

Managing Bipolar Disorder: Misdiagnosis and Quality of Life

Bipolar disorder is a long-term, disabling psychiatric condition that adversely affects virtually every aspect of a patient's life. The estimated lifetime risk for bipolar I disorder, the most severe form of the illness, is between 1% and 2%.^{1,2} Bipolar spectrum disorders, which comprise all forms of the condition, have an estimated lifetime prevalence of 5%.^{3,4} The disorder is characterized by recurrence rates of 50% to 90%⁵⁻⁸ and progressive increases in the frequency and severity of episodes.⁹

Bipolar disorder exacts a heavy toll on the affected individual, the healthcare system, and society. The sixth leading cause of disability among people 15 to 44 years of age, bipolar disorder ranks ahead of a number of other prominent long-term conditions, including osteoarthritis, human immunodeficiency virus infection, diabetes, and asthma.¹⁰

The economic burden of bipolar disorder is substantial. In 1999, disability caused by the condition had an estimated economic impact of \$60 billion, with indirect costs (lost productivity) accounting for about half of the total.¹¹ Another widely cited study determined that the economic burden of bipolar disorder amounted to \$45 billion in 1991, with a majority of the total coming from indirect costs.¹²

The burden of bipolar disorder comes not only from the illness itself but from high rates of comorbid psychiatric and medical conditions. Comorbid drug or alcohol abuse is particularly common. One large study of community-dwelling adults showed that 46% of individuals with bipolar disorder suffered from alcohol abuse or dependence, and 41% had comorbid drug abuse or dependence. Additionally, 21% of patients with bipolar disorder also had a history of panic disorder, and 21% had obsessive-compulsive disorder.¹³⁻¹⁵ Other studies of patients

with bipolar disorder have shown rates of alcohol abuse ranging as high as 69% and rates of drug abuse as high as 60%.¹⁶

Surveys and other studies have consistently documented high rates of psychiatric comorbidity among patients with bipolar disorder. In a study of about 300 patients with bipolar disorder, 65% met diagnostic criteria for at least 1 lifetime comorbid psychiatric disorder.¹⁷ Another survey found that 92% of individuals who met diagnostic criteria for bipolar I disorder also met diagnostic criteria for a lifetime anxiety disorder.¹⁸ A recent literature review revealed frequent associations between bipolar disorder and anxiety disorders, panic disorder, obsessive-compulsive disorder, social phobia, eating disorders, attention-deficit/hyperactivity disorder, and axis II personality disorders.¹⁹

Patients with bipolar disorder also have increased rates of certain medical conditions compared with individuals without the disorder. Various studies have demonstrated associations between bipolar disorder and illnesses such as migraine, thyroid disease, obesity, diabetes, and multiple sclerosis. Additionally, bipolar disorder has been associated with increased mortality related to cardiovascular disease and some forms of cancer.²⁰

In addition to the emotional and physical toll, unemployment is a common consequence of bipolar disorder, as are absenteeism and job-related difficulties. A survey by the National Depressive and Manic-Depressive Association (NDMDA) found an unemployment rate of 60% among people with bipolar disorder. Moreover, 88% of the respondents reported occupational difficulties.²¹ Data from a registry of patients with bipolar disorder also demonstrated an unemployment rate of about 60%.¹²

Work-related absenteeism is common among employed individuals with bipolar disorder. As an example, one primary care study showed that a diagnosis of bipolar disorder was associated with a 7-fold likelihood of missing work because of medical illness compared with people without bipolar disorder.²² A recent literature review evaluated the association between bipolar disorder and work impairment, defined as long-term unemployment, occupational functioning, absenteeism because of emotional problems and somatic complaints, or poor work performance. Regardless of the definition, people with bipolar disorder had higher rates of work impairment compared with people without the disorder, including individuals with other types of mental illness.¹¹

Misdiagnosis frequently complicates attempts at effective management of bipolar disorder. In its most recent survey, the NDMDA found that 69% of patients with bipolar disorder were initially misdiagnosed. In more than one third of cases, 10 years or more passed before a correct diagnosis was made.²¹ The results are consistent with an earlier NDMDA survey showing a misdiagnosis rate of 70%.²³ Corroborating data have come from other investigations. For example, one study showed that 40% of patients with bipolar disorder initially had an incorrect diagnosis of major depression, and another showed that 25% to 50% of major depression cases were, in fact, bipolar disorder.^{24,25}

Misdiagnosis of bipolar disorder can have profound consequences for the clinical course of the illness. Obviously, a delay in effective treatment can place a patient at increased risk for recurrence or long-term episodes of illness. Mood-stabilizing therapy for bipolar disorder might be less effective when initiated after unsuccessful treatment for depression.²⁶ Moreover, antidepressant medications have not been shown to prevent depression in patients with bipolar disorder.²⁷

A recent study found that about 14% of the patients in the study with major depressive disorder showed symptoms of mania within the past year, suggesting that they may be misdiagnosed.²⁸ These patients

report significantly lower quality of life than patients with major depressive disorder as measured by the Short Form-8, a questionnaire designed to assess physical, social, and emotional functioning, and the more comprehensive Psychological General Well-Being Scale.

Misdiagnosis also increases the economic consequences of bipolar disorder. A delay in initiation of mood-stabilizing therapy for patients with bipolar disorder has been associated with increased healthcare costs.²⁹ Patients with unrecognized bipolar disorder have higher rates of hospital use and suicide attempts compared with individuals with recognized bipolar disorder.³⁰

Perhaps not surprisingly, many patients with bipolar disorder have poor quality of life, including health-related quality of life. A survey of bipolar patients during euthymia showed that quality of life was similar or worse than that of patients with long-term medical conditions.³¹ Another study showed that a woman who has bipolar disorder with an onset at 25 years of age loses 9 years of life, 12 years of normal health, and 14 years of effective functioning.³² Ten-year follow-up of a group of patients with bipolar disorder showed that about 50% had sustained improvement, whereas 30% to 40% declined functionally over time.³³

A recent review evaluated health-related quality of life, work impairment, and healthcare costs and utilization among patients with bipolar disorder. The analysis showed that bipolar disorder substantially decreases a person's health-related quality of life and increases costs associated with medical care and work impairment. Patients with bipolar disorder had higher rates of healthcare resources compared with patients with depression or long-term medical conditions.¹¹ Another review found that patients with bipolar disorder have lower quality of life than patients with schizophrenia.³⁴

A recent study investigated changes in health-related quality of life in patients with bipolar I or II disorder who were given quetiapine monotherapy during an 8-week, double-blind, placebo-controlled trial. Using the 16-item short form of the Quality of Life Enjoyment and Satisfaction Questionnaire, significant improvement was noted in the

quetiapine treatment groups compared with placebo groups.³⁵

This supplement to *The American Journal of Managed Care* examines 2 key issues in the diagnosis, evaluation, and management of bipolar disorder: misdiagnosis and quality of life. As suggested above, both issues make major contributions to the burdens associated with bipolar disorder.

Roy H. Perlis, MD, explores the magnitude of the problem of misdiagnosis, factors underlying misdiagnosis of bipolar disorder, and some of the consequences of misdiagnosis. Dr Perlis also discusses how to improve the diagnosis of bipolar disorder. The article emphasizes that careful screening for current and past symptoms and close clinical follow-up provide the foundation for accurate diagnosis and more effective management of bipolar disorder.

Lana A. Vornik, MSc, and Robert M. A. Hirschfeld, MD, examine the impact of bipolar disorder on patients' quality of life. They review findings from studies that have included quality-of-life assessment in the evaluation and management of patients with bipolar disorder. They also discuss findings obtained with specific quality-of-life assessment instruments. Finally, they review data related to the impact of treatment on the quality of life of patients with bipolar disorder, particularly the effects of atypical antipsychotics. In general, symptomatic improvement has been associated with improved quality of life in patients with bipolar disorder.

The following articles address highly relevant, contemporary issues in the diagnosis, evaluation, and treatment of bipolar disorder. The information provides insight into topics and principles that have clear applicability to the managed care environment.

REFERENCES

1. Kessler RC, McGonagle KA, Zhao S, et al. Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States. Results from the National Comorbidity Survey. *Arch Gen Psychiatry*. 1994; 51:8-19.
2. Bebbington P, Ramana R. The epidemiology of bipolar affective disorder. *Soc Psychiatry Psychiatr Epidemiol*. 1995;30:279-292.
3. Akiskal HS, Bourgeois ML, Angst J, Post R, Moller H, Hirschfeld R. Re-evaluating the prevalence of and diagnostic composition within the broad clinical spectrum of bipolar disorders. *J Affect Disord*. 2000;59 (suppl 1):S5-S30.
4. Angst J, Gamma A, Benazzi F, Ajdacic V, Eich D, Rossler W. Toward a re-definition of subthreshold bipolarity: epidemiology and proposed criteria for bipolar-II, minor bipolar disorders, and hypomania. *J Affect Disord*. 2003;73:133-146.
5. Goodwin FK, Jamison KR. *Manic-Depressive Illness*. New York, NY: Oxford University Press; 1990.
6. Goldberg JF, Harrow M, Grossman LS. Course and outcome in bipolar affective disorder: a longitudinal follow-up study. *Am J Psychiatry*. 1995;152:379-384.
7. Dion GL, Tohen M, Anthony WA, Watermaux CS. Symptoms and functioning of patients with bipolar disorder six months after hospitalization. *Hosp Community Psychiatry*. 1988;39:652-657.
8. Keck PE, McElroy SL, Strakowski SM, et al. Outcome and comorbidity in first- compared with multiple-episode mania. *J Nerv Ment Dis*. 1995;183:320-324.
9. Post RM, Susan R, Weiss B. Sensitization, kindling, and carbamazepine: an update on their implications for the course of affective illness. *Pharmacopsychiatry*. 1992;25:41-43.
10. Murray CJ, Lopez AD. Global mortality, disability and the contribution of risk factors: Global Burden of Disease Study. *Lancet*. 1997;349:1436-1442.
11. Dean BB, Gerner D, Gerner RH. A systematic review evaluating health-related quality of life, work impairment, and healthcare costs and utilization in bipolar disorder. *Curr Med Res Opin*. 2004;20:139-154.
12. Wyatt RJ, Henter I. An economic evaluation of manic-depressive illness—1991. *Soc Psychiatry Psychiatr Epidemiol*. 1995;30:213-219.
13. Regier DA, Farmer ME, Rae DS, et al. Comorbidity of mental disorders with alcohol and other drug abuse: results from the Epidemiologic Catchment Area (ECA) study. *JAMA*. 1990;264:2511-2518.
14. Chen YW, Dilsaver SC. Comorbidity of panic disorder in bipolar illness: evidence from the Epidemiologic Catchment Area Survey. *Am J Psychiatry*. 1995;152: 280-282.
15. Chen YW, Dilsaver SC. Comorbidity for obsessive-compulsive disorder in bipolar and unipolar disorders. *Psychiatry Res*. 1995;59:57-64.
16. Cassidy F, Ahearn EP, Carroll BJ. Substance abuse in bipolar disorder. *Bipolar Disord*. 2001;3:181-188.
17. McElroy SL, Altshuler LL, Suppes T, et al. Axis I psychiatric comorbidity and its relationship to historical illness variables in 288 patients with bipolar disorder. *Am J Psychiatry*. 2001;158:420-426.
18. Freeman MP, Freeman SA, McElroy SL. The comorbidity of bipolar and anxiety disorders: prevalence, psychobiology, and treatment issues. *J Affect Disord*. 2002;68:1-23.
19. Krishnan KR. Psychiatric and medical comorbidities of bipolar disorder. *Psychosom Med*. 2005;67:1-8.
20. McElroy SL. Diagnosing and treating comorbid (complicated) bipolar disorder. *J Clin Psychiatry*. 2004;65(suppl 15):35-44.
21. Hirschfeld RM, Lewis L, Vornik LA. Perceptions and impact of bipolar disorder: how far have we really come? Results of the National Depressive and Manic-Depressive Association 2000 survey of individuals with bipolar disorder. *J Clin Psychiatry*. 2003;64:161-174.
22. Olfson M, Fireman B, Weissman MM, et al. Mental disorders and disability among patients in a primary

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- care group practice. *Am J Psychiatry*. 1997;154:1734-1740.
- 23. Lish JD, Dime-Meenan S, Whybrow PC, Price RA, Hirschfeld RM.** The National Depressive and Manic-Depressive Association (DMDA) survey of bipolar members. *J Affect Disord*. 1994;31:281-294.
- 24. Ghaemi SN, Sachs GS, Chiou AM, Pandurangi AK, Goodwin K.** Is bipolar disorder still underdiagnosed? Are antidepressants overutilized? *J Affect Disord*. 1999;52:135-144.
- 25. Angst J, Gamma A, Lewinsohn P.** The evolving epidemiology of bipolar disorder. *World Psychiatry*. 2002;1:146-148.
- 26. Swann AC, Bowden CL, Calabrese JR, Dilsaver SC, Morris DD.** Differential effect of number of previous episodes of affective disorder on response to lithium or divalproex in acute mania. *Am J Psychiatry*. 1999;156:1264-1266.
- 27. Ghaemi SN, Lenox MS, Baldessarini RJ.** Effectiveness and safety of long-term antidepressant treatment in bipolar disorder. *J Clin Psychiatry*. 2001;62:565-569.
- 28. Bolge SC, Rajagopalan K.** Quality of life: misdiagnosed bipolar disorder vs depression on bipolar disorder. Presented at the Fourth European Stanley Conference, September 23-25, 2005; Aarhus, Denmark.
- 29. Li J, McCombs JS, Stimmel GL.** Cost of treating bipolar disorder in the California Medicaid (Medi-Cal) program. *J Affect Disord*. 2002;71:131-139.
- 30. McCombs JS, Thiebaud P, Shi L.** Impact of unrecognized bipolar disorders in patients treated with antidepressant medications [abstract]. *Value Health*. 2003;6:352.
- 31. Cooke RG, Robb JC, Young LT, Joffe RT.** Well-being and functioning in patients with bipolar disorder assessed using the MOS 20-ITEM short form (SF-20). *J Affect Disord*. 1996;39:93-97.
- 32. US Department of Health, Education, and Welfare.** *Medical practice project: a state-of-the-science report for the office of the Science Secretary for the US Department of Health, Education, and Welfare*. Baltimore, Md: Policy Research; 1979.
- 33. Goldberg JF, Harrow M.** Consistency of remission and outcome in bipolar and unipolar mood disorders: a 10-year prospective follow-up. *J Affect Disord*. 2004;81:123-131.
- 34. Namjoshi MA, Buesching DP.** A review of the health-related quality of life literature in bipolar disorder. *Qual Life Res*. 2001;10:105-115.
- 35. Endicott J, Rajagopalan K, Minkwitz M.** Efficacy of quetiapine in improving quality of life in patients with bipolar depression. Presented at the Academy of Managed Care Pharmacy 17th Annual Meeting & Showcase, April 20-23, 2005; Denver, Colo.