National Trends in the Outpatient Diagnosis and Treatment of Bipolar Disorder in Youth

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Context: Although bipolar disorder may have its onset during childhood, little is known about national trends in the diagnosis and management of bipolar disorder in young people.

Objectives: To present national trends in outpatient visits with a diagnosis of bipolar disorder and to compare the treatment provided to youth and adults during those visits.

Design: We compare rates of growth between 1994-1995 and 2002-2003 in visits with a bipolar disorder diagnosis by individuals aged 0 to 19 years vs those aged 20 years or older. For the period of 1999 to 2003, we also compare demographic, clinical, and treatment characteristics of youth and adult bipolar disorder visits.

Setting: Outpatient visits to physicians in office-based practice.

Participants: Patient visits from the National Ambulatory Medical Care Survey (1999-2003) with a bipolar disorder diagnosis (n=962).

Main Outcome Measures: Visits with a diagnosis of bipolar disorder by youth (aged 0-19 years) and by adults (aged ≥ 20 years).

Results: The estimated annual number of youth office-based visits with a diagnosis of bipolar disorder increased from 25 (1994-1995) to 1003 (2002-2003) visits per 100,000 population, and adult visits with a diagnosis of bipolar disorder increased from 905 to 1679 visits per 100,000 population during this period. In 1999 to 2003, most youth bipolar disorder visits were by males (66.5%), whereas most adult bipolar disorder visits were by females (67.6%); youth were more likely than adults to receive a comorbid diagnosis of attention-deficit/hyperactivity disorder (32.2% vs 3.0%, respectively; P<.001); and most youth (90.6%) and adults (86.4%) received a psychotropic medication during bipolar disorder visits, with comparable rates of mood stabilizers, antipsychotics, and antidepressants prescribed for both age groups.

Conclusions: There has been a recent rapid increase in the diagnosis of youth bipolar disorder in office-based medical settings. This increase highlights a need for clinical epidemiological reliability studies to determine the accuracy of clinical diagnoses of child and adolescent bipolar disorder in community practice.

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In clinical practice, the accurate recognition and diagnosis of youth bipolar disorder may be complicated by high rates of psychiatric comorbidity and symptom overlap with other, more prevalent psychiatric disorders. Comorbid attention-deficit/hyperactivity disorder (ADHD) and oppositional defiant disorder are especially common among youth with bipolar disorder. Typical manifestations of ADHD, such as distractibility or hyperactivity, are also present in pediatric bipolar disorder. Severe irritability and mood symptoms can also occur in children and adolescents with ADHD not meeting full criteria for bipolar disorder. Other comorbidities, such as anxiety and conduct disorders, have also been reported in youth with bipolar disorder.

There is currently a dearth of information concerning national trends in the diagnosis of bipolar disorder among children and adolescents and the treatments that these young people receive. To help address this gap in the literature, we describe recent national trends that these young people receive. To help address this gap in the literature, we describe recent national trends in the volume and treatment of office-based medical visits provided to youth and adults diagnosed with bipolar disorder.

METHODS

SOURCE OF DATA

The National Ambulatory Medical Care Survey (NAMCS) is conducted annually by the National Center for Health Statistics. It samples a nationally representative group of visits to non-federally employed office-based physicians who are primarily engaged in direct patient care. The NAMCS uses a multistage probability sample design involving samples of primary sampling units (a county, a group of adjacent counties, or a standard metropolitan statistical area), physician practices within primary sampling units, and patient visits within physician practices. During 1 week, attending physicians or their office staffs complete a 1-page form about demographic, clinical, and treatment characteristics of each patient visit. Visits to other mental health care providers are not included in the survey. Following National Center for Health Statistics recommendations, we combined data from contiguous survey years to establish a larger base on which to derive estimates so as to arrive at more stable annual estimates for survey years with few annual visits. To estimate temporal trends in youth and adult bipolar disorder visits, we grouped visits in the following calendar years: years 1994 to 1995, 1996 to 1997, 1998 to 1999, 2000 to 2001, and 2002 to 2003. To compare current practice patterns in delivery of care to youth and adults with bipolar disorder, we grouped the visits from 1999 to 2003. Response rates through the years varied from 70% to 73%.

VARIABLES

Diagnoses were made by the treating physicians according to the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), and no specific training was provided. Visits were classified as bipolar mania (codes 296.0, 296.1, and 296.4), bipolar depression (code 296.5), bipolar mixed (code 296.6), and bipolar unspecified (codes 296.7-296.80 and 296.89). Although most ICD-9-CM and DSM-IV diagnoses share the same codes, there are some differences between the diagnostic systems. The ICD-9-CM includes 2 codes not present in the DSM-IV: 296.1 (manic disorder, recurrent episode) and 296.81 (atypical manic disorder). The code 296.89 includes bipolar II disorder in DSM-IV, whereas in ICD-9-CM, it refers to manic-depressive psychosis mixed type. Comorbidity was defined as visits that were given an additional code of a mental disorder: codes 290-319, 780.1, or 995.3. Up to 5 ICD-9-CM codes were specified for each patient visit.

Visits for the treatment of bipolar disorder that included psychotropic medications were classified into 5 medication groups: mood stabilizers, antipsychotics, antidepressants, benzodiazepines, and stimulants. Mood stabilizers included lithium carbonate or citrate and anticonvulsants, with anticonvulsants further subdivided into valproate and others (carbamazepine, lamotrigine, topiramate, gabapentin, oxcarbazepine, levetiracetam, and tiagabine hydrochloride). Antipsychotics included second-generation (clozapine, risperidone, olanzapine, quetiapine fumarate, ziprasidone hydrochloride, and aripiprazole) and first-generation (all other) agents. Antidepressants included tricyclics and tetracyclics, selective serotonergic reuptake inhibitors (fluoxetine hydrochloride, sertraline hydrochloride, citalopram hydrobromide, escitalopram oxalate, fluvoxamine maleate, and paroxetine hydrochloride), and other antidepressants (venlafaxine hydrochloride, bupropion hydrochloride, trazodone hydrochloride, nefazodone hydrochloride, mirtazapine, and monoamine oxidase inhibitors). Stimulants included methylphenidate hydrochloride, amphetaminamines, and pemoline. Visits including psychotherapy or counseling were coded as psychotherapy visits.

Data regarding sources of payment for the visit were collapsed into 3 non–mutually exclusive categories: public insurance (Medicare, Medicaid, and other government insurance), private insurance, and a residual category including self-payment, no charge, uncompensated care, workers’ compensation, and unknown payment source.

Data were collected on patient age, sex, race, and ethnicity as determined by physician judgment. Visits were also classified according to whether the physician had ever seen the patient before. Duration of the visit in minutes was recorded as well.

ANALYTIC STRATEGY


To estimate population bipolar disorder visit rates, we used as numerators the weighted national estimates of bipolar disorder visits for youth and adults. Denominators were derived from intercensal estimates of the populations aged 0 to 19 years (youth sample) and 20 years and older (adult sample) from the 1990 and 2000 US census data. We used these estimates to conduct trend analyses of office-based youth and adult visits with a diagnosis of bipolar disorder for years 1994 to 1995, 1996 to 1997, 1998 to 1999, 2000 to 2001, and 2002 to 2003. To estimate the proportion of bipolar disorder visits per total mental health visits, denominators were the weighted NAMCS estimates of total mental health office-based visits. Mental health visits were defined as visits with a psychiatric diagnosis, ICD-9-CM codes 290-319, 780.1, and 995.3, for the 2 age groups. To estimate the proportion of bipolar disorder visits per total office-based visits, denominators were the weighted NAMCS estimates of all office-based visits.

To examine whether the characteristics of bipolar disorder visits vary by age, we compared the treatment provided during bipolar disorder visits between the 2 age groups. Group comparisons are presented with respect to demographic and insur-
ance characteristics, comorbid diagnoses, pharmacological and psychotherapeutic management, and whether the treating physician was a psychiatrist. Because the low number of bipolar disorder visits by youth in years prior to 1999 would result in unreliable estimates, we limit our comparisons to the surveys between 1999 and 2003.

STATISTICAL METHODS

The National Center for Health Statistics weights each NAMCS visit to correct for sampling imperfections. Reported percentages are based on weighted estimates. To assess change over time in youth and adult bipolar disorder visit rates per population, we used a linear regression model with log(rate/(1−rate)) of bipolar disorder visits as the response variable and year, age group (youth vs adult), and their interaction as predictors. To assess change over time in the proportion of bipolar disorder visits over all office-based visits by children and adults, a logistic regression analysis modeled the probability of bipolar disorder visits out of all office-based visits (response variable) as a function of year, age group, and their interaction. In both models, if the interaction term was not significant, the model without the interaction term was tested. In all of the models, adults and youth without a diagnosis of bipolar disorder were the reference categories. Thus, the coefficient of the time variable reflects the rate of increase of adult bipolar disorder visits over time. The rate of increase in youth bipolar disorder visits is obtained by adding the coefficient of time and the coefficient of the interaction terms. The interaction term measures the group difference in the rate of increase in bipolar disorder visits.

The differences between youth and adult visits between 1999 and 2003 with respect to the demographic and clinical characteristics were examined using χ² tests for categorical variables and t tests for continuous variables. Logistic regression analyses were conducted to determine patient demographic and clinical factors associated with bipolar disorder diagnosis. All of the tests were 2-sided and were performed at a significance level of α = .05.

To account for the complex survey design, the SUDAAN version 9.1.3 (SAS Institute, Inc, Cary, North Carolina) statistical software packages were used to estimate means and corresponding standard errors and 95% confidence intervals for the rate estimates, as well as to conduct the logistic regression analyses.

RESULTS

TRENDS IN YOUTH AND ADULT VISITS WITH A BIPOLAR DISORDER DIAGNOSIS

In the United States, the annual number of office-based visits with a diagnosis of bipolar disorder was estimated to increase in youth from 25 (1994-1995) to 1003 (2002-2003) per 100 000 population, whereas in adults it increased from 905 (1994-1995) to 1679 (2002-2003) per 100 000 population. The linear model showed a significant interaction effect between time and age group on the bipolar disorder diagnosis visit rate per population (β = 0.73; SE = 0.13; t = 5.60; P = .001), indicating a faster increase in the bipolar disorder diagnosis visit rate per 100 000 persons in youth (β = 0.90; SE = 0.09; t = 9.80; P < .001) than in adults (β = 0.17; SE = 0.13; t = 1.86; P = .11) during the study period.

The percentage of visits with a mental disorder diagnosis that were for a diagnosis of bipolar disorder increased among youth from 0.42% (1994-1995) to 6.67% (2002-2003) and among adults from 4.77% (1994-1995) to 6.58% (2002-2003). As a percentage of total office-based visits, visits with a diagnosis of bipolar disorder increased among youth from 0.01% (1994-1995) to 0.06% (1996-1997), 0.15% (1998-1999), 0.29% (2000-2001), and 0.44% (2002-2003), and among adults from 0.31% to 0.32%, 0.38%, 0.50%, and 0.50% during the same periods, respectively. Based on the logistic regression analysis, there was also an interaction effect between age group and year (β = 0.53; SE = 0.11; t = 4.82; P < .001), indicating that the bipolar disorder diagnosis visit rate per total office-based visits increased faster in youth than in adults during the study period. Over all of the office-based clinical visits during 1994 to 2003, for every 2 years, the log odds of the bipolar disorder diagnosis visit rate for youth increased by 0.67 (β = 0.67; SE = 0.10; t = 6.59; P < .001), whereas they increased by 0.14 for adults (β = 0.14; SE = 0.03; t = 3.36; P = .007). As a result, the odds ratio between adults and youth with respect to the proportion of visits with bipolar disorder diagnosis per office-based visits changed from 26.8 (95% confidence interval, 10.0-72.2) in 1994 to 1995 to 1.2 (95% confidence interval, 0.7-1.9) in 2002 to 2003.

DEMOGRAPHIC AND CLINICAL CHARACTERISTICS COMPARISON BETWEEN YOUTH AND ADULTS

Between 1999 and 2003, 154 visits to physicians by youth and 808 visits by adults in which a diagnosis of bipolar disorder was received were sampled, representing 763 visits per 100 000 population for youth and 1602 visits per 100 000 population for adults. Approximately two-thirds of the youth bipolar disorder visits were by males, whereas roughly two-thirds of the adult bipolar disorder visits were by females. There were no significant age group differences in the other demographic characteristics. In both groups, most visits were by patients who were white, had previously seen the physician, and paid for the visit with private insurance. Psychiatrists provided care in most vis-
its by both patient age groups. Overall, comorbid mental disorders were as frequent in youth bipolar disorder visits as in adult bipolar disorder visits (Table 1).

In the logistic regression model conducted to determine patient demographic and clinical factors associated with bipolar disorder diagnosis among youth, male sex was associated with an increased likelihood of bipolar disorder diagnosis (odds ratio, 1.93; 95% confidence interval, 1.30-2.87; \( P = .001 \)). After controlling for ADHD, the effect of sex on youth bipolar disorder diagnosis achieved only marginal significance (\( P = .05 \)).

**TREATMENT PROVIDED DURING OFFICE-BASED PHYSICIAN VISITS**

Most visits by both youth and adult patients with a diagnosis of bipolar disorder included the prescription of at least 1 psychotropic medication. The 2 age groups were also similar with respect to visit duration and the proportion of visits that included psychotherapy. Youth and adults received a mood stabilizer in approximately two-thirds of the visits. Anticonvulsants were the mood stabilizers most frequently prescribed in both samples. A similar proportion of youth and adults received a prescription of an antidepressant. Approximately one-third of the visits with antidepressant prescriptions in both age groups did not include prescription of a mood stabilizer. There were no significant differences in the proportions of youth and adult bipolar disorder visits that included a prescription of antipsychotics, although atypical antipsychotics were prescribed proportionately more frequently to youth. Stimulants were prescribed approximately a 7 times greater proportion of youth than adult bipolar disorder visits. By contrast, benzodiazepines were prescribed in approximately a 5 times greater proportion of adult than youth bipolar disorder visits. About 6 in 10 visits in both age groups with bipolar disorder diagnosis included prescription of a combination medication regimen (Table 2).

There has been a recent national increase in the number of office-based visits with a diagnosis of bipolar disorder, with an especially impressive increase among visits by younger patients. While the diagnosis of bipolar disorder in adults increased nearly 2-fold during the 10-year study period, the diagnosis of bipolar disorder in youth increased approximately 40-fold during this period.

The impressive increase in the diagnosis of childhood and adolescent bipolar disorder in US office-based practice indicates a shift in clinical diagnostic practices. In broad terms, either bipolar disorder was historically underdiagnosed in children and adolescents and the problem has now been rectified, or bipolar disorder is currently being overdiagnosed in this age group. Without independent systematic diagnostic assessments, we cannot confidently select between these competing hypotheses.

It is possible that pediatric bipolar disorder, previously underdiagnosed, is now being appropriately recognized at earlier ages. The median age at onset of bipolar disorder has been located between ages 19 and 23 years, indicating that in 50% of patients, the illness starts at a younger age. Long delays in treatment seek-
Table 2. Treatment Provided to Youth and Adult Patients With Bipolar Disorder During Office-Based Physician Visits, 1999-2003a

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Youth Bipolar Disorder Visits (n=154)b</th>
<th>Adult Bipolar Disorder Visits (n=808)b</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. (%)</td>
<td>95% CI</td>
</tr>
<tr>
<td>Any psychotropic medication</td>
<td>141 (90.6)</td>
<td>82.3-95.2</td>
</tr>
<tr>
<td>Mood stabilizer</td>
<td>93 (60.3)</td>
<td>49.7-70.0</td>
</tr>
<tr>
<td>Lithium</td>
<td>21 (12.4)c</td>
<td>7.2-20.6</td>
</tr>
<tr>
<td>Any anticonvulsant</td>
<td>75 (49.0)</td>
<td>37.5-60.5</td>
</tr>
<tr>
<td>Valproate</td>
<td>44 (30.6)</td>
<td>21.2-42.0</td>
</tr>
<tr>
<td>Other</td>
<td>31 (18.4)</td>
<td>11.7-27.6</td>
</tr>
<tr>
<td>Antidepressant</td>
<td>55 (34.0)</td>
<td>26.5-42.4</td>
</tr>
<tr>
<td>Antipsychotic</td>
<td>74 (47.7)</td>
<td>36.0-59.7</td>
</tr>
<tr>
<td>Benzodiazepine</td>
<td>8 (5.2)c</td>
<td>2.2-11.6d</td>
</tr>
<tr>
<td>Stimulant</td>
<td>57 (36.0)</td>
<td>25.9-47.5d</td>
</tr>
<tr>
<td>Any psychotropic combination</td>
<td>104 (62.7)</td>
<td>51.0-73.1</td>
</tr>
<tr>
<td>Mood stabilizer + antidepressant</td>
<td>38 (23.6)</td>
<td>16.9-31.9</td>
</tr>
<tr>
<td>Mood stabilizer + antipsychotic</td>
<td>36 (24.7)</td>
<td>16.8-34.9</td>
</tr>
<tr>
<td>Antipsychotic + antidepressant</td>
<td>26 (16.7)c</td>
<td>10.4-25.6c</td>
</tr>
<tr>
<td>Psychotherapy</td>
<td>62 (41.7)</td>
<td>29.2-55.4</td>
</tr>
</tbody>
</table>

Abbreviation: CI, confidence interval.  
a Data are based on the National Ambulatory Medical Care Survey. Youth are defined as aged 0 to 19 years and adults are defined as aged 20 years and older. Percentages are based on weighted sampling. See the text for definition of the medication grouping.  
b The mean±SD visit durations were 32.6±2.3 minutes for the youth bipolar disorder visits and 30.6±1.1 minutes for the adult bipolar disorder visits.  
c Unreliable estimates based on fewer than 30 visits.  
d Results are statistically significant.
As a separate line of research, it may be helpful to probe the diagnostic processes used in routine clinical practice. For example, it might be informative to assess whether clinicians give more weight to particular clinical presentations, such as high levels of aggression, than to specific DSM-IV symptoms. In research on adult bipolar disorder, there is considerable discordance between structured diagnostic interviews and expert re-interview.24

Visits by youth and adults with a diagnosis of bipolar disorder share several background characteristics, with 2 important exceptions. First, consistent with earlier national studies,23,63,66 visits by adults with a bipolar disorder diagnosis were disproportionately made by females. In line with clinical samples,14,16,65 the reverse was true of youth visits with a bipolar disorder diagnosis. Second, there were different patterns of comorbidity. In agreement with previous studies,14,17,65 we found that comorbid diagnosis of ADHD was higher in the youth visit sample than in the adult visit sample. Our analyses suggest that boys with comorbid ADHD may account for the predominance of males among youth diagnosed with bipolar disorder. Without prospective longitudinal research, it is not possible to determine the extent to which pediatric bipolar disorder is a developmental subtype of adult illness characterized by this sex and comorbidity pattern14,66 or the extent to which highly irritable boys with ADHD are being misdiagnosed as having bipolar disorder.20,67,68

The strength of treatment efficacy data differs markedly between adult and youth bipolar disorder. Evidence supporting current adult prescription practices is well documented.69-71 Meanwhile, treatment efficacy data in pediatric bipolar disorder remain limited mostly to case series and open trials, with only a few double-blind, placebo-controlled published studies.72-75 Evidence for lithium efficacy comes from 1 small, positive, randomized, placebo-controlled trial in a heterogeneous sample including adolescents with and at risk for bipolar disorder with comorbid substance dependence.74

The current analyses have several important limitations. First, diagnoses in the NAMCS are based on the independent judgment of the treating physician rather than on an independent objective assessment. For this reason, the data represent patterns in the diagnosis of bipolar disorder rather than patterns in the treated prevalence of the disorder. Second, no information is available concerning the dosage of the prescribed psychotropic medications. Third, data from the NAMCS are cross-sectional and therefore do not permit examination of duration and succession of treatment trials. Fourth, sample sizes limit efforts to evaluate the independence of associations between patient demographic and clinical characteristics and provision of psychotropic treatment. Fifth, the NAMCS records visits rather than individual patients, and the number of duplicated data for individual patients is unknown. Last, because the sample is restricted to office-based visits, it does not include visits to community mental health centers, hospital outpatient clinics, and various other clinical settings where patients with bipolar disorder receive mental health care, nor does it include mental health care provided by non-physicians.

A rapidly increasing number of office-based visits are being provided for the treatment of young people diagnosed with bipolar disorder. Despite controversy concerning the continuity of pediatric and adult bipolar disorder, there appear to be few differences in the pharmacological management of youth and adult bipolar disorder visits in office-based practice. As noted for other psychiatric conditions,76 physicians may be generalizing pharmacological treatment principles developed from adult clinical trials to the treatment of children and adolescents. There is an urgent need to study the reliability and validity using multiple informant strategies of the diagnosis of child and adolescent bipolar disorder in community practice and to evaluate the effectiveness and safety of pharmacological treatment regimens commonly used to treat youth diagnosed with bipolar disorder.

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Correction

Errors in Funding/Support, Financial Disclosure, Tables, and Text. In the Original Article by Merikangas et al titled “Lifetime and 12-Month Prevalence of Bipolar Spectrum Disorder in the National Comorbidity Survey Replication,” published in the May issue (2007;64[5]:543-552), there were several errors.

First, the following sentence in the Funding/Support section was incorrect: “The preparation of this article was supported by AstraZeneca.” AstraZeneca did not provide any financial or scientific support for this study.

Second, in addition to the financial disclosure of Dr Hirschfeld, that section should have contained the following: “Dr Akiskal is a consultant to or serves on the advisory board of Abbott International, GlaxoSmithKline, and Sanofi-Aventis. Dr Angst is a consultant to or serves on the advisory board of AstraZeneca and Eli Lilly and Company. Mr Greenberg is a consultant to or serves on the advisory board of AstraZeneca, Bristol-Myers Squibb, Eli Lilly and Company, Forest Laboratories, Ortho Biotech, and Sanofi-Aventis. Dr Kessler is a consultant to or serves on the advisory board of AstraZeneca, Bristol-Myers Squibb, Eli Lilly and Company, Sanofi-Aventis, and Wyeth-Ayerst.

Third, Table 1 and Tables 3 through 6 were labeled incorrectly with regard to SD and SE. In Table 1, the mention of SD should have read SE. In Tables 3 through 6, the mentions of SE should have read SD. A corrected version of Table 1 with SDs is available at http://www.hcp.med.harvard.edu/ncs/ftpdir/PA377%20erratum.pdf.

Fourth, the reference to inappropriate pharmacological treatment of bipolar disorder should have been restricted to bipolar disorders I and II and not included subthreshold bipolar disorder.

Errors 3 and 4 were pointed out by Bernard Carroll, MD.