Characteristics of Children With Elevated Symptoms of Mania: The Longitudinal Assessment of Manic Symptoms (LAMS) Study

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Objective: The aim of the Longitudinal Assessment of Manic Symptoms (LAMS) study is to examine differences in psychiatric symptomatology, diagnoses, demographics, functioning, and psychotropic medication exposure in children with elevated symptoms of mania (ESM) compared to youth without ESM. This article describes the initial demographic information, diagnostic and symptom prevalence, and medication exposure for the LAMS cohort that will be followed longitudinally.

Method: Guardians of consecutively ascertained new outpatients 6 to 12 years of age presenting for treatment at one of 4 university-affiliated mental health centers were asked to complete the 10-item Parent General Behavior Inventory Short Form (P-GBI-SF **[AU1]**). Patients with scores ≥ 12 on the P-GBI-SF (ESM+) and a matched sample of patients who screened negative (ESM–) were invited to participate.

Results: 707 children (621 ESM+, 86 ESM–; mean [SD] age = 9.4 [2.0] years) were evaluated. The ESM+ group, compared to the ESM– group, more frequently met *DSM-IV* criteria for a mood disorder ($P < .001$), bipolar spectrum disorders (BPSD; $P < .001$), and disruptive behavior disorders ($P < .01$). Furthermore, they showed poorer overall functioning and more severe manic, depressive, attention-deficit/hyperactivity, disruptive behavioral, and anxiety symptoms. Nevertheless, rates of BPSD were relatively low in the ESM+ group (25%), with almost half of these BPSD patients (12.1% of ESM+ patients) meeting *DSM-IV* criteria for bipolar disorder not otherwise specified. ESM+ children with BPSD had significantly more of the following: current prescriptions for antipsychotics, mood stabilizers, and anticonvulsants; psychiatric hospitalizations; and biological parents with elevated mood. ESM+ children with BPSD were also lower functioning compared to ESM+ children without BPSD.

Conclusions: Although ESM+ was associated with higher rates of BPSD than ESM–, 75% of ESM+ children did not meet criteria for BPSD. Results suggest that longitudinal assessment is needed to examine which factors are associated with diagnostic evolution to BPSD in children with elevated symptoms of mania.

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Evidence that elevated symptoms of mania (ESM) are present in a substantial number of children seeking psychiatric care continues to build.[1–4] Although a portion of children with ESM may meet strict *DSM-IV* criteria for bipolar disorder type I or II, many do not. For example, a study[5,6] of inpatient children found that a relatively high proportion (62.5%) experienced *DSM-III-R* symptoms of mania (defined as euphoria and/or irritability plus 3 of the remaining 5 symptoms on the mania symptom subscale from the Child Symptom Inventory-4R).[6,5] However, of those children with manic symptoms, only a small number met criteria for a bipolar disorder.

Furthermore, the clinical implications of ESM in children are unclear because the presence of manic symptoms does not necessarily mean that a bipolar diagnosis is inevitable.[3,7–9] In one sample of 9- to 13-year-old males meeting *DSM-III-R* criteria for attention-deficit/hyperactivity disorder (ADHD) and manic symptoms, no participants met criteria for a bipolar disorder at 6-year follow-up.[8] In one of the few published epidemiologic studies,[10] adolescents originally reporting some manic symptoms (defined as experiencing a distinct period of abnormally and

persistently elevated, expansive, or irritable mood without meeting diagnostic criteria for a bipolar disorder) rarely developed a bipolar disorder in the 6- to 10-year follow-up period.

Although relatively little is known about the phenomenology, course of illness, or symptom evolution of youth who experience ESM but do not meet *DSM-IV* criteria for a bipolar diagnosis, it appears that inpatient children with manic symptoms experience marked psychosocial dysfunction and a high degree of psychopathology regardless of bipolar diagnostic status.[3,56]

Although there is currently no clear means of distinguishing which children with ESM will eventually develop bipolar disorder, determination of a reliable method is a priority due to the important implications of assigning such a diagnosis to a child. For example, the diagnosis of bipolar disorder implies a lifelong, heritable condition, with psychological and social sequelae for both the child and his or her family. Youth who are assigned a bipolar diagnosis in error may receive inappropriate treatments for years, particularly unnecessary psychotropic medications that carry significant risks. On the other hand, failure to appropriately assign a bipolar spectrum disorder (BPSD) diagnosis may result in a lack of appropriate treatment and prolonged suffering. Thus, making an accurate diagnosis regarding the presence or absence of bipolarity in a child manifesting ESM~~MS~~ has important clinical implications. However, even in adults who have putatively more prototypical presentations of bipolar disorder, there are studies showing that many years typically elapse from the onset of mood symptoms until the correct ~~BP~~ bipolar diagnosis is made.[11,12]

Recent data from the National Ambulatory Medical Care Survey (1999–2003) indicated that over 90% of youth who were given a diagnosis of bipolar disorder in office-based clinical settings received a psychotropic medication for this diagnosis.[13] However, data regarding medication treatment of children with ESM, regardless of diagnosis, are limited. Due to the presence of symptoms that might be construed as indicative of a bipolar diathesis, it is possible that these children may receive medications indicated for patients with more narrowly defined bipolarity. According to treatment recommendations and practice parameters, children with a bipolar disorder may be prescribed atypical antipsychotics, frequently in combination with a mood stabilizer.[14,15] Although these agents may be beneficial to some patients, they also may be associated with substantive risks.

The National Institute of Mental Health–supported Longitudinal Assessment of Manic Symptoms (LAMS) study was designed to prospectively follow an epidemiologically ascertained cohort of children with ESM, as well as a comparison group of outpatient children without ESM, both to delineate the relationship between manic symptoms and bipolarity and to carefully define the characteristics of children with ESM. This article describes the initial demographic information, diagnostic and symptom prevalence, and medication exposure for the LAMS cohort that will be followed longitudinally.

METHOD

Institutional review boards at each of the 4 university-affiliated LAMS sites (Case Western Reserve University, Cincinnati Children's Medical Center, the Ohio State University, and the University of Pittsburgh Medical Center/Western Psychiatric Institute and Clinic) reviewed and approved all procedures in the protocol. Written informed consent from parents/guardians and assent from participants were obtained before any study-related procedures were performed. Parents consented to complete the screening procedure described in the next section, and parents consented and children assented to participate in the longitudinal portion of the study.

Participant Ascertainment

Parents/guardians of all eligible children between the ages of 6 years, 0 months, and 12 years, 11 months, who were new patients to LAMS outpatient clinics (see inclusion and exclusion criteria) were asked to complete the 10-item Parent General Behavior Inventory Short Form (P-GBI-SF)[16,17] to screen for ESM based on their child's behavior over the past 6 months. The items that comprise the P-GBI-SF describe hypomanic, manic, and biphasic symptomatology and have been reported to discriminate bipolar disorder in youth from other diagnoses.[17] Each item is scored from 0 ("never or hardly ever") to 3 ("very often or almost constantly"); total scores range from 0 to 30, with higher scores indicative of greater symptomatology. Each patient whose parent/guardian rated the child at or above a score of 12 (ESM+) on the 10-item P-GBI-SF was invited to participate in the longitudinal portion of the LAMS study. In addition, a smaller comparison group of patients who scored 11 or lower (ESM–) roughly matched in real time on age, sex, race, ethnicity, and Medicaid status was selected to enroll in the longitudinal portion of the study. More details concerning subject ascertainment and the rationale for the cut score of 12 on the P-GBI-SF are described in detail in Horwitz et al.[4]

To be screened for the study, patients must (1) not have received mental health treatment in the outpatient clinics where the LAMS study was being conducted within the past 12 months; (2) be between the ages of 6

years, 0 months, and 12 years, 11 months; (3) speak English; (4) have an accompanying parent/guardian who speaks English; and (5) not have a sibling or other child living in the same household who had already participated in screening for possible LAMS participation. See Horwitz et al[4] for a detailed description of these screening and selection procedures.

Patients rated positively by their parents/guardians for ESM (scoring 12 or higher on the P-GBI-SF; ESM+) and patients not presenting with ESM selected as the comparison group (ESM–) were invited to participate in the longitudinal portion of the study. Of the 1,124 children who screened ESM+, 621, or 55%, accepted the invitation. There were no sociodemographic differences between children/families agreeing to enroll in the longitudinal study and those who did not. ESM– children were sampled with replacement (those who were approached, but refused, were replaced by another demographically matched youth in the ESM– group), resulting in 86 children without ESM also being included in the longitudinal cohort[4] (Figure 1).

Longitudinal Assessment and Follow-Up

After the children and adolescents were assessed at baseline, participants who continued to be eligible were seen every 6 months for up to 5 years. Each of these study visits lasted approximately 2 to 4 hours.

Baseline Assessment

Demographics. Information including age, sex, race, ethnicity, and health insurance status was obtained from parents/guardians. In addition, a brief medical history was collected.

Diagnoses. Children and their guardians were administered the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version~~Episode~~ (K-SADS-PL)[18] with additional depression and manic symptom items derived from the Washington University in St. Louis Kiddie Schedule for Affective Disorders and Schizophrenia ~~(WASH-U-K-SADS)~~.[19,20] Items to assess nonverbal communication, the child's relationship with others, shared enjoyment, and social-emotional reciprocity according to *DSM-IV* criteria were added to the K-SADS-PL to screen for pervasive developmental disorders. The resulting instrument, the K-SADS-PL-W, is a semistructured interview that assesses current and lifetime psychiatric diagnoses and the time course of each illness.

Unmodified *DSM-IV* diagnostic criteria were used in the LAMS study. The criteria for bipolar disorder not otherwise specified (BP-NOS) were clarified for the LAMS study to follow the same criteria used in the Course and Outcome of Bipolar Youth (COBY) Study.[21] BP-NOS was operationalized as follows: (1~~a~~) elated mood plus 2 associated symptoms of mania (eg, grandiosity, decreased need for sleep, pressured speech, racing thoughts, increased goal-directed activity, etc) or irritable mood plus 3 associated symptoms of mania; (2~~b~~) change in the participant's level of functioning (increase or decrease); (3~~c~~) symptoms must be present for a total of at least 4 hours within a 24-hour period; and (4~~d~~) the participant must have had at least 4 episodes of 4 hours' duration or a total of 4 days of the above-noted symptom intensity in his/her lifetime. All diagnoses were reviewed and confirmed by a licensed child psychiatrist or psychologist. It should be noted that once a child met criteria for a BPSD in the LAMS study, that diagnosis was always documented as a current diagnosis (although it could be listed as "in partial/full remission").

Medication history. Each child's parent/guardian provided a complete history of the child's past and currently prescribed psychotropic medications during the interview. For simplicity, some medications have been grouped according to class (anticonvulsants, antidepressants, antipsychotics, stimulants, α_2 agonists, benzodiazepines), whereas others are reported separately.

Functional assessment. The Children's Global Assessment Scale (CGAS)[22] was completed by study interviewers to provide a severity rating of participants' current impairment. The CGAS is a clinical rating scale used to document children's overall functional capacity at home, at school, and with peers over the past 2 weeks. Scores range from 1 (indicating a severely impaired child) to 100 (indicating a child with superior functioning).

Symptomatic assessment. In addition to administration of the K-SADS-PL-W, which ascertained presence or absence of manic and depressive symptoms specifically within the context of a mood episode (ie, "filtered" ratings), "unfiltered" ratings of apparent mood symptoms were also assessed via both parental self-report and clinical rating scales. These unfiltered ratings did not require clinical judgment about the reasons for symptoms to be manifest. Because a key aspect of the LAMS study is the assessment of symptoms, regardless of etiology, over time, these unfiltered ratings were obtained to complement those assessments of affective illness that were manifest only during the presence of a mood disorder.

Unfiltered mania ratings were obtained via parental self-report of their child's functioning over the past 6 months on the P-GBI-SF and via direct interview of parents and children regarding the past 2 weeks using the Young Mania Rating Scale (YMRS)[23] via interview with both the child and parent. Total scores on this 11-item scale range from 0 (no manic

symptoms) to 60. The YMRS has demonstrated good reliability[24] and good ability to discriminate bipolar spectrum disorders from ADHD.[25–27]

Unfiltered depression ratings were obtained via direct interview of parents and children regarding the past 2 weeks using the Children's Depression Rating Scale-Revised (CDRS-R).[28,29] The CDRS-R is a 17-item scale administered as an interview with the child and parent. The instrument has demonstrated good validity and psychometric properties.[28,29] CDRS-R scores range from 17 to 113, with higher scores being indicative of greater depressive symptomatology.

The Child and Adolescent Symptom Inventory-4R (CASI-4R)[30] contains items reflecting *DSM-IV* criteria for emotional and behavioral disorders in children and adolescents. Parent-reported scores on the ADHD, oppositional defiant disorder, and conduct disorder subscales were examined. Frequency of symptoms and the frequency of symptom-related impairment over the past 6 months are scored on a scale of 0 (never) to 3 (very often). The CASI-4R has demonstrated satisfactory internal consistency, test-retest reliability, and convergent/discriminant validity with corresponding scales of the Child Behavior Checklist and the Conners' Parent Rating Scale.[31]

The parent-completed Screen for Child Anxiety Related Emotional Disorders (SCARED-P)[32] quantified symptoms of anxiety over the past 6 months. The SCARED measures 5 aspects of anxiety: (1) panic/somatic, (2) generalized anxiety, (3) separation anxiety, (4) social phobia, and (5) school phobia. The 41 SCARED items are rated from 0 (not true or hardly ever true) to 2 (very true to often true). The SCARED has shown good internal consistency ($\alpha \sim 0.90$)[33] and excellent discriminant validity between children with anxiety disorders and children with nonanxiety psychiatric disorders (all *P* values $\leq .05$).[33]

The Family History Screen[34] was obtained to collect information on 15 psychiatric disorders and suicidal behavior in biological parents. As family history will be described in more detail at a later time, this article only examines presence or absence of elevated mood, defined as a report of ever having experienced a period of feeling extremely happy or high by the youth's biological mother or father.

Interviewer Training and Interrater Reliability

LAMS interviewers were trained in 3 parts: during a 3-day start-up meeting, by rating along with taped interviews, and by leading administrations of the assessment instruments. To prevent rater drift following training, interviewers rated taped administrations of the K-SADS-PL-W, CDRS-R, and the YMRS. The κ for K-SADS-PL-W psychiatric diagnoses was 0.82. More specifically, the κ for bipolar diagnoses was 0.93. In addition, the κ for the CDRS-R and the YMRS were 0.47 and 0.41, respectively, which are within the acceptable levels of item level–weighted κ values suggested in the literature.[35]

Statistical Analyses

Fisher exact tests were used to test for possible differences in distribution of sex, race, ethnicity, Medicaid status, intact families, rates of special education placement, psychiatric hospitalization, *DSM-IV* psychiatric diagnoses, family history of elevated mood, and current and past medications in the ESM+ versus ESM– groups and in the ESM+ group with versus without BPSD. Independent *t* tests were used to examine differences in CGAS, YMRS, P-GBI-SF, CDRS-R, CASI-4R, and SCARED-P scores between ESM+ and ESM– groups and ESM+ youth with versus without BPSD.

The α level for statistical significance was set at $P \leq .05$. It was not adjusted for multiple comparisons performed due to the exploratory nature of this work.

RESULTS

Participant Characteristics

Demographics for the 707 participants appear in Table 1. Compared to ESM– participants, ESM+ participants were significantly less likely to be living in intact families and had significantly lower CGAS scores, indicative of poorer overall functioning. As ESM+ and ESM– participants had been matched on demographic variables, these 2 groups did not differ significantly in regard to age, sex, race (white vs other races), ethnicity (Hispanic vs non-Hispanic), or whether they received public insurance (compared to all other insurance groups). Moreover, the ESM+ and ESM– groups did not differ in the proportion having received special education or in the number of prior psychiatric hospitalizations (see Table 1).

DSM-IV Psychiatric Disorders

Current diagnoses (as defined by *DSM-IV* criteria) and symptoms at baseline appear in Tables 2–45. Fourteen participants (9 [1.4%] ESM+ and 5 [5.8%] ESM–) did not meet criteria for a current *DSM-IV* diagnosis. The ~~average~~ mean number of current diagnoses at baseline was 2.5 (SD = 1.3). Members of the ESM+ group had more diagnoses (mean = 2.6, SD=1.3) than the ESM– comparison group (mean = 2.0, SD=1.2; $t_{705} = 3.95$, $P \leq .001$).

Mood disorders and mood symptoms. As shown in Table 2, when compared to ESM– youth, the ESM+ group more frequently met *DSM-IV* criteria for a mood disorder and bipolar spectrum disorders and had significantly higher YMRS scores at baseline. As expected, the mean P-GBI-SF score in the ESM+ group

was significantly greater than in the ESM– group. While ESM+ and ESM– groups did not differ significantly in the rate of depressive disorders, the ESM+ group received significantly higher CDRS-R scores over the previous 2 weeks (see Table 2).

ADHD and disruptive behavior disorders. ESM groups did not differ significantly in rates of current ADHD, but the ESM+ group scored significantly higher on all 3 CASI-4R ADHD subscales (see Table 3). In addition, compared to the ESM– group, the ESM+ group reported more disruptive behavior disorders (53.1% vs 36.0%) and higher oppositional defiant disorder and conduct disorder subscale scores on the CASI-4R (see Table 3).

Other psychiatric disorders. Table 4 provides comparisons of psychotic, anxiety, adjustment, and pervasive developmental disorders between groups. There was a trend for the ESM– group to have a greater rate of pervasive developmental disorders (11.6%) compared to the ESM+ group (5.6**[AU2]**%). ESM+ and ESM– groups did not differ significantly in the occurrence of psychotic disorders, anxiety disorders, or adjustment disorders. However, SCARED-P total scores were higher in the ESM+ group than in the ESM– group, indicative of more anxiety symptoms over the previous 6 months. Of note, no participants met *DSM-IV* criteria for a substance use disorder.

Psychotropic Medication Exposure

Currently prescribed and past trials of psychotropic medications for participants appear in Table 5. At baseline, 63% (n = 443) of the youth were prescribed at least 1 psychotropic medication. Neither current nor past prescription rates differed significantly for ESM+ and ESM– groups (current: ESM+ vs ESM–, mean [SD] = 1.1 [1.1] vs 1.0 [1.0]; $t_{705} = 0.38$, $P = .71$; past: ESM+ vs ESM–, mean [SD] = 1.4 [2.0] vs 1.6 [2.1]; $t_{705} = 0.62$, $P = .53$). Similarly, prescription rates for specific categories of medication (lithium, anticonvulsants, antidepressants, antipsychotics, stimulants, or α_2 agonists) did not differ between groups (see Table 5).

ESM+ With Bipolar Disorder Versus ESM+ Without Bipolar Disorder

Table 6 includes the comparisons of demographics, family history, diagnoses, currently prescribed medication groups, and current mood symptoms for ESM+ participants with and without BPSD. As shown in Table 6, ESM+ participants with BPSD had more psychiatric hospitalizations and were older, lower functioning, and more likely to have biological mothers and fathers with elevated mood (ever experienced a period of feeling extremely happy or high) than ESM+ participants without BPSD. In addition, ESM+ youth with BPSD had a higher rate of currently prescribed antipsychotics, mood stabilizers, and anticonvulsants. Finally, as expected, ESM+ youth with BPSD had higher scores on all unfiltered mood symptom ratings (P-GBI-SF, YMRS, and CDRS-R). However, ESM+ youth without a BPSD had more current disruptive behavior disorders (conduct disorder, oppositional defiant disorder, and/or disruptive behavior not otherwise specified).

DISCUSSION

These findings underscore several crucial points. First, ESM appear to be a common concern in outpatient psychiatric settings, consistent with emerging literature about the relatively high rate of manic symptoms in other studies. Second, ESM are associated with substantially increased rates of bipolar disorder, which is why measures assessing ESM may prove useful as screening aids.[17,36] Third, ESM are associated with other, nonbipolar diagnoses and/or may be a marker of severe pathology rather than a specific marker of a bipolar diathesis.

In the 707 children and adolescents of the LAMS cohort, the diagnoses most frequently assigned at baseline were ADHD (76.1%), other disruptive behavior disorders (51.1%), mood disorders (40.5%), and anxiety disorders (31.3%). Further, the entire cohort had high rates of comorbidity. Of note is that the ESM+ group met criteria for more diagnoses and had poorer overall functioning than the ESM– group. Furthermore, preliminary results indicate that ESM+ youth with BPSD have lower overall functioning, and more psychiatric hospitalizations, and were more likely to have parents with elevated mood compared to ESM+ youth without BPSD.

Similar to the children described by Carlson and Kelly,[56] many youth who were identified as experiencing ESM did not meet diagnostic criteria for BPSD. Whether or not these children with ESM will eventually develop a bipolar diagnosis, either confirming or refuting the findings of Lewinsohn et al[10] and Hazell et al[8] that no or few youth with manic symptoms will later develop BPSD, will be assessed through longitudinal assessments of this study cohort. This question is a key specific aim of the LAMS study.

As expected, there were some differences in rates of diagnoses between the ESM groups. For instance, ESM+ youth were diagnosed with more bipolar spectrum disorders than those in the ESM– group. However, only one-quarter of youth with ESM actually met diagnostic criteria for a BPSD. (Interestingly, most of that quarter of ESM+ children with BPSD met diagnostic criteria for either BP-NOS [48%] or bipolar I [43%], with very few meeting criteria for bipolar II or cyclothymia.) ESM+ youth were, in fact, more likely to have a disruptive behavior disorder diagnosis than a

bipolar diagnosis. More specifically, over half of the ESM+ group was diagnosed with a disruptive behavior disorder, primarily oppositional defiant disorder, compared to only 36% of the ESM– group.

The ESM+ and ESM– groups did not differ significantly in the number of youth currently diagnosed with a depressive disorder, ADHD, or anxiety disorder. Despite this lack of categorical differences between groups, parents of children in the ESM+ group endorsed significantly greater depressive, ADHD, and anxiety symptoms on the CASI-4R and SCARED-P compared to the ESM– group. This suggests the ESM+ group is more symptomatic across a variety of domains even if these symptoms do not (yet) translate to significantly more diagnoses within those domains.

With such diagnostic diversity found in the ESM+ group, it may be argued that the P-GBI-SF cut score was set too low. However, the P-GBI-SF cut score of 12 for the ESM groups was purposely set to keep sensitivity to true bipolar cases high and also capture a large number of other cases showing similar symptoms for different diagnostic reasons. The second, heterogeneous group will be the more interesting one to follow longitudinally.

Not surprisingly, with over three-fourths of LAMS participants meeting diagnostic criteria for ADHD, stimulants were the most frequently prescribed class of current and past medication. However, with 76% of the overall sample having an ADHD diagnosis, only 39% of the LAMS cohort was currently prescribed a stimulant. Antipsychotic medications were prescribed at a relatively high rate, with nearly a quarter (22%) of all 707 LAMS participants prescribed an antipsychotic at the time of assessment. Although ESM+ and ESM– groups differed in the rates of bipolar spectrum disorders and disruptive behavior disorders, neither current nor past exposure to any medication class examined in this study differed significantly between the groups. However, in the ESM+ group, those children with BPSD were prescribed significantly more antipsychotics (41% vs 17%), anticonvulsants, and mood stabilizers compared to ESM+ participants without BPSD. Finally, although approximately 30% of the participants were diagnosed with an anxiety disorder and 18% of the youth met criteria for a depressive disorder, rates of current selective serotonin reuptake inhibitor (SSRI) prescriptions were relatively low (8.9%). This modest rate may reflect the effect of the Black Box warning for SSRIs.[37] A more detailed examination of community-based prescribing practices is warranted in future examinations of the LAMS study sample.

When examining the ESM+ group, the fact that the children without a bipolar disorder had a greater rate of disruptive behavior disorders supports the possibility that there are 2 main paths that lead to ESM+: (1) having a bipolar disorder and (2) having disruptive behavior disorders and some mood symptoms without meeting diagnostic symptoms criteria for a bipolar disorder.

Limitations

Limitations of this study include the fact that the sample of children was obtained only from outpatient mental health centers associated with university partners. Therefore, the sample does not include children whose parents sought care in other settings or who were currently hospitalized. The sample was focused in Ohio and western Pennsylvania and might not reflect outpatient mental health services utilization patterns in other regions. Further, given that these were all children and families seeking care, they are not representative of the general population of children.

Clinical Implications

Although ESM may be commonly found in children and adolescents, this does not necessarily indicate that BPSDs are common in youth. In fact, the children and adolescents in the ESM+ group were more likely to have an ADHD and/or disruptive behavior disorder rather than a BPSD. Screening for ESM did increase the base rate of BPSD to a quarter of the sample, however, higher than would be anticipated in a general outpatient clinic.[38]

In conclusion, although LAMS participants were selected based on the presence of ESM, their subsequent structured interviews revealed a diverse range of psychiatric disorders. Furthermore, while ESM were associated with higher rates of BPSD, most of these youth did not meet diagnostic criteria for BPSD. Rather, ESM+ youth more commonly had a disruptive behavior disorder. Perhaps most surprising is the fact that the ESM+ youth did not differ from ESM– youth in number of psychotropic medications, a finding that warrants further investigation. The data will provide the opportunity to examine medication use in youth with considerable psychiatric morbidity. Results suggest that the longitudinal assessment of ESM is needed to examine which factors are associated with diagnostic evolution to a bipolar spectrum disorder in patients with ESM and whether such evolution even occurs. Longitudinal data are also needed to identify risk and protective factors associated with long-term outcomes in this vulnerable population.

Drug*[AU3] *names: aripiprazole (Abilify), atomoxetine (Strattera), bupropion (Wellbutrin, Aplenzin, and others), buspirone (BuSpar and others), clonidine (Catapres, Duraclon, and others), clozapine (FazaClo, Clozaril, and others), diphenhydramine (Benadryl and others), guanfacine (Intuniv, Tenex, and others), hydroxyzine (Vistaril and others), lisdexamfetamine (Vyvanse), lithium (Lithobid and others), methylphenidate (Focalin, Daytrana,

and others), mirtazapine (Remeron and others), olanzapine (Zyprexa), paliperidone (Invega), quetiapine (Seroquel), risperidone (Risperdal and others), trazodone (Oleptro and others), venlafaxine (Effexor and others), ziprasidone (Geodon).

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Figure 1. Ascertainment of Subjects for the Longitudinal Assessment of Manic Symptoms (LAMS) Study

Abbreviations: ESM = elevated symptoms of mania, P-GBI-SF = Parent General Behavior Inventory Short Form.