CME

Demographic and Clinical Characteristics of Individuals in a Bipolar Disorder Case Registry

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Background: The goal of this analysis was to characterize a cohort of 3000 persons who self-identified as having bipolar disorder by demographic, clinical, and treatment characteristics and to document the burden that this disorder imposed on their lives.

Method: The Stanley Center Bipolar Disorder Registry used a variety of recruitment methods to reach people with bipolar disorder. The cohort included those currently in treatment and those active in support groups. Registrants completed an interviewer-administered questionnaire to obtain information on demographic characteristics, clinical history, and treatment history.

Results: The median age of the 2839 patients who were analyzed was 40.1 years, 64.5% were women, and over 90% were white. The median age at onset was 17.5 years, and the mean was 19.8 years. Despite the fact that over 60% completed at least some college and 30% completed college, 64% were currently unemployed. The patients' family histories point to a high prevalence of mental disorder in the families, especially mood disorders. Patients were concurrently taking multiple medications, and more than one third were taking at least 3 types of psychotropic medications. This pattern of pharmacotherapy was consistent with participants' overall mood ratings, which demonstrated how unusual it was for them to be symptom-free over a 6-month period.

Conclusion: Our present findings point to the chronicity and severity of bipolar disorder as experienced in the community. We still need to develop better interventions, ensure access to care consistent with current consensus guidelines, and initiate care as early as possible in the course of the condition.

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In the spirit of full disclosure and in compliance with all ACCME Essential Areas and Policies, the faculty for this CME activity were asked to complete a full disclosure statement. The information received is as follows: Dr. Kupfer is a consultant for Hoffman-LaRoche, and is a member of the advisory board for Pfizer, Lilly, and Forest; Dr. Frank is a consultant for Pfizer Italiana, Pfizer USA, Forest, and Lilly; has received research grant support from NIMH, Forest, and Lilly; and is a member of the speakers/advisory board for Pfizer Psychiatry Advisory Board. Drs. Cluss, Grochocinski, Houck, and Stapf have no significant commercial relationships to disclose relative to the presentation.

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Pursuing epidemiologic and intervention studies on populations with low prevalence of a specific health issue is an ongoing challenge for clinical and services researchers. Even though bipolar disorder has a population prevalence estimated at about 1%,[1,2] it can be difficult to recruit a study group that is adequate in size and representative of the overall population. A variety of recruitment methods involve referrals from health providers and self-identification by subjects (recruitment through advertisements, patient groups, and community presentations).[3] These methods are likely to identify very different types of individuals. For example, recruitment performed by health care professionals is likely to yield a group of patients who have more contact with the health services system. Recruitment of individuals through patient groups or public forums increases the chance of finding persons who are not currently in active treatment and those who may have stable conditions. However, such methods are more likely to identify highly motivated patients and those who are more likely to be newly diagnosed and learning about their disorder.

In the past 10 years, there have been numerous reports documenting the lack of recognition of bipolar disorder, the long period of time that passes between diagnosis and the point at which individuals find appropriate professional help, and the difficulty of treating this complex condition. It is becoming clear that bipolar disorder is one in which early onset may be the rule, yet adequate treatment is rarely provided in the early stages of the illness, which could greatly reduce the lifetime burden of this illness. Proving this to be the case could result in improvements in both early detection and the availability of treatment services.

With these concerns in mind, we initiated a bipolar disorder case registry sponsored by the Stanley Center for the Innovative Treatment of Bipolar Disorder of the Department of Psychiatry at the University of Pittsburgh School of Medicine, Pittsburgh, Pa. This registry is a voluntary registry for which participants are self-identified, in contrast to other disease registries that identify cases through mandatory government reporting or from patient lists. The goal of our analysis was to characterize a cohort of almost 3000 persons who self-identified as having bipolar disorder with respect to demographic, illness, and treatment characteristics and to document the burden that this disorder imposes on the lives of patients.

METHOD

The Stanley Center Bipolar Disorder Registry used a variety of recruitment methods with the goal of reaching different subgroups of people with bipolar disorder, including those currently in treatment and those active in support groups. Recruitment was conducted in the local region (southwestern Pennsylvania) and nationally. Recruitment efforts targeted both patients and health care professionals. For example, the Stanley Center invited health care professionals to join their provider consortium, meaning that they could call for informal consultation in the face of difficult treatment issues, and receive a free newsletter on bipolar disorder and local research efforts, as well as invitations to seminars and workshops. Stanley Center staff met with psychiatrists and other mental health specialists at their practice sites and spoke at staff meetings at local mental health agencies. Efforts to contact patients included presentations to patient support groups and to local community groups, advertisements in newspapers and on radio, and distribution of brochures in county assistance offices, provider agencies, and local conferences. A typical week for Stanley Center recruitment staff included presentations and distribution of brochures to the following groups: county medical assistance office staff, consumers and providers at a rural county community support project meeting, a local Alliance for the Mentally Ill group, an agency for mentally retarded adults, and nursing staff at a local general hospital.

An innovative and important avenue of recruitment was the Stanley Center's site on the Internet's World Wide Web. The Center Web site described the provider consortium, the registry, and ongoing clinical trials. Visitors were able to browse provider and consumer newsletters and read about ongoing clinical trials. A toll-free number was given to allow persons to find out more about joining the registry.

Persons who contacted the Stanley Center and identified themselves as having bipolar disorder were invited to join the registry. Those who agreed and completed a signed consent form then completed an interviewer-administered questionnaire to obtain information on demographic characteristics, clinical history, and treatment history. Approximately half of those contacting the Center did not join the registry; many of these respondents were ineligible because they contacted the center to obtain information on behalf of a friend or family member with the disorder. Participants receive quarterly newsletters and information from the Stanley Center and can use a telephone-based resource center. Both the newsletters and the resource hot line provide expert information on current clinical issues and resources for bipolar disorder patients and their families.

Sample

Approximately 3880 persons with bipolar disorder registered with the Stanley Center from its inception in the spring of 1995 through 1999. Individuals over the age of 18 years who identified themselves as having bipolar disorder were eligible. To determine the validity of self-identification, we conducted a face-to-face Structured Clinical Interview for DSM-IV Axis I Disorders-Patient Edition (SCID-I/P)[4] with a subset of 100 of these individuals and found that 93% met criteria for a lifetime bipolar spectrum diagnosis.[3] The analyses presented in this report are limited to the 2839 registry participants living within a 150-mile radius of Pittsburgh who completed surveys at the time they joined the bipolar disorder case registry. This geographic region was chosen for detailed analysis since this was the group to whom we wanted to be able to direct our clinical services.

Variables

Demographic characteristics. Age, race, gender, level of education, marital status, employment status, and income status were available for most subjects.

Clinical and treatment characteristics. Registrants reported the number of lifetime hospitalizations for mental health problems. Any hospitalizations in the year prior to the interview were identified. We asked registrants to list all of their current psychotropic medications. Psychotropic medications were classified into antimanics, anticonvulsants, antidepressants, antipsychotics, and benzodiazepines. Combinations of these medications were also examined and reported. Registrants also indicated whether they were currently in treatment with a psychiatrist. Family history of bipolar disorder, unipolar depression, and schizophrenia were also obtained. Specifically,

Table 1. Diagnosis and Past History of Mood Disorders (N = 2839)[a]

Diagnosis and Past History	Percentage
Patients report that a health professional considered them to be:	
Bipolar	94.3
Manic	17.1
Hypomanic	8.9
Depressed	41.6
Schizoaffective	8.9
Other diagnosis	36.8
Any hospitalization[b]	85.1
Ever hospitalized for:	
Mania[b]	43.2
Depression[b]	59.1
Mixed episode[b]	33.2
Suicide	
Ever attempted suicide	50.3
Ever attempted suicide while manic	13.4
Ever attempted suicide while depressed	46.3
Ever required hospitalization for suicide attempt	34.8
Received ECT at any time	17.1
Medical hospitalizations in past 12 months	19.6

[a] Abbreviation: ECT = electroconvulsive therapy. Percentages add to > 100% due to the possibility that multiple selections could be made.
[b] The median number of hospitalizations for patients with any hospitalization = 3, for patients with mania = 2, for patients with depression = 2, and for patients with mixed episode = 2.

Table 2. Family History of Mood Disorders (N = 2839)

Family Member	Bipolar Disorder (%)	Unipolar Disorder (%)	Schizophrenia (%)
Any family member	54.0	52.1	15.3
Mother	23.1	27.8	3.8
Father	18.0	16.8	2.8
Sibling	18.4	19.1	4.8
Children	8.0	5.1	1.2
Maternal grandparent	8.6	8.1	1.9
Maternal aunt/uncle	9.6	10.3	3.5
Paternal grandparent	6.6	6.1	1.5
Paternal aunt/uncle	6.8	6.7	2.4
Cousin	10.7	7.8	2.9

participants were asked questions about their biologically related family members.

Symptom severity was self-rated monthly for the previous 6 months and the current month on an ordinal scale of –3 for severe depression to +3 for severe mania. A zero score indicated that depression and mania symptoms were absent or minimal. Summary scores over these 7 months were tabulated and reported.

Analyses

The sample of 2839 registrants was divided by gender into 1009 men and 1830 women. Univariate comparisons were performed between the genders on other demographic characteristics, diagnoses, family history of illness, first episode information, and current depression and mania severity. Group t tests were used for continuous measures and chi-square tests for contingency tables were used for categorical variables.

RESULTS

The cohort comprised 2839 participants living within a 150-mile radius of Pittsburgh. The median age of the 2839 Stanley Registry participants was 40.1 years, 64.5% were women, and over 90% were white, consistent with the demographics of the greater Pittsburgh area. One third were currently married, one third were never married, and the remainder were separated, divorced, or widowed. Approximately 45% had children under 18 years of age. Over 90% of the sample had high school diplomas, one third of the subjects had completed college, and 11% had a graduate or professional degree. Almost 65% were unemployed, and almost 40% were receiving disability or welfare support. When the sample is divided by gender, few significant differences are found. However, more men (39.4%) than women (29.9%) had never been married. Men had higher mean educational achievement (college education: men, 63.4%; women, 59.6%), were more likely to be employed (men, 38.8%; women, 34.3%), but also were more likely to be on disability, welfare, or retired (men, 33.7%; women, 30.4%).

As shown in Table 1, the vast majority of the participants in the registry reported that a health professional considered them to have bipolar disorder (94.3%). In over 90% of the cases, this information had been obtained from a physician, usually a psychiatrist. When diagnostic categories were examined, it appeared that more women were considered by professionals to have been depressed (43.5% vs. 38.1%; $\chi^2 = 7.92$, p = .005). Over 85% of the participants reported having had at least 1 psychiatric hospitalization, with almost 60% reporting being hospitalized for depression, and 43% reporting being hospitalized for mania. The median number of hospitalizations for the overall sample was 3.

Over one half of the participants had attempted suicide, with a greater number of women (with depression, 52.5% vs. women without depression, 46.2%; $\chi^2 = 9.73$, p = .002) attempting suicide while depressed than men attempting suicide while depressed (48.4% vs. 42.6%; $\chi^2 = 8.30$, p = .004). Over 17% of the sample had received electroconvulsive therapy (ECT) at some point in their treatment. Notably, almost 20% had been hospitalized for a medical condition in the previous 12 months.

As shown in Table 2, over 50% of the participants reported having at least 1 family member with bipolar disorder, and over 50% reported at least 1 family member with unipolar disorder. More women than men (58.1% vs. 46.6%; $\chi^2 = 35.00$, p = .0001) reported having family members with bipolar disorder. On the basis of participants' reports, it appeared mothers had a greater likelihood of having either bipolar disorder or unipolar disorder than other family members; however, this may

Table 3. Psychotropic Medication Use in Bipolar Disorder (N = 2839)

Medication	Percentage
No. of concurrent psychotropic medications	
0	11.6
1	20.6
2	31.3
3	23.0
4	10.5
≥ 5	3.0
Current use of medication by category	
Antimanic	37.1
Anticonvulsant	42.7
Antidepressant	54.0
Antipsychotic	29.8
Benzodiazepine	25.4
Antimanic only	9.4
Anticonvulsant only	6.7

Figure 1. Distribution of Bipolar Disorder by Age at Onset (N = 2308)

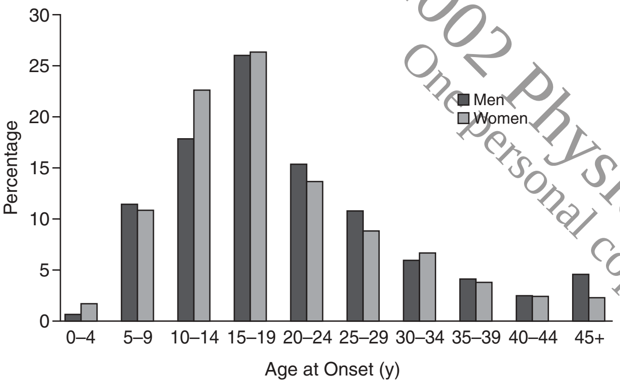

Table 4. Characteristics of the First Episode of Bipolar Disorder (N = 2308)[a]

Characteristics	Percentage
Living situation	
Parents' home	57.6
Own/family home	27.9
Other	14.5
Marital status	
Never married	74.4
Married	21.0
Divorced	2.7
Separated	1.5
Widowed	0.3
Mood	
Depressed	54.2
Manic	21.5
Mixed	24.3
Medication treatment	34.1
Psychotherapy	36.4
Hospitalization	28.2
For mania	10.1
Voluntary	4.9
Involuntary	5.2
For depression	11.2
Voluntary	7.4
Involuntary	3.8
For mixed episode	8.6
Voluntary	5.1
Involuntary	3.5

[a]Mean age at first episode = 19.8 years (median = 17.5 years).

simply represent respondents' greater familiarity with information concerning their mothers' as opposed to other family members' mental health.

Table 3 shows current psychotropic medication usage by the registry participants. It is striking that fewer than 12% of the sample were currently taking no psychotropic medication. Three fourths of the patients were taking 1 to 3 medications. When one examines specific categories of medication, over one third of the patients were taking lithium and over 40% of the patients were taking an anticonvulsant as a mood stabilizer, but very few of the patients were taking lithium or an anticonvulsant drug alone. More than half the patients were taking an antidepressant. Finally, 25% of the sample was taking a benzodiazepine.

In the 2308 participants in whom age at first episode was reported, the median age at onset was 17.5 years with a mean of 19.8 years (Figure 1). We also examined age at onset by dividing the entire sample into 3 cohorts: those born between 1900–1939 (cohort 1); 1940–1949 (cohort 2); and, finally, 1950–1959 (cohort 3). Subjects born after 1959 are too young to provide good estimates. In the earliest birth cohort, the median age at onset was 22.5 years, while the 2 later birth cohorts had a median age at onset of 19 years. ECT was used for treatment in 43.7% of patients in cohort 1, compared with 24.5% in cohort 2 and 19.6% in cohort 3. Reports of suicide attempts have increased across the cohorts: 30.9% in cohort 1, 44.4% in cohort 2, and 51.9% in cohort 3.The hospitalization rate for the first episode was higher in cohort 1 at 40.5% compared to 27.1% in cohort 2 and 27.7% in cohort 3.

As shown in Table 4, at the time of the first episode, over half of the participants were living in their parents' homes, and only one fourth of the sample had been married. With respect to their primary mood during the first episode, half the sample reported experiencing depression, 21.5% reported a manic episode, and one quarter reported a mixed episode. More women than men reported experiencing a depressive first episode. One third of the participants received medication treatment during their first episode, over one third received psychotherapy, and 28.2% were hospitalized. Over 50% of the sample received no treatment for their first episode.

A final area of interest was examining participants' mood ratings in the 6 months prior to participation in the registry and during the current month. There was a greater likelihood that these patients had symptoms of depression rather than mania (63.6% vs. 33.1%). More than half the participants reported at least 1 month of moderate-to-severe depressive symptomatology. Women were more likely to report depression than men (67.1% vs. 57.3%; $\chi^2 = 17.35$, $p = .001$) and to have a higher mean depression symptom score 0.68 ± 0.75 vs. 0.60 ± 0.77; $t = 2.22$, df = 1821, $p = .03$) with a maximum score of 3.

DISCUSSION

Clinical trials have typically used a variety of recruitment methods including referrals from health care providers and self-identification by subjects (recruitment through advertisements, patient groups, and community presentations).[5] On the other hand, epidemiologic surveys generally use population-based methods of identifying samples, including household enumeration[6,7] or random digit dial telephone surveys.[8] While these approaches provide extremely important data on the prevalence of disorders, they are expensive and extremely large numbers of participants are needed to identify an adequate sample of persons with relatively rare conditions. For example, out of 19,182 individuals interviewed in the Epidemiologic Catchment Area (ECA) household enumeration study in 5 communities across the United States, less than 200 persons with bipolar disorder were identified.[9]

Because the focus of services research is understanding patterns of care across populations, study groups have usually been defined from lists of patients receiving care at specific institutions or practices, membership lists of insurance plans, or community-based sampling through random digit dial calling or other means. While these methods generally provide study groups that are more representative of those in treatment, the cost of using such recruitment strategies may be prohibitive for low prevalence conditions. The numbers identified in even very large panels may yield inadequate samples.

In this study of a large group of identified patients with bipolar disorder, several points should be underscored. First, the disorder is clearly one of early onset. The phenomenon of early onset has been documented in other reports, but needs to be put in an appropriate context. Goodwin and Jamison,[10] who discussed age at onset in studies conducted primarily through the 1970s and the 1980s, concluded that the mean age at onset was 28.1 years in an overall sample of 4200 patients. However, it is noteworthy that the ECA study[11] showed a mean age at onset of 21.2 years. In general, studies conducted before 1980 report a somewhat later onset, although the age at onset data comparing gender differences show a preponderance of individuals between 15 and 24 years of age.[10] Clayton and colleagues, in their study on Swiss males, demonstrated that in a group of 26 subjects with bipolar disorder, the median age at onset was 20 years with a range of 10 to 34 years.[1] Even the most conservative recent estimates show at least one quarter of patients with bipolar disorder have an onset before age 20, even when the onset is defined as a full episode rather than the presence of several symptoms.

Other striking findings in this report include the current functioning of this patient sample. Despite the fact that over 60% completed at least some college and 30% completed college, 64% are currently unemployed. The disparity between employment status and income versus level of education indicates severe impairment. These findings are consistent with the reports in the last 6 years published by Goldberg and colleagues[12] and Gitlin and Hammen.[13] Is this level of impairment a necessary consequence of the disorder, or does it result from inadequate efforts to address depressive symptomatology in a (perhaps wrongminded) effort to prevent mania?

Second, the family histories, although not obtained with research-level family history methodology, point to a high prevalence of mental disorder in the families of registry participants, especially mood disorders. These figures almost certainly represent an underestimate of the prevalence figures that would have been obtained using a family interview method. These figures raise serious questions about the capacity of key family members to aid young individuals suffering early episodes of illness in obtaining appropriate care.

Third, patients are concurrently taking multiple medications and more than one third are taking at least 3 types of psychotropic medications. This pattern of pharmacotherapy is consistent with participants' overall mood ratings, which demonstrates how unusual it is for them to be symptom-free over a 6-month period. Yet, one wonders whether any of the individual pharmacotherapies has been maximized before the addition of adjunctive medication and whether some of the symptoms participants report might not really represent collateral effects of complex drug regimens.

One important final issue involves the suitability of persons with bipolar disorder to accurately characterize that diagnosis. As indicated earlier,[3] we found that 93% of individuals met DSM-IV criteria for a lifetime bipolar spectrum diagnosis. This subset of 100 was assessed randomly from the original 800 members of the registry and accurately reflected this original cohort. We have examined other cohorts of the registry and found no major differences in the groups except when age at onset is used to divide up the groups. Not surprising, the use of electroconvulsive treatment and initial hospitalization is lower in the younger cohorts, but the rate of suicide attempts has appeared to increase. While we tentatively conclude that individuals with bipolar disease can self-identify themselves accurately, they probably underestimate the type or amount of comorbid psychiatric disorder (although the group did self-identify substance disorder as the most frequent comorbid psychiatric condition). Finally, we do not have concurrent clinical ratings of their self-ratings of mood changes over the previous 6 months. There is a growing consensus, however, that bipolar patients spend the greatest amount of time in a mild depressive state. Certainly, this area needs more attention clinically.

All of our present findings point to the chronicity and severity of bipolar disorder as experienced in the community. While thought of until recently as a problem solved, bipolar disorder is anything but that. Clearly we need to develop better interventions and initiate them as early as possible in the course of this pernicious condition. In implementing the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) (information available at http://www.stepbd.org), the National Institute of Mental Health has recognized that much work needs to be done in this area. Yet, it will be several years before the outcomes of this major initiative are known. In the interim, we should, at a minimum, attempt to ensure access to care consistent with current consensus guidelines[14] for all individuals who suffer from manic depressive disorder.

Disclosure of off-label usage: The authors have determined that, to the best of their knowledge, no investigational information about pharmaceutical agents has been presented in this article that is outside U.S. Food and Drug Administration–approved labeling.

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