Clinician Prescribing Patterns in Adolescents with Bipolar Spectrum Disorders

Micaiah Peele, BS; Melissa DelBello, MD, MS; Christina Klein, PhD, MPH; Jeffrey Welge, PhD; Thomas Blom, MS

University of CINCINNATI

Background

- Bipolar spectrum disorders (BSD) are characterized by periods of mood instability that include episodes of mania/hypomania and often depression.
- Onset of BSD typically occurs during adolescence.[1]
- Patients often require multiple medications from different pharmacologic classes to achieve mood stabilization and treat co-occurring psychiatric disorders, such as attention-deficit hyperactivity disorder.[2]
- Although polypharmacy is often necessary, it is a challenge due to increased risk for side effects, decreased patient adherence, and higher cost.[3]
- Prior studies suggest that polypharmacy among youth with mood disorders is correlated with a higher number of psychiatric admissions, longer hospitalizations, placement outside the biological family, violence/aggression, developmental disorders, and intellectual disabilities.[4]

Study Aim

- The aim of the present study was to characterize the relationships among demographic characteristics and clinical factors of youth with BSD and the prescribing patterns of clinicians who treat these youth.

Methods

We conducted secondary analyses of data obtained from the MOBILITY (Metformin for Overweight and Obese Children with Bipolar Spectrum Disorders Treated with Second-Generation Antipsychotics) cohort. MOBILITY is a large, pragmatic study that enrolled 1565 patients from 64 US mental health sites.

Patients included in the study were:
- 8-19 years of age
- Current or past diagnosis of BSD
- BMI ≥85th percentile
- Prescribed at least one second-generation antipsychotic (SGA)[5]

Variables analyzed:
- Patient sex assigned at birth (SaaB), race, ethnicity, study site type (community vs academic), enrollment setting (inpatient vs outpatient) and insurance type (public vs private).
- Clinician-reported psychiatric diagnoses at baseline
- Clinician-reported prescribed mediations at baseline

Statistical analysis:
- Two-sample t-tests examined univariate relationships between number of psychiatric medications and each of the demographic variables.
- Linear regression examined associations *between* number of diagnoses, age, sex assigned at birth, ethnicity, race, insurance type (public vs private), study site type (academic vs. community mental health center), enrollment setting (inpatient vs. outpatient), and number of prescribed medications at baseline.

Results

N=1565 participants
- 53% male SaaB
- 65% Caucasian/White
- Mean age in years: 13.9 (SD=2.9)
- Mean number of psychiatric diagnoses: 2.6 (1.2)
- Mean prescribed psychotropic medications: 2.8 (1.2)

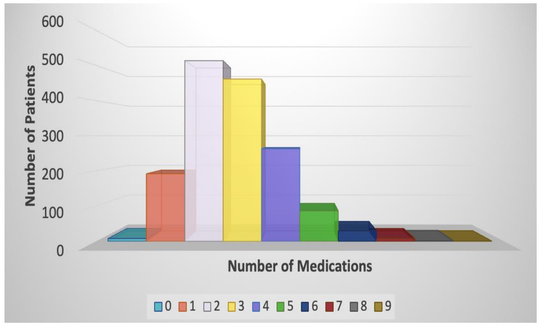
Table 1. Psychiatric Medications Prescribed at Baseline by Class.

Medication Class	N	%
Any SGA	1530	97.8
Any Antidepressant	789	50.4
Any Stimulant	605	38.7
Any Non-Stimulant ADHD Treatment	548	35.0
Any Anxiolytic	252	16.1
Any Mood Stabilizer	250	16.0

Note. ADHD=Attention Deficit Hyperactivity Disorder

- Aripiprazole (41.5%) was the most prescribed SGA (Table 1).
- Methylphenidate/dexmethylphenidate (21.7%) was the most prescribed stimulant.
- Guanfacine (20.5%) was the most prescribed non-stimulant for ADHD.
- Hydroxyzine (7.0%) was the most prescribed anxiolytic.
- Lithium (6.1%) was the most prescribed mood stabilizer.

Figure 1. Number of Medications Prescribed at Baseline.



- 513 (32.8%) participants were prescribed two medications (Figure 1).
- The second most common number of medications prescribed was three (n=461, 29.5%).

Table 2. Rates of Comorbid Psychiatric Diagnoses at Baseline.

Diagnosis	N	%
ADHD	853	54.5
Anxiety Disorders	439	28.1
Impulse Control Disorders	325	20.8
Disruptive Behavior Disorders	256	16.4
Trauma Disorders	227	14.5
Autism Spectrum Disorders	173	11.1
Intellectual Disabilities	79	5.0
Schizophrenia	54	3.5
Obsessive-Compulsive Disorder	47	3.0

Results (Con't)

Table 3. Two-Tailed T-Tests Comparing Average Number of Medications and Demographic Variables.

Variable	Category	n	Mean	SD	T-stat	P-Value
SaaB	Male	829	2.9	1.2	5.66	<0.001
	Female	736	2.6	1.2		
Site type	Community	773	2.8	1.3	0.86	0.391
	Academic	792	2.8	1.2		
Insurance	Private	651	2.8	1.2	0.67	0.503
	Public	914	2.8	1.3		
Ethnicity	Hispanic	202	2.5	1.1	3.37	<0.001
	Non-Hispanic	1361	2.8	1.2		
Enrollment Setting	Inpatient	125	2.3	1.1	4.83	<0.001
	Outpatient	1440	2.8	1.2		
Race	Caucasian/ White	1023	2.9	1.3	5.79	<0.001
	Non-Caucasian/ Non-White	480	2.5	1.1		

Note. $\alpha = 0.05$, "Non-Caucasian/Non-White" includes Asian, Black, Native American, Biracial, Native Hawaiian/Other Pacific Islander, or Other.

- The results of the t-test indicated SaaB (Male > Female), ethnicity (non-Hispanic > Hispanic), enrollment setting (outpatient > inpatient), and race (Caucasian/White > non-Caucasian/non-White) were each significantly associated with a higher number of medications prescribed at baseline in this sample (Table 3).

Table 4. Linear Regression Model Predicting Number of Psychiatric Medications.

Variable	Effect Size, d	P-value
Age, years	-0.04	0.392
SaaB	0.22	<0.001
Ethnicity	0.06	0.257
Race	0.26	<0.001
Site type	0.04	0.414
Insurance	-0.04	0.391
Enrollment setting	0.20	<0.001
Number of diagnoses	0.40	<0.001

- The linear regression results indicated male SaaB ($p<0.001$), Caucasian/White race ($p < 0.001$), outpatient enrollment setting (vs. inpatient; $p < 0.001$), and a higher number of psychiatric diagnoses ($p < 0.001$) were significantly associated with a higher number of prescribed psychotropic medications in youth with BSD (Table 4).

Discussion

- Male SaaB were prescribed more medications than females. This could possibly be due to higher rates of ADHD in male SaaB.
- Consistent with our hypothesis, number of psychiatric diagnoses predicted the number of medications prescribed at baseline.
- Non-Hispanic and Caucasian/White patients were more likely to be on a greater number of medications. This may be related to access to care.
- Outpatient enrollment setting (vs. an inpatient setting) was also significantly associated with a higher number of prescribed medications, which may be related to continuity of care in an outpatient setting compared to inpatient.
- Rates of polypharmacy were low compared to previous literature.

Limitations
- We only examined baseline medications instead of examining medications at baseline, 12 months, and 24 months.
- We did not examine duration or dose of medication exposure.

Future directions
- Future analyses will evaluate associations between demographic and clinical characteristics and longitudinal medication exposure.

References

1. Perlis RH, Dennehy EB, Miklowitz DJ, et al. Retrospective age at onset of bipolar disorder and outcome during two-year follow-up: Results from the step-bd study. *Bipolar Disord, 11:* 391–400, 2009. https://doi.org/10.1111/j.1399-5618.2009.00686.

2. Constantine RJ, Boaz T, Tandon R. Antipsychotic polypharmacy in the treatment of children and adolescents in the fee-for-service component of a large state Medicaid program. *Clinical Therapeutics*. 32:949-959, 2010. doi:10.1016/j.clinthera.2010.04.021

3. Toteja N, Gallego JA, Saito E, et al. Prevalence and correlates of antipsychotic polypharmacy in children and adolescents receiving antipsychotic treatment. *Int J Neuropsychopharmacol* 17:1095-1105, 2014. doi:10.1017/S1461145712001320

4. Saldaña SN, Keeshin BR, Wehry AM, et al. Antipsychotic polypharmacy in children and adolescents at discharge from psychiatric hospitalization. *Pharmacotherapy: Journal Human Pharmacology Drug Therapy*. 34:836-844, 2014. doi:10.1002/phar.1453

5. Welge JA, Correll CU, Sorter MT, et al. Metformin for overweight and obese children with bipolar spectrum disorders treated with second-generation antipsychotics (mobility): Protocol and methodological considerations for a large pragmatic randomized clinical trial. *JAACAP Open*. 1:60-73, 2023. doi:10.1016/j.jaacop.2023.03.004

Acknowledgements

The MOBILITY study was funded through Patient-Centered Outcomes Research Institute. Financial support through Department of Psychiatry and Behavioral Neuroscience Medical Student Scholars Program.