

Bipolar Disorder: Disease Burden

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Abstract

Bipolar disorder is a chronic, severe, recurrent mood disorder. Traditional estimates of the prevalence of the disorder may underestimate the actual total disease burden. The condition can occur across a wide spectrum of ages, but the most common age of onset appears to be between the ages of 15 and 19. Bipolar disorder is often underdiagnosed or misdiagnosed, with profound negative clinical and economic consequences. Medical and psychiatric comorbidity is common in patients with bipolar disorder. Functional disability because of bipolar disorder is comparable with that of many chronic medical conditions. It has been estimated that the total annual societal cost of bipolar disorder may be as high as \$45 billion.

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Epidemiology of Bipolar Disorder

Bipolar disorder is a chronic psychiatric illness characterized by recurrent episodes of mania, hypomania, mixed states, and depression. Various studies have estimated the prevalence of bipolar disorder to be between 1% and 2%. The National Comorbidity Survey suggested a lifetime prevalence of 1.6%.¹ The Epidemiologic Catchment Area (ECA) surveys have suggested a lifetime prevalence of 1.3%.² An epidemiologic study of 38 000 community-dwelling individuals in 10 countries found prevalence rates similar to those reported for the United States.³ However, a recent study suggested a substantially higher prevalence of 3.7% for bipolar spectrum disorders.⁴ Many estimates from community surveys may not include milder forms of bipolar disorder (eg, bipolar II disorder, bipolar disorder not otherwise specified), which could result in underestimation of the true prevalence of the spectrum of the disorder.⁵

Men and women have similar rates of bipolar illness.^{3,6} Some evidence suggests that women are more likely to be hospital-

ized during manic episodes, and that rapid cycling occurs more often in women than in men.^{6,7} Women also appear more likely to have predominantly depressive features, rather than manic features over the course of the illness.⁸

Bipolar disorder can occur for the first time at any age. However, the peak period of onset is between the ages of 15 and 19.² A National Depressive and Manic-Depressive Association (NDMDA) survey found that 59% of patients with bipolar disorder experienced their first symptoms during childhood or adolescence.⁸ However, bipolar disorder can also manifest for the first time in later years. One study showed that new onset of mania occurred in 9.3% of a group of patients older than 60 years of age with affective disorders.⁹ Another recent report noted that 6.1% of adults aged 60 and older with bipolar disorder appear to have illness of relatively recent onset.¹⁰

Recurrence rates for bipolar disorder are high even with ongoing therapy. One study found a 73% relapse rate at 5 years, and two thirds of the patients had multiple relapses.¹¹ Other estimates place the relapse rate at about 90%, with nearly half of the relapses occurring within 2 years.¹²

Misdiagnosis and Its Consequences

Misdiagnosis of bipolar disorder is a frequent occurrence and represents a major obstacle to appropriate treatment. In one study, 40% of a group of patients with bipolar disorder had received an incorrect diagnosis of major depression.¹³ Another study found that 25% to 50% of major depression cases were, in fact, bipolar disorder.¹⁴ The NDMDA survey showed that 70% of patients with bipolar disorder were initially misdiagnosed, most often as having major depression. Half of the patients had consulted multiple physicians or other professionals.⁸ On average, 8

years passed before the correct diagnosis of bipolar disorder was made.¹⁵ Reasons for misdiagnosis are manifold, including that patients may not share information regarding manic symptoms with their physicians, depressive symptoms can be easily mistaken for unipolar depressive illness, and, finally, symptoms of bipolar disorder may frequently overlap with those of other psychiatric disorders, including schizophrenia, attention-deficit disorder, and personality disorders.^{16,17}

Misdiagnosis of bipolar disorder leads to a variety of negative consequences, perhaps the most obvious being a delay in effective therapy. One study found that direct health-care costs were significantly higher for patients who had delayed use of or did not use mood stabilizers during the first year of treatment for bipolar disorder.¹⁸ Additionally, mood stabilizing therapy may be less effective when initiated after unsuccessful therapy for depressive episodes.¹⁹ In particular, misdiagnosis of bipolar disorder as unipolar depression has substantial clinical implications. Antidepressants have not been shown to be more effective than mood stabilizers in the treatment of acute bipolar depression, and have been shown to be less effective than mood stabilizers in preventing depressive relapse in bipolar disorder.²⁰ Antidepressant therapy can also have a destabilizing effect on the clinical course of bipolar disorder.²¹⁻²³ Finally, psychoeducational approaches specific for bipolar illness are supported by evidence-based treatment guidelines,²⁴ and individuals who are misdiagnosed do not receive the benefits of appropriate psychoeducation.

Failure to recognize bipolar disorder has substantial economic consequences. A California study found that patients with unrecognized bipolar disorder have higher rates of hospital use and suicide attempts compared with patients with recognized bipolar disorder.²⁵

Functional Impairment

Bipolar disorder is the sixth leading cause of medical disability worldwide among people 15 to 44 years of age. Bipolar disorder is associated with a greater degree of disability than a number of prominent chronic med-

ical conditions, including osteoarthritis, human immunodeficiency virus infection, diabetes, and asthma.²⁶

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Bipolar disorder is associated with high rates of unemployment, job-related difficulties, and interpersonal stress. Two large surveys revealed unemployment rates of about 60%, even among college-educated patients.^{27,28} In one of the surveys, 88% of respondents reported occupational difficulties.²⁷ The other survey also showed that 65% of respondents had difficulty maintaining long-term relationships, and 64% had difficult relationships with their children.²⁸

Many patients with bipolar disorder have a poor quality of life, particularly when the condition goes untreated or when comorbid conditions exist. A survey of bipolar patients during euthymia found that their quality of life was similar to or below that of patients with long-term medical conditions.²⁹ A US government study concluded that a woman with bipolar disorder with onset at age 25 loses 9 years of life, 12 years of normal health, and 14 years of effective functioning.³⁰ A 10-year follow-up of patients with bipolar disorder found that about 50% of patients had sustained improvement, whereas 30% to 40% experienced functional decline over time.³¹

A recent review of health, life, work impairment, and healthcare costs and utilization among patients with bipolar disorder showed that this illness imposes a tremendous burden on patients and the healthcare system, including decreased health-related quality of life and increased costs associated with medical care and work

impairment.³² Patients with bipolar disorder used healthcare services more than patients with depression or chronic medical conditions. Inpatient costs were the largest contributor to the cost of care. Treatment to prevent recurrence was found to be the most effective way to reduce costs. The authors concluded that limited data suggest that appropriate management of bipolar disorder can improve health-related quality of life and functioning while reducing use and cost.

Suicide

Patients with bipolar disorder have a higher risk of suicide than patients with any other psychiatric or medical illness.³³ According to one study, the odds ratio for suicide attempts in bipolar disorder was 6.2, which was higher than any other axis I psychiatric disorder, including depression.³⁴ Another study showed that patients with bipolar disorder had a higher lifetime history of suicide attempt than patients with any other psychiatric disorder.³⁵ Rates of suicidal ideation and attempts range between 35% and 50%.^{28,33,36} The Stanley Center Bipolar Disorder Registry reported that 50% of patients enrolled had attempted suicide, and 35% of the attempts resulted in hospitalization.²⁸ The rate of completed suicide is approximately 20%.³¹

Comorbidity and Bipolar Disorder

Patients with bipolar disorder have high rates of medical and psychiatric comorbidity. The ECA study found that among patients with bipolar disorder, 46% had alcohol abuse or dependence, 41% had drug abuse or dependence, 21% had panic disorder, and 21% had obsessive-compulsive disorder.³⁷⁻³⁹ Persons with bipolar I disorder were more than 3 times as likely to have alcohol abuse or dependence and 7 times more likely to have drug abuse or dependence compared with the general population.³⁷ Patients with bipolar disorder were 26 times more likely to have panic disorder and 8 times more likely to have obsessive-compulsive disorder than were people in the general population without a mood disorder.^{38,39}

In another study, 65% of a group of patients with bipolar disorder also met *Diagnostic and Statistical Manual of*

Mental Disorders, Fourth Edition criteria for at least 1 comorbid lifetime axis I psychiatric disorder. The most common comorbidities were anxiety disorders and substance use. The authors found evidence that axis I comorbidity was associated with an earlier age of onset of bipolar disorder and worsening course of bipolar illness.⁴⁰

Other studies have confirmed frequent comorbidity of bipolar disorder with anxiety, substance use, and conduct disorders. Various reports have documented cooccurrence of bipolar disorder with a variety of other psychiatric disorders, including anorexia nervosa, bulimia nervosa, binge-eating disorder, attention-deficit/hyperactivity disorders, sexual disorders and addictions, impulse-control disorders, autism spectrum disorders, and Tourette's syndrome.⁴¹ The clinical implications of comorbidity are profound. One report noted that in bipolar patients the presence of substance use disorder doubles the risk of suicide,⁴² and another report found that quality of life among individuals with bipolar disorder and substance abuse is significantly affected by the severity of substance dependence.⁴³

General medical disorders also frequently occur with bipolar disorder. These include migraine, thyroid disease, and type 2 diabetes. Community studies have demonstrated associations between bipolar disorder and migraine, Tourette's syndrome, multiple sclerosis, and obesity. Bipolar disorder has been associated with increased mortality from cardiovascular disease and some forms of cancer.⁴¹ It has been suggested that the risk of developing dementia is increased when there are a greater number of episodes in bipolar disorder.⁴⁴

Economic Burden

Bipolar disorder imposes a substantial economic burden on the healthcare system. One study estimated that the total economic burden of the condition exceeded \$45 billion in 1991. Of that total, actual treatment costs accounted for \$7 billion.⁴⁵ Another report placed the estimated cost of bipolar disorder at \$10 billion in 1990.⁴⁶ A more recent study found that total lifetime costs for patients with bipolar disorder onset in 1998 was \$24 billion.⁴⁷

Conclusion

Bipolar disorder poses a major challenge to the healthcare system. The condition is frequently misdiagnosed and may be more common than previously thought. Recurrence rates are high, even with ongoing therapy. Bipolar disorder affects many aspects of a patient's life. Loss of function is common, and quality of life is often greatly reduced. Unemployment rates are high among patients with bipolar disorder, and individuals often have difficulty in the workplace and in social and personal relationships. Individuals with bipolar disorder have high rates of psychiatric and medical comorbidity, which contributes to increased utilization of healthcare resources. The estimated annual societal cost of bipolar disorder ranges from \$10 billion to \$45 billion.

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. Weissman MM, Bland RC, Canino GJ, et al. Cross-national epidemiology of major depression and bipolar disorder. *JAMA*. 1996;276:293-299.
4. Hirschfeld RMA, Calabrese JR, Weissman M. Lifetime prevalence of bipolar I and II disorders in the United States. Abstract presented at: The 155th Annual Meeting of the American Psychiatric Association; May 18-23, 2002; Philadelphia, Pa.
5. Dunner DL. Clinical consequences of under-recognized bipolar spectrum disorder. *Bipolar Disord*. 2003;5:456-463.
6. Hendrick V, Altshuler LL, Gitlin MJ, Delrahim S, Hammen C. Gender and bipolar illness. *J Clin Psychiatry*. 2000;61:393-396.
7. Leibenluft E. Women with bipolar illness: clinical and research issues. *Am J Psychiatry*. 1996;153:163-173.
8. 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.
9. Yassa R, Nair V, Nastase C, Camille Y, Belzile L. Prevalence of bipolar disorder in a psychogeriatric population. *J Affect Disord*. 1988;14:197-201.
10. Sajatovic M, Blow F, Ignacio RV, Kales HC. New-onset bipolar disorder in later life. *Am J Geriatr Psychiatry*. 2005;13:282-289.
11. Gitlin MJ, Swendsen J, Heller TL, Hammen C. Relapse and impairment in bipolar disorder. *Am J Psychiatry*. 1995;152:1635-1640.
12. Bowden CL, Krishnan A. Pharmacotherapy for bipolar depression: an economic assessment. *Expert Opin Pharmacother*. 2004;5:1101-1107.
13. 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.
14. Angst J, Gamma A, Lewinsohn P. The evolving epidemiology of bipolar disorder. *World Psychiatry*. 2002;1:146-148.
15. Baldessarini R, Tondo L, Hennen J. Treatment delays in bipolar disorders. *Am J Psychiatry*. 1999;156:811-812.
16. Thomas P. The many forms of bipolar disorder: a modern look at an old illness. *J Affect Disord*. 2004;79(suppl 1):S3-S8.
17. Bowden CL. A different depression: clinical distinctions between bipolar and unipolar depression. *J Affect Disord*. 2005;84:117-125.
18. 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.
19. 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.
20. Ghaemi SN, Hsu DJ, Soldani F, Goodwin FK. Antidepressants in bipolar disorder: the case for caution. *Bipolar Disord*. 2003;5:421-433.
21. Wehr TA, Goodwin FK. Rapid cycling in manic-depressives induced by tricyclic antidepressants. *Arch Gen Psychiatry*. 1979;36:555-559.
22. Wehr TA, Sack DA, Rosenthal NE, Cowdry RW. Rapid cycling affective disorder: contributing factors and treatment responses in 51 patients. *Am J Psychiatry*. 1988;145:179-184.
23. Altshuler LI, Hendrick V, Parry B. Pharmacological management of premenstrual disorder. *Harv Rev Psychiatry*. 1995;2:233-245.
24. Fountoulakis KN, Vieta E, Sanchez-Morno J, Kaprinis SG, Goikolea JM, Kaprinis GS. Treatment guidelines for bipolar disorder: a critical review. *J Affect Disord*. 2005;86:1-10.
25. McCombs JS, Thiebaud P, Shi L. Impact of unrecognized bipolar disorders in patients treated with antidepressant medications [abstract]. *Value Health*. 2003;6:352.
26. Murray CJ, Lopez AD. Global mortality, disability and the contribution of risk factors: Global Burden of Disease Study. *Lancet*. 1997;349:1436-1442.
27. Hirschfeld MA, 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.
28. Kupfer DJ, Frank E, Grochocinski VJ, Cluss PA, Houck PR, Stapf DA. Demographic and clinical characteristics of individuals in a bipolar disorder case registry. *J Clin Psychiatry*. 2002;63:120-125.
29. 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.
30. United States 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. Policy Research, Baltimore, Maryland, USA, 1979.

31. **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.
32. **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.
33. **Woods SW.** The economic burden of bipolar disease. *J Clin Psychiatry.* 2000;61(suppl 13):38-41.
34. **Chen YW, Dilsaver SC.** Lifetime rates of suicide attempts among subjects with bipolar and unipolar disorders relative to subjects with other Axis I disorders. *Biol Psychiatry.* 1996;39:896-899.
35. **Kessler RC, Borges G, Walters EE.** Prevalence of and risk factors for lifetime suicide attempts in the National Comorbidity Survey. *Arch Gen Psychiatry.* 1999;56:617-626.
36. **Suppes T, Leverich GS, Keck PE, et al.** The Stanley Foundation Bipolar Treatment Outcome Network II. Demographics and illness characteristics of the first 261 patients. *J Affect Disord.* 2001;67:45-59.
37. **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.
38. **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.
39. **Chen YW, Dilsaver SC.** Comorbidity for obsessive-compulsive disorder in bipolar and unipolar disorders. *Psychiatry Res.* 1995;59:57-64.
40. **McElroy SL, Altshuler LL, Tuppes 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.
41. **McElroy SL.** Diagnosing and treating comorbid (complicated) bipolar disorder. *J Clin Psychiatry.* 2004;65(suppl 15):35-44.
42. **Comtois KA, Russo JE, Roy-Byrne P, Ries RK.** Clinicians' assessment of bipolar disorder and substance abuse as predictors of suicidal behavior in acutely hospitalized psychiatric inpatients. *Biol Psychiatry.* 2004;56:757-763.
43. **Singh J, Mattoo SK, Sharan P, Basu D.** Quality of life and its correlates in patients with dual diagnosis of bipolar affective disorder and substance dependence. *Bipolar Disord.* 2005;7:187-191.
44. **Kessing LV, Anderson PK.** Does the risk of developing dementia increase with the number of episodes in patients with depressive disorder and in patients with bipolar disorder? *J Neurol Neurosurg Psychiatry.* 2004;75:1662-1666.
45. **Wyatt RJ, Henter I.** An economic evaluation of manic-depressive illness—1991. *Soc Psychiatry Psychiatr Epidemiol.* 1995;30:213-219.
46. **Greenberg PE, Stiglin LE, Finkelstein SN, Berndt ER.** The economic burden of depression in 1990. *J Clin Psychiatry.* 1993;54:405-418.
47. **Begley CE, Annegers JF, Swann AC, et al.** The lifetime cost of bipolar disorder in the US: an estimate for new cases in 1998. *Pharmacoeconomics.* 2001;19:483-495.