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The Relationship of Persistent Manic Symptoms to the Diagnosis of Pediatric Bipolar Disorder

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Abstract

Objective—The diagnosis of Bipolar Spectrum Disorders (BPSDs; Bipolar I and II, Cyclothymic Disorder, and Bipolar NOS) in youth remains controversial. The present study evaluated the possibility that the presence of persistent manic symptoms over a relatively short interval may increase the probability of a BPSD diagnosis.

Method—Data were obtained from the screening and baseline assessments of an ongoing prospective longitudinal study examining the diagnosis and phenomenology of youth presenting to outpatient centers at ages 6–12 with elevated symptoms of mania (ESM+) and a control group of youth without ESM (ESM−). Youth were classified into four groups: Persistent ESM+, Remitted ESM+, Persistent ESM−, and Progressed to ESM+.

Results—Individuals with Persistent ESM+ were more likely to have a BPSD (relative risk=3.04, 95% CI=2.15 – 4.30). Using two administrations of a parent-report measure of manic symptoms spaced over a relatively brief interval (Median=4.0, M=6.1, SD=5.9 weeks) improved the prediction of BPSD over using only the first administration [ΔR^2=.10, $\Delta\chi^2(1)$=50.06, p<.001]. Likelihood ratios indicated that Persistent ESM− substantially decreased the probability of BPSD. While high levels of Persistent ESM+ increased the probability of a BPSD diagnosis, the final positive predictive value was only sufficient to signify the need for more thorough clinical evaluation.

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Conclusions—In many cases, obtaining repeated parent report of mania symptoms substantially altered the probability of a BPSD diagnosis and may be a useful adjunct to a careful clinical evaluation. Future waves of data collection from this longitudinal study will be crucial for devising clinically-useful methods for identifying or ruling out pediatric BPSD.

Keywords

Pediatric Bipolar Disorder; Mania Symptoms; Longitudinal

Bipolar Spectrum Disorders (BPSDs; Bipolar I and II, Cyclothymic Disorder, and Bipolar not otherwise specified (NOS)) are chronic, debilitating illnesses with considerable controversy surrounding their pediatric presentation.[1] Over half (60%) of adults with bipolar disorder experience their first symptoms during adolescence.[2,3] Nearly one-third (30%) experience symptoms prior to age 13.[2,3] In clinical settings, children are increasingly likely to be given a bipolar diagnosis.[4–7] Although controversy remains about the nature of bipolar spectrum presentations in youth,[8] both “classic” and other spectrum presentations (BP-II, BP-NOS, cyclothymic disorder) are often associated with substantial suffering.[9] Increased prevalence in clinical settings,[10] combined with poor long-term outcomes, make accurate and early diagnosis of BPSD an important challenge with considerable public health significance.

The few available studies examining prodromal symptoms for BPSD suggest that symptoms of mania may be indicative of early stages of illness,[11–14] although many studies examining early symptoms concentrate on children of parents with BPSD,[15–18] and few have used prospective designs.[19–21] Growing evidence indicates a large number of children receiving psychiatric care present with elevated symptoms of mania (ESM).[22–24] A substantial proportion of youth with ESM suffer from considerable dysfunction, although many do not meet strict DSM criteria for BPSD.[24–27]

Previous papers have described the participant characteristics[28] and study design[29] of the NIMH-funded Longitudinal Assessment of Manic Symptoms (LAMS) study. This article extends previous studies by describing diagnostic differences between youth with parent-reported manic symptoms that persist over two assessment points (Persistent ESM+) versus youth with manic symptoms that remit (Remitted ESM+) or are consistently low across two time points (Persistent ESM−). It was hypothesized that individuals with Persistent ESM+ would have higher rates of BPSD diagnoses than other youth. In this study, ESM is conceptualized as a phenotype that when positive and persistent (Persistent ESM+), is related to and potentially predictive of current or future BPSD diagnosis, but is not redundant with BPSD. This study’s secondary aim was to evaluate clinical utility of tracking manic symptoms over two time points in determining the presence of pediatric BPSD. Parent reports on brief rating scales have been particularly powerful at reducing the tendency to over-diagnose bipolar disorder.[10,30] We expected that including information from two assessment time points would further increase the accuracy of predicting BPSD.

Method

Participants

The LAMS study was designed to examine the relationships between ESM and DSM diagnoses in a cohort of 6–12 year old children recruited from 10 outpatient mental health clinics associated with four universities in Ohio and Western Pennsylvania. This report includes data collected during the screening and baseline assessments from the longitudinal portion of the LAMS study for 692 enrolled children.[28,29]

Parents/guardians of youth completed the Parent General Behavior Inventory-10 Item Mania Scale (PGBI-10M)[31] to screen for elevated symptoms of mania (ESM). The PGBI-10M is a 10-item parent report instrument that collects hypomanic, manic, and biphasic mood symptoms and discriminates BPSD from other diagnoses.[31] Items are scored from 0 (never or hardly ever) to 3 (very often or almost constantly). All participants whose parent/guardian scored the PGBI-10M at or above 12 (ESM+; N=1124 out of 2622 screened) were invited to participate in the longitudinal phase of the LAMS study. Scores of 12 or higher were used to identify a cohort enriched for BPSD but that would likely include substantial proportions of children with other non-BPSD psychiatric difficulties. In addition, a matched group of children (age, sex, race/ethnicity and insurance status) who scored below 12 (ESM−) were recruited. Baseline evaluations occurred 3–6 weeks after the screening assessment (median=4.0, M=6.1, SD=5.9 weeks, inter-quartile range=2–8). Due to variability between ESM+ and ESM− groups in the time between screening and baseline assessments, time interval was included in subsequent analyses. Youth were excluded if they or their guardian did not speak English, if there was evidence that manic symptoms were due to a general medical condition, or if the youth had autism.

Procedures were reviewed and approved by the Institutional Review Boards at each of four participating major mid-western medical center sites. Parents/guardians provided written informed consent prior to screening. Caregivers and youth gave written informed consent/assent prior to baseline.

Measures

At the baseline assessment, youth and their caregivers were administered the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Episode (K-SADS-PL)[32] supplemented with additional mood onset and offset items from the WASH-U K-SADS[33] to assess for current and past psychiatric disorders. Bachelor's, master's and doctoral level interviewers were trained by rating taped interviews and leading administrations while experienced interviewers rated concurrently. Inter-rater reliability for K-SADS-PL-W psychiatric diagnoses was excellent, K=0.82 (0.93 for bipolar diagnoses). All diagnoses were confirmed by a licensed child psychiatrist or psychologist.

The PGBI-10M was collected again at baseline. In addition, the child's manic-like symptoms were assessed via clinician rating using the Young Mania Rating Scale (YMRS; total scores 0–60).[34] Ratings of depressive-like symptoms were assessed using the Children's Depression Rating Scale-Revised (CDRS-R).[35] The CDRS-R is a 17-item interviewer administered measure (total scores 17– 113). Both the YMRS and CDRS-R have demonstrated good internal consistency and inter-rater reliability.[35–38] The YMRS and CDRS-R were administered in an "unfiltered" manner (i.e., presence of cross-sectional symptoms did not need to be linked to a mood episode). They were used for clinical description only because they were derived from the same interview as the diagnoses.

ESM Groups

Youth were classified into one of four groups based on their screening and baseline assessment PGBI-10M total scores (Figure 1). Participants who scored ≥ 12 on the PGBI-10M at both screen and baseline were classified in the Persistent ESM+ group (*n*=383). Participants who scored ≥ 12 at screening but scored < 12 at baseline on the PGBI-10M were included in the "Remitted ESM+" group (*n*=225). It is possible that symptoms were simply fluctuating in the Remitted ESM+ group. The Persistent ESM− group (*n*=73) was comprised of youth who scored <12 on the PGBI-10M at both screen and baseline. Finally, a small group of participants (*n*=11) scored <12 at screening, but ≥12 at

baseline (Progressed to ESM+). Due to this group's small size, their findings are included only for descriptive purposes.

Statistical Analyses

Preliminary analyses examined ESM group differences on demographic and clinical symptom severity measures using univariate analysis of variance or chi-square.

Chi-square analyses examined the relationship between the four ESM groupings and seven DSM diagnostic groups. The latter were: any BPSD, any depressive disorder; any ADHD, any other disruptive behavior disorder (DBD), any psychotic disorder, any anxiety disorder, and Asperger's disorder or pervasive developmental disorder (PDD) NOS. The Course and Outcome of Bipolar Youth (COBY) study definition of BP-NOS was used in the present study.[9] Importantly, this definition of BP-NOS requires episodic fluctuations. Children with chronic mood symptoms without clear mood fluctuations are not included in the COBY definition of BP-NOS.

Chi-square analyses also examined the relationship between ESM groups and the presence versus absence of suicidal ideation or behavior. Summary scores of 3 or higher (3=thoughts of suicide, mostly when angry) on item 13 of the CDRS-R were used to indicate the presence of significant suicidal ideation/behavior. For the primary analysis of BPSD, $p<.05$ was used. For other diagnoses and suicidal ideation/behavior, a conservative Bonferroni correction ($p<.05/7=.007$) determined significance. Power was >.90 for small to medium effect sizes (all $r>.15$) for all analyses, even after Bonferroni correction.

In addition to chi-square, relative risk (95% CI) was calculated. For the present design, relative risk is superior to odds ratio based on interpretability of findings[39,40] and because individuals were not selected on the basis of having a disorder.[41]

The clinical utility of repeated PGBI-10M administrations was evaluated by first examining the consistency of scores over time using an intraclass correlation coefficient. Next, the incremental validity of using both PGBI-10M administrations versus only the screening score to predict BPSD diagnosis was evaluated using hierarchical logistic regression. PGBI-10M total score at screening was the independent variable in the initial step, total score at baseline was the independent variable in the second step. Given the large sample size, only substantial increases in variance ($\Delta R^2>.03$) were considered meaningful.

To enhance the clinical utility of this information, multilevel diagnostic likelihood ratios (DLRs) are presented.[42,43] DLRs quantify the ability of low and high scores to alter the post-test probability of BPSD.[44,45] A DLR > 1 indicates increased probability while a DLR < 1 indicates decreased probability. The first set of DLRs was calculated for screening administration only. The following multi-level divisions were used to investigate whether extreme scores yield additional information: low (PGBI-10M<12), elevated (12–19), and very high (20+).[44] The second set of DLRs used both screening and baseline PGBI-10M total scores. ESM groupings were similar to those used above, except: 1) Persistent ESM+ was divided into *very high* (20+ at both administrations) and *elevated* scores (at least one score between 12 and 19, with both scores 12 or greater); and 2) Remitted ESM+ and Progressed to ESM+ were collapsed into an *Inconsistent ESM* category, because these combinations were unlikely to substantially influence the probability of BPSD.

The value of using PGBI-10M administrations to determine the probability of BPSD diagnosis was evaluated using a Bayesian framework for combining conditional probabilities to yield a revised probability estimate. Several prior probabilities were used as starting points: .02, .05, .15, .25, and .50. The lowest prior probabilities (.02 and .05)

approximate settings where the base rate of BPSD approximates epidemiological estimates.[46,47] The .50 prior probability mimics clinical uncertainty.[48] The .15 and .25 probabilities provide more realistic estimates for outpatient mental health settings. These prior probabilities could also represent a starting point based on knowledge of the base rate of BPSD *combined with* family history (.15=2nd degree relative; .25=1st degree relative).[49]

Finally, Receiver Operating Characteristic (ROC) curve analyses evaluated the diagnostic efficiency of the average of the two PGBI-10M scores. This examines performance using a simple and more familiar way of combining the test information.

Results

Participant Characteristics

Table 1 displays sample sizes and demographic characteristics of youth classified as Persistent ESM+, Remitted ESM+, Persistent ESM−, and Progressed to ESM+. Almost 2/3 (63%) of individuals with ESM+ at screening continued to have ESM+ at baseline (Persistent ESM+). The four ESM groups did not differ in age, sex, or insurance status. Youth with ESM− at screening had longer times between screening and assessment due to the recruitment strategy, which immediately enrolled ESM+ in the longitudinal phase but delayed the ESM− screens for a matching procedure. Youth with Persistent ESM+ returned more quickly than other groups and youth with Remitted ESM+ fell in between. For this reason, and to conservatively estimate differences between ESM groups, time from screening to baseline follow-up was included as a covariate in regression models predicting BPSD. Race and ethnicity differences were minor and largely accounted for by the small Progressed to ESM+ group. As expected, baseline YMRS and CDRS-R scores were lowest in youth with Persistent ESM− and highest in those with Persistent ESM+.

ESM Status and Diagnoses

Individuals with Persistent ESM+ had 3 times greater risk of being diagnosed with a BPSD relative to other patterns of ESM (Table 2). Increases in the risk of BPSD in individuals with Persistent ESM+ were most striking when comparing this group to the Persistent ESM− group (6.10; 95% CI=2.33–19.14). Increases were less dramatic, but substantial, when comparing this group to the Remitted ESM+ group (2.79; 95% CI=1.89–4.20). No relative risk estimates for non-BPSD diagnoses survived Bonferroni correction (all $p>.007$).

Potential Clinical Utility of Repeated PGBI-10M Administrations

Individual differences in manic symptoms over the screening to baseline time period were stable, with an intra-class correlation=.73. Including the second (baseline) PGBI-10M administration improved prediction of a BPSD diagnosis substantially over using only the screening (first) administration, even when time between screening and baseline assessments was included in the model [(ΔR^2=.10, $\Delta\chi^2(1)$=46.95, $p<.001$].

Table 3 presents DLRs and post-test probabilities of any BPSD diagnosis across a range of clinically relevant prior probabilities. Screening DLRs tended to be less helpful than DLRs based on two administrations. DLRs based on two administrations were useful in both the low (<12) and very high ranges (20+). Post-test probabilities for DLRs based on two administrations were substantially reduced for individuals showing Persistent ESM−. Reductions in the post-test probability of BPSD were likely sufficient to rule out the need for further expensive evaluation. DLRs for individuals showing very high (20+) Persistent ESM+ greatly increased the probability of BPSD. Clinicians could use DLRs flexibly in combination with prior probabilities other than those shown in the table. One of the easiest ways is by means of a probability “nomogram” as shown in Figure 2.[43] Interested readers

could use the nomogram to combine the prior value and DLR to re-create the tabled values as a way of practicing with the tool. However, even for the highest prior probability, the increase was meaningful, but only sufficient to signify the need for additional evaluation.

Results of ROC analysis indicated adequate efficiency of the average of PGBI-10M scores (AUC=.68, SE=.02, 95% CI=.63–.72). A cut score of 12 provided good sensitivity (.88) but also a large proportion of false alarms (.62). A cut score of 20 reduced sensitivity (.36) but also decreased the false alarm rate substantially (.14).

Discussion

The majority of individuals (63%) whose parents reported ESM at screening continued to show ESM ~4 weeks later. Persistent or increasing levels of ESM showed a strong association with BPSD diagnoses. Persistent ESM did not increase the odds of having other diagnoses or suicidal ideation/behavior. Persistently elevated PGBI-10M scores (≥20) appear to be a useful and fairly specific predictor of BPSD and not other diagnoses. However, only a minority of individuals with moderate levels of Persistent ESM+ met criteria for a BPSD diagnosis. Moderate levels of ESM also occur in individuals with other common disorders, such as ADHD.

Longitudinal assessment of manic symptoms is more helpful than a single assessment for predicting the presence of BPSD. The present findings support using two administrations of the PGBI-10M, even if only a brief period of time (approximately 1 month) elapses between assessments. Assessing stability over time in symptom level further enhanced prediction of BPSD diagnosis, despite the changeable and complex mood symptom patterns often seen in BPSD.[1,8]

Using a DLR approach increases the consistency of test result interpretation, improves accuracy over unaided interpretation, and reduces risk of overdiagnosing BPSD.[50,51] In the DLR framework, combining results from two administrations appears quite useful for "ruling out" a BPSD diagnosis, even in clinical settings with a moderate base rate. Broader application of this approach may improve resource allocation (i.e., time, effort, cost).[52] Adding a second PGBI-10M administration resulted in substantial improvement in detecting BPSD without inflating the false positive rate – avoiding the pitfall of "overdiagnosis." Elevated scores that remain stable or scores that increase at follow-up should be viewed as a "red flag" requiring additional assessment.

The DLR framework may be enhanced by iteratively including family history. Existing evidence indicates a 5-fold (DLR=5) increase in the probability of BPSD when a first-degree relative is diagnosed with BPSD.[10,53] Clinics that routinely use a broad-band instrument such as the Child Behavior Checklist[54] might follow-up high scores on the Externalizing scale[30] with a PGBI-10M, then repeat the PGBI before referring the family for a more detailed diagnostic interview that includes careful probing of BPSD symptoms. Using multiple gates would filter referrals and increase the procedure's specificity.

The DLR approach is analogous to using a weather report. The report will sometimes be wrong, but it can be a guide for behavior. For example, if the report says 50% probability of rain, a reasonable response would be to bring a rain coat. Alternatively, if it says ~0% chance of rain, making plans to be outdoors would be appropriate. Adopting this system allows a person to make better choices over the long run but will not prevent all instances of getting rained on. In most assessment cases, a thorough clinical assessment ultimately will be required.

The simpler and more familiar approach involving averaging screening and baseline PGBI-10M scores resulted in only modest efficiency in detecting the presence of BPSD. This is to be expected in a cohort enriched for manic symptoms but not specifically ascertained for BPSD. The modest efficiency observed further supports a more nuanced approach – part of a broader clinical assessment strategy - that considers scores across two administrations.

Large increases (i.e., > 6 points) in PGBI-10M scores were rare in this cohort. A small group (n=11) of eleven individuals were ESM− at screening but progressed to ESM+ at baseline. Interestingly, these individuals showed a substantially higher percentage of BPSD diagnoses relative to individuals with consistently low scores (27.3% vs. 5.5%). The small group size precludes inferences, but future waves of follow-up may help to determine whether increases over time in PGBI-10M scores serve as a strong prognostic indicator of BPSD onset.

Limitations

The LAMS cohort intentionally selected new outpatient children with high or low scores on the PGBI-10M. Thus, the present findings are particularly helpful for devising assessment strategies in outpatient settings. However, results may be less applicable to inpatient samples or the larger, non-clinical population. Furthermore, the variable time between screening and baseline assessments, while not altering results statistically, and the merging of BP-NOS with other bipolar disorders represent limitations that influence the generalizability of findings. Larger epidemiological studies will be needed to determine whether the present findings generalize to the non-clinical population.

Future Directions

Several important questions remain regarding the relationship between ESM and BPSD. Will youth with Persistent ESM+ without BPSD develop BPSD later? Will individuals with remitted ESM+ and BPSD show a rapidly fluctuating course of symptoms? How can repeated parent reports be combined with clinician observations or other risk factors to enhance detection of BPSD? Follow-up assessments of the LAMS cohort will be essential to providing answers to these questions. Empirical approaches, such as growth mixture modeling, are particularly promising for clarifying pediatric-specific BPSD phenotypes and developing clinically useful diagnostic classification.

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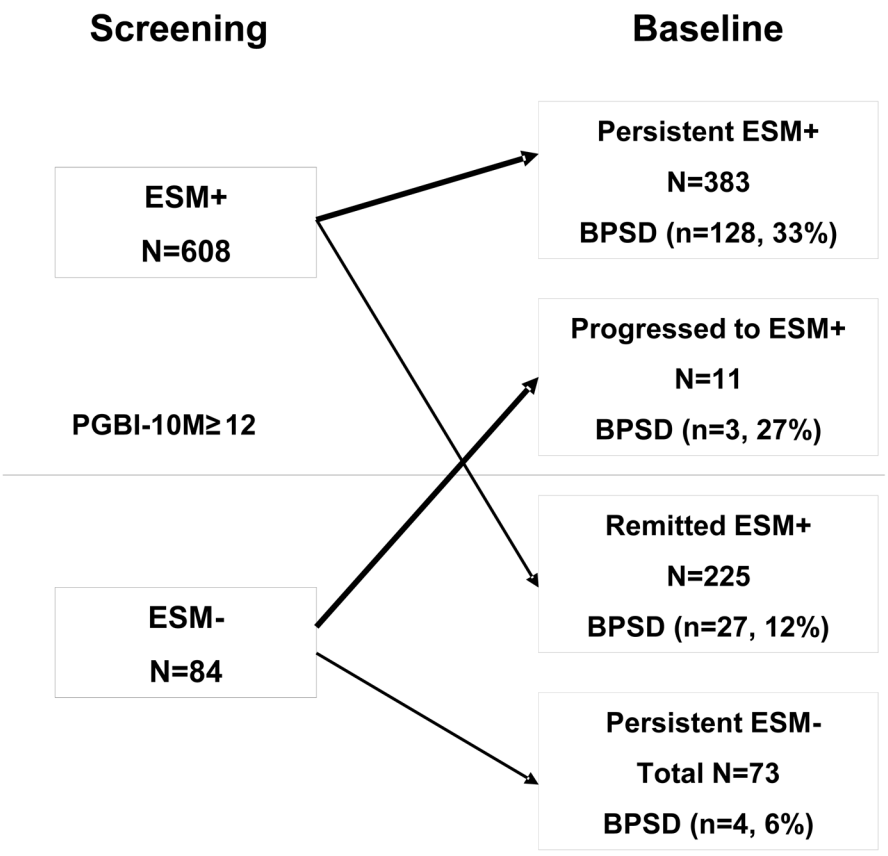

Figure 1.
Elevated Symptoms of Mania (ESM) status at screening and baseline and Bipolar Spectrum Disorder (BPSD) diagnosis.

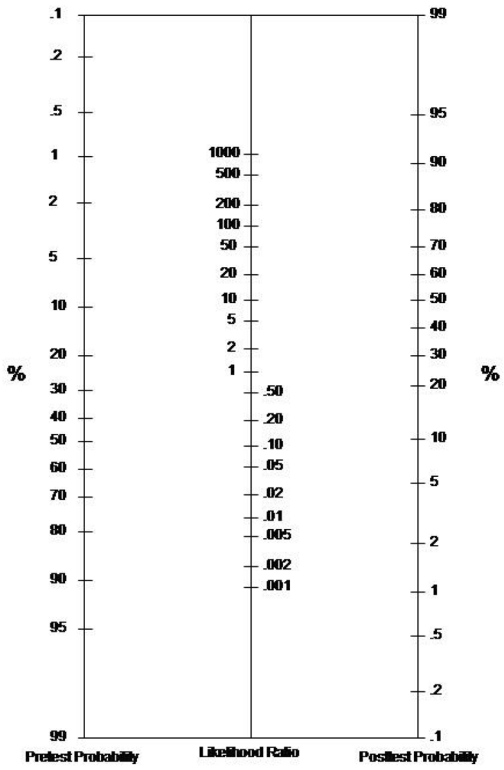

Figure 2.

Nomogram for combining prior probability and diagnostic likelihood ratios (adapted from Jaeschke et al., 1994, JAMA).

Note: Use the nomogram to combine starting probability (such as the base rate of bipolar disorder in the clinical setting) with information gleaned from test scores or risk factors. Find the staring probability (such as a 5% or 6% prevalence of bipolar disorder in an outpatient clinic[10] and mark it on the left-hand column. Find the diagnostic likelihood ratio associated with the test result (e.g., the values in Table 3) and mark it on the middle column. Connect the two dots and cross the third line to estimate the revised probability.

Table 1

Demographic characteristics and baseline clinical symptoms of Elevated Symptoms of Mania (ESM) groups.

	Persistent ESM +	Remitted ESM +	Persistent ESM −	Progressed to ESM+	F/X^2 (p)
N	383	225	73	11	
Mean Age (SD) at Screening	9.2 (1.9)	9.2 (2.0)	9.4 (1.6)	10.5 (1.5)	1.61 (.186)
Time (weeks) from Screening to Baseline	4.7 (4.0)	6.8 (7.7)	10.8 (5.2)	10.8 (5.1)	29.06 (<.001)
Sex (% Male)	65.5	69.8	78.1	54.5	5.73 (.126)
Race					
White %	66.8	60.0	74.0	36.4	
African-American %	24.3	32.0	19.2	18.2	25.39 (<.001)
Multi-Racial or Other Race %	8.9	8.0	6.8	45.5	
Ethnicity (% Hispanic)	4.7	3.6	1.4	36.4	28.28 (<.001)
Insurance Status					
Medicaid Only %	48.2	45.7	41.1	63.6	
Private Insurance %	45.8	50.7	54.8	36.4	6.35 (.705)
Self-pay %	1.5	0.9	0.0	0.0	
Medicaid and Private %	4.5	2.7	4.1	0.0	
Baseline YMRS	20.1 (9.2)	14.0 (7.7)	9.9 (6.6)	13.6 (9.1)	43.59 (<.001)
Baseline CDRS-R	36.8 (10.6)	32.8 (10.4)	30.5 (9.4)	35.0 (13.6)	11.38 (<.001)

YMRS=Young Mania Rating Scale, CDRS-R=Children's Depression Rating Scale-Revised

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Table 2

Diagnostic rates (%), Odds Ratios, and Diagnostic Likelihood Ratios (DLR) by Elevated Symptoms of Mania (ESM) groups. Numbers represent percents within each ESM group.

		Persistent ESM + n=383	Remitted ESM + n=225	Persistent ESM − n=73	Progressed to ESM+ n=11	Persistent ESM vs. All Others	
	n	%	%	%	%	Relative Risk (95% CI)	X^2 (p)
Any Bipolar Spectrum Diagnosis:	162	33.4	12.0	5.5	27.3	3.04 (2.15–4.30)	47.93 (<.001)
BP1	71	15.4	3.1	2.7	27.3		
BP2	3	0.8	0.0	0.0	0.0		
Cyclothymic Disorder	11	2.6	0.4	0.0	0.0		
BP-NOS	77	14.6	8.4	2.7	0.0		
Any Depressive Spectrum Diagnosis:	115	18.5	14.7	12.3	27.3	1.27 (.90–1.79)	1.94 (.164)
MDD	46	6.8	5.8	6.8	18.2		
Dysthymic Disorder	15	2.1	2.2	1.4	9.1		
Depressive Disorder NOS	54	9.4	6.7	4.1	0.0		
Any Attention-Deficit/Hyperactivity Diagnosis	528	79.9	71.1	74.0	72.7	1.11 (1.02–1.21)	6.13 (.013)
Any Disruptive Behavior Disorder Diagnosis	354	54.3	51.1	37.0	36.4	1.15 (.99–1.34)	3.41 (.065)
Any Psychotic Diagnosis	16	2.9	1.8	1.4	0.0	1.78 (.62–5.05)	1.19 (.275)
Any Anxiety Diagnosis	214	31.3	31.6	28.8	18.2	1.03 (.82–1.29)	0.07 (.797)
Any Autism Spectrum Diagnosis	44	4.7	7.1	13.7	0.0	.56 (.31–1.00)	3.96 (.047)
Suicidal Thoughts or Behavior	110	18.3	15.1	6.8	9.1	1.18 (1.01–1.39)	3.64 (.057)

Note. ESM=Elevated Symptoms of Mania; BP=Bipolar Disorder; DBD=disruptive behavior disorder (conduct or oppositional-defiant disorder; PDD=pervasive developmental disorder; MDD=major depressive disorder. X^2 (p) test difference between Persistent ESM+ and all other groups. Diagnostic groupings are any diagnosis regardless of the presence of BPSD. Thus, diagnostic groups are not reflective of comorbidities within BPSD.

Table 3

Multilevel Diagnostic Likelihood Ratios (DLRs) for Elevated Symptoms of Mania (ESM) groups based on a single versus repeated assessment of hypomania symptoms.

PGBI-10M				Post-Test Probability of BPSD				
Screening Administration	**n**	**Category**	**DLR**	**Prior =.02**	**Prior =.05**	**Prior =.15**	**Prior=.25**	**Prior =.50**
<12	84	Low	.30	.01	.02	.05	.09	.23
12–19	386	Elevated	.97	.02	.05	.15	.24	.49
20+	222	Very High	1.42	.03	.07	.20	.32	.59
Two Administrations								
Persistent ESM− (<12)	73	Low	.19	<.01	.01	.03	.06	.16
Inconsistent ESM	236	Neutral	.48	.01	.03	.08	.14	.32
Persistent ESM+ (12–19)	290	Elevated	1.45	.03	.07	.20	.33	.59
Persistent ESM+ (20+)	93	Very High	2.36	.05	.11	.29	.44	.70

Note: Prior probabilities of .15 and .25 are estimates based on the combination of an outpatient setting base rate and second and first degree family history, respectively. DLR=Diagnostic Likelihood Ratio, Prior=Prior Probability. DLRs <.50 are useful for decreasing the probability of a BPSD diagnosis and DLRs >2.0 are useful for increasing the probability of a BPSD diagnosis.