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Research report

Diagnostic certainty of a voluntary bipolar disorder case registry

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Abstract

Background: Strategies for identifying and recruiting persons with bipolar disorder are of importance as interest in studying this relatively uncommon, but highly disabling illness increases. The development and implementation of a bipolar disorder case registry and the assessment of diagnostic certainty of the resulting sample are described. *Methods*: Eight hundred and four individuals who self-reported a history of bipolar disorder were recruited. Telephone interviewers gathered demographic information and clinical, medical and treatment history information. One hundred randomly-selected registrants completed an in-person structured diagnostic interview. Self-report of diagnosis was compared to the results of the diagnostic interview. *Results*: Ninety three percent of registrants interviewed met criteria for a lifetime bipolar spectrum diagnosis; of those, 76.3% were diagnosed with bipolar I disorder. Agreement between self-reported and SCID diagnoses was 93%, indicating that self-report of a bipolar diagnosis is highly reliable. Two-thirds had experienced at least one other lifetime Axis I diagnosis, with substance abuse/dependence (55.9%) and panic disorder (19.4%) the most common comorbidities. *Limitations*: Since nearly all of the sample have previously been diagnosed as having bipolar disorder by a professional, the sample's representativeness of the population as a whole may be somewhat limited. *Conclusions*: Persons with bipolar disorder can accurately identify themselves as having the disorder via a telephone interview, indicating that a case registry method is a useful strategy for recruiting very large samples of persons with this disorder. Such large samples will allow for further study of treatment variations among patient subgroups, of pathways to treatment, and of the effectiveness of new treatments.

Keywords: Bipolar disorder; Manic depression; Registry

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1. Introduction

Bipolar disorder is a serious and long-term psychiatric disorder. Estimates of lifetime prevalence range from 1.2% for bipolar I and II subtypes combined (Weissman et al., 1988) to 5% to 8% when the proposed bipolar III subtype (Akiskal, 1996) is included. Effects of the characteristically recurrent episodes of mania and major depression can be disabling and may include difficulties such as job loss, marital problems including divorce, disruption of other interpersonal relationships, and suicide (Goodwin and Jamison, 1990). The scientific study of the biological mechanisms in the etiology and treatment of bipolar disorder is critical because of the difficulty of treating the illness successfully over the lifetime and because of the high costs associated with the illness. Study of a disease such as bipolar disorder, which is relatively infrequent but which is associated with high morbidity, can be complex and expensive, however, because of the difficulty associated with identifying a sufficiently large sample of subjects for study. Several research approaches have been taken to studying individuals with bipolar disorder, including epidemiological studies in the general population, cross-sectional mailed surveys of people known to have bipolar disorder, and treatment studies or clinical trials including subjects with the illness who have been identified in academic medical settings.

1.1. Epidemiological samples

A significant advantage of population-based epidemiological studies is that such studies may be broadly interpreted to be representative of the population as a whole. In prospective epidemiological studies, a large number of individuals is interviewed, with such individuals either selected randomly or as part of a stratified or household sample. Retrospective epidemiological studies or case control studies compare large numbers of known cases with controls. Examples of this approach are the Epidemiologic Catchment Area (ECA) study (described in Regier et al., 1984) and the National Comorbidity Survey (Kessler et al., 1996) which interviewed US community samples of approximately 20,000 and 8000 people, respectively.

An important disadvantage of epidemiological studies, however, is that with a relatively uncommon condition such as bipolar disorder, an inordinately large sample of the general population must be interviewed to obtain a relatively small number of subjects with the disorder of interest (e.g., less than 200 cases in the ECA and less than 100 cases in the National Comorbidity Survey). Second, because the purpose of population studies is to gather information about a very broad range of symptoms and problems, there typically is not much depth to the information collected about any specific diagnosis, which is especially problematic for a complex, multiphasic illness such as bipolar disorder. A third disadvantage is that most epidemiological surveys are cross-sectional in nature and do not allow for tracking of cases over the course of the illness. Case control studies, while less costly than prospective studies, have the additional disadvantage of identification bias, since such studies generally have included only those patients who present at academic medical centers. Recall bias, in which persons with an illness tend to recall illness-related events, risks, and symptoms more frequently than controls, may be another disadvantage in case control studies.

1.2. Cross-sectional mailed survey method

With a mailed survey, information can be gathered from a large sample of affected individuals, as in the survey conducted by the National Depressive and Manic–Depressive Association (Lish et al., 1994). A disadvantage to this approach, however, is that such surveys are cross-sectional and generally provide no mechanism for longitudinal follow up. Also, there is often no independent confirmation of respondents' self-reported diagnosis so that some percentage of respondents may not have the disorder of interest. Survey representativeness also can be problematic if only a minority of those who receive the survey return them. Respondents tend to be more highly motivated than persons who do not reply, so that those with more chaotic lives or unstable clinical courses tend to be underrepresented in the final sample. Likewise, literacy issues and the limit to the amount of information that can be collected in a single, written form decrease the comprehensiveness of information gathered.

1.3. Treatment studies/clinical trials

In a third approach to the identification of bipolar individuals, clinical samples of affected persons are recruited to test alternative treatment strategies for subsets of bipolar symptoms. Advantages to this approach are: subjects usually have a verified diagnosis of bipolar disorder; in-depth information generally is gathered on the subject pool; and subjects often are evaluated and followed for an extended period of time. Disadvantages of treatment studies, however, are that very small numbers of subjects typically are enrolled and that sampling tends to occur from only very limited recruitment sources, such as a specific psychiatric inpatient unit at an academic medical center or from responders to advertisements. Additionally, treatment studies usually have very strict inclusion and exclusion criteria, significantly limiting the generalizability of results. To date, this method has been the most common for assessing efficacy of pharmacological and therapeutic treatments for bipolar disorder.

1.4. The Stanley Center Voluntary Bipolar Disorder Case Registry

Although the contributions made to the understanding of bipolar disorder from the three approaches described above are incontrovertibly important, their cumulative limitations are significant when studying a high morbidity, relatively low frequency illness such as bipolar disorder. Because of these limitations a fourth alternative – a case registry – has been utilized by researchers from the Stanley Center for the Innovative Treatment of Bipolar Disorder of the Department of Psychiatry of the University of Pittsburgh School of Medicine. A case registry is a system of ongoing registration of ''data concerning all cases of a particular disease or other health-relevant condition in a defined population such that the cases can be related to a population base'' (Last et al., 1995). Registries have been developed for various medical disorders and procedures such as angioplasty (e.g., Faxon et al., 1996) and tumors (e.g. Enayati and Traverso, 1997), for psychiatric disorders such as schizophrenia (Kendler et al., 1996) and Alzheimer's Disease (described in Clark et al., 1997), and for other general purposes such as the twin registries in Scandinavian countries (e.g. Danish Twin Registry, Kyvik et al., 1995). Utilizing a registry to study disease makes the most sense when the disease of interest is: a definable condition; one associated with chronic morbidity, disability, and/or long term health care needs and, therefore, with high cost; and of relatively low prevalence. This method of sample collection has the benefit of having a large, affected pool of willing research participants who can be followed over time in naturalistic studies of disease progression and/or who can participate in multiple serial or parallel studies of either global disorder-related issues or sub-studies focusing on specific demographic or clinical populations.

Stanley Center recruitment goals have been to maximize the total number of patients available for study and longitudinal follow up while minimizing the costs associated with their identification, in order to achieve a broad range of patient characteristics, geographical variation, referral sources, and treatment history variability. The sample is labeled a ''voluntary registry'' to distinguish it from true registries in which every identified case of the disorder of interest is enrolled. Although we cannot enroll every person with bipolar disorder in our geographic region, recruitment strategies are designed to gather the largest possible number of bipolar volunteers from a broad range of clinical and general community sources. The advantage to this recruitment method is that it is inclusive rather than exclusive and allows for the gathering of a very large sample of bipolar subjects.

In a registry which studies a specific definable condition, it is critical to have procedures for defining who is a case since all registered cases must have the characteristic, disorder, problem, or condition under investigation to report with any certainty the findings which emerge. In tumor registries, for example, cases are identified on the basis of tissue pathology. An angioplasty registry enrolls only individuals who have undergone a specific, documented surgical procedure. Individuals contact the Stanley Center Registry because they believe they have bipolar disorder and not because their disorder was identified by us initially through some objective, independent method. The validity of our study, therefore, is highly dependent upon whether regis-

trants are accurate when they self-report their ''caseness.'' In this report we describe our methods for determining the diagnostic certainty of our voluntary bipolar disorder case registry sample. Previous literature suggests that individuals with this disorder experience long delays before receiving an accurate diagnosis (Lish et al., 1994), resulting in the accrual of significant chronic symptomatology and sometimes disability before diagnosis. Therefore, we hypothesized that people who contact a registry claiming to have bipolar disorder would be highly likely to have it, probably the result of living with significant symptomatology for long periods of time.

2. Methods

2.1. Recruitment

Since the spring of 1995, the Stanley Center Registry has registered 804 individuals with bipolar disorder who live within 150 miles of Pittsburgh, PA. The recruitment approach emphasizes unique partnerships with consumer advocacy groups, with community mental health and primary care providers, and with non-mental health public agencies and groups in order to develop a sample which is representative of the population who suffer from bipolar disorder. Efforts are made to reach various subgroups of people with bipolar disorder: those individuals who are currently in treatment for the disorder, previously-diagnosed individuals who are not in treatment currently, and people who believe that they may have the disorder but who have not previously been diagnosed.

2.2. Interview methods

In response to these public relations contacts, persons who are self-identified as having bipolar disorder call the Stanley Center using either a local number or a well-publicized, toll-free phone number. After a signed consent form is returned in the mail, a telephone interview is completed to gather information about registrant demographics, clinical history, treatment history, and current and past medical history. In exchange for continued participation, registrants receive quarterly newsletters and have access to a telephone resource center, both of which provide expert information on current clinical issues and resources for bipolar patients and family members.

2.3. Diagnostic measures

Registrants are asked during the telephone interview, ''Has any health professional ever told you that you were suffering from: bipolar disorder or manic depression, mania, hypomania, depression, schizophrenia, or other psychiatric disorder?'' A random 20% of all registered individuals are selected to complete a face-to-face Structured Clinical Interview for DSM-IV Axis I Disorders-Patient Edition (SCID: First et al., 1995). Those selected are interviewed either in our office or their homes and are reimbursed $25. Psychiatric records are requested to complement the SCID interviews. Interviewers are experienced psychiatric nurse clinicians and master's level psychiatric social workers and counselors who have completed a 30-hour SCID training program consisting of didactic presentations, observation of taped and live interviews performed by senior clinician-interviewers, role-playing of interviews, and supervised pilot interviews before performing interviews on their own.

A comparison of demographic and clinical characteristics of registry subjects who received a SCID interview and those who did not was performed to test for group differences on these variables. Chi-square tests were used to assess statistical significance for categorical variables. The percent agreement was assessed for self-reported diagnostic status and SCID diagnosis.

3. Results

3.1. Sample description

Demographic and clinical information for the sample are presented in Table 1. There were 136 registrants invited to complete a SCID interview. One hundred (74%) were completed and are discussed in this report. Thirty-six of the invited registrants refused to be interviewed. Comparison of the 100 registrants who completed the SCID inter-

Table 1
Demographic characteristics by SCID status $N = 804$

	No SCID $n = 704$	SCID $N = 100$
Gender		
Male	36.1	41.0
Female	63.9	59.0
Age		
18–24	6.1	2.0
25–34	22.0	19.0
35–44	37.5	39.0
45–54	24.3	25.0
55–64	8.2	11.0
65 +	1.9	4.0
Race		
White	93.5	93.0
Non-White	6.5	7.0
Marital Status		
Never Married	30.4	21.0
Married	33.8	45.0
Separated	8.1	5.0
Divorced	25.9	29.0
Widowed	1.9	0.0
Employment		
Not Employed	60.1	63.0
Employed	39.9	37.0
Education		
< High School	4.0	3.0
High School Diploma	24.6	23.0
Some College	31.5	33.0
College Degree	24.6	24.0
Graduate or Professional	15.3	17.0
Clinical Characteristics		
Ever Hospitalized	82.2	85.0
For Mania	43.9	51.0
For Depression	53.8	55.0
For Mixed Episode	24.3	24.0
Attempted Suicide	50.4	47.0
Currently in Treatment	96.0	96.0

No distributions were significantly different (Chi-Square Test, $p < 0.05$)

view to the other 704 subjects in the sample indicate no statistically significant differences between the groups for any demographic or clinical factors. The group for whom we have SCID results, therefore, generally is representative demographically and clinically of the larger non-SCID registry sample.

Nearly half (45.2%) of the 804 registrants were referred to the registry from a health professional, the result of public relations efforts to mental health agencies, hospitals, mental health professionals and non-mental health medical practitioners such as internal medicine and family practice physicians. Another quarter (21.5%) of registrants was recruited through community public relations efforts such as informational literature in county public assistance offices, libraries, newsletters, bus ads, and conferences. Area mental health support groups referred 11.2% of these registrants, with the Internet and other miscellaneous sources providing the remaining 22.1% of the referrals.

3.2. SCID results

Table 2 summarizes the results of the SCID interviews. Of participants who completed structured diagnostic interviews, 93 (93%) were found to have a lifetime bipolar spectrum diagnosis (bipolar I, II, other bipolar disorder, or schizoaffective disorder, bipolar type), with 71 (76.3%) of those having a diagnosis of bipolar I disorder. Only 7 registrants (7%) in the SCID group did not meet criteria for any bipolar diagnosis.

Table 3 shows that Axis I diagnostic comorbidities were prevalent over the lifetime in the sample, with greater than two-thirds ($n = 65$, 69.9%) of those with a bipolar disorder having experienced at least one lifetime Axis I comorbidity. More than half of the sample had suffered from a substance abuse/dependence disorder ($n = 52$, 55.9%) at some point in their lifetime while more than one in five had experienced a panic disorder ($n = 18$, 19.4%). In addition, there were 9 (9.7%) registrants who had experienced a post traumatic stress disorder. The table reports on the lesser number of registrants who had other comorbidities. Of those with comorbidities,

Table 2
Participants selected for SCID: lifetime diagnosis

	N	
Bipolar I	71	
Bipolar II	18	
Other bipolar disorder	1	
Schizoaffective disorder, bipolar type	3	
Not Bipolar	7	
• Major depression		3
• Dysthymia		1
• Mood disorder due to GMC		1
• Substance-induced mood disorder		1
• Schizoaffective disorder, depressed		1
Total	100	

Table 3
Comorbid Axis I diagnoses bipolar: subjects ($N = 93$)

	N	%
No comorbid diagnoses	28	30.1%
Substance abuse/dependence	52	55.9%
Panic disorder	18	19.4%
Post traumatic stress disorder	9	9.7%
Obsessive compulsive disorder	5	5.4%
Social phobia	3	3.2%
Specific phobia	4	4.3%
Generalized anxiety	3	3.2%
Hypochondriasis	1	1.1%
Anorexia nervosa	3	3.2%
Bulimia nervosa	3	3.2%
Binge eating disorder	2	2.2%
Substance-induced mood disorder	1	1.1%
Agoraphobia without panic disorder	1	1.1%

the majority ($n = 38$, 58.5%) had only one other lifetime Axis I diagnosis; 16 (24.6%) had two other diagnoses; 9 (13.8%) had three; and 2 (3.1%) had experienced four other lifetime Axis I diagnoses. These data compare with data from the National Comorbidity Survey (Kessler et al., 1997) which indicate that 100% of persons in a highly selected subsample of persons with bipolar I disorder ($N = 29$) had at least one other lifetime psychiatric disorder. Of this group, 92.9% had experienced some anxiety disorder, with simple phobia (66.6%) and agoraphobia (62.4) most common. Seventy-one percent had experienced a lifetime substance abuse or dependence disorder and 81.7% had experienced a conduct and/or adult antisocial disorder.

3.3. Diagnostic certainty of self-reported bipolar status

The self-reported and SCID diagnoses in our sample agreed 93.0% of the time for both a positive and negative bipolar status. By self-report in the initial interview, 94 (94%) registrants who also completed a SCID identified themselves as having been diagnosed with bipolar disorder by a professional, compared to 674 of the 704 (95.7%) in the non-SCID group (chi square = 0.62, $p = 0.44$). The 6 SCID completers (6%) who answered no to the question of having received a professional diagnosis were included in the registry because they reported at the initial interview that they had reason to believe they suffered from the disorder. Of these 6, half met criteria on the SCID for a bipolar spectrum diagnosis; the remaining 3 were found to have met criteria for major depression only ($n = 2$) and schizoaffective disorder, depressive type ($n = 1$). Four subjects (4%) said they had been diagnosed with bipolar disorder by a professional, but the SCID did not confirm the diagnosis ($n = 1$ dysthymia, $n = 1$ major depression, $n = 1$ mood disorder due to a general medical condition, and $n = 1$ substance induced mood disorder).

4. Discussion

The results of this study demonstrate the validity of our self-selected registry sample. Persons who report over the phone that they have been diagnosed with bipolar disorder do accurately identify themselves. Only 4.3% of the group who reported that they had been diagnosed with bipolar disorder failed to meet diagnostic criteria following a structured diagnostic interview. Although there is only a small number of subjects in our report who believed that they had bipolar disorder but had *not* been previously diagnosed, ($n = 6$ in the SCID group), our data suggest that such persons may be correct half the time.

Study analyses demonstrate that our registry recruitment strategy has resulted in a remarkably high proportion of the sample having the disorder of interest. Using this method, we have been able to recruit the largest sample of persons with bipolar disorder ever gathered for study. The large sample size, combined with the high level of diagnostic validity shown in the current study, provides strong evidence that a voluntary case registry can be a useful strategy for identifying and recruiting persons with bipolar disorder. Our large sample will allow for the development of studies of treatment variation among income groups, of provider characteristics, and of paths to treatment, as well as providing a mechanism for clinical trial recruitment. For clinical trials, a large diagnostically certain sample will become more important as we move from studies of treatment efficacy to a focus on treatment effectiveness, when the importance of generalizability of

results to persons other than those treated at academic medical centers will increase.

One limitation of the current sample is that because 94% had already been diagnosed as having the disorder by a professional, the sample may not be fully representative of the population of persons with bipolar disorder. If population estimates of the prevalence of bipolar disorder are correct, there are many other as-yet undiagnosed cases in the community who have not been identified by our sampling strategy. Future recruitment strategies will need to address the issue of how to make the registry more accessible and inviting to other subgroups of people with bipolar disorder.

Future reports will describe the psychiatric, psychosocial, medical and treatment characteristics of the Stanley Center Registry sample over the longitudinal course of the study and will compare this sample with other bipolar samples described in the literature. These reports will draw upon a second registry interview that is completed approximately one year after the first and focuses on gathering SES, life event and treatment information for the year around the time of the individual's first-ever episode of mania or depression and for the year prior to the interview. Global monthly ratings of mood, life events, medication use, and longitudinal information about general medical history also will be investigated.

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