

# Mood Disorders and Suicide

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The mood disorders unipolar major depression and bipolar disorder increase the risk of suicidal ideation, attempted suicide, and death by completed suicide. This article reviews the epidemiologic data on the relationship between mood disorders and suicide, with an emphasis on the substantial risk of suicide, while reassessing older data that may no longer apply. Widespread underdiagnosis and undertreatment of major depression and bipolar disorder contribute to an unacceptable risk of suicide, a preventable tragedy. *(J Clin Psychiatry 2001;62[suppl 25]:27-30)*

Many people who struggle with mood disorders may think of killing themselves, yet ultimately decide to live; conversely, most people who kill themselves have mood disorders, and in many instances, their deaths are preventable. Contemplated and completed suicide represents hopelessness, despair, and the fatal outcome of the 2 major mood disorders, major depression and bipolar disorder. The actual risk of death from suicide for those with mood disorders varies from study to study, but compared with the general population, people with mood disorders are unequivocally at increased risk of suicide.<sup>1</sup> A few weeks before people complete suicide, most have contact with their physicians,<sup>2,3</sup> and many are neither diagnosed with a mood disorder nor treated.<sup>4-6</sup> Since treatment lowers the risk of suicide, many of these deaths could have been prevented.<sup>7,8</sup> Thus, detection and treatment of mood disorders are the cornerstones of preventing suicide. This article will review the epidemiology and complex relationship between mood disorders and suicide.

## RISK OF SUICIDE IN MAJOR DEPRESSION

The lifetime risk of death by suicide in major depression is frequently cited as 15%.<sup>9</sup> When this statistic from the Guze and Robins article is cited, an important detail often missing is that the 15% rate of death refers to those patients who required inpatient care before 1970 and who

were then followed for 5 to 10 years. The generalizability of this rate of death from suicide to outpatients today is, at best, questionable. Additionally, the treatments widely available to treat depression in 1970 would frequently result in death when taken as an overdose; if ingested all at once, just a 2-week supply of a tricyclic antidepressant results in cardiac death.<sup>10,11</sup> The newer generation of antidepressants is less toxic when taken as an overdose; the modern treatments used to alleviate depression (and its attendant suicidal ideation and behaviors) cannot be used by depressed patients to kill themselves.<sup>12</sup> Thus, the 15% lifetime risk of death by suicide in depressed patients is most likely a gross overestimate for today's outpatients.

An additional line of reasoning for revising the suicide rate comes from epidemiologic data. Several researchers have extrapolated rates of mood disorders and suicide from large-scale epidemiologic studies.<sup>13,14</sup> Using Guze and Robin's assumption of a 15% lifetime rate of death from suicide and the rates of depression in the United States,<sup>15</sup> the rate of suicide should be about 4 times higher than actually observed.<sup>13</sup> By modeling data available as of 1994, the risk of completed suicide for people with major depression is estimated at about 3.4%, with men having a risk of death of about 7% and women about 1%. The modeling also suggests that depressed males below the age of 25 years are over 10 times more likely to die from suicide as compared to females in their age group. Similarly, a meta-analysis of suicide studies in psychiatric patients found an overall estimate of the risk of death from suicide of about 6% for affective disorders.<sup>14</sup> One could reasonably conclude that the actual lifetime risk of death from suicide for major depression is between 3.4% and 6%, but this overall estimate omits important distinctions among subpopulations. To show such differences, a meta-analysis examined suicide rates in 3 distinct groups: inpatients who had been hospitalized following suicidal behavior, inpatients with affective disorders, and predominantly affective disorder

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outpatients; lifetime risk of suicide was found to be 8.6%, 4.0%, and 2.2%, respectively.<sup>16</sup>

More direct evidence of the risk of suicide from major depression is available from the National Comorbidity Survey.<sup>15,17</sup> This study assessed a representative cross-sectional community sample with the obvious constraint that respondents were alive; those who had already died by suicide were not available for analysis. Compared to those without any disorder, those with major depression had odds ratios for suicidal ideation and suicidal plans of 11.0 and 9.6, respectively. Among those with ideation, the odds ratio for having a plan or a planned attempt was 1.7 and 2.1; the odds ratio for those without a plan who had an impulsive attempt was 1.9. The number of psychiatric comorbid conditions, regardless of the specific conditions, dramatically increased the odds ratio for all of the studied aspects of suicidality.

Data on lifetime risk of suicide inform the field but fail to be of clinical use. A more time-sensitive assessment of risk of suicide is needed. It appears that the period of highest risk for attempted suicide is both early in the course of a major depressive episode and within the first few years of onset of the disorder. Those who attempt suicide do so more frequently in the first 3 months of an episode and within 5 years of the onset of depression.<sup>18</sup> Greater anxiety may also predict suicide early in the course of the disorder, while hopelessness predicts long-term risk.<sup>19,20</sup> For some, however, their anxiety may prevent them from killing themselves; if their anxiety falls short of being intolerable, patients may actually be too anxious about dying or causing themselves pain. When these patients are treated with anxiolytics alone, their suicidal risk may actually increase.<sup>21</sup>

### RISK OF SUICIDE FOR BIPOLAR DISORDER

In contrast to major depression, bipolar disorder is made up of several distinct states: depression, hypomania, mania, and mixed states, all with or without psychosis. Since patients can move between states and experience multiple states in their lifetimes, it is not surprising that patients with bipolar disorder kill themselves more frequently than those with major depression. It has been estimated that the lifetime risk of suicide attempts for bipolar disorder is between 25% and 50%,<sup>22</sup> with different states associated with different risks of suicide. Mania confers the lowest risk for completed suicide, while those bipolar patients with mixed symptoms or dysphoric mania (mania with depressive symptoms) present the highest risk.<sup>23-27</sup> Those with mania, however, may still have higher rates of attempted suicide compared to those with major depression.<sup>17</sup> In contrast, those with major depression may have more suicidal intent than those with bipolar I with mixed states.<sup>28</sup>

The higher risk of suicide associated with dysphoric mania, compared to other bipolar states, may be due to

longer episodes coupled with a lower response to treatment.<sup>29-31</sup> Mood-stabilizing anticonvulsants, such as carbamazepine and valproate, may improve the distress and associated suicidal thoughts and actions experienced by dysphoric patients, although this relationship remains speculative.<sup>32,33</sup> The increased risk of suicide across all states of bipolar disorder could result from drug and alcohol abuse, a common and corrosive comorbid condition. Substance and alcohol abuse occurs in up to 60% of all bipolar I patients.<sup>34,35</sup> But those with dysphoric mania or rapid cycling are at the highest risk of substance abuse.<sup>34,36</sup> Another possible reason for the higher risk of suicide among those in mixed states may be that manic symptoms during a depressed episode, especially irritability and tension, are particularly difficult to tolerate and cause patients to feel trapped.<sup>33</sup> Suicide is one way to rid oneself of this intolerable state.<sup>37</sup>

Bipolar II patients, with episodes of major depression interspersed with periods of hypomania, are also a high-risk group for suicide.<sup>38-40</sup> Patients with a history of suicide attempts were found to have a greater prevalence of alcoholism, bipolar II, and schizotypal features.<sup>38</sup> When inpatients were ranked for their level of suicidality, those with bipolar II disorder were the highest followed by major depressive disorder, bipolar I disorder with mainly mixed episodes, and substance abuse disorders.<sup>28</sup> This is one of the few studies that ranked bipolar II patients as more suicidal than bipolar I patients with mixed episodes. Although other studies refute this finding, bipolar II subtypes have been found to be associated with a high risk of suicide.<sup>41,42</sup>

The high risk of suicide among bipolar II patients may be due to misdiagnosis; many are misdiagnosed as having a personality disorder or major depression. Cycling and mixed states can result when these patients are treated with antidepressants alone.<sup>43</sup> As described earlier, these states themselves are associated with a high risk of suicide.

Although dysphoric mania is the bipolar subtype associated with the highest risk of completed suicide, bipolar patients in depressive episodes are also at risk. Those bipolars who attempt suicide were found to do so more often during a depressive episode than during a nondepressive episode.<sup>7</sup> Similarly, high-intent bipolar suicide attempters and completers had more depressive pathology.<sup>44</sup> These relationships, however, should be tempered by the underdiagnosis of dysphoric mania, which is usually diagnosed and treated as agitated depression instead.

The risk of suicide appears to be associated with onset at an earlier age and then remains constant over one's lifetime without any relationship to the duration of illness.<sup>45</sup>

### SUICIDE AND TREATMENT

There are increasing amounts of evidence for the efficacy of various treatments in preventing suicide. Most notably, considerable data support the beneficial effect of

lithium on suicide rates,<sup>46,47</sup> as well as indicate an important link between higher rates of antidepressant prescribing and lower rates of suicides.<sup>8</sup> Additionally, psychosocial interventions may potentially be beneficial for individuals who are at high risk for suicide (see Gray and Otto,<sup>48</sup> this issue, for a review).

Unfortunately, despite the availability of treatments that help prevent suicide and the undeniable link between mood disorders and high rates of suicide, mood disorders continue to be underdiagnosed and undertreated. Studies have reported that as many as one half to three quarters of major mood disorders may go undiagnosed.<sup>29,49</sup> Additionally, reports of patient treatment history<sup>5</sup> and of expert consensus<sup>50</sup> have concluded that major depression in particular is overwhelmingly undertreated.

### SUMMARY

Major depression and bipolar disorder cause people to kill themselves. Suicide is a public health tragedy when widely available and effective treatments are underutilized. The key to prevention is the apparently simple combination of detection and treatment of mood disorders in patients, but all too often, these patients linger without either a diagnosis or treatment. Public education and greater detection and treatment in primary care (major depression) and psychiatry (bipolar disorder) may ultimately reduce suicide rates.

*Drug name:* carbamazepine (Tegretol and others).

*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.

### REFERENCES

- Henriksson MM, Aro HM, Marttunen MJ, et al. Mental disorders and comorbidity in suicide. *Am J Psychiatry* 1993;150:935–940
- Anderson U, Anderson M, Rosholm J, et al. Contacts to the health care system prior to suicide: a comprehensive analysis using registers for general and psychiatric hospital admissions, contacts to general practitioners and practicing specialists and drug prescriptions. *Acta Psychiatr Scand* 2000; 102:126–134
- Appleby L, Shaw J, Amos T, et al. Suicide within 12 months of contact with mental health services: national clinical survey. *BMJ* 1999;318:1235–1239
- Keller MG, Klerman GL, Lavori PW, et al. Treatment received by depressed patients. *JAMA* 1982;248:1848–1855
- Oquendo MA, Malone KM, Ellis SP, et al. Inadequacy of antidepressant treatment for patients with major depression who are at risk for suicidal behavior. *Am J Psychiatry* 1999;156:190–194
- Rost K, Zhang M, Fortney J, et al. Persistently poor outcomes of undetected major depression in primary care. *Gen Hosp Psychiatry* 1998;20:12–20
- Rihmer Z, Rutz W, Pihlgren H, et al. Depression and suicide on Gotland: an intensive study of all suicides before and after a depression-training programme for general practitioners. *J Affect Disord* 1995;35:147–152
- Isacsson G, Bergman U, Rich CL. Epidemiological data suggest antidepressants reduce suicide risk among depressives. *J Affect Disord* 1996;41: 1–8
- Guze SB, Robins E. Suicide and primary affective disorders. *Br J Psychiatry* 1970;117:437–438
- Gallant DM. Antidepressant overdose: symptoms and treatment. *Psychopathology* 1987;20(suppl 1):75–81
- Halper JP, Mann JJ. Cardiovascular effects of antidepressant medications. *Br J Psychiatry* 1988;153(suppl 3):87–98
- Kapur S, Mieczkowski T, Mann JJ. Antidepressant medications and the relative risk of suicide attempt and suicide. *JAMA* 1992;268:3441–3445
- Blair-West GW, Cantor CH, Mellsop GW, et al. Lifetime suicide risk in major depression: sex and age determinants. *J Affect Disord* 1999;55: 171–178
- Inskip HM, Harris EC, Barraclough B. Lifetime risk of suicide for affective disorder, alcoholism, and schizophrenia. *Br J Psychiatry* 1998;172:35–37
- 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
- Bostwick JM, Pankratz VS. Affective disorders and suicide risk: a reexamination. *Am J Psychiatry* 2000;157:1925–1932
- 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
- Malone KM, Haas GL, Sweeney JA, et al. Major depression and the risk of attempted suicide. *J Affect Disord* 1995;34:173–185
- Fawcett J, Scheftner WA, Fogg L, et al. Time-related predictors of suicide in major affective disorders. *Am J Psychiatry* 1990;147:1189–1194
- Beck AT, Weissman A, Lester D, et al. The measurement of pessimism: the Hopelessness Scale. *J Consult Clin Psychol* 1974;68:371–377
- Placidi GPA, Oquendo MA, Malone KM, et al. Anxiety in major depression: relationship to suicide attempts. *Am J Psychiatry* 2000;157: 1614–1618
- Robins LN, Regier DA, eds. *Psychiatric Disorders in America: The Epidemiologic Catchment Area Study*. New York, NY: Free Press; 1991
- Dilsaver SC, Yuan-Who C, Swann AC, et al. Suicidality in patients with pure and depressive mania. *Am J Psychiatry* 1994;151:1312–1315
- Goldstein RB, Black DW, Nasrallah A, et al. The prediction of suicide. *Arch Gen Psychiatry* 1991;48:418–422
- Strakowski SM, McElroy SL, Keck PE Jr, et al. Suicidality among patients with mixed and manic bipolar disorder. *Am J Psychiatry* 1996;153: 674–676
- Freeman MP, McElroy SL. Clinical picture and etiological models of mixed states. *Psychiatr Clin North Am* 1999;22:535–547
- Goldberg JF, Garno JL, Portera L, et al. Correlates of suicidal ideation in dysphoric mania. *J Affect Disord* 1999;56:75–81
- Tondo L, Baldessarini RJ, Hennen J, et al. Suicide attempts in major affective disorder patients with comorbid substance use disorders. *J Clin Psychiatry* 1999;60(suppl 2):63–69
- Keller MB, Lavori PW, Coryell W, et al. Differential outcome of pure manic, mixed/cycling, and pure depressive episodes in patients with bipolar illness. *JAMA* 1986;255:3138–3142
- Secunda SK, Swann A, Katz MM, et al. Diagnosis and treatment of mixed mania. *Am J Psychiatry* 1987;144:96–98
- Prien RF, Himmelhoch JM, Kupfer DJ. Treatment of mixed mania. *J Affect Disord* 1988;15:9–15
- Clothier J, Swann AC, Freeman T. Dysphoric mania. *J Clin Psychopharmacol* 1992;12:13S–16S
- McElroy SL, Keck PE Jr, Pope HG Jr, et al. Clinical and research implications of the diagnosis of dysphoric or mixed mania or hypomania. *Am J Psychiatry* 1992;149:1633–1644
- Himmelhoch JM, Mulla D, Neil JF, et al. Incidence and significance of mixed affective states in a bipolar population. *Arch Gen Psychiatry* 1976; 33:1062–1066
- Sonne SC, Brady KT. Substance abuse and bipolar comorbidity. *Psychiatr Clin North Am* 1999;22:609–625
- Brady KT, Lydiard RB. Bipolar affective disorder and substance abuse. *J Clin Psychopharmacol* 1992;12:17S–22S
- Goodwin FK, Jamison KR. *Manic-Depressive Illness*. New York, NY: Oxford University Press; 1990
- Bulik CM, Carpenter LL, Kupfer DJ, et al. Features associated with suicide attempts in recurrent major depression. *J Affect Disord* 1990;18:29–37
- Rihmer Z, Barsi J, Arato M, et al. Suicide in subtypes of primary major depression. *J Affect Disord* 1990;18:221–225
- Amsterdam JD, Garcia-Espana F, Fawcett J, et al. Efficacy and safety of fluoxetine in treating bipolar II major depressive episode. *J Clin Psychopharmacol* 1998;18:435–440
- Lester D. Suicidal behavior in bipolar and unipolar affective disorders: a meta-analysis. *J Affect Disord* 1993;27:117–121
- Vieta E, Benabarre A, Colom F, et al. Suicidal behavior in bipolar I and

- bipolar II disorder. *J Nerv Ment Dis* 1997;185:407–409
43. Rihmer Z, Pestalicy P. Bipolar II disorder and suicidal behavior. *Psychiatr Clin North Am* 1999;22:667–673
44. Michel K. Suicide risk factors: a comparison of suicide attempters with suicide completers. *Br J Psychiatry* 1987;150:78–82
45. Ahrens B, Berghofer A, Wolf T, et al. Suicide attempts, age and duration of illness in recurrent affective disorders. *J Affect Disord* 1995;36:43–49
46. Crundwell JK. Fluoxetine and suicidal ideation: a review of the literature. *Int J Neurosci* 1993;68:73–84
47. Tondo L, Jamison KR, Baldessarini RJ. Effect of lithium maintenance on suicidal behavior in major mood disorders. *Ann N Y Acad Sci* 1997;836:339–351
48. Gray SM, Otto MW. Psychosocial approaches to suicide prevention: applications to patients with bipolar disorder. *J Clin Psychiatry* 2001;62(suppl 25):56–64
49. Mann JJ, Oquendo M, Underwood MD, et al. The neurobiology of suicide risk: a review for the clinician. *J Clin Psychiatry* 1999;60(suppl 2):7–11
50. Hirschfeld RMA, Keller MB, Panico S, et al. The National Depressive and Manic-Depressive Association consensus statement on the undertreatment of depression. *JAMA* 1997;277:333–340

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