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2007

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### Recommended Citation

Luby, Joan L.; Meade Stalets, Melissa; and Belden, Andy C., "Psychotropic prescriptions in a sample including both healthy and mood and disruptive disordered preschoolers: relationships to diagnosis, impairment, prescriber type, and assessment methods." *Journal of Child and Adolescent Psychopharmacology*. 17, 2. 205-216. (2007).

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# Psychotropic Prescriptions in a Sample Including Both Healthy and Mood and Disruptive Disordered Preschoolers: Relationships to Diagnosis, Impairment, Prescriber Type, and Assessment Methods

Joan L. Luby, M.D., Melissa Meade Stalets, M.A., and Andy C. Belden, Ph.D.

## ABSTRACT

**Objective:** Epidemiological data has shown that psychotropic medications are being prescribed to preschoolers at increasing rates. The diagnostic context and functional impairment of these preschoolers remains unknown. This investigation aimed to address these questions in a sample of preschoolers who were either without symptoms (healthy) or with mood and disruptive disorders by assessing them using a structured diagnostic interview and measure of impairment.

**Method:** Preschoolers aged 3.0 to 5.11 without symptoms and those with symptoms of mood and disruptive disorders were recruited from primary care and daycare sites in the St. Louis area to participate in a psychiatric evaluation that included information about psychotropic prescriptions from community practitioners.

**Results:** Seven percent of preschoolers ( $n = 19$ ) out of a total sample of  $n = 267$  were prescribed psychotropic medications. Fifty-two percent of preschoolers in the total sample met criteria for an Axis I psychiatric disorder. Presence of an Axis I disorder was significantly related to psychotropic prescription ( $p < 0.01$ ). Among preschoolers who met criteria for an Axis I disorder 12% received psychotropics (Dx/Rx group). The Dx/Rx group was more impaired than those with a diagnosis who were not prescribed psychotropics ( $p < 0.001$ ). Among preschoolers taking psychotropic medications, two failed to meet criteria for any Axis I disorder.

**Conclusion:** In this sample, most psychotropic medications were prescribed for impaired preschoolers with an Axis I diagnosis. These findings shed some light on the prescribing trends among mood and disruptive disordered preschoolers.

## INTRODUCTION

**E**PIDEMIOLOGICAL INVESTIGATIONS have revealed that psychotropic medications have been prescribed to preschool aged children

over the last decade at rates that raise concern when the fact that they have not been tested for efficacy or approved by the Food and Drug Administration (FDA) for use in this young age group is considered (Coyle 2000). Prior studies

also indicate that these prescribing trends have been accelerating in the past five years (Pathak et al. 2004; Rappley et al. 1999; Zito and Safer 2005; Zito et al. 2000). However, several important issues have yet to be addressed by the investigations done to date, preventing a full understanding of the key contributors and underlying factors giving rise to the public health problem. One issue is that most of the available data describes patterns of psychotropic medication prescribing in preschoolers enrolled in Medicaid or other federal or state funded insurance programs (Rushton and Whitmire 2001; Zito et al. 2000). While these samples give us a picture of psychotropic prescribing in specific subpopulations, they are not representative of the general population.

Another critical and unexplored issue in the available pharmaco-epidemiological studies is that the diagnostic context of these prescriptions remains unknown. One exception to this is a study that addressed prescriptions in relation to symptoms in a preschool sample from a health maintenance organization (DeBar et al. 2003). Further, it is unclear whether appropriate diagnostic assessments were conducted and what DSM-IV diagnoses if any, or types and degree of functional impairment, were being targeted by these prescriptions. A related factor that remains unknown is the medical specialty and training (e.g., general practitioner versus child psychiatrist) of prescribing practitioners. Yet another key question that needs to be addressed is whether medications are prescribed before, after, or in conjunction with a trial of psychotherapy or other psychosocial interventions in these very young children. Obtaining information about these issues would further clarify the nature of the preschool prescribing trend and could be useful to direct public health education and intervention efforts necessary to minimize and prevent inappropriate prescribing.

During the same period that these prescribing trends have arisen, significant progress has been made in the area of clarifying age-appropriate assessment techniques and diagnostic nosologies of mental disorders in preschool children (Task force on research diagnostic criteria: Infancy and Preschool 2003). However, it remains unclear whether these age-appropriate methods and/or diagnostic criteria are being utilized in the psychopharmacologic treatment decisions for pre-

school populations. In addition, the efficacy of a few early psychotherapeutic and behavioral techniques for the treatment of specific preschool onset disorders has now been established (e.g., Hood and Eyberg 2003; Faja and Dawson 2006). The positive and in some cases enduring ameliorative effects of early interventions in these specific areas suggests a possible window of opportunity for early intervention during the preschool period. Based on these new findings and current prescribing trends of psychotropic medications to preschool-age children, there is a clear need for additional information regarding the use of psychotropic medications among this young and potentially vulnerable and/or potentially uniquely treatable age group.

The aim of this investigation was to explore the rates and types of psychotropic medications prescribed by community practitioners in a sample of healthy or mood and disruptive disordered preschool children who had undergone a comprehensive research diagnostic assessment. We also sought to investigate the methods of clinical assessment used by these community practitioners as well as the recommendation and use of psychotherapy in advance of psychotropic prescribing.

## METHOD

### *Participants and procedure*

Preschoolers between 3.0 and 5 years 11 months of age (5.11) were recruited from community pediatric or primary care practices and preschools/daycares in the St. Louis metropolitan area for participation in a study of early emotional development and mood disorders. Participants were ascertained using the Preschool Feelings Checklist (PFC; Luby et al. 2004) a validated screening checklist that identified children with symptoms of depression and disruptive disorders as well as those without behavioral problems. To achieve an ethnically and socio-economically diverse sample, a demographically broad range of primary care and daycare settings in the St. Louis metropolitan area was selected for participation in the study.

Approximately 6,000 checklists were distributed to the recruiting sites and from those  $n = 1,474$  checklists were returned to the Washing-

ton University School of Medicine (WUSM) Early Emotional Development Program (EEDP). Using the PFC, and previously established thresholds, the study population was over-sampled for preschoolers with mood and disruptive symptoms. This was done by design so that a large group of preschoolers with these disorders could be obtained to facilitate the main study aims, which were to investigate the nosology of preschool mood disorders. Previous findings have illustrated that a score  $\geq 3$  on the PFC is highly sensitive and moderately specific for mood disorders as well as moderately sensitive for disruptive disorders (Luby et al., 2004). Caregivers of preschoolers between 3.0 and 5.11 years of age and with a PFC score  $\geq 3$  and  $< 1$ , as well as those with a PFC scores = 1 based on the presence of the symptom of anhedonia, were contacted by phone for a screening interview. Those without anhedonia and a score of 1 and those with a score of 2 were excluded. Eight hundred and ninety-nine ( $n = 899$ ) caregivers of preschoolers were contacted by phone to establish if any exclusion criteria (e.g., neurological disorders, autistic spectrum disorders, developmental delays) were present and that all inclusion criteria were met. Those who met all inclusion and exclusion criteria ( $n = 416$ ) were invited for study participation and  $n = 302$  agreed and participated in the full assessment.

Trained research assistants (separate parent and child interviewers) evaluated preschool study participants and their primary caregivers at WUSM EEDP. The study protocol was reviewed and approved by the Human Research Protection Office. Prior to the evaluation, parents gave informed consent, and the children assented to the study protocol. Preschoolers participated in a comprehensive evaluation of developmental capacities and mental health status in both dyadic and individual testing formats. The primary caregiver (94% were biological mothers) was interviewed about their child's behaviors, emotions and development. In addition, caregivers completed four self-report take-home questionnaires.

For the purpose of this investigation, the primary caregivers of all preschool participants reported to be taking psychotropic medications were subsequently contacted by telephone. Additional information about the specialty of the prescribing practitioner as well as the method of

clinical diagnostic assessment was obtained. Assessment methods were categorized in the following way: a specialty preschool mental health assessment was defined by the use of a multi-session dyadic play format, a general child mental health assessment was defined as being seen by a child psychiatrist in a format typically used for older children (without observations of dyadic play) and no formal mental health assessment was defined as being seen by a non-mental health practitioner in a single office visit. In addition, information about whether any form of psychotherapy was recommended or initiated prior to, or concurrent with, medication prescription was also sought. For the purpose of the following analyses, psychotherapy was defined broadly as any treatment by a clinician that focused directly on children's behaviors and emotions. This could include psychodynamic, cognitive and/or behavioral therapies. It did not include therapies such as physical therapy, speech and language or occupational therapy. These treatments were categorized as "developmental therapies" and were considered separately. Out of  $n = 20$  preschoolers who were reported as receiving medication,  $n = 18$  participants were successfully contacted by phone and provided the requested information,  $n = 2$  could not be contacted or failed to return calls.

### *Measures*

Information about mental health, prescriptions taken by the child, and treatment (i.e., developmental as well as psychotherapeutic) was obtained using the Health and Behavior Questionnaire (HBQ; Armstrong et al. 2003) an age-appropriate measure with established validity (Essex et al. 2002). The HBQ assessed "regular" medication use defined as "taken daily for at least one month." This measure was completed by caregivers prior to coming to the EEDP. Trained interviewers who remained blind to children's diagnostic status administered all other study measures. Preschoolers' degree of impairment, ranging from no impairment to severe impairment was established using the Preschool Early Childhood Functional Assessment Scale (PECFAS; Hodges 1994) an age appropriate measure of impairment with established validity. The PECFAS is rated by trained interviewers who achieve re-

liability with an outside site using standardized testing materials (Murphy 1999). The PECFAS is rated on the basis of parental response to probes about their child's functioning. Items are designed to address impairment in functioning as a result of symptoms and address 3 contexts (home, school and community) and 4 domains (behavior towards others, moods/emotions, self-harm, thinking and communication). Parents were also interviewed extensively by a trained interviewer about their child's moods and behaviors using the Preschool Age Psychiatric Assessment (PAPA; Egger et al. 1999). The PAPA is a comprehensive age-appropriate semi-structured interview with established construct validity and test-re-test reliability (Egger et al. 2006). Diagnostic modules of the PAPA contain developmentally sensitive translations of relevant mental health symptoms. Diagnoses were based on standard computerized DSM-IV algorithms. For mood disorders, symptom criteria only were used (duration criteria were set aside). Preschoolers in the study sample fell into the following diagnostic categories based on the application of DSM-IV algorithms: Major Depressive Disorders (MDD), Bipolar-I (BP), ADHD, Oppositional Defiant Disorder (ODD), Conduct Disorder (CD) and Anxiety Disorders (alone and in varying co-morbid combinations). Preschoolers who did not meet criteria for any of these disorders were categorized as healthy.

#### *Data analysis*

Chi-square analyses were conducted to test for differences between psychotropic medication use and demographic characteristics such as, age, gender, and gross household income. An odds ratio was computed to examine the expected increase in likelihood that children who were taking psychotropic medication(s) would have been diagnosed with a DSM-IV Axis-I disorder in the current study. Next, descriptive statistics (i.e., percentages) were calculated to examine the proportion of children taking certain classes of psychotropic medication in relation to diagnostic classification, prescriber-type, and assessment method. To test the likelihood that preschoolers taking psychotropic medications had or were receiving psychotherapy and/or developmental therapy,

odds ratio tests were calculated. Last, Mann-Whitney and odds ratio tests were calculated to examine expected differences between preschoolers' psychotropic medication use and functional impairment. Functional impairment was measured and tested as a dimensional as well as dichotomous (i.e., severe versus not severe functional impairment) variable.

## RESULTS

### *Psychotropic prescriptions and demographic factors*

Out of the total sample of  $n = 302$ ,  $n = 35$  were missing the pertinent prescribing information due to failing to complete the HBQ. Thus, relevant data about psychotropic medication use was available for  $n = 267$  preschoolers. There were no demographic or diagnostic differences between preschoolers of caregivers who completed the HBQ and those who did not. The study sample had a diverse socioeconomic and ethnic composition consistent with the ethnic composition of the St. Louis metropolitan area (see Table 1). Among the sub-sample with data about medication use, 7% (i.e.,  $n = 19$  out of  $n = 267$ ) were reported to be taking psychotropic medication. Alpha agonists (guanfacine and clonidine) were included as psychotropic medications (although originally designed for cardiac treatments) due to their use (and some available investigations) in clinical practice to control impulsivity in young children. Gender was related to medication use,  $\chi^2(df1, n = 267) = 6.09, p < 0.01$ , with rates of psychotropic medication use approximately four times higher among boys than girls. Gender was also related to meeting criteria for any DSM-IV Axis I diagnosis (i.e., yes or no). Boys were almost twice as likely to be diagnosed with any Axis I disorder compared to girls. Age was related to medication status,  $\chi^2(df2, n = 267) = 8.40, p < 0.01$ , with  $n = 1$ , 3-year-old child taking psychotropics (stimulant & alpha agonist) compared to  $n = 8$ , 4-year olds ( $n = 1$  stimulant and antipsychotic,  $n = 1$  alpha agonist and antipsychotic,  $n = 1$  lithium and antipsychotic,  $n = 3$  stimulants,  $n = 1$  antipsychotic,  $n = 1$  alpha agonist,) and  $n = 10$ , 5-year-old children ( $n = 1$  alpha agonist and



TABLE 1. DEMOGRAPHIC CHARACTERISTICS OF THE STUDY SAMPLE

	DSM		No DSM	
	DX/RX n = 17	DX/No RX n = 123	DX/RX n = 2	DX/No RX n = 125
Gender % (n)				
Male	77% (13)	55% (68)	100% (2)	44% (54)
Female	23% (4)	45% (55)	X	56% (70)
Age in Years				
3	6% (1)	32% (39)	X	28% (35)
4	47% (8)	40% (49)	X	48% (60)
5	47% (8)	29% (35)	100% (2)	23% (29)
Ethnicity (child)				
White	59% (10)	47% (57)	50% (1)	65% (81)
Black	35% (6)	43% (53)	50% (1)	39% (36)
Hispanic	6% (1)	4% (5)	X	2% (3)
Asian or Pacific Indian	X	3% (3)	X	2% (2)
Mixed racial background	X	3% (3)	X	2% (2)
Caregivers' education				
No college	23% (4)	20% (24)	X	14% (17)
Some college	53% (9)	42% (52)	50% (1)	31% (38)
4-year degree	6% (1)	20% (24)	50% (1)	26% (32)
Beyond 4-year degree	X	4% (5)	X	7% (8)
Professional degree	18% (3)	15% (18)	X	22% (26)
Marital status				
Married	59% (10)	50% (61)	50% (1)	67% (83)
Separated	X	4% (5)	X	2% (2)
Divorced	12% (2)	12% (15)	X	4% (5)
Widowed	X	X	X	2% (2)
Never married	29% (5)	34% (41)	50% (1)	26% (32)
Income				
0-\$20,000	31% (5)	29% (31)	X	21% (24)
\$20,001-\$40,000	19% (3)	21% (23)	X	11% (13)
\$40,001-\$60,000	31% (5)	16% (17)	50% (1)	17% (20)
\$60,000+	19% (3)	34% (37)	50% (1)	51% (59)

DSM DX/RX = *Diagnostic and Statistical Manual* Diagnosis, diagnosis/prescription; DX/No RX = *Diagnostic and Statistical Manual* Diagnosis, diagnosis/no prescription; No DSM = No *Diagnostic and Statistical Manual* Diagnosis

antipsychotic,  $n = 7$  stimulants,  $n = 2$  antipsychotics). Preschoolers' age did not differ as a function of diagnostic status (i.e., BP, MDD, ADHD/ODD/CD, anxiety, and healthy) in the sub-sample ( $n = 267$ ) included in these analyses. When examining the presence or absence of a DSM-IV Axis I disorder (but not taking into account specific disorders), results indicated the presence of any Axis I disorder was significantly related to psychotropic medication use,  $\chi^2 (df1, n = 267) = 11.25, p < .01$ . Preschoolers with a

DSM-IV Axis I diagnosis were almost 9 (CI = 1.954 to 38.182) times more likely to be taking a psychotropic medication than those with no DSM-IV Axis I disorder (see Table 2).

*Psychotropic prescriptions and DSM-IV diagnosis*

Of the children with a DSM-IV Axis I diagnosis according to parent report on the PAPA, 12% ( $n = 17$ ) were taking psychotropic med-

**TABLE 2. VARIABLES ASSOCIATED WITH PSYCHOTROPIC MEDICATION PRESCRIPTION DURING PRESCHOOL PERIOD**

	<i>Odds ratio</i>	<i>Confidence interval</i>
Male gender	3.84**	1.24–11.90
≥55 months vs. ≤54 months	4.90**	1.58–15.21
In psychotherapy	46.46***	13.95–154.70
Met criteria for BP-1	21.36***	7.47–61.02
Met criteria for disruptive disorder (ADHD, ODD, CD)	7.73***	2.49–24.04
Met criteria for any Axis I disorder	8.63**	1.95–38.18

\*\* $p < .01$ ; \*\*\* $p < .001$

BP-1 = bipolar 1; ADHD = attention-deficit/hyperactivity disorder; ODD = oppositional defiant disorder; CD = conduct disorder

Note: Confidence intervals above and throughout this paper are large simply because the point estimates are large. If one were to examine the log odds ratios of the gender and psychotherapy findings above, it becomes clear that distances between the lower and upper ends of the interval in relation to the point estimate are very similar.

ication. Five children (29%) of those on medications were prescribed two psychotropic medications. Among those taking psychotropic medications in the sample as a whole ( $n = 19$ ), 11% ( $n = 2$ ) did not meet diagnostic criteria for any of the DSM-IV Axis I disorders assessed. Of note, Autistic Spectrum Disorders (ASDs) were not assessed and attempts were made to screen out participants with ASDs (which was an exclusion criterion for study participation). Within the sub-group on medication, specific psychotropic medications prescribed within different diagnostic groups, are outlined in Table 3. Of particular interest was that all preschool participants taking an atypical antipsychotic met DSM-IV symptom criteria for a diagnosis of BP-1 with co-morbid MDD (see

Table 3). Conversely, 42% of preschoolers who met symptom criteria for BP-1 had been prescribed a psychotropic medication.

#### *Psychotropic prescriptions and prescriber type and assessment method*

Among the  $n = 19$  preschoolers who were taking a psychotropic medication, information regarding type of prescriber was available for 18 children (prescriber type unknown for 1 combination prescription). Of these preschoolers, 33% ( $n = 6$ :  $n = 3$  atypical antipsychotic,  $n = 2$  stimulant,  $n = 1$  atypical antipsychotic and alpha agonist combination) of the prescriptions were written by child psychiatrists, 33% ( $n = 6$ :  $n = 5$  stimulant,  $n = 1$  alpha ago-

**TABLE 3. DSM-IV DIAGNOSIS AND MEDICATION PRESCRIBED**

	<i>Healthy</i> ( $n = 2$ )	<i>Anxiety</i> ( $n = 1$ )	<i>MDD</i> ( $n = 1$ )	<i>CD</i> ( $n = 1$ )	<i>ADHD</i> <i>/ODD</i> ( $n = 1$ )	<i>MD/ADHD/</i> <i>ODD</i> ( $n = 2$ )	<i>MDD/BP/≥</i> <i>1 Disruptive*</i> ( $n = 11$ )	<i>Total</i> <i>RX</i>
Stimulant	2	0	1	1	1	2	5	12
Antipsychotic	0	0	0	0	0	0	7	7
Alpha Agonist	0	1	0	0	0	0	2	3
Lithium	0	0	0	0	0	0	1	1
Total $n$	2	1	1	1	1	2	11	

\*Within this group four children were taking two separate psychotropic medications concurrently

MDD = major depressive disorder; CD = conduct disorder; ADHD/ODD = attention-deficit/hyperactivity disorder/oppositional defiant disorder; MDD/ADHD/ODD = major depressive disorder/attention-deficit/hyperactivity disorder/oppositional defiant disorder; MDD/BP = major depressive disorder/bipolar disorder; RX = prescription

nist) were written by pediatricians, 22% ( $n = 4$ :  $n = 2$  stimulants,  $n = 1$  atypical antipsychotic and alpha agonist combination,  $n = 1$  stimulant and alpha agonist combination) by pediatric neurologists and 11% ( $n = 2$ :  $n = 1$  stimulant,  $n = 1$  stimulant and atypical antipsychotic combination) were written by nurse practitioners working in a child psychiatry office. Information about the type of assessment received prior to psychotropic prescription was available for  $n = 17$  preschoolers. Nine (53%) caregivers reported their child did not receive any formal mental health assessment prior to being prescribed medication. Six preschoolers (35%) received a general child mental health assessment and two preschoolers (12%) received a specialized preschool mental health assessment. All preschool subjects who received prescriptions from their pediatrician or neurologist did not receive a formal mental health evaluation (defined above). Among those who were prescribed by a child psychiatrist  $n = 4$  received a general mental health assessment and  $n = 2$  received a specialized infant/preschool assessment. Both subjects ( $n = 2$ ) prescribed by a nurse practitioner working under the supervision of a child psychiatrist received a general mental health evaluation. Of note was that both participants who received medications but who did not meet criteria for an Axis I DSM-IV diagnosis based on the PAPA received their prescriptions from a pediatrician. Regarding the type of assessment conducted for this subgroup, this data was missing from one and the mother of the second preschooler reported receiving no formal psychiatric assessment. Both medicated preschoolers without a DSM-IV diagnosis were boys (see Table 1).

#### *Psychotropic prescriptions and psychotherapy and developmental therapies*

Fifteen out of  $n = 19$  or 79% of preschoolers taking psychotropic medications had previous or current psychotherapy of some form. Within the entire study sample (i.e.,  $n = 267$ )  $n = 30$  preschoolers had previously or were currently participating in some form of psychotherapy (broadly defined as described above). Preschoolers in psychotherapy were 46.45 (CI = 13.952 to 154.704) times more likely to be pre-

scribed a psychotropic medication than preschoolers who were not in psychotherapy. Among the 2 preschoolers who were on medication and did not meet criteria for a DSM-IV diagnosis, 1 received no psychotherapy either prior to or concurrent with the medication treatment. Of the  $n = 19$  preschoolers prescribed psychotropic medications, 16% ( $n = 3$ ) had received some form of developmental therapy (i.e., school resource room, speech/language therapy, physical and/or occupational therapy) in the last year.

#### *Psychotropic prescriptions and functional impairment*

Mann-Whitney U tests were conducted to evaluate potential differences in preschoolers' impairment scores in relation to psychotropic medication use and the presence or absence of a DSM-IV Axis I diagnosis. The first analysis examined whether there was a significant difference in impairment between children prescribed psychotropic medication versus not taking medication among preschoolers with an Axis I diagnosis. Results indicated that preschoolers who were prescribed psychotropic medication and who had an Axis I diagnosis had significantly higher impairment scores on all seven subscales of the PECFAS as well as on the PECFAS total impairment score,  $z = -4.66$ ,  $p < 0.0001$ , compared to preschoolers with an Axis I diagnosis who were not prescribed psychotropic medications.

To examine the likelihood that preschoolers taking psychotropic medications would be rated as severely impaired on the PECFAS overall as well as within its seven subscales, odd ratios were computed. Analyses indicated that preschoolers who had been prescribed a psychotropic medication were 11 (CI = 3.48 to 32.25) times more likely to have been given the most severe rating on one or more of the PECFAS subscales compared to those not on medication. Odds ratios (and confidence intervals) for specific subscales are provided in Table 4. Of particular interest was the finding that preschoolers taking psychotropic medication were 20 (CI = 5.63 to 76.85) times more likely to have been rated "severely impaired" on the social subscale and 16 (CI = 1.38 to 188.78)



TABLE 4. ODDS OF RATING OF "SEVERE" IMPAIRMENT BY DOMAIN MEDICATED VERSUS NOT MEDICATED

	<i>Odds ratios</i>	<i>Confidence interval</i>
School	11.78***	3.09–44.96
Home	7.84***	2.45–25.07
Community	Did not occur	Did not occur
Social	20.80***	5.63–76.85
Mood	16.13**	1.38–188.77
Self-harm	3.69 (ns)	0.32–43.05
Thinking/communication	1.06 (ns)	0.943–1.20

\*\* $p < .01$ ; \*\*\* $p < .001$

Note: Large confidence interval explanation as in Table 2.

times more likely to have rated as severely impaired on the mood subscale.

Mann-Whitney U tests were conducted to test whether preschoolers who were prescribed an antipsychotic (in this study all were atypical antipsychotics) were more impaired than preschoolers who were prescribed any psychotropic medication outside of this class (e.g., stimulant, alpha agonist, other mood stabilizer). Results indicated that preschoolers who were prescribed antipsychotics were significantly more impaired on the PECFAS home behavior ( $z = -3.11, p < 0.005$ ), social behavior ( $z = -2.40, p < 0.01$ ), moods/emotions ( $z = -2.19, p < 0.02$ ), self-harm ( $z = -2.88, p < 0.01$ ), thinking/communication ( $z = -2.85, p < 0.01$ ) subscales, as well as on the total PECFAS impairment scale ( $z = -2.78, p < 0.01$ ) compared to preschoolers prescribed psychotropic medication outside of this class.

## DISCUSSION

Study findings report on psychotropic medication use in a sample of preschoolers for whom structured research diagnostic assessments and measures of impairment have also been obtained. These data provide new information about the association between diagnosis from a validated age-appropriate semi-structured diagnostic interview and level of functional impairment and their relationship to

psychotropic medication use in specific diagnostic areas in preschool aged children. While the available literature has consistently reported high rates of psychotropic prescribing to preschoolers, the available data to date have not yet informed the issue of whether the children receiving these prescriptions met criteria for DSM-IV Axis I psychiatric disorders and if so which disorders were the primary target of treatment. Of note was the finding that 90% (17 out of 19) of preschoolers between the ages of 3.0 and 5.11 who were prescribed a psychotropic medication met criteria for a DSM-IV Axis 1 disorder based on an age appropriate structured research diagnostic interview. In keeping with these findings, preschoolers on psychotropic medications had a much higher likelihood of being rated as "severely impaired" on a structured measure. The highest odds ratios for impairment were found in the social and mood domains suggesting that difficulty in these areas may trigger pharmacologic interventions.

Another clear and notable finding was the higher rate of psychopharmacological treatment of externalizing/disruptive behavioral problems compared to those with internalizing disorders only. In particular, psychopharmacologic treatment for preschoolers meeting symptom criteria for BP-I (42% of those prescribed a medication met symptom criteria for BP-I), in which disruptive features are prominent, was the highest of any disorder targeted. Further, every atypical antipsychotic prescrip-

tion written was for a child who met symptom criteria for BP-I (in addition to other co-morbid disorders). In contrast, no antidepressants were prescribed in this preschool population that contained  $n = 72$  (27%) preschoolers who met all DSM-IV symptom criteria for MDD. This difference in rates of prescribing antidepressants compared to antipsychotics is of interest because both classes of medications are similarly lacking in safety and efficacy data for preschool aged children. Several factors may have contributed to the difference in prescribing of these two classes of medications, including the under identification of depressive syndromes and the recent FDA "Black Box" warning for antidepressants. However, the socially disruptive nature of the externalizing disorders for which antipsychotics were prescribed may be the most important factor. The finding of one depressed preschooler who was prescribed a stimulant medication was notable along these lines. The disruptive disorders are often viewed by caregivers and clinicians as requiring greater urgency for behavioral control, given the potential for self-harm and aggression towards others.

Another notable finding was the unique characteristics of the two preschoolers who did not meet criteria for a DSM-IV diagnosis but who were prescribed stimulants. Both prescriptions were written by pediatricians and at least one was known to be administered without formal psychiatric evaluations. Further both participants were boys and one also received psychotherapy. Notably, these two children were significantly less impaired (according to the PECFAS) compared to the  $n = 17$  preschoolers taking medications who also met criteria for a DSM-IV Axis 1 disorder. It is possible that these children received clinical diagnoses from their prescribing community practitioner even though they did not meet criteria for the DSM-IV diagnoses assessed as a part of our research assessment. The use of stimulants in both "undiagnosed" preschoolers suggests that disruptive behavior that included inattention and/or impulsivity was being targeted. Alternatively, it is also possible that medication was effective in minimizing symptoms to a point below diagnostic thresholds at the time of the research diagnostic assessment. Based on

the very small number of children in this interesting group, it is premature to draw conclusions. However larger scale studies that address the relationship between diagnosis and stimulant prescriptions among primary care physicians would be of interest to investigate this issue further.

Results suggest that the overall rate of psychopharmacological treatment in the study sample was comparable or lower than (when sampling differences are considered) those reported in population based samples. However, this comparison is not straightforward based on the fact that this study sample was oversampled for preschoolers with behavioral and emotional symptoms and therefore is not a representative community sample. Seven percent (7%) of preschoolers in the study sample were found to be on psychotropic medications. This rate in a sample with high rates of psychiatric disorders would seem to represent a lower rate than the 5.9-6.3% prevalence rate of psychotropics found in a recent population based study of youths less than 20 years of age (Zito et al. 2003). However, in a more targeted preschool-age Oregon HMO study of psychotropic usage, 16% of a sample of 743 preschoolers was taking psychotropics (DeBar et al. 2003). Based on differences in sampling characteristics, it is difficult to compare this rate to the prescription rate found in the study sample presented here.

Further, among preschoolers meeting diagnostic criteria for Axis I disorders (which included ADHD, ODD, CD, MDD, BP and anxiety disorders) rates of prescribing in the study sample were also lower than those reported in preschool pharmacoepidemiology studies. For example, among  $n = 223$  Medicaid enrollees in Michigan younger than age 4 with a clinical diagnosis of ADHD, 57% took at least 1 medication (Rappley et al. 2002). This compares to only 22% of those with a diagnosis of ADHD based on a structured research interview in the study sample presented here.

The finding that boys are more likely to be treated with psychotropic medication than girls is consistent with previous findings in larger and older samples (Shireman et al. 2005; Rushton and Whitmire 2001) as well as in other larger and younger Health Maintenance Orga-

nization (HMO) samples (Zito et al. 2003). These findings may be explained by the fact that disruptive behaviors were the most common target of psychopharmacologic treatment, and higher rates of disruptive behavioral disorders have been found in preschool aged boys (Egger and Angold, 2006).

Notably, preschoolers meeting DSM-IV symptom criteria for BP-I (with other co-morbid disorders) had the highest rate of psychotropic medication use. While this diagnosis remains highly controversial in preschool children, preliminary evidence for the validity of the BP-I syndrome has been previously provided (Luby and Belden 2006). This finding is consistent with other findings from the same study sample showing that this group demonstrated the highest levels of impairment; levels significantly higher even than those groups with other Axis 1 disorders (Luby and Belden 2006). However, given the absence of prospective, double-blind, placebo-controlled studies of treatment for preschool onset BP, this finding suggests that prescriptions to preschoolers with symptoms of mania and/or severe mood instability may be an important source of the public health problem in preschool psychotropic prescribing. These findings suggest that studies of age-appropriate treatments, to include both psychotherapeutic and psychopharmacologic, as well as further studies of the nosology of early onset BP are now needed.

The prescription of more than 1 psychotropic medication to preschool children (found in 5 cases) is also of interest given the higher risks involved and the paucity of data, not only on use of single agents, but even further on the use of combinations. Of note was that none of these combination prescriptions was written by a pediatrician. Although the sub-sample of preschoolers on multiple psychotropic medications was too small for further analysis in this sample, further investigation of this prescribing practice would be of paramount importance.

Another issue apparent from the study findings was the high rates of impairment found among the group of children undergoing treatment with a psychotropic medication. While details of pre- and post-treatment impairment are not known, and it is also unclear for how long the study participants were treated be-

yond the 1 month period assessed by the HBQ, this finding is notable. This finding taken together with other study findings and the extant literature underscores the need for specific study of the efficacy of these medications.

Several features of the study design and sample characteristics limit these findings. The relatively small subgroup of preschoolers on psychotropic medication on which many of the analyses are based is a limitation. The reliance of this small group suggests the reader should interpret the findings with caution due to an increased likelihood of statistical error, such as a lack of power to identify potentially important but small effect sizes. The fact that the same rater conducted the psychiatric interview (although was not privy to formal diagnostic group classification) and the measure of impairment could have given rise to rater bias. The sole reliance on parent report to derive psychiatric diagnosis without accounting for observation of the child and child informant measures is a design limitation. Another limitation is the restricted focus on mood and disruptive disorders and the exclusion of preschoolers with ASDs. The latter group is of importance as preschoolers with ASDs are a frequent target of psychotropic medications and are worthy of independent study.

The nosology of many preschool disorders, and internalizing disorders in particular, remains understudied and substantial ambiguities remain in the application of several psychiatric diagnoses to preschool age children. Nevertheless, these findings from a diagnostically well-characterized sample are informative and add new details to the relatively small body of empirical data regarding psychotropic medication use in preschool age children. These findings underscore the need for continued investigation in this area. They also provide some reassurance that based on standardized research assessments, those children who meet criteria for Axis I diagnoses and who are impaired appear to be the primary targets of psychotropic treatment in the community. Also reassuring was the majority of preschoolers on psychotropic medications were also in some form of psychotherapy. While this does not confirm that these psychotropic treatments were the optimal or even appropriate treatments in each case, it does suggest that chil-

dren who are symptomatic and impaired as a group were being targeted in this sample of mood and disruptive disordered preschoolers.

### AUTHOR DISCLOSURE

The authors do not have any corporate, commercial, or financial relationships that pose conflicts of interest.

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