

## Serious Mental Illness in Childhood: What Longitudinal Data on Manic Symptoms Can Tell Us

Elevated symptoms of mania (ESM) are increasingly prevalent among children seeking care for psychiatric distress. Characterized as marked extremes in mood accompanied by intense irritability, ESM is the hallmark feature of bipolar disorder,<sup>1</sup> which is also being diagnosed in children at increasingly high rates. However, ESM does not on its own indicate a bipolar diagnosis, and there is currently no reliable means of predicting whether a child with ESM will ultimately develop bipolar disorder.<sup>2</sup> In order to better understand the diagnostic course of ESM and identify key predictors of progression to a bipolar spectrum disorder, researchers at Case Western Reserve University and collaborating institutions are conducting the first ever longitudinal study of youth who have been selected explicitly for their presentation with this important risk factor.

Bipolar spectrum disorders (BPSDs) are chronic mental illnesses which severely affect childhood wellbeing. In youth, BPSDs are characterized by aggression, attention problems, anxiety, depression, and delinquency.<sup>3</sup> In the school environment, the condition has been shown to have a significant negative impact on work effort, peer relationships, extracurricular involvement, and academic achievement, with delayed or lowered graduation rates and lower college entry rates.<sup>4</sup> Furthermore, research suggests that among adolescents

with psychiatric conditions, those with bipolar disorder have the highest rates of injury- and overdose-related hospitalization and service use, indicating a high burden of both suffering and health care expenses.<sup>5</sup> A recent study among adult bipolar patients is indicative of the high health care costs of the disorder: total health expenditures in the first year after diagnosis averaged \$19,116 per patient, compared with \$4,348 in health care expenses incurred by the average, non-bipolar member in the same managed care health plan.<sup>6</sup> When compared with major depressive disorder in youth, adolescent bipolar disorder has been associated with more suicide attempts, higher rates of multiple attempts, younger age at first attempt, and greater lethality of attempts.<sup>3</sup>

Diagnoses of BPSD in children (including bipolar I and II disorders, cyclothymic disorder, and bipolar disorder not otherwise specified [NOS]) are rising sharply. In a national sample of youth age 0–19 who visited a health care provider for any reason, the annual number of visits with a bipolar diagnosis rose from 25 to 1003 per 100,000—a 40-fold increase—between 1995 and 2003.<sup>7</sup> The possibility of high pediatric BPSD rates is supported by data showing that up to 60% of afflicted adults experienced the onset of symptoms during childhood or adolescence.<sup>1</sup> It is now estimated that as many as 1 million

youth in the U.S. may suffer from the condition.<sup>8</sup> Still, the presentation of pediatric BPSD remains highly controversial. BPSD may manifest differently before and after puberty, making classification challenging. Moreover, it can be difficult to distinguish BPSD from other psychiatric disorders common in youth (e.g., ADHD, depression, conduct disorder), as many symptoms overlap and the disorders often co-occur.<sup>1</sup>

A bipolar label indicates a lifelong, heritable condition that carries social and psychological ramifications for the child and his or her family.<sup>2</sup> Children who are incorrectly diagnosed with BPSD may be subject to years of inappropriate and costly treatments, including the prescription of antipsychotic medications which present significant health risks. Conversely, failure to appropriately assign a bipolar diagnosis can lead to unnecessary suffering resulting from an indefinite delay in treatment. Given the rising prevalence of BPSD in clinical settings, the lasting consequences that accompany such a diagnosis, and the implications for providing treatment, accurately identifying bipolarity in children with ESM presents a critical challenge. This research and policy brief summarizes the ongoing work of CWRU scholars and collaborators to gather and analyze longitudinal data addressing this need and discusses some of the practice and policy implications.

## The Longitudinal Assessment of Manic Symptoms (LAMS) Study

Dr. Findling is an internationally-recognized researcher whose work has focused on pediatric psychopharmacology and serious psychiatric disorders in children and adolescents. He is the coordinating principal investigator of the Longitudinal Assessment of Manic Symptoms (LAMS) study, funded by the National Institute of Mental Health (NIMH).

### Design

The LAMS study was designed to describe the course of Elevated Symptoms of Mania (ESM) from childhood to adolescence and delineate the relationship between ESM and bipolarity by following a clinic-based cohort of children over time.<sup>1,2</sup> Between December 2005 and December 2008, children age 6–12 were recruited from 10 out-patient mental health clinics and screened for presence/absence of ESM. These clinics are associated with the collaborating universities of the LAMS study: CWRU, University of Cincinnati, Ohio State University, and University of Pittsburgh.

In the screening phase, parents or guardians were asked to rate their children's symptoms according to the Parent General Behavior Inventory 10-Item Mania Scale (PGBI-10M).<sup>1</sup> All children who scored 12 or higher on the scale were considered to be ESM positive (ESM+) and were invited to enroll in the LAMS study. For every 10 ESM+ children, a child scoring < 12 (ESM-) was matched demographically with an ESM+ child and invited to enroll. A baseline assessment of enrolled children was conducted 3–6 weeks after screening and involved diagnosis, collection of medication histories, functional and symptomatic assessments, and collection of demographic variables (child's age, sex, race/ethnicity, and insurance status).<sup>2</sup> Children were then followed up every six months for up to five years. This brief contains findings from the screening and baseline assessments only. Follow-up data are still being analyzed.

### Key Findings

**Screening.** Initial assessment using the PGBI-10M was completed for a total of 2,622 patients, with 707 children ultimately enrolled in the study: 621 ESM positive and 86 ESM negative.<sup>2</sup> Results from screening show that **four PGBI-10M items contributed most strongly to the difference in ESM+ versus ESM- scores:** Days or more 1) depressed/irritable, than days or more extremely high, elated, overflowing with energy; 2) unusually happy and intensely energetic, but everything gets on nerves and makes angry; 3) of extreme happiness or energy, yet also anxious or tense; and 4) unusually happy and energetic, yet also struggles with rage or urge to smash/destroy.<sup>1</sup> **The majority of children who were ultimately diagnosed with BPSD were rated ESM+ at screening, suggesting that these symptoms are also highly associated with BPSD.**

**Diagnoses and Related Factors.**<sup>2</sup> Of the 707 children enrolled in the study, the most common diagnoses at baseline were ADHD (76.1%), other disruptive behavior disorders (51.1%), mood disorders (40.5%), and anxiety disorders (31.3%). 22.9% of participating children were diagnosed with a bipolar spectrum disorder (BPSD). Co-morbidity (i.e., meeting criteria for multiple diagnoses) was common in both the ESM+ and ESM- groups, but children who had ESM+ had more concurrent diagnoses and poorer overall functioning than children in the control group. Among children who were ESM+ (N=621), those with BPSD (N=155) had lower



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overall functioning, more psychiatric hospitalizations, and were more likely to have parents with elevated mood than those without BPSD.

63% of youth who had ESM+ at the time of screening continued to display manic symptoms at the baseline assessment 3-6 weeks later.<sup>9</sup> It is of particular interest that those children with persistently high or increasing scores on the PGBI-10M (score  $\geq 20$ ) were three times as likely to be diagnosed with BPSD than ESM+ children whose symptoms had subsided, or ESM- children who remained negative.

Importantly, persistently elevated symptoms of mania did not increase the odds of being diagnosed with any other conditions (e.g., ADHD, depression, anxiety, psychotic disorders, disruptive behavior disorders, autism spectrum disorders), suggesting that persistent ESM+ may be a fairly specific predictor of BPSD and not other diagnoses.

These findings highlight a number of important points:

- **Results are consistent with those of other studies in that manic symptoms seem to be relatively common in children seeking outpatient psychiatric care.**
- **Elevated symptoms of mania are associated with significantly higher rates of bipolar disorder, with 25% of ESM+ versus 8.1% of ESM- children meeting the criteria for a BPSD diagnosis.<sup>2</sup>**
- **Manic symptoms that persist at high levels over a relatively short time period (1 month) may increase the likelihood of a child eventually meeting the criteria for a BPSD diagnosis. At the same time, however, isolated episodes as well as moderately persistent levels of ESM were shown to be common in other conditions such as ADHD.<sup>9</sup>**

**Service Usage and Treatment.<sup>5</sup>** At baseline, children diagnosed with BPSD had higher rates of inpatient admissions in their lifetimes (22%) and in the past year (14%) than did those diagnosed with other conditions. Among children diagnosed with BPSD, those with major impairment were more likely to be accessing multiple services (e.g., outpatient, inpatient, alternative, school and classroom-based), to have reported lifetime use of intensive and outpatient services, and to have received both therapy and medication (vs. medication alone) when compared to those with mild impairment. Among the entire cohort, ethnic minorities and children covered by Medicaid were more likely to have received therapy alone (which is covered in full by Medicaid) versus a medication-therapy combination when compared with their white and/or privately insured counterparts. **This finding points to economic disparities in treatment options as well as potential cultural differences in attitudes regarding the appropriateness of certain interventions for mental illness.**

In light of recent trends in the literature suggesting that antipsychotics are being prescribed to children at significantly increasing rates, data were also collected on participants' prescription histories. Assessment yielded unexpected results showing that the majority of children in the LAMS study had not, in fact, been prescribed an antipsychotic medication.<sup>10</sup> In this sample, the only factors associated with receiving an antipsychotic were the narrowly-defined bipolar I disorder, psychotic disorders such as schizophrenia, and higher socioeconomic status. **These data do not support the troubling hypothesis at times portrayed in the media and elsewhere<sup>11,12</sup> that the rise in antipsychotic use may be driven by the broadening definition of "bipolar spectrum disorders" and subsequent rising rates of BPSD diagnoses.**

### Future Directions<sup>13</sup>

In 2010, the LAMS study was awarded a \$7.8 million renewal grant from the National Institute of Mental Health. The new funds will allow Dr. Findling and his team to continue following the original cohort of children for an additional five years. By extending the study, researchers will be able to gather data as these children age into adolescence and young adulthood—periods of greater risk for developing a bipolar spectrum disorder.

In addition to continued monitoring, researchers are also launching an innovative collaboration with colleagues in radiology and pediatrics to incorporate two neuroscience-based technologies: *neurocognitive testing* which assesses the youths' attention capacities and abilities to process new information, and *neuroimaging* which maps brain activity through functional magnetic resonance imaging (fMRI). With this new ability to examine brain functioning, researchers hope to identify markers of underlying biological mechanisms that may predispose individuals to bipolarity.

Given the opportunity for combined analysis of ESM, neurocognitive performance, functional abnormalities, and clinical outcomes over time, the LAMS study now has an enhanced capacity for developing more accurate pediatric diagnostic measures, determining the most appropriate points for intervention, and gaining a better understanding of the factors influencing mental illness trajectories.

## Implications for Policy and Practice

**Service Use** Baseline data indicate that among children experiencing elevated symptoms of mania, mental health service utilization begins at an early age (averaging 6–7 years old) and spans multiple service sectors.<sup>5</sup> **These results highlight the importance of coordination between sectors—particularly school and outpatient settings—to maximize the effectiveness and efficiency of care.** Public policy both locally and nationally has sought to strengthen the school-based connection. For instance, the Mental Health in Schools Act of 2011 seeks to provide comprehensive school mental health programs that are culturally, linguistically, and age appropriate. Locally, the Ohio Mental Health Network for School Success (OMHNSS) facilitates school-community-family collaboration on issues of student mental health, and the Effective Practice Integration Council (EPIC) supports school-based mental health services through partnerships between school districts and several Ohio universities. Both programs have received funding from the U.S. Substance Abuse and Mental Health Services Administration (SAMHSA), and are working to document the effectiveness of school-based mental health services and encourage evidence-based practices.

**Treatment** Despite evidence that combined use of medication and psychosocial therapy is often the most effective option for youth with serious mental illnesses, a minority of enrolled children had received such combination treatment. Moreover, combination treatment was independently associated not only with the severity of the child's condition, but with non-clinical factors such as race and insurance coverage. **In addition to underscoring the need for practitioners and families to be well informed regarding the range of treatment**

**options, these findings provide motivation for proactively addressing treatment disparities.** The Patient Protection and Affordable Care Act (PPACA) addresses this need in part by requiring that mental health services be included in the essential benefits package that all qualified insurance plans provide. Lastly, given that older children in the study had a higher likelihood of hospitalization, early intervention in both outpatient and school settings may help to avert later hospitalization and to reach those children who are receiving suboptimal care or no treatment at all.<sup>5</sup> With its emphasis on prevention, the PPACA supports this need as well.

**Diagnosis** Persistently elevated scores on the Parent General Behavior Inventory 10-Item Mania Scale (PGBI-10M) were shown to be fairly specific predictors of a bipolar diagnosis, with two assessments separated by as little as 3 weeks being more predictive than a single assessment.<sup>9</sup> **These results are directly applicable in clinics that routinely administer broad-band screening tests such as the Child Behavior Checklist. Children with high scores on the Externalizing scale (indicating hyperactivity and aggression) could be followed-up with two administrations of the PGBI-10M before being referred for a more specialized bipolar assessment.** This process would filter specialist referrals and increase screening specificity. LAMS researchers recommend using a "diagnostic likelihood ratio" approach for BPSD based on the two PGBI scores. Analogous to a weather report, such an approach may be used as a guide which, though not fail-safe, would improve the consistency and accuracy of test result interpretation and reduce the risk of overdiagnosis.

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