharmacologic treatment of severe irritability and problem behaviors in autism: A systematic review and meta-analysis. Pediatrics 2016; 137: S124–S135. DOI: 10.1542/peds.2015-2851K

[58] Ghaleiha A, Ghyasvand M, Mohammadi MR et al. Galantamine efficacy and tolerability as an augmentative therapy in autistic children: A randomized, double-blind, placebo-controlled trial. J Psychopharmacol 2014; 28: 677–685. DOI: 10.1177/0269881113508830

[59] Ure A, Cox GR, Haslam R et al. Acetylcholinesterase inhibitors for autistic spectrum disorders. Cochrane Database Syst Rev 2023; 6: CD013851. DOI: 10.1002/14651858.CD013851.pub2

[60] Anagnostou E, Chaplin W, Watner D et al. Factor analysis of repetitive behaviors in Autism as measured by the Y-BOCS. J Neuropsychiatry Clin Neurosci 2011; 23: 332–339. DOI: 10.1176/jnp.23.3.jnp332

[61] Research Units on Pediatric Psychopharmacology Autism Network. Randomized, controlled, crossover trial of methylphenidate in pervasive developmental disorders with hyperactivity. Arch Gen Psychiatry 2005; 62: 1266–1274. DOI: 10.1001/archpsyc.62.11.1266

[62] Greenhill LL, Abikoff HB, Arnold LE et al. Medication treatment strategies in the MTA Study: Relevance to clinicians and researchers. J Am Acad Child Adolesc Psychiatry 1996; 35: 1304–1313. DOI: 10.1097/00004583-199610000-00017

[63] Greenhill LL, Swanson JM, Vitiello B et al. Impairment and deportment responses to different methylphenidate doses in children with ADHD: The MTA titration trial. J Am Acad Child Adolesc Psychiatry 2001; 40: 180–187. DOI: 10.1097/00004583-200102000-00012

[64] Glennon J, Purper-Ouakil D, Bakker M et al. Paediatric European Risperidone Studies (PERS): Context, rationale, objectives, strategy, and challenges. Eur Child Adolesc Psychiatry 2014; 23: 1149–1160. DOI: 10.1007/s00787-013-0498-3

[65] Center for Drug Evaluation and Research. Applicarion Number: NDA 20-272/S-036/041 NDA 20-588/S-024/028/029 NDA 21-444/S-008/015 2006

[66] Mano-Sousa BJ, Pedrosa AM, Alves BC et al. Effects of risperidone in autistic children and young adults: A systematic review and meta-analysis. Curr Neuropharmacol 2021; 19: 538–552. DOI: 10.2174/1570159X18666200529151741

[67] Janssen Pharmaceutical Companies. RISPERDAL-package insert. 2007

[68] Cohen D, Raffin M, Canitano R et al. Risperidone or aripiprazole in children and adolescents with autism and/or intellectual disability: A Bayesian meta-analysis of efficacy and secondary effects. Res Autism Spectr Disord 2013; 7: 167–175. DOI: 10.1016/j.rasd.2012.08.001