

Use of Psychotropic Medication in Children and Adolescents With Autism Spectrum Disorders

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KEY WORDS

autism spectrum disorders, psychotropic medications, medical comorbidity, psychiatric comorbidity

ABBREVIATIONS

ADHD—attention-deficit/hyperactivity disorder

ASD—autism spectrum disorder

ATN—Autism Treatment Network

CBCL—Child Behavior Checklist

CSHQ—Child Sleep Health Questionnaire

DSM-IV-TR—*Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision*

GI—gastrointestinal

OCD—obsessive-compulsive disorder

SSRI—selective serotonin reuptake inhibitor

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abstract

OBJECTIVES: The goal of this study was to examine rates of psychotropic medication use and identify associated child and family characteristics among children and adolescents with autism spectrum disorder (ASD) enrolled in an autism registry maintained by the Autism Treatment Network (ATN).

METHODS: The sample, derived from the ATN registry, consists of 2853 children aged 2 to 17 years with diagnoses of ASD supported by *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*, and the Autism Diagnostic Observation Schedule with available data on medication use. As part of initial enrollment in the registry, parents completed questionnaires on current psychotropic medication use, psychiatric and medical conditions, and demographics.

RESULTS: Of the 2853 children, 763 (27%) were taking ≥ 1 psychotropic medication; 15% were prescribed 1 medication, 7.4% received 2 medications, and 4.5% received ≥ 3 . Among children aged 3 to 5 years, 11% were taking ≥ 1 psychotropic medication; among 6- to 11-year-old children, 46%; and 66% of adolescents aged 12 to 17 years were taking at ≥ 1 psychotropic medication. A parent report of comorbid diagnosis of attention-deficit/hyperactivity disorder, bipolar disorder, obsessive-compulsive disorder, depression, or anxiety was associated with a high rate of use, with 80% receiving ≥ 1 psychotropic medication. Only 15% of children with no comorbid psychiatric disorder were taking psychotropic medication. Psychotropic medication use was also related to sleep and gastrointestinal problems.

CONCLUSIONS: The prescription of psychotropic medications in this registry sample is highly related to comorbid psychiatric disorder. Other factors associated with use include medical comorbidities, race, ethnicity, and older age. *Pediatrics* 2012;130:S69–S76

The autism spectrum disorders (ASDs) have received increased attention over the past 2 decades, with rising rates of recognition and diagnosis. With the increasing number of identified cases has come a concomitant increase in the use of a variety of psychotropic medications as part of the individual's overall treatment plan. Surveys of the topic over this time period have documented use in various populations.¹⁻⁵

The parent-completed surveys conducted by Lam et al noted direct associations of medication use with older age, intellectual disability, and more restrictive home and educational placements.² Across 3 regional surveys, use of any psychotropic medication was reported in 30% to 45% of individuals. These authors found varying demographic correlates with use of specific classes of medications, but the surveys lacked information regarding specific indications or target symptoms in this population. The survey conducted by Witwer and Lecavalier⁶ showed correlation of medication class with behavioral subscale scores and adaptive behavior. For example, children with high hyperactive and conduct problem scores were more likely to receive antipsychotics and psychostimulants. Lower adaptive behavior scores were associated with higher antipsychotic and mood stabilizer use.

When used, medications are generally chosen to treat specific symptoms because there are no currently available pharmacologic agents with proven efficacy to treat the core ASD symptoms. This has led to the use of medicines known to be effective for other specific target symptoms or behaviors commonly seen in ASD, such as attention and distractibility, obsessive or compulsive behaviors, anxiety, and depression. Other factors affecting use and choice of medication, such as IQ, functional level, and other comorbidities, have not been routinely addressed in previous studies.

The goal of this study was to examine the reported use of psychotropic medications in children and youth with ASD and receiving care through the Autism Speaks Autism Treatment Network (ATN), a multisite consortium of autism programs across the United States and Canada. We were particularly interested in describing use by drug class, age, and race/ethnicity, as well as by presence or absence of (1) psychiatric comorbidity, (2) other medical comorbidity, and (3) behavioral symptoms.

METHODS

Study Sample

The Autism Speaks ATN, a collaboration among 17 academic health centers in the United States and Canada, has developed a common registry for children enrolled in the several sites. Families are offered the opportunity to participate in the registry, which requires written consent and sharing of additional personal health information and completion of additional questionnaires. The study is approved by the institutional review board at each site. Main registry inclusion criteria are age 2 to 18 years and confirmation of a diagnosis of autism, Asperger disorder, or pervasive developmental disorder not otherwise specified using a battery of assessments including *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision* (DSM-IV-TR) criteria and administration of the Autism Diagnostic Observation Schedule. Parents provided information regarding previous diagnoses, testing, and treatments. Clinicians accepted parent reports of comorbid psychiatric diagnoses, which reflect both parents' understanding of their child's condition and other physicians' description to parents and presumed rationale for treatment. Medications reported by parents were those received at time of enrollment

and confirmed by ATN clinicians. All data collected were entered into the registry database by trained study coordinators at each site. The registry database is maintained by the EMMES Corporation (Bethesda, MD). Enrollment for the registry (based on the date of consent) began in December 2007. The study sample included all children enrolled in the ATN Registry from December 2007 to the end of April 2011.

Study Variables

Use of Psychotropic Medications

Receipt of psychotropic medications at the time of enrollment into the ATN registry was the primary study measure. We categorized medications as stimulants, selective serotonin reuptake inhibitors (SSRIs), α -adrenergic agents, and antipsychotic medications. Concurrent use of >1 medication was identified, as well as class of medication. We did not determine dose or timeframe of medication taking.

Demographics

Demographic characteristics included child gender, age, and race/ethnicity. We categorized age as <3 years, 3 to 5 years, 6 to 11 year, and 12 to 17 years; race and ethnicity (from parent report) were categorized as Native American or Alaskan Native, Asian, black or African American, Native Hawaiian or Pacific Islander, white, black Canadian, and mixed race. Because of the small numbers in some categories, these were collapsed to white/Caucasian and nonwhite/Caucasian. Ethnicity was categorized as Hispanic or Latino origin and non-Hispanic or non-Latino.

Comorbid Conditions

Parents reported comorbid psychiatric conditions at the time of enrollment in the registry. Conditions included attention-deficit/hyperactivity disorder (ADHD), bipolar disorder,

TABLE 1 Medication Use by Age (N = 2843)

Age group (n)	Any medication, n (%)	2 medications, n (%)	≥3 medications, n (%)	Stimulant, n (%)	α-agonist, n (%)	SSRI, n (%)	Atypical antipsychotic, n (%)
<3 y (367)	2 (1)	0	0	1	1	0	0
3–5 y (1147)	119 (10)	23 (2)	10 (1)	39 (3)	54 (4)	17 (1.4)	46 (4)
6–11 y (951)	422 (44)	119 (13)	60 (6)	247 (26)	111 (12)	136 (14)	129 (14)
12–17 y (276)	176 (64)	55 (20)	31 (11)	92 (33)	39 (14)	88 (32)	64 (23)
Total	760 (27)	208 (7)	130 (5)	379 (13)	205 (7)	241 (8)	239 (8)

obsessive-compulsive disorder (OCD), anxiety, and depression.

The initial medical history questionnaire queried gastrointestinal (GI) symptoms, specifically constipation, diarrhea, abdominal pain, and GI allergy. We dichotomized children into those with and without reported GI symptoms. To determine the presence of sleep disorders, we used the Child Sleep Health Questionnaire (CSHQ), a 33-item parent completed questionnaire.⁷ Insofar as the CSHQ has been studied well only to age 10 years, we limited analyses of sleep disorder associations with psychotropic medication use to children <11 years old.⁸ Total CSHQ scores >41 have been reported as a sensitive cutoff for clinically significant sleep problems. We also included presence or absence of seizures by parent report. Additional child characteristics included externalizing, internalizing, and total scale scores on the Child Behavior Checklist (CBCL), a validated measure of behaviors. We used cutoff scores of 70 on the CBCL scales as denoting risk for behavioral problems.⁹

Control Variables

Previous research has shown associations of ASD diagnostic category and cognitive status with use of medications. We controlled for these as well as insurance status (private, public, or Medicaid) and parental educational status in multivariable analyses.

Analysis

We initially determined variations in use of medications by age and race, using χ^2 to determine significance. We then examined variations in use by psychiatric comorbidities, other medical comorbidities, and behavioral symptoms in multivariable analyses, controlling for age, IQ, primary caregiver education, insurance, ASD diagnosis, race, and ethnicity when noted. Adjusted odds ratios are provided for medication use.

RESULTS

Medication information was available for 2853 children enrolled in the ATN Registry. Of the 2853, 763 (27%) were prescribed ≥1 psychotropic medica-

tion; 15% received 1 medication, 7.4% received 2 medications, and 4.5% reported receiving ≥3.

Use of Psychotropic Medication by Age

Medication use varied substantially by age. Only 1% of children under age 3 years were reported as using any psychotropic medication. Among children aged 3 to 5 years, 10% were taking ≥1 psychotropic medication; among 6- to 11-year old children, 44%; and among 12- to 17-year-olds, 64% were taking ≥1 psychotropic medication. Table 1 provides information on the specific psychotropic medications by age group.

Demographic Variations in Psychotropic Medication Use

There were no significant variations in medication use by IQ or gender. Children with private insurance had a higher rate of psychotropic medication receipt compared with children with other or no insurance (P = .003; see Table 2). Nonwhite (19%) and

TABLE 2 Medication Use by Race/Ethnicity and Insurance Status

	Any medication, n (%)	2 medications, n (%)	≥ 3 medications, n (%)	Stimulant, n (%)	α-agonist, n (%)	SSRI, n (%)	Atypical antipsychotic, n (%)
Race (N = 2853)	P < .0001	P = .003	P = .16	P < .0001	P = .22	P = .0002	P = .35
Caucasian (n = 2226)	610 (27)	181 (8)	108 (5)	328 (15)	167 (8)	213 (10)	193 (9)
Non-Caucasian (n = 627)	112 (18)	29 (5)	22 (4)	53 (8)	38 (6)	30 (5)	47 (8)
Ethnicity (N = 2759)	P = .0002	P < .003	P < .05	P < .02	P = .23	P = .0003	P < .03
Hispanic or Latino (n = 278)	45 (16)	8 (3)	6 (2)	24 (9)	15 (5)	8 (3)	14 (5)
Non-Hispanic or Latino (n = 2481)	658 (26)	198 (8)	120 (5)	345 (14)	183 (7)	229 (9)	222 (9)
Insurance status (N = 2840)	P = .003	P = .06	P = .32	P = .075	P < .0004	P < .01	P < .01
Private (n = 1306)	365 (28)	107 (8)	49 (4)	195 (15)	92 (7)	133 (10)	118 (9)
Public (n = 922)	227 (25)	57 (6)	36 (4)	110 (12)	87 (9)	59 (6)	89 (10)
Other/none (n = 625)	130 (21)	35 (6)	16 (3)	76 (12)	26 (4)	51 (8)	33 (5)

TABLE 3 Medication Use by Psychiatric or Medical Comorbidity

Condition	Any medication use		2 medications		≥3 medications		Stimulants		α-agonist		SSRI		Atypical antipsychotic	
	n (%) using	OR (95% CI)	n (%) using	OR (95% CI)	n (%) using	OR (95% CI)	n (%) using	OR (95% CI)	n (%) using	OR (95% CI)	n (%) using	OR (95% CI)	n (%) using	OR (95% CI)
Depression	27 (90)	9.47 (2.69–33.43) ^a	7 (23)	1.32 (0.50–3.48)	4 (13)	2.30 (0.69–7.69)	12 (40)	1.49 (0.65–3.40)	4 (13)	1.31 (0.42–4.04)	15 (50)	3.85 (1.66–8.96)	11 (37)	3.94 (1.60–9.72)
Bipolar ^b	18 (95)	NA	6 (32)	NA	2 (10)	NA	10 (53)	NA	3 (16)	NA	4 (21)	NA	10 (53)	NA
ADHD	193 (82)	17.10 (11.42–25.62)	61 (26)	4.65 (3.02–7.16)	36 (15)	7.57 (4.18–13.70)	154 (66)	21.98 (15.51–31.99)	49 (21)	4.14 (2.65–6.46)	52 (22)	1.64 (1.07–2.53)	51 (22)	3.03 (1.97–4.66)
OCD	51 (77)	5.60 (2.91–10.79)	18 (27)	2.60 (1.37–4.94)	12 (18)	4.16 (1.96–8.80)	24 (37)	1.76 (0.99–3.14)	14 (21)	2.61 (1.34–5.11)	30 (46)	5.20 (2.87–9.43)	19 (29)	2.71 (1.43–5.14)
Anxiety	73 (79)	7.52 (4.24–13.34)	26 (28)	3.09 (1.78–5.37)	14 (15)	3.53 (1.75–7.11)	30 (33)	1.40 (0.84–2.33)	16 (17)	2.07 (1.11–3.84)	48 (52)	9.31 (5.48–15.81)	26 (28)	3.56 (2.03–6.22)
GI problems	312 (29)	1.25 (0.99–1.58) ^c	90 (8)	1.37 (0.95–1.98)	41 (4)	1.00 (0.62–1.62)	148 (14)	0.87 (0.66–1.15)	84 (8)	1.23 (0.86–1.75)	117 (11)	1.23 (0.89–1.72)	112 (10)	1.82 (1.28–2.58)
No GI problems	222 (24)	1.00	54 (8)	1.00	33 (4)	1.00	130 (14)	1.00	58 (6)	1.00	76 (8)	1.00	56 (6)	1.00
Sleep problems	357 (30)	1.40 (1.08–1.82)	96 (8)	1.32 (0.88–1.97)	54 (5)	1.74 (0.97–3.10)	191 (16)	1.42 (1.04–1.94)	105 (9)	1.98 (1.27–3.07)	123 (10)	1.04 (0.73–1.49)	116 (10)	1.45 (0.99–2.12)
No sleep problems	151 (26)	1.00	41 (7)	1.00	16 (3)	1.00	73 (13)	1.00	28 (5)	1.00	62 (11)	1.00	45 (8)	1.00

Results from multivariable analyses controlling for age, gender, race/ethnicity, and insurance status. CI, confidence interval; NA, not applicable; OR, odds ratio.

^a Bipolar population too small for stable estimates.

^b Psychiatric condition comparisons: use of medications among those with the comorbid condition compared with children without that condition.

^c Other comorbidity comparisons: use of medications among those with GI or sleep problems compared with children without reported problems.

white/Latino (18%) children had significantly lower use of psychotropic medications than white/non-Latino children (26%).

Psychotropic Medications and Comorbid Psychiatric and Medical Diagnoses

Of the 442 children with a comorbid diagnosis of ADHD, bipolar disorder, OCD, depression, or anxiety, 362 (82%) were on ≥1 psychotropic medication. Of these, 39% received only 1 psychotropic medication, 26% received 2, and 16% received ≥3 (Table 3). Among children with a diagnosis of ADHD, although the most common medication used was stimulants, these children also had higher use of α-agonists and atypical antipsychotics. Only 16% of children without a psychiatric comorbidity used psychotropic medication. Children whose parents reported GI symptoms or sleep problems had higher use of medications (29% and 30%, respectively) than children whose parents reported no such problems.

Psychotropic Medications and CBCL Subscales

Children did not significantly differ on the CBCL internalizing problem scores with regard to psychotropic medication use ($P = .52$; Table 4). Children with CBCL total problems score >70 (36%) were more likely to take psychotropic medications than children with lower scores (22%; $P < .0001$). Results for the externalizing problems score were similar, and these children were more likely to receive an atypical antipsychotic.

DISCUSSION

Among subjects in the Autism Speaks ATN registry, 27% received psychotropic medications; rates were much higher among older children. These

TABLE 4 Rates of Medication Use by CBCL Problem Scores

	Any medication		Two medications		≥3 medications	
	<i>n</i> (%) using	OR (95% CI)	<i>n</i> (%) using	OR (95% CI)	<i>n</i> (%) using	OR (95% CI)
Internalizing						
≤70	393 (25.4)	1.00	105 (6.8)	1.00	56 (3.6)	1.00
>70	132 (28.3)	1.21 (0.92–1.59) ^{a,b}	39 (8.4)	1.44 (0.95–2.18)	15 (3.2)	0.78 (0.42–1.43)
Externalizing						
≤70	418 (24.8)	1.00	117 (7)	1.00	53 (3.1)	1.00
>70	107 (32.8)	2.37 (1.72–3.27)	27 (8.3)	1.82 (1.13–2.95)	18 (5.5)	2.09 (1.15–3.80)
Total Problems						
≤70	321 (22.2)	1.00	84 (5.8)	1.00	39 (2.7)	1.00
>70	204 (35.9)	2.09 (1.61–2.70)	60 (10.5)	2.07 (1.41–3.02)	32 (5.6)	1.78 (1.07–2.98)

Results from multivariable analyses controlling for age, gender, race/ethnicity, and insurance status. CI, confidence interval; OR, odds ratio.

^a Comparing children with scores >70 with those with scores ≤70.

^b $P < .0001$.

rates compare with reports in the literature ranging from 24% to ~80%.^{1–5} The high predominance of children under age 5 in the registry likely explains the relatively low overall rate. This study found 10% of children under age 6 used medications, 44% among those in the 6 to 11 age range, and 64% for children over age 12. Rates of medication use in these older groups are similar to other reports in the literature. The sample in Mandell's study had <2% under age 3 and 19% under age 6, with 76% between 6 and 18. Younger children are less likely to be prescribed these medications, and newly diagnosed children are less likely to have these medications prescribed at their first visit.

Access to health care by health insurance coverage may be another factor. Children with other or no insurance had lower rates of medication use. This could reflect differences in complexity, and it could also reflect variations in access associated with different insurance coverage.

We found variations in medication use related to race and ethnicity, with white/Caucasians and non-Hispanic or Latino subjects more likely to receive medication. Almost 27% of white/Caucasian subjects were receiving medication versus 18% of non-whites ($P < .0001$). Non-Hispanic/Latino showed similar proportions with 26.5% receiving medication

versus 16% Hispanic/Latino ($P = .0002$). White/Caucasian and non-Hispanic/Latino subjects were also more likely to receive ≥3 medications.

Medical comorbidities also influence psychotropic usage. Parent-reported GI problems and sleep problems were both associated with increased use of these medicines. Much current research addresses medical symptoms in efforts to better define broader phenotypes of ASD, with increasing evidence that ASD represents a whole-body disorder, affecting other organ systems (GI, endocrine, immunologic) as well as the central nervous system.¹⁰ Buie¹¹ and others have described responses to GI conditions including common ASD behaviors such as repetitive movements and self-injurious behaviors. Sleep problems, common in ASD, have been associated with increased behavioral problems as measured by the CBCL.^{12–14}

We examined variables from the CBCL to determine associations with clusters of behaviors apart from comorbid psychiatric diagnoses. Although we found no influence of internalizing problems, there was a relationship with clinically significant scores on the externalizing problems scale and the CBCL Total Score. The externalizing problems scale addresses disruptive behaviors such as oppositional behaviors, aggression, and attention problems.

As previously noted, no medications specifically address the core symptoms of ASD. Psychotropic medication use is directed at target symptoms and behaviors, usually guided by the effectiveness of medications for other psychiatric disorders that appear to be comorbid with the patient's ASD. We found strong relationships between medication use and parent reports of other psychiatric conditions. Subjects with a comorbid diagnosis of depression received medication 94% of the time, and those with comorbid bipolar disorder, ADHD, OCD, or anxiety all received medication at least 80% of the time. Comorbid psychiatric diagnoses are difficult to identify in younger children, but as children mature, the symptoms become more apparent. It also should be noted that these are parent reports of these diagnoses. DSM-IV-TR does not allow the formal diagnosis of these disorders in a patient with autism; for this reason, it may be more accurate to consider these as symptoms of these disorders. Only 15% of children with ASD and no comorbid psychiatric diagnosis received medication. For this group, clinicians may have followed DSM-IV-TR guidelines and did not make a comorbid psychiatric diagnosis but felt the patient had symptoms significant enough to warrant medication treatment. However, studies have shown

that a high proportion of prescriptions for psychotropic medications such as anxiety medications fail to have a corroborating diagnosis in the medical record.^{15–17} Our data do not allow confirmation via medical records or other sources.

The use of the 4 categories of psychotropic medications tracked in this study has increased over the past 2 decades. In 2002, Langworthy-Lam, Aman, and colleagues¹ surveyed 1538 families in North Carolina and repeated this with a similar study of families in Ohio in 2003.² They found similar results in each state, with 45% of individuals receiving psychotropic medications, most commonly antidepressants (eg, fluoxetine), antipsychotics (eg, risperidone), and stimulants (eg, methylphenidate). Analysis of a large commercial claims and encounters database found nearly 57% received a psychotropic medication.³ Among Medicaid-enrolled children with autism spectrum disorders,⁴ 56% received ≤ 1 psychotropic medication, with 20% receiving ≥ 3 . They found these medicines were being prescribed to a significant proportion of this population, with 18% of those aged ≤ 2 on medications and 32% of those in the 3- to 5-year old preschool age group. An examination of data from the National Ambulatory Medical Care Survey and the outpatient portion of the National Hospital Ambulatory Medical Care Survey found $\sim 80\%$ of ASD visits were prescribed psychotropic medications, with a mean of 2.4 medications prescribed at any given visit.⁵

Prescriptions for stimulant medications, typically for ADHD, have steadily risen. ADHD symptoms are common in individuals with ASD, and stimulant medications are frequently prescribed. A recent review¹⁸ found evidence for effectiveness of stimulants, noradrenergic reuptake inhibitors, antipsychotics, and α -adrenergic agonists. Studies conducted by the Research

Units on Pediatric Psychopharmacology Autism Network have demonstrated benefit of methylphenidate for ADHD symptoms, although the effect size was less than that seen in typically developing children, and adverse effects were more frequent.¹⁹ Additional review of this population revealed improvement in hyperactive and impulsive symptoms more than symptoms of inattention,²⁰ with no benefit on oppositional defiant symptoms and no worsening of stereotypies. Methylphenidate also improved social communication and social initiation, response to bids for joint attention, self-regulation, and regulated affective state.²¹ Another pair of prospective and retrospective studies conducted in a specialty center in England demonstrated benefit of methylphenidate for ADHD symptoms in ASD, but to a lesser extent than in typically developing subjects.²² A more recent review confirmed this general response in several studies.²³

The effectiveness of SSRIs in treating OCD led to use of these medications as potential treatments for repetitive behaviors and stereotypies in ASD. The benefits of these medications for symptoms of anxiety, which are common in ASD, have led to their use for this symptom. Reviews of several studies examining citalopram, escitalopram, fluoxetine, fluvoxamine, and sertraline suggested benefit in ASD,^{24,25} but problems with study methodologies have raised some doubts. A subsequent rigorous study of citalopram failed to demonstrate benefit for repetitive behaviors.²⁶ A similar study of fluoxetine also showed no benefit. A recent Cochrane review of SSRI use in treatment of ASD found no evidence of effect.²⁷

The antipsychotic medications, especially the atypical antipsychotics, have been studied extensively over the past 20 years. The second-generation

(atypical) antipsychotics have gained popularity because of initial evidence that risk of movement disorder side effects may be less than with first-generation antipsychotics. The antipsychotic group of medicines is primarily used to treat aggression, self-injurious behavior and severe temper tantrums, a cluster of symptoms collectively referred to as irritability.²⁸ Risperidone has been shown to improve irritability symptoms; improvements in restricted, repetitive, and stereotyped patterns of behavior; interest; and activities.²⁹

Since 2006, the US Food and Drug Administration has approved 2 atypical antipsychotic medications for treatment of irritability in autistic disorder (risperidone for children 5 to 16 years and aripiprazole for those aged 6 to 17 years), and the α -agonists guanfacine and clonidine have been approved for treatment of ADHD in new extended release formulations for children aged 6 to 17 years. The evidence for effectiveness of medications is gradually accumulating,^{30,31} and physician prescription of these medicines to treat ASD and comorbid psychiatric conditions will likely increase with time. Families often have difficulty determining whether medication is needed as part of the treatment plan for a child or adolescent with ASD and challenging behavior. Autism Speaks and the Autism Intervention Research Network on Physical Health have developed a Medication Decision Aid and Toolkit that is posted on the Autism Speaks web site as a means of helping families and providers minimize polypharmacy by identifying specific reasons for medication use and increasing awareness of the need for an approach that uses both medication and behavioral interventions.

Our study has several limitations. The data used are collected from families upon entry into the ATN Registry.

Approximately one-third of subjects have a diagnosis before coming to this registry; as a result, parent report of comorbid diagnoses and treatment with psychotropic medications often represents care provided outside the ATN site. Criteria used for making these diagnoses, whether some comorbid symptoms are secondary to these medicines, the perceived effectiveness of these medicines, and the temporal relationship between initiation of these medications and any other therapies the child may be receiving are not known. Similarly, the data do not permit determination of the effectiveness of any previous treatments or if any previous treatment trials provided appropriate time and monitoring. We have minimal information on socioeconomic status and a predominantly Caucasian

population, permitting little study of cultural differences in diagnosis or medication use.

Our study does confirm that significant numbers of children and adolescents with ASD are prescribed psychotropic medications, with supportive findings of behavioral problems on CBCL. There has been a trend for increasing use of these medicines over the past 20 years for a variety of reasons, and as knowledge of their efficacy is acquired, it is likely that this will continue to increase. Future studies should include factors such as nonmedical therapies (applied behavioral analysis techniques, parent behavioral training, speech therapy, occupational therapies) and examine both their use and their time of initiation relative to start of

medication to determine their impact on reducing or delaying medication use. The role of cultural differences and health disparities also needs attention because these have become more apparent as factors affecting both seeking and receiving health care services. Furthermore, the effects of children receiving coordinated care through a medical home model should also be examined because this may facilitate earlier referral to early intervention and other, nonmedical therapies. Finally, there is a need for better outcome measures for autism spectrum disorders to ascertain the benefits of the therapies individuals receive. Such measures could help clinicians determine any broader benefits for the well-being of these patients beyond the direct effect on target symptoms.

REFERENCES

- Langworthy-Lam KS, Aman MG, Van Bourgondien ME. Prevalence and patterns of use of psychoactive medicines in individuals with autism in the Autism Society of North Carolina. *J Child Adolesc Psychopharmacol*. 2002;12(4):311–321
- Aman MG, Lam KS, Collier-Crespin A. Prevalence and patterns of use of psychoactive medicines among individuals with autism in the Autism Society of Ohio. *J Autism Dev Disord*. 2003;33(5):527–534
- Oswald DP, Sonenklar NA. Medication use among children with autism spectrum disorders. *J Child Adolesc Psychopharmacol*. 2007;17(3):348–355
- 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(3). Available at: www.pediatrics.org/cgi/content/full/121/3/e441
- Gerhard T, Chavez B, Olfson M, Crystal S. National patterns in the outpatient pharmacological management of children and adolescents with autism spectrum disorder. *J Clin Psychopharmacol*. 2009;29(3):307–310
- Witwer A, Lecavalier L. Treatment incidence and patterns in children and adolescents with autism spectrum disorders. *J Child Adolesc Psychopharmacol*. 2005;15(4):671–681
- Owens JA, Spirito A, McGuinn M. The Children's Sleep Habits Questionnaire (CSHQ): Psychometric properties of a survey instrument for school-aged children. *Sleep*. 2000;23(8):1043–1051
- Goodlin-Jones BL, Sitnick SL, Tang K, Liu J, Anders TF. The Children's Sleep Habits Questionnaire in toddlers and preschool children. *J Dev Behav Pediatr*. 2008;29(2):82–88
- Achenbach T, Rescorla L. *Child Behavior Checklist*. Burlington, VT: ASEBA; 2000
- Campbell DB, Buie TM, Winter H, et al. Distinct genetic risk based on association of MET in families with co-occurring autism and gastrointestinal conditions. *Pediatrics*. 2009;123(3):1018–1024
- Buie T, Campbell DB, Fuchs GJ III, et al. Evaluation, diagnosis, and treatment of gastrointestinal disorders in individuals with ASDs: A consensus report. *Pediatrics*. 2010;125(suppl 1):S1–S18 doi:10.1542/peds.2009-1878C
- Schreck KA, Mulick JA, Smith AF. Sleep problems as possible predictors of intensified symptoms of autism. *Res Dev Disabil*. 2004;25(1):57–66
- van der Helm E, Gujar N, Walker MP. Sleep deprivation impairs the accurate recognition of human emotions. *Sleep*. 2010;33(3):335–342
- Gujar N, McDonald SA, Nishida M, Walker MP. A role for REM sleep in recalibrating the sensitivity of the human brain to specific emotions. *Cereb Cortex*. 2011;21(1):115–123
- Mojtabai R, Olfson M. Proportion of antidepressants prescribed without a psychiatric diagnosis is growing. *Health Aff (Millwood)*. 2011;30(8):1434–1442
- Comer JS, Olfson M, Mojtabai R. National trends in child and adolescent psychotropic polypharmacy in office-based practice, 1996–2007. *J Am Acad Child Adolesc Psychiatry*. 2010;49(10):1001–1010
- Mark TL. For what diagnoses are psychotropic medications being prescribed? A nationally representative survey of physicians. *CNS Drugs*. 2010;24(4):319–326
- Aman MG, Farmer CA, Hollway J, Arnold LE. Treatment of inattention, overactivity, and impulsiveness in autism spectrum disorders. *Child Adolesc Psychiatr Clin N Am*. 2008;17(4):713–738, vii
- Research Units on Pediatric Psychopharmacology Autism Network. Randomized, controlled, crossover trial of methylphenidate in pervasive developmental disorders with hyperactivity. *Arch Gen Psychiatry*. 2005;62(11):1266–1274
- Posey DJ, Aman MG, McCracken JT, et al. Positive effects of methylphenidate on

- inattention and hyperactivity in pervasive developmental disorders: an analysis of secondary measures. *Biol Psychiatry*. 2007; 61(4):538–544
21. Jahromi LB, Kasari CL, McCracken JT, et al. Positive effects of methylphenidate on social communication and self-regulation in children with pervasive developmental disorders and hyperactivity. *J Autism Dev Disord*. 2009;39(3):395–404
 22. Santosh PJ, Baird G, Pityaratstian N, Tavare E, Gringras P. Impact of comorbid autism spectrum disorders on stimulant response in children with attention deficit hyperactivity disorder: A retrospective and prospective effectiveness study. *Child Care Health Dev*. 2006;32(5):575–583
 23. Murray MJ. Attention-deficit/hyperactivity disorder in the context of autism spectrum disorders. *Curr Psychiatry Rep*. 2010; 12(5):382–388
 24. Posey DJ, Erickson CA, Stigler KA, McDougle CJ. The use of selective serotonin reuptake inhibitors in autism and related disorders. *J Child Adolesc Psychopharmacol*. 2006;16(1–2):181–186
 25. Kolevzon A, Mathewson KA, Hollander E. Selective serotonin reuptake inhibitors in autism: A review of efficacy and tolerability. *J Clin Psychiatry*. 2006;67(3):407–414
 26. King BH, Hollander E, Sikich L, et al; STAART Psychopharmacology Network. Lack of efficacy of citalopram in children with autism spectrum disorders and high levels of repetitive behavior: Citalopram ineffective in children with autism. *Arch Gen Psychiatry*. 2009;66(6):583–590
 27. Williams K, Wheeler DM, Silove N, Hazell P. Selective serotonin reuptake inhibitors (SSRIs) for autism spectrum disorders (ASD). *Cochrane Database Syst Rev*. 2010;8(8):CD004677
 28. McDougle CJ, Stigler KA, Erickson CA, Posey DJ. Atypical antipsychotics in children and adolescents with autistic and other pervasive developmental disorders. *J Clin Psychiatry*. 2008;69(suppl 4):15–20
 29. 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(6):1142–1148
 30. Research Units on Pediatric Psychopharmacology Autism Network. Risperidone treatment of autistic disorder: longer-term benefits and blinded discontinuation after 6 months. *Am J Psychiatry*. 2005;162(7): 1361–1369
 31. Jesner OS, Aref-Adib M, Coren E. Risperidone for autism spectrum disorder. *Cochrane Database Syst Rev*. 2007;(1): CD005040

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