Objective: This study clarified the early characteristics of substance use disorders in patients with first-episode bipolar I disorder.

Method: The authors evaluated substance use disorders, associated factors, and clinical course, prospectively, in the first 2 years of DSM-IV bipolar I disorder with standardized methods.

Results: Baseline substance use disorder was found in 33% (37 of 112) of the patients at baseline and in 39% at 24 months. Anxiety disorders were more frequent in the patients with than without substance use disorder (30% and 13%, respectively). Associations of alcohol dependence with depressive symptoms and cannabis dependence with manic symptoms were suggested. Patients using two or more substances had worse outcomes.

Conclusions: Since substance use disorders were frequent from the beginning of bipolar I disorder and were associated with anxiety disorders and poor outcome, early interventions for substance use disorder and anxiety might improve later outcome.

Patients with bipolar I disorder have high risks of co-morbid substance use disorders, with lifetime prevalence as high as 50%–60% (1). Substance use disorder comorbidity is eventually associated with worse bipolar I disorder outcome and higher suicidal risk, but very little is known about substance use disorder in early bipolar I disorder (2–5). Therefore, we analyzed data from the McLean-Harvard First Episode Mania Study to evaluate the timing of specific substance use disorders, associated risk factors, and relationships to clinical outcomes in the first 24 months of follow-up.
abuse. Of 22 subjects using one substance only (group 2), 17 used alcohol, four cannabis, and one heroin; the 15 in group 3 abused two or more substances (Table 1). Dependence was ranked as follows: 23 with alcohol, 11 cannabis, five cocaine, and one hallucinogen; abuse was ranked as follows: seven with alcohol, four cannabis, one cocaine, and two hallucinogens. For both dependence and abuse, there was considerable overlap in use of different drugs (average=1.8 per substance use disorder case). The prevalence of substance use disorder rose to 38.8% at 24 months (31 of 80 with a second SCID assessment).

Polydrug use subjects (group 3) versus nonabusers (group 1) were younger, less well educated, more likely to have a family history of psychiatric illness, and to be seen initially in mixed states. Subgroups with no abuse and monodrug use were similar in all of these baseline measures, and the subgroups did not differ by sex or race. Co-morbidity with any anxiety disorder was more common with substance use disorders. Patients with polydrug use spent more time ill during follow-up (especially in mixed episodes). Syndromal recovery was similar across subgroups. Other morbidity at 2 years (including initial depression severity and time spent in major depression/dysthymia or mania) did not differ significantly among subgroups (Table 1).

We also compared 2-year outcomes of patients with no substance use disorder versus alcohol-dependent (N=23) versus cannabis-dependent patients (N=11). Patients with no substance use disorder spent similar proportions of time in manic and depressive illness (mean=14.4%, SD=19.5%, versus mean=13.5%, SD=21.9%; ratio=1:1.1). Cannabis-dependent subjects spent more time in mania (mean=26.8%, SD=34.0%, versus mean=11.5%, SD=19.1%; ratio=2.3:1), whereas alcohol-dependent patients spent much more time depressed (mean=11.9%, SD=22.9%, in mania versus mean=21.9%, SD=29.5%, in depression; ratio=1:1.8). However, these findings did not reach statistical significance, and there was a considerable overlap in the use of both drugs.

**Discussion**

This preliminary assessment indicated that the prevalence of substance use disorder was already substantial among first-episode, DSM-IV bipolar I subjects (33%), reaching 39% by 24 months. Syndromal recovery from index mania occurred at similar rates across substance use disorder subgroups. However, overall morbidity during follow-up was particularly severe among patients with polysubstance use disorder, whereas patients with monosubstance use disorder had surprisingly good early outcomes. A previously suggested (3) association of alcohol with depression and cannabis with mania was found and warrants further study.

Of note, patients with comorbid substance use disorder were more likely than nonusers to be diagnosed with a DSM-IV anxiety disorder. A link between anxiety and substance use disorders in major affective disorders has been proposed (4), but the cause-effect relationships remain unclear. Substance use might sometimes ameliorate anxi-

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**TABLE 1. Characteristics of Patients With First-Episode Bipolar I Disorder Regarding Substance Use Disorders**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Patients With No Substance Use Disorder (group 1, N=75)</th>
<th>Patients With Monosubstance Use Disorder (group 2, N=22)</th>
<th>Patients With Polysubstance Use Disorder (group 3, N=15)</th>
<th>Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
<td>N</td>
<td>%</td>
</tr>
<tr>
<td>Male sex</td>
<td>42</td>
<td>56.0</td>
<td>11</td>
<td>50.0</td>
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<tr>
<td>Non-Caucasian race</td>
<td>14</td>
<td>18.7</td>
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<td>18.2</td>
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<tr>
<td>Education &lt;16 years</td>
<td>44</td>
<td>58.7</td>
<td>19</td>
<td>86.4</td>
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<td>Family psychiatric history</td>
<td>39</td>
<td>66.1</td>
<td>15</td>
<td>83.3</td>
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<tr>
<td>Anxiety disorder</td>
<td>10</td>
<td>13.3</td>
<td>6</td>
<td>27.3</td>
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<tr>
<td>Initial hospitalized episode</td>
<td></td>
<td></td>
<td>7</td>
<td>46.7</td>
</tr>
<tr>
<td>Manic</td>
<td>62</td>
<td>82.7</td>
<td>17</td>
<td>77.3</td>
</tr>
<tr>
<td>Mixed</td>
<td>13</td>
<td>17.3</td>
<td>5</td>
<td>22.7</td>
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<tr>
<td>Syndromal recovery</td>
<td>72</td>
<td>96.0</td>
<td>20</td>
<td>90.9</td>
</tr>
</tbody>
</table>

* DSM-IV substance abuse or dependence at first hospitalization. Polysubstance use defined by use of two or more agents.
* The three groups were compared with each other unless otherwise noted.
* Fisher’s exact test.
* The patients with no substance abuse were compared with those with monosubstance and polysubstance abuse disorder combined (df=1).
* The patients with polysubstance use disorder were compared with those with no substance use disorder and those with monosubstance use disorder combined (df=1, 109).
BRIEF REPORTS

Anxiety symptoms or anxiety worsened by substance use disorder. The evident association suggests the testable hypothesis that very early clinical interventions in new bipolar I disorder aimed at limiting both anxiety symptoms and substance use disorder might contribute to improved outcomes.

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