Long-Term Implications of Early Onset in Bipolar Disorder: Data from the First 1000 Participants in the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD)

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Background: *Early onset of mood symptoms in bipolar disorder has been associated with poor outcome in many studies; however, the factors that might contribute to poor outcome have not been adequately investigated.*

Methods: *The first consecutive 1000 adult bipolar patients enrolled in the National Institute of Mental Health's Systematic Treatment Enhancement Program for Bipolar Disorder were assessed at study entry to determine details of their age of onset of mood symptoms. Clinical course, comorbidity, and functional status and quality of life were compared for groups with very early (age < 13 years), early (age 13–18 years), and adult (age > 18 years) onset of mood symptoms.*

Results: *Of 983 subjects in whom age of onset could be determined, 272 (27.7%) experienced very early onset, and 370 (37.6%) experienced early onset. Earlier onset was associated with greater rates of comorbid anxiety disorders and substance abuse, more recurrences, shorter periods of euthymia, greater likelihood of suicide attempts and violence, and greater likelihood of being in a mood episode at study entry.*

Conclusions: *Very early or early onset of bipolar disorder might herald a more severe disease course in terms of chronicity and comorbidity. Whether early intervention might modify this risk merits further investigation.*

Key Words: Bipolar disorder, age of onset, quality of life, comorbidity

The complex variation of clinical presentations in bipolar disorder has been widely acknowledged (Lenox et al 2002). This heterogeneity hinders attempts to determine prognosis, to define effective treatments, and to elucidate genetic and other factors that might contribute to disease development. Age at illness onset represents one clinical marker that might be useful in defining more homogeneous subgroups in bipolar disorder. Indeed, early onset of illness has been suggested as a marker of greater genetic loading in bipolar disorder (Bellivier et al 1998; McMahon et al 1994; Pauls et al 1992; Somanath et al 2002; Strober et al 1988; Taylor and Abrams 1981), perhaps indicative of a unique mode of inheritance (Grigoroiu-Serbanescu et al 2001).

Three 2-year follow-up studies suggest that early-onset bipolar disorder is associated with a more severe disease course, though definitions of outcome and "early onset" varied (Carlson et al 2002; Geller et al 2002; Tohen et al 2000). A 5-year prospective follow-up study (Strober et al 1995) suggested recurrence rates similar to those seen in adult studies (Keller et al 1993). With longer-term follow-up, however, the difference in outcome might be less clear. Three smaller studies with follow-up of 10 years or more suggested relatively good long-term outcome for adolescent-onset bipolar patients (Bashir et al 1987; Jarbin et al 2003; McGlashan 1988).

In addition, the clinical differences among early-onset bipolar patients that might contribute to overall poor outcome in some samples are not well characterized. Early age of onset could simply indicate greater overall severity, or it could predispose the patient to other features of illness course that contribute to poor outcome. For example, early onset has been associated with increased risk for suicide attempt (Bellivier et al 2001; Tsai et al 1999), poorer lithium response (Schurhoff et al 2000), more psychotic features (Bellivier et al 2001; McGlashan 1988; Schurhoff et al 2000), more mixed episodes (Schurhoff et al 2000), greater rates of neuropsychological dysfunction (Taylor and Abrams 1981), and greater comorbidity with panic disorder (Schurhoff et al 2000) or drug or alcohol abuse (Bashir et al 1987). The independent relationship between these features and outcome in terms of functional status or quality of life is rarely assessed in age-of-onset studies. If the factors associated with early onset that contribute to poorer outcome could be identified, they might suggest more specific approaches to early intervention to limit the morbidity of early-onset bipolar disorder (Conus and McGorry 2002).

Therefore, to clarify the relationship of age of onset with long-term outcome, we examined the prevalence and clinical implications of early and very-early onset in bipolar disorder, assessed retrospectively. In a large cohort of systematically evaluated subjects participating in a multicenter study of bipolar disorder, we compared early-onset groups with an adult-onset group in terms of retrospective measures of disease course, comorbidity, and functional and quality of life measures. We hypothesized that, consistent with previous shorter-term fol-

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Received September 9, 2003; revised December 31, 2003; accepted January 13, 2004.

0006-3223/04/$30.00
doi:10.1016/j.biopsych.2004.01.022

low-up studies, earlier onset of illness would indeed be associated with a poorer course, particularly for the very-early-onset group, and that much of this difference could be explained by greater Axis I comorbidity.

Material and Methods

The Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) is a multicenter National Institute of Mental Health–funded project designed to evaluate the longitudinal outcome of patients with bipolar disorder. The overall study combines a large, prospective, naturalistic study and a series of randomized, controlled trials, which share a battery of common assessments (Sachs et al 2003). To enter STEP-BD, patients are required to be at least 15 years of age and to meet DSM-IV criteria (First et al 1996) for bipolar I disorder, bipolar II disorder, cyclothymia, bipolar disorder not otherwise specified (NOS), or schizoaffective manic or bipolar subtypes. Exclusion criteria are limited to unwillingness or inability to comply with study assessments or inability to give informed consent. After a complete description of the study to the participants, written informed consent was obtained. For subjects aged 15–17 years, written assent was obtained, with written informed consent obtained from a parent or legal guardian. For the present report, only patients who met lifetime criteria for bipolar I disorder, bipolar II disorder, or bipolar disorder NOS and who had completed baseline diagnostic assessments were considered. The study protocol was approved by the Institutional Review Boards of all participating institutions.

Procedures

Diagnoses were obtained by semi-structured interview by doctoral-level clinicians using the Mini International Neuropsychiatric Interview (MINI version 4.4; Sheehan et al 1998). The MINI is a brief, structured interview designed to identify the major Axis I psychiatric disorders in the DSM-IV and ICD-10. In validation and reliability studies, the MINI was compared with the Structured Clinical Interview for DSM-III-R (patient version) and found to have acceptably high validation and reliability scores.

For the present study, all clinician- and patient-rated instruments examined were collected cross-sectionally at study initiation, regardless of treatment or clinical status. Information on the course and severity of bipolar symptoms, including age of onset, history of suicide attempts, and the longest period of time euthymic ("mood has been consistently normal") in the past 2 years was elicited as part of the baseline semi-structured interview, the Affective Disorders Evaluation (ADE) (Sachs et al 2003). Measures of quality of life and functional status, including the clinician-rated Global Assessment of Functioning (GAF; First et al 1996), and the patient-rated Quality of Life Enjoyment and Satisfaction Questionnaire (QLESQ; Endicott et al 1993) and Range of Impaired Functioning Tool (LIFE-RIFT; Leon et al 1999) were also collected.

Age of onset for first depressive and first manic, hypomanic, or mixed episode was determined by the evaluator as part of the ADE. With this instrument, after establishing the presence of at least one prior or current depressive and one prior or current manic, hypomanic, or mixed episode using DSM-IV criteria, the evaluator systematically inquired about prior episodes with these or similar symptoms to determine the age of onset of the first episode of each type. As the index or presenting episode (depression or mood elevation) is not explicitly recorded, for the purposes of this analysis it was derived from the earlier of the two ages of onset (depressive and manic/hypomanic/mixed). For subjects for whom the first episode of each pole occurred at the same age, initial polarity was recorded as indeterminate.

Statistical Analysis

For all categoric variables, χ^2 tests were used to compare three groups: very early, early, and adult onset of mood symptoms. If any cell count was less than five, Fisher's exact tests were used. For continuous variables, the appropriate tests of analysis of variance (parametric or nonparametric) were used to compare the three groups. For those variables that were correlated with duration of illness, regression models were used to adjust for the effect of duration of illness. Logistic regression models were used for the analysis of any binary outcome variables, cumulative logistic regression models were used for discrete outcome variables with more than two levels, and generalized regression models were used for continuous outcome variables. For all analyses, if the overall test was found to be statistically significant ($p < .05$), pairwise post hoc comparisons were conducted. For pairwise comparisons, Bonferroni correction for multiple comparisons was performed.

Results

Demographic and Diagnostic Characteristics

Subjects in this study are drawn from the first consecutive 1000 participants in STEP-BD. For this analysis, only the 983 subjects with diagnoses of bipolar I, II, or NOS in whom age of first mood symptoms could be determined were included. Among these subjects, mean age of onset was 17.37 years (SD 8.67); 272 (27.7%) experienced very early onset, and 370 (37.6%) experienced early onset, leaving 341 (34.7%) in the adult-onset group. For the entire group, 41.2% were male, 91.5% were Caucasian, and the mean age at the time of evaluation was 40.6 years. The proportions of the group diagnosed as bipolar I, II, and NOS were 71.6%, 24.3%, and 4.1%, respectively. The first episode of mood disorder was depression in 22.2% and mania in 56.8%; for the remaining 21.0%, first depression and mania occurred within 1 year, and precise pole-of-onset was not determined.

Demographic and clinical characteristics of the three groups, based on age of onset, are presented in Table 1. Overall, the groups were similar in terms of ethnicity, gender, and bipolar subtype. Whereas age at study entry was somewhat greater in the adult-onset group, duration of illness (defined as years since onset of mood symptoms) was greatest in the very-early-onset group.

Rates of comorbid lifetime Axis I diagnoses, including anxiety disorders, substance use disorders, eating disorders, and attention-deficit/hyperactivity disorder (ADHD), are described in Table 2. In general, comorbidity was greatest in the very-early-onset group, followed by the early-onset group.

Tables 3 and 4 display features of lifetime and recent illness course. After age at study entry and duration of illness were controlled for in a multiple regression, the earlier-onset age groups remained associated with greater number of lifetime mood episodes as a whole ($\chi^2 = 13.82$, $p = .001$), as well as greater number of lifetime depressive episodes ($\chi^2 = 28.97$, $p < .0001$) and manic episodes ($\chi^2 = 12.93$, $p = .002$). Multiple regression also indicated, relative to the adult onset group, a greater likelihood of making at least one suicide attempt (adjusted odds ratio 2.85, 95% CI 1.99-4.09 for very early onset; adjusted odds ratio 1.78, 95% CI 1.28-2.46 for early onset) but not

Table 1. Demographic Features of Bipolar Patients with Prepubertal, Adolescent, and Adult Onset of Mood Symptoms

Characteristic	*df*	Statistic	*p*	First Episode at <13 y (*n* = 272)	First Episode at 13–18 y (*n* = 370)	First Episode at >18 y (*n* = 341)	Total Sample (*n* = 983)
Caucasian	2	$\chi^2 = .23$	.89	90.8%	91.9%	91.5%	91.5%
Male	2	$\chi^2 = .06$	.97	40.6%	41.5%	41.4%	41.2%
Mean Age at Entry (y)	2	KW $\chi^2 = 83.3$	<.0001[a, b]	38.3 (SD 11.9, median 38.5)	37.4 (SD 12.2, median 37.0)	45.7 (SD 12.3, median 45.0)	40.6 (SD 12.7, median 41.0)
Mean Duration of Illness at Entry (y)	2	KW $\chi^2 = 100.5$	<.0001[a,b,c]	29.6 (SD 12.2, median 30.0)	22.0 (SD 12.2, median 21.0)	19.3 (SD 12.2, median 18.0)	23.2 (SD 12.9, median 22.0)
Bipolar Subtype	4	$\chi^2 = .42$	.84				
I				72.8%	69.7%	72.7%	71.6%
II				23.9%	25.7%	23.2%	24.3%
NOS				3.3%	4.6%	4.1%	4.1%
Polarity First Episode	4	$\chi^2 = 26.6$	<.0001				
Mania				24.3%	20.8%	22.0%	22.2%
Depression				63.6%	58.7%	49.3%	56.8%
Bimodal (mania and depression within 1 y)				12.1%	20.5%	28.7%	21.0%

KW, Kruskal-Wallis; NOS, not otherwise specified.
[a] $p < .05$ for pairwise comparison of prepubertal- and adult-onset groups.
[b] $p < .05$ for pairwise comparison of adolescent- and adult-onset groups.
[c] $p < .05$ for pairwise comparison of prepubertal- and adolescent-onset groups.

a greater prevalence of psychotic features. Subjects with very early or early onset were also more likely to present in a mood episode, particularly a depressive or mixed state, and to report a greater number of mood episodes over the preceding year.

Finally, we examined three measures that capture aspects of functioning and quality of life and compared them between onset age groups with multiple regression. For these models, terms for age of onset, illness duration, clinical status at study entry, comorbid anxiety, substance use, and ADHD, and number of mood episodes in the past year were included. Onset age group [$F(2) = 3.08$, $p = .047$] represented a significant predictor of quality of life as reflected by the QLESQ, but not of functioning as reflected by the GAF or LIFE-RIFT. Overall illness duration was not significantly associated with any of the three functioning/quality-of-life measures; however, greater number of prior depressive episodes was associated with poorer functioning as measured by the LIFE-RIFT [$F(1) = 10.11$, $p = .001$].

Discussion

In this cohort of 983 subjects with bipolar disorder I, II, or NOS, 272 reported onset of mood symptoms before age 13. Early onset in general was associated with a more severe historical disease course, as reflected in greater comorbidity for most Axis I disorders, greater chronicity represented by more mood episodes and a greater proportion of days depressed, and greater lifetime risk of suicide attempts. Functioning and quality of life at study entry was significantly poorer among early- and very-early-onset subjects; this seemed to be mediated in part by chronicity and greater likelihood of being in a mood episode at study entry.

Differences between the early- and very-early-onset groups suggest that vulnerabilities to different illness features might diminish with age, but at varying rates. For alcohol and drug abuse or dependence, the similarity of early- and very-early-onset groups might indicate that the vulnerability persists through adolescence. Conversely, for panic with agoraphobia, the vulnerability might be greatest among subjects with very-early onset and diminish through adolescence.

Overall, these results are consistent with other reports of poorer course with early onset of illness observed in small, shorter-term (2-year) prospective studies. An analysis of 89 bipolar patients with early onset reported slow recovery and relapse rates of greater than 50% (Geller et al 2002). Another study, which included 159 bipolar patients, found lesser rates of syndromal and functional recovery among those with onset before age 30 (Tohen et al 2000). Finally, among 123 bipolar I patients, onset before age 19 was associated with poorer functional and clinical outcomes (Carlson et al 2002).

Our results must be reconciled with some previous longer-term studies, which generally found lesser differences or no differences between early- and later-onset bipolar patients in terms of disease course. A 5-year prospective study of 54 adolescents with bipolar disorder found recurrence rates similar to those observed in observational studies of adults (Strober et al 1995). Similarly, a prospective follow-up over a mean of 10.5 years, which included 25 bipolar patients with onset before age 19, found generally good outcomes, at least compared with early-onset schizophrenia spectrum illness (Jarbin et al 2003). Another small 10-year study of adolescent-onset bipolar disorder also reported relatively good long-term outcome, despite a "stormy" first year of illness (Bashir et al 1987). Likewise, in one 15-year follow-up study, outcomes in 35 adolescent-onset patients were as good or better than outcomes in 31 adult-onset patients (McGlashan 1988).

Apart from the larger sample size in the present study, another important difference is the separation of very-early and early onset; the significantly greater vulnerability of very-early-onset bipolar patients might have been obscured by the inclusion of adolescent-onset patients in previous studies. This cohort is also predominantly Caucasian, which might influence its generalizability.

Table 2. Comorbid Axis I Diagnoses Among Prepubertal-, Adolescent-, and Adult-Onset Bipolar Patients

Comorbid Diagnosis	Onset Age < 13 y (*n* = 272)	Onset Age 13–18 y (*n* = 370)	Onset Age > 18 y (*n* = 341)	Wald χ^2 (2 df)	*p*	Adjusted Odds Ratio (Age < 13 y vs. > 18 y)	95% CI of Odds Ratio (Age < 13 y vs. > 18 y)	Adjusted Odds Ratio (Age 13–18 y vs. > 18 y)	95% CI of Odds Ratio (Age 13–18 y vs. > 18 y)
Any Anxiety Disorder	69.2% (*n* = 180)	53.9% (*n* = 192)	38.3% (*n* = 127)	48.87	<.0001[a, b, c]	3.60	2.50–5.16	1.89	1.39–2.56
Panic w/ Agoraphobia	18.5% (*n* = 48)	11.8% (*n* = 42)	8.2% (*n* = 27)	12.72	.002[a, c]	2.59	1.52–4.40	1.52	.91–2.53
Panic w/o Agoraphobia	8.9% (*n* = 23)	9.6% (*n* = 34)	6.0% (*n* = 20)	2.47	.29	1.27	.66–2.43	1.58	.89–2.81
Agoraphobia w/o Panic	11.2% (*n* = 29)	5.1% (*n* = 18)	4.8% (*n* = 16)	10.95	.004[a, c]	2.64	1.35–5.17	1.07	.54–2.14
Social Phobia	31.2% (*n* = 81)	23.4% (*n* = 83)	13.3% (*n* = 44)	22.77	<.0001[a, b]	2.84	1.85–4.38	1.97	1.32–2.95
GAD	29.3% (*n* = 76)	18.6% (*n* = 66)	12.7% (*n* = 42)	19.61	<.0001[a, b, c]	2.68	1.73–4.18	1.55	1.02–2.37
OCD	13.5% (*n* = 35)	8.7% (*n* = 31)	7.8% (*n* = 26)	5.03	.08	1.82	1.03–3.22	1.13	.65–1.94
PTSD	27.3% (*n* = 71)	16.4% (*n* = 58)	11.2% (*n* = 37)	24.48	<.0001[a, b, c]	3.13	1.97–4.97	1.58	1.01–2.46
Alcohol Abuse/Dependence	47.3% (*n* = 123)	46.6% (*n* = 166)	31.9% (*n* = 106)	15.89	.0004[a, b]	1.73	1.22–2.46	1.82	1.33–2.49
Drug Abuse/Dependence	34.2% (*n* = 89)	33.4% (*n* = 119)	15.1% (*n* = 50)	40.86	<.0001[a, b]	3.47	2.28–5.28	2.96	2.03–4.31
Bulimia	8.1% (*n* = 21)	7.0% (*n* = 25)	2.7% (*n* = 9)	9.73	.008[a, b]	3.67	1.59–8.47	2.81	1.29–6.14
Anorexia	5.4% (*n* = 14)	4.5% (*n* = 16)	1.8% (*n* = 6)	7.35	.025[a, b]	4.07	1.47–11.29	2.74	1.05–7.10
ADHD	20.4% (*n* = 53)	7.6% (*n* = 27)	5.7% (*n* = 19)	34.41	<.0001[a, c]	4.67	2.60–8.38	1.39	.75–2.55

CI, confidence interval; GAD, generalized anxiety disorder; OCD, obsessive-compulsive disorder; PTSD, posttraumatic stress disorder; ADHD, attention-deficit/hyperactivity disorder.
[a] $p < .05$ for pairwise comparison of prepubertal- and adult-onset groups.
[b] $p < .05$ for pairwise comparison of adolescent- and adult-onset groups.
[c] $p < .05$ for pairwise comparison of prepubertal- and adolescent-onset groups.

Several limitations of this investigation should be noted. A disadvantage of the retrospective approach is that, unlike in first-episode studies, age of first episode must be determined in many cases 10 or more years after onset. Errors in recall, as well as other potential confounders, such as "effort after meaning," might distort first episodes or recognition of concurrent illness. To address recall bias, age at study entry was included in multivariate analyses. Age at study entry likewise did not seem to influence reporting of concurrent or comorbid diagnoses.

An additional complication arises in very-early-onset patients, in whom episodes might not be as distinct as in adults, and modified diagnostic criteria might be required (Leibenluft et al 2003). Various criteria for determining age of onset might differ in their reliability (Egeland et al 1987). Indeed, in our cohort, the mean age of onset is somewhat earlier than in other reports (Bellivier et al 2003), though more similar to patient self-report (Hirschfeld et al 2003). Interviewers trained in DSM-IV diagnosis using the MINI and other instruments attempted to determine with the patient the age of first episode; at a minimum, this age probably captures age of first mood symptoms sufficient to impact function, which might be a more clinically relevant concept in any case (Egeland et al 1987). In particular, it might be less vulnerable than age of first treatment or first hospitalization to Berkson's bias and thus allow a more independent assessment of comorbid illness.

A related limitation is that other features of illness course were also determined retrospectively. Particularly for the prior year, illness states might be assessed with at least moderate confidence in many patients (Judd et al 2002, 2003) Still, recognizing this concern, we intend to follow this cohort prospectively for at least 2 years.

Beyond retrospective assessment, another critical issue in integrating the results of our study with previous findings is the variability in the definition of early onset. One approach uses admixture analysis (Bellivier et al 2001, 2003; Gibbons et al 1984), in which the "best fit" to a distribution curve is determined. Using this approach, one group suggested three distributions, with mean age of onset of 16.9, 26.9, and 46.2 years (Bellivier et al 2001), and identified clinical differences between these groups; however, that analysis failed to control for the potential confounding effect of duration of illness, and it might have lacked the sample size to detect a smaller, very-early-onset group such as that which we describe. We instead elected to determine groups on the basis of thresholds likely to be clinically relevant in other respects, including onset of puberty and end of adolescence, recognizing that these thresholds are somewhat arbitrary and imperfect.

Despite these limitations, this study shows that individuals with very early onset of mood symptoms who go on to have a bipolar course might be at risk for a particularly severe course, associated with greater comorbidity, greater recurrence and chronicity, and greater risk of making a suicide attempt. In most respects, patients with early onset are intermediate in severity between very-early- and adult-onset individuals; however, in some cases (for example, with respect to lifetime substance abuse or dependence), the two earlier-onset groups are similar but distinct from the adult-onset group. This might indicate different vulnerability periods for different comorbidities: for example, patients who develop, or continue to experience, mood symptoms during adolescence might be at greater risk for substance abuse than those who develop mood symptoms later. Whether these early-onset groups represent scientifically useful distinctions for investigating genetic or other neurobiological

Table 3. Lifetime Illness Features Among Prepubertal-, Adolescent-, and Adult-Onset Bipolar Patients

Illness Feature	Onset Age < 13 y ($n = 272$)	Onset Age 13–18 y ($n = 370$)	Onset Age > 18 y ($n = 341$)	Wald χ^2 (2 df)	p	Adjusted Odds Ratio (Age < 13 y vs. > 18 y)	95% CI of Odds Ratio (Age < 13 y vs. > 18 y)	Adjusted Odds Ratio (Age 13–18 y vs. >18 y)	95% CI of Odds Ratio (Age 13–18 y vs. > 18 y)
Suicide Attempt	49.8% ($n = 132$)	37.0% ($n = 136$)	24.6% ($n = 84$)	32.58	<.0001[a, b, c]	2.85	1.99–4.09	1.78	1.28–2.46
Violence	28.6% ($n = 77$)	25.3% ($n = 94$)	15.7% ($n = 54$)	14.36	.001[a, b]	2.13	1.41–3.22	1.82	1.25–2.64
Presence of Psychotic Features	37.0% ($n = 96$)	41.2% ($n = 147$)	43.7% ($n = 141$)	2.37	.31	.93	.66–1.32	.95	.70–1.29
No. of Mood Episodes, Lifetime				13.82	.001[a, b, c]	N/A	N/A	N/A	N/A
0	1.7%	3.9%	4.2%						
1	.6%	1.6%	4.2%						
2	1.2%	6.3%	5.9%						
3	2.3%	2.8%	6.3%						
4	1.8%	3.9%	8.8%						
5–12	13.5%	22.1%	33.9%						
13–52	28.6%	28.3%	19.2%						
≥53	50.3%	31.1%	17.6%						
No. of Manic Episodes, Lifetime				12.93	.002[a, b, c]	N/A	N/A	N/A	N/A
0	.4%	.3%	1.3%						
1	4.4%	8.0%	8.8%						
2	2.8%	7.7%	12.3%						
3–4	12.1%	15.5%	20.7%						
5–9	11.2%	14.3%	23.3%						
10–20	15.7%	18.2%	16.3%						
20–50	10.0%	11.3%	4.4%						
Too many to count	43.4%	24.7%	12.9%						
No. of Depressive Episodes, Lifetime				28.97	<.0001[a, b, c]	N/A	N/A	N/A	N/A
0	0%	1.2%	5.0%						
1	2.4%	4.1%	9.7%						
2	2.4%	4.1%	7.7%						
3–4	6.9%	11.6%	19.5%						
5–9	8.9%	21.7%	18.8%						
10–20	17.0%	15.4%	16.4%						
20–50	17.4%	15.4%	7.1%						
Too many to count	44.9%	26.7%	15.8%						

CI, confidence interval; N/A, not applicable.
[a] $p < .05$ for pairwise comparison of prepubertal- and adult-onset groups.
[b] $p < .05$ for pairwise comparison of adolescent- and adult-onset groups.
[c] $p < .05$ for pairwise comparison of prepubertal and adolescent-onset groups.

Table 4. Recent Illness Course at Study Entry Among Prepubertal-, Adolescent-, and Adult-Onset Bipolar Patients

Illness Feature	Onset Age < 13 y (n = 272)	Onset age 13–18 y (n = 370)	Onset age > 18 y (n = 341)	Statistics	p
Mood State at Study Entry				χ^2 (4) = 22.12	.0002[a, b, c]
Syndromal	49.1%	40.3%	31.1%		
Depressed	27.7%	25.1%	22.3%		
Manic/hypomanic	5.5%	7.3%	4.7%		
Mixed	15.9%	7.9%	4.1%		
Subsyndromal symptoms	11.1%	9.7%	12.9%		
Recovered/Recovering	39.9%	50.0%	56.0%		
Longest Euthymia, Past 2 Years (months)	4.2	4.0	5.8	F = 6.72	.0013[a, b]
No. of Manic Episodes, Past Year	3.1	2.0	1.4	F = 12.96	<.0001[a, c]
No. of Depressive Episodes, Past Year	2.8	2.5	1.7	F = 5.15	.006[a, b]
Days Depressed, Past Year (%)	42.8%	40.2%	38.0%	F = 2.23	.11
Days Elevated, Past Year (%)	30.5%	27.1%	24.8%	F = 5.08	.006[a]
Days Irritable, Past Year (%)	43.5%	39.5%	32.8%	F = 9.66	<.0001[a, b]
Days Anxious, Past Year (%)	45.0%	42.4%	35.2%	F = 8.31	.0003[a, b]

[a] $p < .05$ for pairwise comparison of prepubertal- and adult-onset groups.
[b] $p < .05$ for pairwise comparison of adolescent- and adult-onset groups.
[c] $p < .05$ for pairwise comparison of prepubertal- and adolescent-onset groups.

factors in disease will require further study. Likewise, whether early diagnosis and treatment represent an opportunity to influence this course by reducing chronicity and addressing comorbidity merits further investigation.

This research was supported by a National Alliance for Research on Schizophrenia and Depression Young Investigator Award and a National Institute of Mental Health (NIMH) K23 Career Development Award (to RHP). This project has been funded in whole or in part with Federal funds from the NIMH, National Institutes of Health, under contract N01 MH80001.

We report no conflict of interest. Any opinions, findings, and conclusions or recommendations expressed in this publication are those of the authors and do not necessarily reflect the views of the National Institute of Mental Health. This article was approved by the publication committee of the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD).

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