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.

M any 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.1 A few weeks before people complete suicide, most have contact with their physicians,2,3 and many are neither diagnosed with a mood disorder nor treated.4–6 Since treatment lowers the risk of suicide, many of these deaths could have been prevented.7,9 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%.9 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.10,11 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.12 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.13,14 Using Guze and Robin’s assumption of a 15% lifetime rate of death from suicide and the rates of depression in the United States,15 the rate of suicide should be about 4 times higher than actually observed.13 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.14 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...
Outpatients; lifetime risk of suicide was found to be 8.6%, 4.0%, and 2.2%, respectively.16

More direct evidence of the risk of suicide from major depression is available from the National Comorbidity Survey.15,17 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 co-morbid 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.14 Greater anxiety may also predict suicide early in the course of the disorder, while hopelessness predicts long-term risk.19,20 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.21

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%,22 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.23–27 Those with mania, however, may still have higher rates of attempted suicide compared to those with major depression.17 In contrast, those with major depression may have more suicidal intent than those with bipolar I with mixed states.28

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.29–31 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.2,23,32 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.34,35 But those with dysphoric mania or rapid cycling are at the highest risk of substance abuse.34,36 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.33 Suicide is one way to rid oneself of this intolerable state.37

Bipolar II patients, with episodes of major depression interspersed with periods of hypomania, are also a high-risk group for suicide.38–40 Patients with a history of suicide attempts were found to have a greater prevalence of alcoholism, bipolar II, and schizotypal features.38 When patients 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.29 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.31,42

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.32 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 bipolar who attempt suicide were found to do so more often during a depressive episode than during a nondepressive episode.7 Similarly, high-intent bipolar suicide attempters and completers had more depressive pathology.38 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.43

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,\textsuperscript{46,47} as well as indicate an important link between higher rates of antidepressant prescribing and lower rates of suicides.\textsuperscript{8} Additionally, psychosocial interventions may potentially be beneficial for individuals who are at high risk for suicide (see Gray and Otto,\textsuperscript{48} 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.\textsuperscript{29,49} Additionally, reports of patient treatment history\textsuperscript{5} and of expert consensus\textsuperscript{50} 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**

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