Symptom and Demographic Predictors of Psychotropic Medication use in ADHD and Autism

Susan D. Mayes, James G. Waxmonsky, Raman Baweja*, Richard E. Mattison, Hasan Memon, Usman Hameed and Daniel Waschbusch

Department of Psychiatry H073, Hershey Medical Center, 500 University Dr. Hershey, PA 17033, USA

Abstract: ADHD symptoms, oppositional behavior, aggression, and irritability are common in children with ADHD-Combined and autism and are often targeted for treatment with medication. The goal of our study was to determine symptom, diagnostic, and demographic variables that influence the classes of psychotropic medications used to treat children with ADHD-Combined, ADHD-Inattentive, and autism. The sample comprised 1,407 children with autism and 1,036 children with ADHD (without autism) 2-17 years of age. Medications most often prescribed were ADHD medications (22% stimulant, 2% atomoxetine), 8% antipsychotic, 6% SSRI, and 5% alpha agonist. Children with ADHD-Combined and children with autism did not differ in the proportion prescribed a psychotropic and were more likely to be treated with medication than children with ADHD-Inattentive. ADHD severity ratings, oppositional defiant disorder, conduct disorder, anxiety, depression, irritability, and low IQ increased the likelihood of medication use and predicted medication classes. Older age was the most significant predictor of medication treatment. Race, sex, and parent occupation were not predictors. The findings were positive in that symptoms and not demographics determined medication treatment. Interestingly, the presence of learning problems was not a predictor of medication use, despite studies showing that ADHD medication can improve academic performance.

Keywords: Psychotropic medication, symptoms, demographics, ADHD-Combined, ADHD-Inattentive, autism.

Placebo controlled studies of children who have ADHD or autism have shown that ADHD medications (stimulants and atomoxetine), antipsychotics, and alpha agonists can decrease ADHD symptoms. These studies investigated ADHD medications in children with ADHD [1-3] and in children with autism [4-8], antipsychotics in children with ADHD [9-11] and autism [12], and alpha agonists in children with ADHD [13-15] and autism [16-18]. Studies also demonstrated that ADHD medication can improve academic performance and achievement test scores [2, 19-21].

ADHD medications, antipsychotics, and alpha agonists also reduced oppositional and aggressive behavior in controlled trials. Studies included children with ADHD treated with an ADHD medication [2, 3, 20, 22] or antipsychotic [9-11, 23] and children with autism treated with an antipsychotic [12, 24, 25] or alpha agonist [17, 26]. For children with ADHD, methylphenidate reduced irritability [3, 27]. For children with autism, irritability decreased with an antipsychotic [28-30], an SSRI [31], and an alpha agonist [17]. Controlled studies of children with ADHD demonstrated that anxiety and depression decreased with methylphenidate [2] and anxiety decreased with risperidone [32].

*Address correspondence to this author at the Department of Psychiatry H073, Hershey Medical Center, 500 University Dr. Hershey, PA 17033, USA;
Tel: (717) 531-8515; Fax: (717) 531-6250;
E-mail: rbaweja@pennstatehealth.psu.edu

ADHD symptoms, oppositional behavior, aggression, and irritability are common in ADHD-Combined presentation (ADHD-C) and autism, and anxiety is common in autism. Most children with autism have ADHD [33], and maternal ADHD ratings and attention test scores are similar for children with ADHD and children with autism [34]. Most (51% to 68%) children with autism and with ADHD-C have oppositional defiant disorder/ODD [35-39], and 39% with ADHD-C and 45% with autism were considered by their mothers as often or very often irritable [39]. Further, children with autism and normal intelligence did not differ from children with an anxiety disorder in maternal ratings of anxiety [40]. ADHD symptoms, behavior problems, irritability, and anxiety are often targeted for treatment with medication, and the aforementioned studies demonstrate that different classes of medication can reduce these symptoms.

Correlates of Medication Use

ADHD and Autism Diagnoses

Children with ADHD are almost exclusively prescribed an ADHD medication, usually a stimulant, with percentages ranging from 70% to 88% [41-43]. In contrast, smaller percentages of children with autism are treated with a psychotropic, with a median of 55% across eleven studies [44-54]. The most commonly prescribed medications in these autism studies were antipsychotics, most often risperidone (median 31% of children across studies), stimulants (median 23%), and

E-ISSN: 2310-8231/19

antidepressants, usually SSRIs (median 21%), followed by alpha agonists and anticonvulsant/mood stabilizers.

Comorbid Conditions

Psychotropic medication use increased with the presence of comorbid conditions, such as ADHD, ODD, conduct disorder (CD), bipolar disorder, anxiety, depression, and aggression in children with autism [44, 45, 48-50, 52, 54]. Children with ADHD treated with a stimulant plus another medication were more likely to have a comorbid psychiatric disorder [43, 55], and antipsychotic use was associated with high levels of psychiatric comorbidity in children with ADHD [56].

IQ

In individuals with autism, antipsychotic use was greater in those with intellectual disability (ID) than without ID [44, 52]. In a study restricted to individuals with autism and an IQ $\geq$ 70, psychotropic medication use was not related to IQ [50]. No studies were located analyzing the relationship between IQ and medication use in children with ADHD.

Age

Psychotropic treatment increased with age across studies of children with autism [44, 45, 48-50, 52, 54]. The only exception was a curvilinear relationship for stimulant use, with greatest use in middle childhood [44]. Polypharmacy also increased with age in autism [45]. For children with ADHD, stimulant use was greater in 10- to 14-year-olds than in 5- to 9-year-olds [57], but other studies showed a nonsignificant relationship with age [58, 59].

Sex

Two studies reported that psychotropic medication use did not differ between boys and girls with autism [48, 54], whereas another study found greater psychotropic treatment in males [49]. In other autism studies, boys were more often treated with an ADHD medication than girls, and girls with autism were more often prescribed an antidepressant, mood stabilizer, or SSRI [48, 50]. In elementary students with ADHD, male gender was a significant predictor of ADHD medication use [58]. According to insurance claims general population data, stimulant medication use was 2-3 times more common in boys than girls [60, 61], which is expected given the greater prevalence of ADHD in boys.

SES and Race

Studies investigating differences in psychotropic medication use as a function of SES in children with autism reported a nonsignificant relationship [48, 54]. Findings regarding race in autism were inconsistent. One study [49] found that psychotropic medication was more commonly used by whites than nonwhites, whereas another study [54] reported that Hispanics had greater psychotropic use than whites. Medicaid data for children with ADHD who were prescribed a stimulant showed that blacks had the highest frequency of treatment with a stimulant plus an antipsychotic [55].

Purpose

No study has simultaneously analyzed diagnostic, symptom, and demographic predictors of different classes of psychotropic medication prescribed for children with ADHD-C, ADHD-Inattentive presentation (ADHD-I), and autism. This is important in order to understand variables that determine what medication class is more likely to be prescribed than others, despite similar or overlapping symptoms in children with autism and in children with ADHD. Diagnoses in our study were based on comprehensive clinical evaluations, unlike previous studies relying on medical record reviews or parent report, which may not yield reliable diagnoses and may indicate an obvious diagnosis (e.g., ADHD) without considering additional possibilities (e.g., autism). This is important because many children with autism are initially diagnosed with only ADHD [62, 63]. Prior studies also failed to analyze ADHD-C and ADHD-I separately, which is critical to do because of significant differences in symptom profiles and comorbidity between the two subtypes. For example, children with ADHD-C and autism both have higher rates of irritable, oppositional, and aggressive behavior than children with ADHD-I [2, 39, 40, 64, 65]. Our study covers a broad age range (2-17 years) and IQ range (9-149), allowing for the determination of potential age and IQ predictors not possible in other studies using restricted ranges. Much remains to be learned about age and medication use. Some studies noted in our introduction reported a positive linear relationship and others a curvilinear relationship. Results regarding sex and race are also inconsistent. Our analyses consider all of these variables simultaneously to determine which are significant independent predictors of medication use.

METHODS

Sample

The study was approved by the Institutional Review Board, which waived informed consent because

analyses were conducted retrospectively on existing clinical data. The sample comprised 2,443 children referred to a psychiatry diagnostic clinic, 1,407 with autism (with or without ADHD) and 1,036 with ADHD without autism. The children were 2-17 years of age (*M* = 7.3, *SD* = 3.1) with IQs ranging from 9 to 149 (*M* = 96.6, *SD* = 22.6). In all, 90.9% were white, 74.5% were male, and 36.5% had a parent with a professional or managerial occupation.

All children underwent a diagnostic evaluation by a licensed PhD psychologist. The evaluation included a diagnostic interview with the parents, parent and teacher questionnaires and rating scales using the Pediatric Behavior Scale/PBS [66], review of educational records, administration of psychological tests (IQ, achievement, and neuropsychological), and clinical observations of the child during the evaluation. All children in the ADHD group had a DSM-IV or DSM-5 (whichever version was current when the child was evaluated) diagnosis of ADHD and fulfilled the following criteria: (1) symptoms of ADHD observed during psychological testing and (2) ratings of short attention span or distractible as often or very often a problem on the PBS by at least two raters (mother, father, teacher). Children were classified with ADHD-C if the median mother, father, and teacher rating on the PBS impulsive and hyperactive items was often or very often a problem. Children were classified with ADHD-I if the median impulsive and hyperactive rating was less than often a problem.

Children in the autism sample had a DSM-IV or DSM-5 diagnosis of autism (i.e., autistic disorder, Asperger's disorder, or autism spectrum disorder) and a score in the autism range on the Checklist for Autism Spectrum Disorder/CASD [67]. The CASD is a 30-item diagnostic measure normed and standardized on 2,469 children (1-18 years, IQs 9-146) with autism, other clinical disorders, and typical development [67]. In the national standardization study, the CASD identified children with and without autism with 99.5% accuracy. The CASD differentiates children with autism from children with intellectual disability, learning disability, traumatic brain injury, language disorder, ADHD, ODD, anxiety disorder, apraxia of speech, and reactive attachment disorder [34, 67-69]. Concurrent validity is strong with high diagnostic agreement (93%-98%) between the CASD and the Childhood Autism Rating Scale, the Gilliam Asperger's Disorder Scale, and the Autism Diagnostic Interview-R [70, 71]. Children with autism who also had ADHD symptoms were only included in the autism sample. These children were not given an additional clinical diagnosis of ADHD if they were evaluated at the time of the DSM-IV, which did not permit an ADHD diagnosis with autism. Maternal ADHD ratings were used to estimate ADHD diagnoses in children with autism. In the autism sample, 79.7% had elevated (often or very often a problem) maternal ratings on the total ADHD subscale (ADHD-C) and 8.9% had elevated ratings on attention deficit but not on impulsivity/hyperactivity (ADHD-I).

Instrument

The 165 items on the PBS were rated by mothers on a 4-point scale from never to very often a problem. The PBS assesses multiple diagnostic categories including ODD, conduct disorder, ADHD, anxiety, depression, and learning problems. The PBS corresponds well with established measures of psychopathology [72, 73] and has been used to diagnose and differentiate psychological problems in several published studies [e.g., 34, 40, 74, 75].

Medications

Medications for each child were the medications with which the child was treated at the time of the evaluation as reported by parents. The number of children treated with a psychotropic was 809 (33.1% of the total sample). Medication classes most often prescribed were 24.0% ADHD medication (22.1% stimulant and 2.3% atomoxetine), 7.8% antipsychotic (most often risperidone), 5.5% SSRI (most often sertraline), and 4.9% alpha agonist (clonidine or guanfacine). The remaining and less frequently prescribed medications were combined in an "other" category and included an anticonvulsant, nonSSRI antidepressant, lithium, anxiolytic, and amantadine. Polypharmacy (two or more prescribed medication classes) for the total sample was 12.3% (*n* = 300).

Variables

Dependent variables were (1) any psychotropic medication, (2) polypharmacy, and (3) specific medication class. Predictor variables were those diagnoses and symptoms noted in our introduction to be positively affected by medication (and therefore, a possible reason for selecting certain medications) and major demographic variables that may influence medication use. The variables were (1) diagnoses: autism (with or without ADHD), ADHD-C (without autism), ADHD-I (without autism), autism+ADHD-C, ODD, and ID (IQ < 80), (2) PBS symptom scores:

ADHD total (attention deficit, impulsivity, and hyperactivity), irritable/angry mood and tantrums, oppositional behavior (disobedient, defiant, and uncooperative), CD symptoms (aggressive, cruel, bully, fight, lie, steal, and destructive), anxious, depressed, and learning problems, and (3) age, IQ, sex, race, and parent occupation (professional vs. other). The ODD symptom cluster was divided into affective symptoms (irritable, angry, and tantrums) and oppositional behavior (disobedient, defiant, and uncooperative), which were analyzed separately because of research supporting that these are independent constructs [76, 77].

Data Analyses

Differences between frequencies of children treated and not treated with a psychotropic for each of the diagnostic and demographic predictor variables were analyzed using χ^2 and phi. To investigate a possible nonlinear relationship between age and medication use, differences in medication use between four age groups (2-5, 6-8, 9-12, and 13-17 years) were analyzed with χ^2 and phi. All independent variables were entered in stepwise binary regression analysis to predict (1) any psychotropic medication, (2) polypharmacy, and (3) each of the five medication classes. All reported *p*-values are two-tailed and have a Bonferroni correction for the number of comparisons made.

RESULTS

Percentages of children with ADHD or autism for each comorbid condition and demographic category treated with a psychotropic are presented in Table **1**. As shown, children with ADHD-C without autism and children with autism with or without ADHD did not differ in the proportion prescribed a psychotropic, but medication use was significantly lower in ADHD-I than ADHD-C and autism. Children who had both autism and ADHD-C were more likely to be medicated (37.7%) than children who had autism and ADHD-I (16.0%), χ^2 = 23.2, ϕ = .14, p < .0001). Polypharmacy was greater in autism and ADHD-C than in ADHD-I (χ^2 = 31.2, ϕ = .14, p < .0001 and χ^2 = 18.3, ϕ = .13, p < .0001), but did not differ between ADHD-C and autism (χ^2 = 5.0, ϕ = .05, p = .18).

Children with each of the comorbid conditions were more likely to be treated with a psychotropic than children without the condition (Table **1**). In contrast, demographic variables were not significantly associated with medication use, with the exception of age. Medication use for all classes and for polypharmacy increased with increasing age until adolescence, when the 13-17 year group did not differ significantly from the 9-12 year group (Table **2**). There were only three exceptions to this pattern. Treatment with an SSRI was greater in 13- to 17-year-olds than in 9- to 12-year-olds, treatment with an alpha agonist did

Table 1: Percent of Children with Autism and/or ADHD Treated with Any Psychotropic Medication (*N* = 2,443)

	n	%		*n*	%	χ^2	ϕ
	medicated			medicated			
Autism[1]	1407	33.3%	ADHD-C without autism	1036	32.8%	4.6	.05
Autism[1]	1407	33.3%	ADHD-I without autism	302	20.2%	20.0	.11[2]
ADHD-C without autism	734	38.0%	ADHD-I without autism	302	20.2%	30.8	.17[2]
ODD[4]	1055	40.8%	No ODD	1388	27.3%	49.0	.14[2]
Oppositional behavior[4]	1419	69.0%	Not oppositional	1024	31.0%	59.9	.16[2]
Irritable/angry/tantrums[4]	1012	39.3%	Not irritable	1431	28.7%	30.1	.11[2]
CD symptoms[4]	444	48.2%	No CD	1999	29.8%	55.7	.15[2]
Anxious[4]	885	43.3%	Not anxious	1558	27.3%	64.7	.16[2]
Depressed[4]	321	54.5%	Not depressed	2122	29.9%	76.4	.18[2]
Learning problem[4]	993	37.2%	No learning problem	1450	30.3%	12.4	.07[3]
Intellectual disability	481	33.7%	IQ $\geq$ 80	1962	33.0%	0.1	.01
Male	1821	34.2%	Female	622	30.1%	3.5	.04
White	2220	33.5%	Nonwhite	223	29.1%	1.7	.03
Professional parent	891	30.1%	Nonprofessional	1552	34.9%	5.8	-.05

[1]with or without ADHD. [2]χ^2 and ϕ p < .0001. [3]χ^2 and ϕ p < .01. [4]rated by mothers as often or very often a problem on the PBS.

Table 2: Percent of Children with Autism and/or ADHD Prescribed each Medication Class by Age Group (*N* = 2,443)

Medication class	Years				χ^2	post hoc $p < .05$
	2-5	6-8	9-12	13-17		
	n = 736	*n* = 933	*n* = 600	*n* = 174		
Any psychotropic	13.9%	35.2%	48.3%	51.1%	213.3	2-5 < 6-8 < 9-12, 13-17
ADHD medication	8.2%	25.9%	37.2%	35.1%	172.0	2-5 < 6-8 < 9-12, 13-17
Antipsychotic	3.8%	8.8%	10.7%	9.8%	25.3	2-5 < 6-8, 9-12, 13-17
SSRI	0.3%	4.8%	10.0%	15.5%	96.7	2-5 < 6-8 < 9-12 < 13-17
Alpha agonist	2.6%	4.6%	7.7%	6.9%	20.0	2-5, 6-8 < 9-12, 13-17
Other medication	2.3%	5.9%	10.0%	10.3%	39.7	2-5 < 6-8 < 9-12, 13-17
Polypharmacy	3.3%	12.5%	20.3%	21.3%	104.8	2-5 < 6-8 < 9-12, 13-17

Note. All χ^2 *p*-values < .0001.

Table 3: Diagnostic and Demographic Predictors of Psychotropic Medication Use in Children with ADHD or Autism (*N* = 2,443)

Medication class[1]	n	Most significant predictor	χ^2 (Classification accuracy)	Remaining significant predictors[2]	χ^2 (Classification accuracy)
Any psychotropic	809	Older	212.6 (67.8%)	ADHD score, Autism, CD, Anxious	440.3 (72.0%)
Polypharmacy	300	Older	94.0 (87.7%)	ADHD score, Anxious, Autism, Oppositional, lower IQ	317.8 (88.0%)
ADHD medication	586	Older	154.6 (74.4%)	ADHD score	345.6 (75.9%)
Antipsychotic	191	Irritable	87.2 (92.2%)	lower IQ, Older, Autism+ADHD-C, CD, Anxiety	228.7 (92.1%)
SSRI	134	Older	85.4 (94.5%)	Anxious, Autism, Depressed	195.5 (94.6%)
Alpha agonist	120	ADHD score	60.0 (95.1%)	Anxious, Older, Autism+ADHD-C, Oppositional	126.2 (95.1%)
Other medication	150	Older	42.9 (93.9%)	lower IQ, Irritable, Depressed	114.7 (93.9%)

Predictor variables entered: Autism (with or without ADHD); ADHD-C (no autism); ADHD-I (no autism); Autism+ADHD; ODD = oppositional defiant disorder; ID = intellectual disability (IQ < 80); ADHD score = total PBS ADHD score; Irritable = irritable, angry, tantrums; Oppositional = oppositional behavior; CD = conduct disorder symptoms; Anxious; Depressed, Learning problem, Age, IQ, White, Male, Professional parent occupation.
[1]With or without another medication.
[2]In order of significance.
Note. All χ^2 values $p < .01$.

not differ significantly between the 2-5 and 6-8 year old groups, and antipsychotic use did not differ between the 6-8 and 9-12 year old groups. Diagnostic and demographic variables that were significant predictors of medication use are presented in Table **3**. Older age was overall the most significant predictor, followed by a more severe score on the PBS ADHD subscale.

DISCUSSION

Age

Older age was the most powerful predictor of medication use overall and was a significant predictor for all seven medication groups (any psychotropic, polypharmacy, ADHD medication, antipsychotic, alpha agonist, SSRI, and "other" medication). Several factors may contribute to the increase in medication use with age. FDA guidelines recommend prescribing most of the medications in our study after age 5. Safety concerns and limited research on long-term side effects in young children may dissuade practitioners and parents from using medication in young children. Autism and ADHD are chronic disorders and, therefore, symptoms are unlikely to entirely resolve with time. At older ages, prescribers and parents may be ready to consider medication as a treatment option. Further,

symptoms may be more problematic in school age than in preschool children because the symptoms interfere with school performance, classroom behavior, and participation in sports and community activities.

Interestingly, the association between medication use and age did not follow a steady linear pattern. Psychotropic use tended to plateau in adolescence, with the exception of a continued increase with age for SSRIs. The latter is expected because anxiety and depression were both significant predictors of SSRI use (which was not the case for the other medication classes) and anxiety and depression have an older mean age of onset than ADHD, autism, and ODD [78, 79]. The plateau in medication use in adolescence for nonSSRI medications may reflect diminished compliance and the increasing role of adolescents in determining their treatment. Treatment with an alpha agonist (unlike all other medication groups) was not significantly less frequent in the 2-5 than 6-8 year old group. For many young children in our study, parents reported that alpha agonists were prescribed to treat sleep problems. Practitioners may be more comfortable prescribing medication for sleep than for behavior problems.

ADHD Symptom Score

The second most powerful predictor of medication use was the total score on the ADHD subscale rated by mothers, which was a significant predictor for any medication, polypharmacy, ADHD medication, and alpha agonists. In our total sample, 93% of the children had elevated maternal ratings of ADHD, which was a major referral complaint. The importance of the elevated maternal ADHD subscale score in predicting medication use suggests that prescribers were listening to mothers. The medication class most often prescribed in our sample was an ADHD medication (24%), versus the other classes (antipsychotic 8%, SSRI 6%, and alpha agonist 5%). For children treated with two or more classes of medication, an ADHD medication was the medication most often combined with another medication. ADHD medication had only two significant predictors (age and ADHD rating). All other medication groups had more than two significant predictors.

Autism

A diagnosis of autism was a significant predictor for any medication, polypharmacy, antipsychotic, SSRI, and alpha agonist, but not an ADHD medication. In our sample, 89% of children with autism had elevated ADHD ratings, consistent with other studies showing the vast majority of children with autism have ADHD [33]. It is important to recognize the high probability of ADHD in children with autism so it can be treated.

ADHD-C versus ADHD-I

Children with ADHD-I (versus ADHD-C and autism) were the least likely to be prescribed medication, and ADHD-I was not a significant predictor of medication use, unlike autism and ADHD-C. This suggests that medication is not often prescribed to treat only attention problems and is more likely to be prescribed for behavior problems. Attention problems may interfere with learning and academic performance, but without impulsivity and hyperactivity, inattention may not be disruptive to others or the classroom, home, and community environments, which may explain why attention problems alone are not treated. This is potentially problematic because controlled studies demonstrate that ADHD medication can improve attention in children with ADHD and with autism [e.g., 2-4, 20, 22], as well as academic performance [2, 19-21, 80]. Learning problems are common and equally prevalent in children with ADHD-I and ADHD-C [81]. Differences in medication use and comorbidity between ADHD-C and ADHD-I highlight the importance of analyzing these two subtypes separately in future research, which has typically not been done.

Comorbidity

Children who had each of the comorbid mental health conditions (autism, ADHD, ODD, CD, oppositional behavior, irritability, anxiety, and depression) were significantly more likely to be treated with a psychotropic than children without each condition. When all comorbid conditions were considered simultaneously in regression analysis, each was a significant and independent predictor for one or more medication class. However, the combination of comorbid predictors was different for each medication class. Polypharmacy and antipsychotic use had more significant predictors than any other medication category, suggesting that children treated with polypharmacy and/or an antipsychotic were more complex and had more comorbid conditions than children treated with other medication classes.

Irritability versus Oppositional Behavior

Irritability was the most significant predictor of antipsychotic use. Controlled studies show that antipsychotics decrease irritability in autism [28-30],

and risperidone and aripiprazole are approved by the FDA for this purpose. Irritability also predicted "other" medication use, which included mood stabilizing anticonvulsants. In contrast, oppositional behavior did not predict antipsychotic use or medication in the "other" category. However, oppositional behavior (and not irritability) predicted treatment with an alpha agonist and polypharmacy. Therefore, irritability and oppositional behavior individually were predictors of different medication classes, but ODD (which combines irritability and oppositional behavior) was not a significant predictor of any medication group. This distinction lends further support for the bi-dimensional conceptualization of ODD, as indicated by research findings [76, 77].

IQ

Lower IQ was an independent predictor of only two medication groups: polypharmacy and "other" medication. When low IQ is combined with the other comorbid conditions, the child is more impaired and possibly perceived as more in need of additional medication treatment, increasing the rate of polypharmacy. Medications in the "other" medication class included anticonvulsants. Epilepsy is associated with lower IQ, which would increase the likelihood of anticonvulsant use and, therefore, also polypharmacy.

Sex, Race, Parent Occupation, and Learning Problems

Sex, race, parent occupation, and learning problems were the only variables that were not significant predictors of medication use for all medication classes. This is contrary to some, but not all, studies reviewed in our introduction. Most previous studies relied on univariate analyses to determine correlates of medication use and, therefore, did not demonstrate that these demographic variables were independently related to medication use after controlling for other variables, particularly comorbidity. All comorbid conditions in our study were independent predictors of two or more medication groups. Together, these findings are positive because symptoms and not demographics determined medication use. It is important for future studies to control for comorbid conditions through multivariate analyses when investigating the influence of demographics on prescribing practices. Interestingly, the presence of learning problems was not a significant predictor of medication use, despite studies showing that stimulants can improve academic performance and achievement test scores in children with ADHD [2, 19-21].

LIMITATIONS

A variety of additional factors affecting the decision to medicate children need to be considered in future research. Particularly influential are parents' [82] and physicians' [83] attitudes regarding medication use, insurance coverage and other access barriers, and changes in prescribing practices over time, which were not analyzed in our study. Our sample involved children referred to a psychiatry diagnostic clinic, which is a limitation in that the children were likely more symptomatic than nonreferred children and may not yet have received a formal diagnosis of ADHD or autism. Our sample was from a single practice site and was predominantly white, so findings need to be replicated in other and more racially diverse settings.

DIRECTIONS FOR FUTURE RESEARCH

Overall, older age was the most powerful predictor of medication use in our study of 2- to 17-year-olds with autism and/or ADHD. Continued research on long-term outcome and safety as a function of the age at which medication treatment is initiated is needed. The FDA has approved some psychotropic medications for preschool children (e.g., age 3 for amphetamines in ADHD and age 5 for risperidone to treat irritability in autism). It remains to be determined if the risk to benefit ratio for psychotropic medications differs across ages. ADHD-C and autism have common overlapping comorbidities, especially oppositional behavior, irritability, and aggression [2, 38, 39]. Controlled studies reviewed in our introduction demonstrate that different medications are effective in reducing these symptoms. Evidence-based research also supports the effectiveness of behavioral interventions in the treatment of preschoolers and older children with autism or ADHD [3, 84, 85]. Future research should continue to explore the most effective combination of pharmacological, behavioral, and psychosocial interventions for treating ADHD and autism and their shared comorbid problems.

REFERENCES

[1] Mayes SD, Sanderson DL, Bixler EO, Humphrey FJ, Mattison RE. Methylphenidate and ADHD: Influence of age, IQ, and neurodevelopmental status. Dev Med Child Neurol 1994; 36: 1099-1107. https://doi.org/10.1111/j.1469-8749.1994.tb11811.x

[2] MTA Cooperative Group. A 14-month randomized clinical trial of treatment strategies for attention-deficit/hyperactivity disorder. Arch Gen Psychiatry 1999; 56: 1073-86. https://doi.org/10.1001/archpsyc.56.12.1073

[3] Waxmonsky J, Pelham WE, Gnagy E, Cummings MR, O'Connor B, Majumdar A, *et al*. The efficacy and tolerability

of methylphenidate and behavior modification in children with attention-deficit/hyperactivity disorder and severe mood dysregulation. J Child Adolesc Psychopharmacol 2008; 18: 573-88.
https://doi.org/10.1089/cap.2008.065

[4] Arnold LE, Aman MG, Cook AM, Witwer AN, Hall KL, Thompson S, *et al*. Atomoxetine for hyperactivity in autism spectrum disorders: Placebo-controlled crossover pilot trials. J Am Acad Child Adolesc Psychiatry 2006; 45: 1196-1205.
https://doi.org/10.1097/01.chi.0000231976.28719.2a

[5] Handen BL, Johnson CR, Lubetsky M. Efficacy of methylphenidate among children with autism and symptoms of attention-deficit hyperactivity disorder. J Autism Dev Disord 2000; 30: 245-55.
https://doi.org/10.1023/A:1005548619694

[6] Harfterkamp M, Buitelaar JK, Minderaa RB, van de Loo-Neus G, van der Gaag RJ, Hoekstra PJ. Atomoxetine in autism spectrum disorder: No effects on social functioning; some beneficial effects on stereotyped behaviors, inappropriate speech, and fear of change. J Child Adolesc Psychopharmacol 2014; 24: 481-5.
https://doi.org/10.1089/cap.2014.0026

[7] Harfterkamp M, van de Loo-Neus G, Minderaa RB, van der Gaag RJ, Escobar R, Schacht A, *et al*. A randomized double-blind study of atomoxetine versus placebo for attention-deficit/hyperactivity disorder symptoms in children with autism spectrum disorder. J Am Acad Child Aolesc Psychiatry 2012; 51: 733-41.
https://doi.org/10.1016/j.jaac.2012.04.011

[8] RUPP. Randomized, controlled, crossover trial of methylphenidate in pervasive developmental disorders with hyperactivity. Arch Gen Psychiatry 2005; 62: 1266-74.
https://doi.org/10.1001/archpsyc.62.11.1266

[9] Aman MG, Binder C, Turgay A. Risperidone effects in the presence/absence of psychostimulant medicine in children with ADHD, other disruptive behavior disorders, and subaverage IQ. J Child Adolesc Psychopharmacol 2004; 14: 243-54.
https://doi.org/10.1089/1044546041649020

[10] Gadow KD, Arnold LE, Molina BSG, Findling RL, Bukstein OG, Brown NV. Risperidone added to parent training and stimulant medication: Effects on attention-deficit/hyperactivity disorder, oppositional defiant disorder, conduct disorder, and peer aggression. J Am Acad Child Adolesc Psychiatry 2014; 53: 948-59.
https://doi.org/10.1016/j.jaac.2014.05.008

[11] Snyder R, Turgay A, Aman M, Binder C, Fisman S, Carroll A. Effects of risperidone on conduct and disruptive behavior disorders in children with subaverage IQs. J Am Acad Child Adolesc Psychiatry 2002; 41: 1026-36.
https://doi.org/10.1097/00004583-200209000-00002

[12] Nagaraj R, Singhi P, Malhi P. Risperidone in children with autism: Randomized, placebo- controlled, double-blind study. J Child Neurol 2006; 21: 450-5.
https://doi.org/10.1177/08830738060210060801

[13] Kollins S, Lopez FL. Psychomotor functioning and alertness with guanfacine extended release in subjects with attention-deficit/hyperactivity disorder. J Child Adolesc Psychopharmacol 2011; 21: 111-20.
https://doi.org/10.1089/cap.2010.0064

[14] Newcorn JH, Stein MA, Childress AC, Youcha S, White C, Enright G, *et al*. Randomized, double-blind trial of guanfacine extended release in children with attention-deficit/hyperactivity disorder: Morning or evening administration. J Am Acad Child Adolesc Psychiatry 2013; 52: 921-30.
https://doi.org/10.1016/j.jaac.2013.06.006

[15] Wilens TE, McBurnett K, Turnbow J, Rugino T, White C, Youcha S. Morning and evening effects of guanfacine extended release adjunctive to psychostimulants in pediatric ADHD: Results from a phase III multicenter trial. J Atten Disord 2017; 21: 110-19.
https://doi.org/10.1177/1087054713500144

[16] Handen BL, Sahl R, Hardan AY. Guanfacine in children with autism and/or intellectual disabilities. J Dev Behav Pediatr 2008; 29: 303-8.
https://doi.org/10.1097/DBP.0b013e3181739b9d

[17] Jaselskis CA, Cook EH, Fletcher KE, Leventhal BL. Clonidine treatment of hyperactive and impulsive children with autistic disorder. J Clin Psychopharmacol 1992; 12: 322-6.
https://doi.org/10.1097/00004714-199210000-00005

[18] Scahill L, McCracken JT, King BH, Rockhill C, Shah B, Politte L, *et al*. Extended-release guanfacine for hyperactivity in children with autism spectrum disorder. Am J Psychiatry 2015; 172: 1197-206.
https://doi.org/10.1176/appi.ajp.2015.15010055

[19] Baweja R, Mattison RE, Waxmonsky JG. Impact of attention-deficit hyperactivity disorder on school performance: What are the effects of medication? Pediatr Drugs 2015; 17: 459-77.
https://doi.org/10.1007/s40272-015-0144-2

[20] Evans SW, Pelham WE, Smith BH, Bukstein O, Gnagy EM, Greiner AR, *et al*. Dose- response effects of methylphenidate on ecologically valid measures of academic performance and classroom behavior in adolescents with ADHD. Experim Clin Psychopharmacol 2001; 9: 163-75.
https://doi.org/10.1037/1064-1297.9.2.163

[21] Kavale K. The efficacy of stimulant drug treatment for hyperactivity: A meta-analysis. J Learn Disabil 1982; 15: 280-9.
https://doi.org/10.1177/002221948201500508

[22] Gillberg C, Melander H, von Knorring A-L, Janols L-O, Thernlund G, Hagglof B, *et al*. Long-term stimulant treatment of children with attention-deficit hyperactivity disorder symptoms. Arch Gen Psychiatry 1997; 54: 857-64.
https://doi.org/10.1001/archpsyc.1997.01830210105014

[23] Aman MG, Bukstein OG, Gadow KD, Arnold LG, Molina BSG, McNamara N, *et al*. What does risperidone add to parent training and stimulant for severe aggression in child attention- deficit/hyperactivity disorder? J Am Acad Child Adolesc Psychiatry 2014; 53: 47-60.
https://doi.org/10.1016/j.jaac.2013.09.022

[24] McCracken JT, McGough J, Shah B, Cronin P, Hong D, Aman MG, *et al*. Risperidone in children with autism and serious behavioral problems. New Eng J Med 2002; 347: 314-21.
https://doi.org/10.1056/NEJMoa013171

[25] Pandina GJ, Bossie CA, Youssef E, Zhu Y, Dunbar F. Risperidone improves behavioral symptoms in children with autism in a randomized, double-blind, placebo-controlled trial. J Autism Dev Disord 2007; 37: 367-73.
https://doi.org/10.1007/s10803-006-0234-7

[26] Politte C, Scahill L, Figueroa J, McCracken JT, King B, McDougle CJ. A randomized, placebo-controlled trial of extended-release guanfacine in children with autism spectrum disorder and ADHD symptoms: An analysis of secondary outcome measures. Neuropsychopharmacol 2018; 43: 1772-8.
https://doi.org/10.1038/s41386-018-0039-3

[27] de la Cruz LF, Simonoff E, McGough JJ, Halperin JM, Arnold E, Stringaris A. Treatment of children with attention-deficit/hyperactivity disorder (ADHD) and irritability: Results from the multimodal treatment study of children with ADHD(MTA). J Am Acad Child Adolesc Psychiatry 2015; 54: 62-70.
https://doi.org/10.1016/j.jaac.2014.10.006

[28] Ghanizadeh A, Ayoobzadehshirazi A. A randomized double-blind placebo-controlled clinical trial of adjuvant buspirone for irritability in autism. Pediatr Neurol 2015; 52: 77-81.
https://doi.org/10.1016/j.pediatrneurol.2014.09.017

[29] McDougle CJ, Scahill L, Aman MG, McCracken JT, Tierney E, Davies M, *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: 1142-8. https://doi.org/10.1176/appi.ajp.162.6.1142

[30] Owen R, Sikich L, Marcus RN, Corey-Lisle P, Manos G, McQuade RD. Aripiprazole in the treatment of irritability in children and adolescents with autistic disorder. Pediatrics 2011; 124: 1533-40. https://doi.org/10.1542/peds.2008-3782

[31] King BH, Hollander E, Sikich L, McCracken JT, Scahill L, Bregman JD. Lack of efficacy of citalopram in children with autism spectrum disorders and high levels of repetitive behavior. Arch Gen Psychiatry 2009; 66: 583-90. https://doi.org/10.1001/archgenpsychiatry.2009.30

[32] Arnold LE, Gadow KD, Farmer CA, Findling RL, Bukstein O, Molina BSG. Comorbid anxiety and social avoidance in treatment of severe childhood aggression: Response to adding risperidone to stimulant and parent training; mediation of disruptive symptom response. J Child Adolesc Psychopharmacol 2015; 25: 203-12. https://doi.org/10.1089/cap.2014.0104

[33] Joshi G, Faraone SV, Wozniak J, Tarko L, Fried R, Galdo M, *et al*. Symptom profiles of ADHD in youth with high-functioning autism spectrum disorder: A comparative study in psychiatrically referred populations J Atten Disord 2017; 21: 846-55. https://doi.org/10.1177/1087054714543368

[34] Mayes SD, Calhoun SL, Mayes RD, Molitoris S. Autism and ADHD: Overlapping and discriminating symptoms. Res Autism Spectr Disord 2012; 6: 277-85. https://doi.org/10.1016/j.rasd.2011.05.009

[35] Biederman J, Faraone SV, Milberger S, Jetton JG, Chen L, Mick E, *et al*. Is childhood oppositional defiant disorder a precursor to adolescent conduct disorder? Findings from a four-year follow-up study of children with ADHD. J Am Acad Child Adolesc Psychiatry 1996; 35: 1193-1204. https://doi.org/10.1097/00004583-199609000-00017

[36] Efron D, Scriberras E. The diagnostic outcome of children with suspected attention hyperactivity disorder following multidisciplinary assessment. J Paediatr Child Health 2010; 46: 392-7. https://doi.org/10.1111/j.1440-1754.2010.01750.x

[37] Faraone V, Biederman J, Weber W, Russell RL. Psychiatric, neuropsychological, and psychosocial features of DSM-IV subtypes of attention-deficit/hyperactivity disorder: Results from a clinically referred sample. Psychol Med 1998; 36: 159-65. https://doi.org/10.1017/S003329170500471X

[38] King S, Waschbusch DA. Aggression in children with attention-deficit/hyperactivity disorder. Expert Rev Neurother 2010; 10: 1581-94. https://doi.org/10.1586/ern.10.146

[39] Mayes SD, Waxmonsky J, Calhoun SL, Kokotovich C, Mathiowetz C, Baweja R. Disruptive mood dysregulation disorder (DMDD) symptoms in children with autism, ADHD, and neurotypical development and impact of co-occurring ODD, depression, and anxiety. Res Autism Spectr Disord 2015; 18: 64-72. https://doi.org/10.1016/j.rasd.2015.07.003

[40] Mayes SD, Calhoun SL, Murray MJ, Ahuja M, Smith LA. Anxiety, depression, and irritability in children with autism relative to children with other neuropsychiatric disorders and typical development. Res Autism Spectr Disord 2011; 5: 474-85. https://doi.org/10.1016/j.rasd.2010.06.012

[41] Hauck TS, Lau C, Wing LLF, Kurdyak P, Tu K. ADHD treatment in primary care: Demographic factors, medication trends, and treatment predictors. Canadian J Psychiatry 2017; 62: 393-402. https://doi.org/10.1177/0706743716689055

[42] Wolraich ML, Lindgren S, Stromquist A, Milich R, Davis C, Watson D. Stimulant medication use by primary care physicians in the treatment of attention deficit hyperactivity disorder. Pediatrics 1990; 86: 95-101.

[43] Zito JM, Safer DJ, dosReis S, Magder LS, Gardner JF, Zarin DA. Psychotherapeutic medication patterns for youths with attention-deficit/hyperactivity disorder. Arch Pediatr Adolesc Med 1999; 153: 1257-63. https://doi.org/10.1001/archpedi.153.12.1257

[44] Aman MG, Lam KSL, Van Bourgondien ME. Medication patterns in patients with autism: Temporal, regional, and demographic influences. J Child Adolesc Psychopharmacol 2005; 15: 116-26. https://doi.org/10.1089/cap.2005.15.116

[45] Coury DL, Anagnostou E, Manning-Courtney P, Reynolds A, Cole L, McCoy R, *et al*. Use of psychotropic medication in children and adolescent with autism spectrum disorders. Pediatrics 2012; 130: S69-76. https://doi.org/10.1542/peds.2012-0900D

[46] Frazier TW, Shattuck PT, Narendorf SC, Cooper BP, Wagner M, Spitznagel EL. Prevalence and correlates of psychotropic medication use in adolescents with an autism spectrum disorder with and without caregiver-reported attention-deficit/hyperactivity disorder. J Child Adolesc Psychopharmacol 2011; 21: 571-9. https://doi.org/10.1089/cap.2011.0057

[47] Logan SL, Carpenter L, Leslie S, Garrett-Mayer E, Hunt KJ, Charles J, *et al*. Aberrant behaviors and co-occurring conditions as predictors of psychotropic polypharmacy among children with autism spectrum disorders. J Child Adolesc Psychopharmacol 2015; 25: 323-36. https://doi.org/10.1089/cap.2013.0119

[48] Madden JM, Lakoma MD, Lynch FL, Rusinak D, Owen-Smith AA, Coleman K, *et al*. Psychotropic medication use among insured children with autism spectrum disorder. J Autism Dev Disord 2017; 47: 144-54. https://doi.org/10.1007/s10803-016-2946-7

[49] Mandell DS, Morales KH, Marcus SC, Stahmer AC, Doshi J, Polsky DE. Psychotropic medication use among Medicaid-enrolled children with autism spectrum disorders. Pediatrics 2008; 121: e441-8. https://doi.org/10.1542/peds.2007-0984

[50] Martin A, Scahill L, Klin A, Volkmar FR. Higher-functioning pervasive developmental disorders: Rates and patterns of psychotropic drug use. J Am Acad Child Adolesc Psychiatry 1999; 38: 923-31. https://doi.org/10.1097/00004583-199907000-00024

[51] Oswald DP, Sonenklar NA. Medication use among children with autism spectrum disorders. J Child Adolesc Psychopharmacol 2007; 17: 348-55. https://doi.org/10.1089/cap.2006.17303

[52] Rosenberg RE, Mandell DS, Farmer JE, Law JK, Marvin AR, Law PA. Psychotropic medication use among children with autism spectrum disorders enrolled in a national registry, 2007-2008. J Autism Dev Disord 2010; 40: 342-51. https://doi.org/10.1007/s10803-009-0878-1

[53] Schubert JR, Camacho F, Leslie D. Psychotropic medication trends among children and adolescents with autism spectrum disorder in the Medicaid program. Autism 2014; 18: 631-7. https://doi.org/10.1177/1362361313497537

[54] Spencer D, Marshall J, Post B, Kulakodlu M, Newschaffer C, Dennen T, *et al*. Psychotropic medication use and polypharmacy in children with autism spectrum disorders. Pediatrics 2013; 132: 833-40. https://doi.org/10.1542/peds.2012-3774

[55] Kamble P, Chen H, Johnson ML, Bhatara V, Aparasu RR. Concurrent use of stimulants and second-generation antipsychotics among children with ADHD enrolled in Medicaid. Psychiatr Services 2015; 66: 404-10. https://doi.org/10.1176/appi.ps.201300391

[56] Sultan RS, Wang S, Crystal S, Olfson M. Antipsychotic treatment among youths with attention-deficit/hyperactivity disorder. JAMA Network Open 2019. https://doi.org/10.1001/jamanetworkopen.2019.7850

[57] Zito JM, Safer DJ, dosReis S, Gardner JF, Magder L, Soeken K, *et al*. Psychotropic practice patterns for youth: A 10-year perspective. Archives of Ped Adolescent Med 2003; 157: 17-25. https://doi.org/10.1001/archpedi.157.1.17

[58] Kamimura-Nishimura KI, Epstein JN, Froehlich TE, Peugh J, Brinkman WB, Baum R, *et al*. Factors associated with attention deficit hyperactivity disorder medication use in community care settings. J Pediatrics In press.

[59] Sawyer MG, Rey JM, Graetz BW, Clark JT, Baghurst PA. Use of medication by young people with attention-deficit/hyperactivity disorder. Med J Australia 2002; 177: 21-5. https://doi.org/10.5694/j.1326-5377.2002.tb04624.x

[60] Burcu M, Safer DJ, Zito JM. Antipsychotic prescribing for behavioral disorders in US youth: Physician specialty, insurance coverage, and complex regimens. Pharmacoepidemiol Drug Safety 2016; 25: 26-34. https://doi.org/10.1002/pds.3897

[61] Cox ER, Motheral BR, Henderson RR, Mager D. Geographic variation in the prevalence of stimulant medication use among children 5 to 14 years old: Results from a commercially insured US sample. Pediatrics 2003; 111: 237-43. https://doi.org/10.1542/peds.111.2.237

[62] Clark T, Feehan C, Tinline C, Vostanis P. Autistic symptoms in children with attention deficit-hyperactivity disorder. Eur Child Adolesc Psychiatry 1999; 8: 50-5. https://doi.org/10.1007/s007870050083

[63] Miodovnik A, Harstad E, Sideridis G, Huntington N. Timing of the diagnosis of attention-deficit/hyperactivity disorder and autism spectrum disorder. Pediatrics 2015; 136: 830-7. https://doi.org/10.1542/peds.2015-1502

[64] Connor DF, Steeber J, McBurnett K. A review of attention-deficit/hyperactivity disorder complicated by symptoms of oppositional defiant disorder or conduct disorder. J Dev Behav Pediatrics 2010; 31: 427-40. https://doi.org/10.1097/DBP.0b013e3181e121bd

[65] Mayes SD, Calhoun SL, Aggarwal R, Baker C, Mathapati S, Anderson R. Explosive, oppositional, and aggressive behavior in children with autism compared to other clinical disorders and typical development. Res Autism Spectr Disord 2012; 6: 1-10. https://doi.org/10.1016/j.rasd.2011.08.001

[66] Lindgren SD, Koeppl GK. Assessing child behavior problems in a medical setting: Development of the Pediatric Behavior Scale. In RJ Prinz, editor. Advances in behavioral assessment of children and families. Greenwich, CT: JAI 1987; pp. 57-90.

[67] Mayes SD. Checklist for Autism Spectrum Disorder. Wood Dale, IL: Stoelting. 2012. https://doi.org/10.1037/t03996-000

[68] Mayes SD, Calhoun SL, Waschbusch D, Baweja R. Autism and reactive attachment/disinhibited social engagement disorders: Co-occurrence and differentiation. Clin Child Psychol Psychiatry 2017; 22: 620-31. https://doi.org/10.1177/1359104516678039

[69] Tierney C, Mayes SD, Lohs SR, Black A, Gisin E, Veglia M. How valid is the Checklist for Autism Spectrum Disorder when a child has apraxia of speech? J Dev Behav Pediatr 2015; 36: 569-74. https://doi.org/10.1097/DBP.0000000000000189

[70] Mayes SD, Calhoun SL, Murray MJ, Morrow JD, Yurich KKL, Mahr, F, *et al*. Comparison of scores on the Checklist for Autism Spectrum Disorder, Childhood Autism Rating Scale (CARS), and Gilliam Asperger's Disorder Scale (GADS) for children with low functioning autism, high functioning autism or Asperger's disorder, ADHD, and typical development. J Autism Dev Disord 2009; 39: 1682-93. https://doi.org/10.1007/s10803-009-0812-6

[71] Murray MJ, Mayes SD, Smith LA. Brief report: Excellent agreement between two brief autism scales (Checklist for Autism Spectrum Disorder and Social Responsiveness Scale) completed independently by parents and the Autism Diagnostic Interview-Revised. J Autism Dev Disord 2011; 41: 1586-90. https://doi.org/10.1007/s10803-011-1178-0

[72] Bixler EO, Vgontzas AN, Lin H-M, Calhoun S, Vela-Bueno A, Fedok F, *et al*. Sleep disordered breathing in children in a general population sample: Prevalence and risk factors. Sleep 2009; 32: 731-6. https://doi.org/10.1093/sleep/32.6.731

[73] Mayes SD, Gordon M, Calhoun SL, Bixler EO. Long-term temporal stability of measured inattention and impulsivity in typical and referred children. J Atten Disord 2014; 18: 23-30. https://doi.org/10.1177/1087054712448961

[74] Conrad AL, Richman L, Lindgren S, Nopoulos P. Biological and environmental predictors of behavioral sequelae in children born preterm. Pediatrics 2010; 125: e83-9. https://doi.org/10.1542/peds.2009-0634

[75] Waxmonsky J, Mayes SD, Calhoun SL, Fernandez-Mendoza J, Waschbusch D, Bixler EO. The association between disruptive mood dysregulation disorder symptoms and sleep problems in children with and without ADHD. Sleep Med 2017; 37: 180-6. https://doi.org/10.1016/j.sleep.2017.02.006

[76] Burke JD, Boylan K, Rowe R, Duku E, Stepp SD, Hipwell AE, *et al*. Identifying the irritability dimension of ODD: Application of a modified bifactor model across five large community samples of children. J Abnorm Psychol 2014; 123: 841-51. https://doi.org/10.1037/a0037898

[77] Waschbusch D, Baweja R, Babinski D, Mayes SD, Waxmonsky J. Irritability and limited prosocial emotions/callous-unemotional traits in elementary school age children. Behav Therapy 2019. https://doi.org/10.1016/j.beth.2019.06.007

[78] Costello EJ, Copeland W, Angold A. Trends in psychopathology across the adolescent years: What changes when children become adolescents, and when adolescents become adults? J Child Psychol Psychiatry 2011; 52: 1015-25. https://doi.org/10.1111/j.1469-7610.2011.02446.x

[79] Kessler RC, Berglund P, Demler O, Jin R, Merikangas KR, Walters EE. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the national comorbidity survey replication. Arch Gen Psychiatry 2005; 62: 593-602. https://doi.org/10.1001/archpsyc.62.6.593

[80] Shaywitz S, Shaywitz B, Wietecha L, Wigel S, McBurnett K, Williams D, *et al*. Effect of atomoxetine treatment on reading and phonological skills in children with dyslexia or attention-deficit/hyperactivity disorder and comorbid dyslexia in a randomized, placebo-controlled trial. J Child Adolesc Psychopharmacol 2017; 27: 19-28. https://doi.org/10.1089/cap.2015.0189

[81] Mayes SD, Calhoun SL. Frequency of reading, math, and writing disabilities in children with clinical disorders. Learn Individ Differences 2006; 16: 145-57. https://doi.org/10.1016/j.lindif.2005.07.004

[82] Waschbusch DA, Cunningham CE, Pelham WE, Rimas HL, Greiner AR, Gnagy EM, *et al*. A discrete choice conjoint experiment to evaluate parent preferences for treatment of young, medication naïve children with ADHD. J Clin Child Adolesc Psychol 2011; 40: 546-61. https://doi.org/10.1080/15374416.2011.581617

[83] Fremont WP, Nastasi R, Newman N, Roizen NJ. Comfort level of pediatricians and family medicine physicians diagnosing and treating child and adolescent psychiatric disorders. Internat J Psychiatry Med 2008; 38: 153-68. https://doi.org/10.2190/PM.38.2.c

[84] Panerai S, Suraniti GS, Catania V, Zingale M, Ferri R, Raggi A, *et al*. (2019): Early results from a combined low-intensive psychoeducational intervention for preschoolers with autism spectrum disorder. Disabil Rehabil 2019. https://doi.org/10.1080/09638288.2018.1522553

[85] Eldevik S, Hastings RP, Hughes JC, Jahr E, Eikeseth S, Cross S. Meta-analysis of early intensive behavioral intervention for children with autism. J Clin Child Adolesc Psychol 2009; 38: 439-50. https://doi.org/10.1080/15374410902851739

Received on 20-11-2019 Accepted on 10-12-2019 Published on 16-12-2019

DOI: https://doi.org/10.12970/2310-8231.2019.07.03