Relationship of Persistent Manic Symptoms to the Diagnosis of Pediatric Bipolar Spectrum Disorders

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Objective: The diagnosis of bipolar spectrum disorders (BPSDs [bipolar I and II disorders, cyclothymic disorder, and bipolar disorder not otherwise specified]) 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 *DSM* diagnosis.

Method: Data were obtained from the screening and baseline assessments collected from 2005 through 2008 of an ongoing prospective, longitudinal study (Longitudinal Assessment of Manic Symptoms) examining the diagnosis and phenomenology of youth (N = 692) presenting to outpatient centers at ages 6–12 years. Youth were assessed for elevated symptoms of mania (ESM) with the Parent General Behavior Inventory–10-Item Mania Scale (PGBI-10M), the primary outcome measure. Screening and baseline scores separated individuals into those with ESM (ESM+; PGBI-10M score ≥ 12) and a control group of youth without ESM (ESM–; PGBI-10M score < 12). Youth were classified into 4 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 2 administrations of the PGBI-10M spaced over a relatively brief interval (median = 4.0, mean = 6.1, SD = 5.9 weeks) improved the prediction of BPSD over using only the first administration ($\Delta R^2 = 0.10$, $\Delta\chi^2_1 = 50.06$, $P < .001$). 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.

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.

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Bipolar spectrum disorders (BPSDs) (bipolar I and II disorders, cyclothymic disorder, and bipolar disorder 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 years.[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 (bipolar II disorder, bipolar disorder 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 articles have described the participant characteristics[28] and study design[29] of the National Institute of Mental Health–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 2 assessment points (persistent ESM+) versus youth with manic symptoms that remit (remitted ESM+) or are consistently low across 2 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 2 time points in determining the presence of pediatric BPSD. Parent reports on brief rating scales have been particularly

powerful at reducing the tendency to overdiagnose bipolar disorder.[10,30] We expected that including information from 2 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- to 12-year-old children recruited from 10 outpatient mental health clinics associated with 4 universities in Ohio and western Pennsylvania. This report includes data collected from 2005 through 2008 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 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 = 1,124 of 2,622 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, mean = 6.1, SD = 5.9 weeks; interquartile 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.

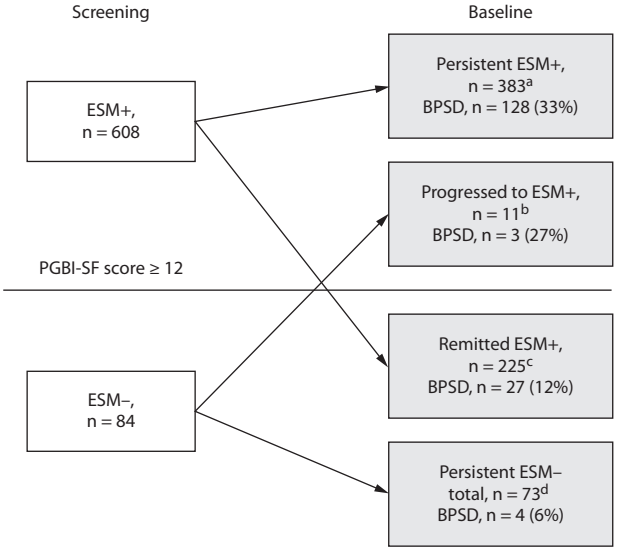
Procedures were reviewed and approved by the institutional review boards at each of 4 participating major midwestern medical center sites. Parents/guardians provided written informed consent prior to screening. Caregivers and youth gave written informed consent/assent prior to baseline.

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 Washington University in St Louis Kiddie Schedule for Affective Disorders and Schizophrenia (WASH-U-KSADS)[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. Interrater reliability for psychiatric diagnoses was excellent, $\kappa = 0.82$ (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 interrater reliability.[35–38] The YMRS and CDRS-R were administered in an "unfiltered" manner (ie, presence of cross-sectional symptoms did not need to be linked to a mood episode). They were used only for clinical description because they were derived from the same interview as the diagnoses.

Figure 1. Elevated Symptoms of Mania (ESM) Status at Screening and Baseline and Bipolar Spectrum Disorder (BPSD) Diagnosis



[a]Persistent ESM+ = screen + baseline PGBI-10M scores ≥ 12.
[b]Progressed to ESM+ = screen PGBI-10M score < 12 + baseline PGBI-10M score ≥ 12.
[c]Remitted ESM+ = screen PGBI-10M score ≥ 12 + baseline PGBI-10M score < 12.
[d]Persistent ESM– = screen + baseline PGBI-10M scores < 12.

Elevated Symptoms of Mania Groups

Youth were classified into 1 of 4 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 composed of

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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 χ^2.

χ^2 Analyses examined the relationship between the 4 ESM groupings and 7 *DSM* diagnostic groups. The latter were any BPSD, any depressive disorder, any attention-deficit/hyperactivity disorder (ADHD), any other disruptive behavior disorder, any psychotic disorder, any anxiety disorder, and Asperger's disorder or pervasive developmental disorder NOS. The Course and Outcome of Bipolar Youth (COBY) study definition of *bipolar disorder NOS* was used in the present study.[9] Importantly, this definition of bipolar disorder NOS requires episodic fluctuations. Children with chronic mood symptoms without clear mood fluctuations are not included in the COBY definition of bipolar disorder NOS.

χ^2 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 $r > 0.15$) for all analyses, even after Bonferroni correction.

In addition to χ^2, 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, and total score at baseline was the independent variable in the second step. Given the large sample size, only substantial increases in variance ($\Delta R^2 > 0.03$) were considered meaningful.

To enhance the clinical utility of this information, multilevel diagnostic likelihood ratios are presented.[42,43] Diagnostic likelihood ratios quantify the ability of low and high scores to alter the posttest probability of BPSD.[44,45] A diagnostic likelihood ratio > 1 indicates increased probability while a diagnostic likelihood ratio < 1 indicates decreased probability. The first set of diagnostic likelihood ratios was calculated for screening administration only. The following multilevel divisions were used to investigate whether extreme scores yield additional information: low (PGBI-10M score < 12), elevated (PGBI-10M score 12–19), and very high (PGBI-10M score 20+).[44] The second set of diagnostic likelihood ratios used both screening and baseline PGBI-10M total scores. Elevated symptoms of mania 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 1 PGBI-10M 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: 0.02, 0.05, 0.15, 0.25, and 0.50. The lowest prior probabilities (0.02 and 0.05) approximate settings in which the base rate of BPSD approximates epidemiologic estimates.[46,47] The 0.50 prior probability mimics clinical uncertainty.[48] The 0.15 and 0.25 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 (0.15 = second-degree relative; 0.25 = first-degree relative).[49]

Finally, receiver operating characteristic curve analyses evaluated the diagnostic efficiency of the mean of the 2 PGBI-10M scores. This analysis 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 two-thirds (63%) of individuals with ESM+ at screening continued to have ESM+ at baseline (persistent ESM+). The 4 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+.

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Table 1. Demographic Characteristics and Baseline Clinical Symptoms of Elevated Symptoms of Mania (ESM) Groups

Variable	Persistent ESM+	Remitted ESM+	Persistent ESM–	Progressed to ESM+	F/χ^2	*P*
n	383	225	73	11		
Age at screening, mean (SD), y	9.2 (1.9)	9.2 (2.0)	9.4 (1.6)	10.5 (1.5)	1.61	.186
Time from screening to baseline, mean (SD), wk	4.7 (4.0)	6.8 (7.7)	10.8 (5.2)	10.8 (5.1)	29.06	<.001
Boys, %	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
Multiracial or other race	8.9	8.0	6.8	45.5		
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 score, mean (SD)	20.1 (9.2)	14.0 (7.7)	9.9 (6.6)	13.6 (9.1)	43.59	<.001
Baseline CDRS-R, score, mean (SD)	36.8 (10.6)	32.8 (10.4)	30.5 (9.4)	35.0 (13.6)	11.38	<.001

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

Table 2. Diagnostic Rates, Odds Ratios, and Diagnostic Likelihood Ratios by Elevated Symptoms of Mania (ESM) Groups

Variable	n	Persistent ESM+ (n = 383), %	Remitted ESM+ (n = 225), %	Persistent ESM– (n = 73), %	Progressed to ESM+ (n = 11), %	Persistent ESM vs All Others[a] Relative Risk (95% CI)	χ^2	*P*
Any bipolar spectrum diagnosis	162	33.4	12.0	5.5	27.3	3.04 (2.15–4.30)	47.93	<.001
Bipolar I disorder	71	15.4	3.1	2.7	27.3			
Bipolar II disorder	3	0.8	0.0	0.0	0.0			
Cyclothymic disorder	11	2.6	0.4	0.0	0.0			
Bipolar disorder 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 (0.90–1.79)	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[b]	354	54.3	51.1	37.0	36.4	1.15 (0.99–1.34)	3.41	.065
Any psychotic disorder diagnosis	16	2.9	1.8	1.4	0.0	1.78 (0.62–5.05)	1.19	.275
Any anxiety disorder diagnosis	214	31.3	31.6	28.8	18.2	1.03 (0.82–1.29)	0.07	.797
Any autism spectrum disorder diagnosis	44	4.7	7.1	13.7	0.0	0.56 (0.31–1.00)	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

[a]χ^2 And *P* value test difference between persistent ESM+ and all other groups. Diagnostic groupings are any diagnosis regardless of the presence of bipolar spectrum disorder. Thus, diagnostic groups are not reflective of comorbidities within bipolar spectrum disorder.
[b]Conduct or oppositional defiant disorder.
Abbreviations: MDD = major depressive disorder, NOS = not otherwise specified.

Elevated Symptoms of Mania 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 (relative risk = 6.10; 95% CI, 2.33–19.14). Increases were less dramatic, but substantial, when comparing this group to the remitted ESM+ group (relative risk = 2.79; 95% CI, 1.89–4.20). No relative risk estimates for non-BPSD diagnoses survived Bonferroni correction (all *P* values > .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 intraclass correlation = 0.73. Including the second (baseline) PGBI-10M administration improved prediction of a BPSD diagnosis substantially over using only the screening (first) administration ($\Delta R^2 = 0.10$, $\Delta\chi^2_1 = 50.06$, $P < .001$), even when time between screening and baseline assessments was included in the model ($\Delta R^2 = 0.10$, $\Delta\chi^2_1 = 46.95$, $P < .001$).

Table 3 presents diagnostic likelihood ratios and posttest probabilities of any BPSD diagnosis across a range of clinically relevant prior probabilities. Screening diagnostic likelihood ratios tended to be less helpful than diagnostic likelihood ratios based on 2 administrations. Diagnostic likelihood ratios based on 2 administrations were useful in both the low (PGBI-10 score < 12) and very high ranges (PGBI-10 score 20+). Posttest probabilities for diagnostic likelihood ratios based on 2 administrations were substantially reduced for individuals showing persistent ESM–.

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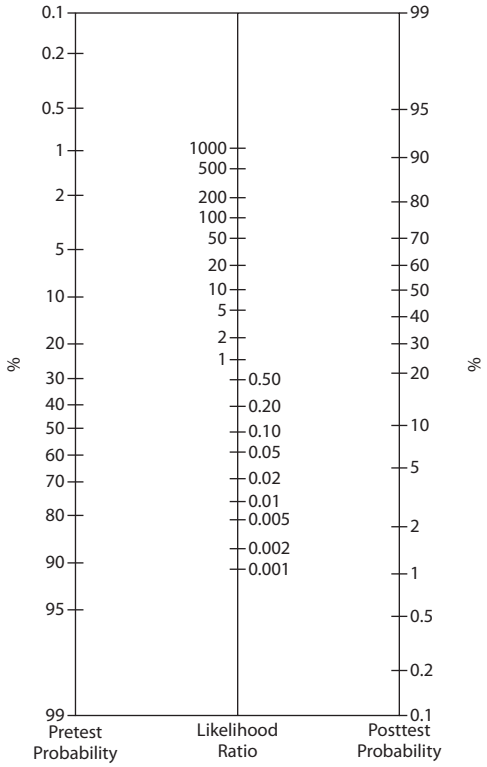
Table 3. Multilevel Diagnostic Likelihood Ratios (DLRs) for Elevated Symptoms of Mania (ESM) Groups Based on a Single Versus Repeated Assessment of Hypomania Symptoms

				Posttest Probability of Bipolar Spectrum Disorder[a]				
Variable	n	Category	DLR[b]	Prior Probability = 0.02	Prior Probability = 0.05	Prior Probability = 0.15	Prior Probability = 0.25	Prior Probability = 0.50
Screening administration								
PGBI-10M score								
< 12	84	Low	0.30	0.01	0.02	0.05	0.09	0.23
12–19	386	Elevated	0.97	0.02	0.05	0.15	0.24	0.49
20+	222	Very high	1.42	0.03	0.07	0.20	0.32	0.59
Two administrations								
Persistent ESM– (PGBI-10M score < 12)	73	Low	0.19	< 0.01	0.01	0.03	0.06	0.16
Inconsistent ESM	236	Neutral	0.48	0.01	0.03	0.08	0.14	0.32
Persistent ESM+ (PGBI-10M score 12–19)	290	Elevated	1.45	0.03	0.07	0.20	0.33	0.59
Persistent ESM+ (PGBI-10M score 20+)	93	Very high	2.36	0.05	0.11	0.29	0.44	0.70

[a]Prior probabilities of 0.15 and 0.25 are estimates based on the combination of an outpatient setting base rate and second- and first-degree family history, respectively.
[b]DLRs < 0.50 are useful for decreasing the probability of a bipolar spectrum disorder diagnosis, and DLRs > 2.0 are useful for increasing the probability of a bipolar spectrum disorder diagnosis.
Abbreviation: PGBI-10M = Parent General Behavior Inventory–10-Item Mania Scale.

Figure 2. Nomogram for Combining Prior Probability and Diagnostic Likelihood Ratios[a]



[a]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 starting 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 (eg, the values in Table 3) and mark it on the middle column. Connect the 2 dots and cross the third line to estimate the revised probability.

Reductions in the posttest probability of BPSD were most likely sufficient to rule out the need for further expensive evaluation. Diagnostic likelihood ratios for individuals showing very high (PGBI-10 score 20+) persistent ESM+ greatly increased the probability of BPSD. Clinicians could use diagnostic likelihood ratios 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 diagnostic likelihood ratio to recreate 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 receiver operating characteristic curve analysis indicated adequate efficiency of the mean of PGBI-10M scores (area under the curve = 0.68; SE = 0.02; 95% CI, 0.63–0.72). A cut score of 12 provided good sensitivity (0.88) but also a large proportion of false alarms (0.62). A cut score of 20 reduced sensitivity (0.36) but also decreased the false-alarm rate substantially (0.14).

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 2 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 diagnostic likelihood ratio approach increases the consistency of test result interpretation, improves accuracy over unaided interpretation, and reduces risk of overdiagnosing BPSD.[50,51] In the diagnostic likelihood ratio framework, combining results from 2 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 (ie, 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 diagnostic likelihood ratio framework may be enhanced by iteratively including family history. Existing evidence indicates a 5-fold (diagnostic likelihood ratio = 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 diagnostic likelihood ratio 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 a weather 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 2 administrations.

Large increases in PGBI-10M scores (ie, > 6 points) were rare in this cohort. A small group (n = 11) of 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, nonclinical population. Furthermore, the variable time between screening and baseline assessments, while not altering results statistically, and the merging of bipolar disorder NOS with other bipolar disorders represent limitations that influence the generalizability of findings. Larger epidemiologic studies will be needed to determine whether the present findings generalize to the nonclinical 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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