

The Risk of Suicide in Patients With Bipolar Disorders

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Patients with bipolar disorder have a high risk of committing suicide, but determining the exact risk is complicated. For many years, the lifetime suicide risk in bipolar disorder was accepted as 15%, but recent researchers have suggested that the lifetime suicide risk may be lower. The group of bipolar patients at highest risk of suicide are young men who are in an early phase of the illness, especially those who have made a previous suicide attempt, those abusing alcohol, and those recently discharged from the hospital. The risk is also increased in patients who are in the depressed phase of bipolar illness, who have mixed states, or who have psychotic mania. Lithium prophylaxis appears to decrease suicide attempts.
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Patients with affective disorders, and particularly bipolar disorders, have a high risk of committing suicide compared with those with other psychiatric and medical disorders; however, determining their exact risk of suicide is difficult for several reasons. First, suicide attempts and completed suicides are easier to identify than suicidal thoughts, which range from fleeting to intrusive and persistent. The relationship of suicidal ideation to completed suicide has not been well studied in bipolar disorder. Second, interpreting suicide rates is complicated. Most cohort studies are of an untreated or partially compliant population, and ethical considerations preclude a clinical study of suicidality in medicated versus nonmedicated patients. Third, few, if any, studies of suicide separate patients by severity of illness. Most studies are done with hospitalized patients, which slants the data toward severely ill patients. Fourth, changes in suicide rates are difficult to decipher since diagnostic criteria vary across time, and treatments also change. Finally, methodological problems confound interpretation. For example, the bipolar and unipolar distinctions became standard in the literature only over the past decade. The enormous variability across follow-up studies has resulted in uncertainty concerning the risk for suicide.

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In 1970, Guze and Robins¹ were the first to review and systematically document the extent of suicide risk in what was then termed manic-depressive illness. They found in every study that at least 12% of deaths among manic-depressive patients were the result of suicide. In 9 studies, 12% to 19% of deaths were due to suicide, and in 8 studies, the suicide rate ranged from 35% to 60%. The researchers concluded that by the time all the patients in the studies they had examined had died, about 15% would have committed suicide, which would make the rate in manic-depressive illness at least 30 times higher than that in the general population. Twenty years later, Goodwin and Jamison² similarly found in 30 studies that 19% of patients had died due to suicide. Recently, however, some researchers have found a lower risk for suicide in patients with bipolar disorder.

REASSESSMENT OF SUICIDE RISK IN AFFECTIVE DISORDERS

Evidence from several recent sources indicates that the suicide rate in persons with major depression is probably less than previously thought. Blair-West and colleagues³ calculated the lifetime risk of suicide in major depression in the United States by adding the lifetime risk of suicide in each age category. Their estimate of the lifetime suicide rate for major depression was 2.5%. They calculated that the lifetime risk would increase to 3.5% if the actual suicide rate was 40% greater than what is reported in official statistics. The discrepancy between this low suicide rate and the usually quoted rate of 15% may be the result of sampling biases. For example, most of the early studies of suicides were based on severely depressed inpatients, while the great majority of persons with major depression are treated as outpatients if they are treated at all. Some of

Table 1. Model Predicting Proportion of Cohort to Die From Suicide*

Disorder	Proportion Assumed Dead (%)			
	10	20	30	100
Alcohol dependence	10	9	8	7
Affective disorder	27	23	20	6
Schizophrenia	41	22	12	4

*From reference 4, with permission. Model assumes that specified proportion of the cohort have died.

Table 2. Mortality Figures for Bipolar Index Group and General Population*

Cause	Observed Deaths (% index group)	Expected Deaths (% general population)	Mortality Ratio
Suicide	15.7	0.67	23.4
Cardiovascular	42.1	14.0	3.0
Respiratory	33.3	1.08	3.1

*From reference 6, with permission.

the early studies also targeted patients with endogenous or melancholic features, who are at higher risk of suicide. Most studies did not distinguish primary from secondary depression or bipolar from unipolar depression, although there is some evidence that persons with secondary depression and bipolar depression are at higher risk of suicide. The rate of suicide across the spectrum of bipolar illnesses is unknown.

"True" lifetime risk of suicide would be calculated by following cohorts until all members of the cohort are dead. Although no adequately defined cohort of affectively ill patients has ever been followed until all were dead, the lifetime suicide risk of 15% has been widely accepted for years. This risk was originally derived from mortality reports published between 1921 and 1975 and from calculations performed before computerized modeling techniques became available. Inskip et al.⁴ used mathematical modeling techniques to reassess the lifetime risk of suicide in individuals with affective disorder. The authors first selected 27 mortality studies of affective disorder from an earlier meta-analysis, which assessed the suicide risk in all mental disorders.⁵ The authors plotted the proportion of deaths against the proportion of deaths from suicide and extrapolated the data points to cohort extinction (Table 1). When this method was used, the lifetime risk of suicide in affective disorder was estimated at 6%. Higher percentages of suicide are seen soon after the onset of the disorder, when only a small proportion of the cohort has died; for example, when only 10% of the cohort had died, suicide accounted for 27% of the deaths. Lifetime risk of suicide was calculated to be 4% for schizophrenia. As with affective disorders, the risk of suicide in schizophrenia was highest early in the course of the illness. Although the lifetime risk of suicide for alcohol dependence (7%) was similar to that for affective disorders and schizophrenia, it was distributed more evenly over the course of the alcohol dependence.

Table 3. Suicide in Bipolar Disorder*

Report	Date	Country	Suicides (N)	
			Observed	Expected
Angst	1986	Switzerland	13	1.36 ^a
Black et al	1987	USA	7	0.48
Bratfos and Haug	1968	Norway	4	0.09
Carlson et al	1974	USA	2	0.03 ^a
Coppen et al	1991	England	0	0.12
Dunner et al	1976	USA	8	0.06 ^a
Friis et al	1991	Norway	2	0.02 ^a
Kay and Petterson	1977	Sweden		
		Prelithium	3	0.41 ^a
		Postlithium	0	0.15 ^a
Lundquist	1945	Sweden	18	1.00 ^a
Müller-Oerlinghausen et al	1992	Germany	3	0.05 ^a
Newman and Bland	1991	Canada	19	1.38
Noreik	1975	Norway	6	0.14 ^a
Perris and d'Elia	1966	Sweden	3	0.23
Tsuang	1978	USA	5	0.66

*From reference 5, with permission. Standardized mortality ratio = 1505 (95% CI, 1225–1844), total observed suicides = 93; expected total suicides = 6.18.

^aExpected mortality ratio calculated by the authors.

The authors concluded that the overall suicide risk in affective disorders is lower than the risk generally accepted but is particularly high close to the time of diagnosis.

Sharma and Markar⁶ also found that suicide was a major cause of mortality early in the course of bipolar illness, with the mortality ratio for suicide being 23.4 times that in the general population (Table 2). The bipolar patients were also at increased risk of early death from cardiovascular and respiratory disease. Other studies have demonstrated an increased risk of cardiac deaths in patients with depression.^{7,8}

A meta-analysis of suicide risk among those with bipolar disorder was carried out by Harris and Barraclough⁵ based on a combined population of 3700 bipolar patients from 14 studies in 7 countries (Table 3). Some patients were followed for as long as 70 years. The authors tried to avoid overestimating suicide risk by taking measures such as including only papers with a minimum of 2 years of follow-up and excluding those reporting more than 10% loss of subjects at follow-up. Combining the studies gave a total suicide risk 15 times (range, 0 to 133 times) the expected; the wide range indicated the variability across studies. The meta-analysis showed that increased risk of suicide was associated with the time since hospital discharge, including both recent discharges and those up to 5 years before. In addition, a history of suicide attempts and comorbid alcohol abuse were also associated with an increased risk of suicide.

SUICIDE RISK AND PHASE OF BIPOLAR ILLNESS

Suicide deaths from manic-depressive illness are usually assumed to be associated with the depressed phase of

the illness, rather than with mania. As early as 1936, however, Jameison⁹ reported on suicides occurring during depressive mania (mixed states). These suicides were likely to occur soon after discharge from hospital. A recent study by Dilsaver et al.¹⁰ assessed suicidality by using the Schedule for Affective Disorders and Schizophrenia (SADS) suicide subscale in a group of 93 patients who met Research Diagnostic Criteria for bipolar I (N = 75) or schizoaffective disorder (N = 18). In their study, only 1 (2.0%) of the 49 patients who had pure mania was suicidal, compared with 24 (54.5%) of the 44 patients with depressive (mixed) mania, a highly significant difference ($p = .0001$). The authors concluded that a subgroup of patients in the manic state may be mildly to extremely suicidal. Pure mania may be more of a research concept than a clinical reality, however, since as mania becomes more severe, it also tends to become more complicated and have depressive or dysphoric features.

Of 31 bipolar I individuals in a Finnish suicide study,¹¹ suicide occurred during a major depressive episode in 79%, during a mixed state in 11%, or during or immediately after remission of psychotic mania in another 11%. There were significant gender differences among the suicides in this study. Fifty-eight percent of the suicides were by men who were younger at the time of suicide than the women who committed suicide (43.3 years vs. 54.6 years). More than half the men but none of the women were alcohol dependent ($p = .0002$). All the bipolar I suicide completers had been treated, the majority in their last year of life, and nearly half were in treatment at the time of death. In contrast to the unipolar depressed suicide victims, the bipolar victims had more divorces, longer treatment histories, and more frequent hospitalizations. Since the bipolar disorder was complicated with comorbid illnesses in 71% of the suicide victims, comorbidity may be a risk factor for suicide in bipolar disorder.

Suicide Attempts

At least 25% to 50% of patients with bipolar disorder attempt suicide at one or more times in their lifetime,² but the epidemiology of parasuicide (suicide attempts) is quite distinct from that of suicide, with attempters more likely to be women than men, to use less lethal means, to act in the presence of others or to notify others of their intent. Women attempt suicide 2 to 3 times more often than men; however, women may be more willing than men to admit previous suicide attempts, while men may be more prone to risk-taking behavior and car accidents that are seldom explored in surveys of suicide attempts.

Nordström et al.¹² studied suicide risk in a sample of 346 mood disorder patients, including 55 who were diagnosed with DSM-III bipolar disorder. Ninety-two were hospitalized after a suicide attempt including 8 with bipolar disorder. Survival analysis was used to study the potential of a current suicide attempt to predict suicide risk in

hospitalized patients and to compare the suicide risk in patients with and without a current suicide attempt. They found a substantially increased cumulative suicide risk over an 11-year observation period in patients with a current suicide attempt, as opposed to those without (15% vs. 5%). A current suicide attempt was a strong predictor of suicide risk in the short term with a 12% risk of dying of suicide within the next year. Fifteen (56%) of the 27 patients who committed suicide during the 11-year study did so in the first year.

Tuckman and Youngman¹³ proposed that the more closely a parasuicide approximated the epidemiologic profile of a completed suicide, the greater the risk of subsequent death from the same cause. The Epidemiologic Catchment Area study¹⁴ revealed a much higher rate of suicide attempts in individuals with bipolar disorder or major depression than in those with no lifetime history of psychiatric illness. Patients with bipolar disorder who have a family history of suicide are significantly more likely to attempt suicide than those without (38% vs. 14%, $p < .0001$).¹⁵

Lithium for Prophylaxis Against Suicidal Behavior

Isometsä et al.¹¹ studied 1397 suicides in Finland in a 12-month period, including 31 with bipolar I illness. Of those suicide completers who were receiving treatment at the time of death, only 11% of the depressed were receiving adequate doses of antidepressants, and none had received electroconvulsive therapy. One goal of the study was to evaluate the usefulness of lithium in suicide prevention. Of the 20 who received lithium in the last 3 months of life, 95% were bipolar or schizoaffective, bipolar type. Lithium treatment was adequate, as judged by the mean of the last 3 serum lithium levels, for half of the victims who received it: in 5 patients, the mean was above, and in 5 it was below, 0.60 mmol/L. Noncompliance with lithium was a major problem. Eighty-five percent reported continuous or intermittent noncompliance with psychopharmacologic treatment in the previous 2 years. Two subjects used overdoses of lithium as their lethal method. Most of the suicides seemed to occur in patients who were not receiving adequate treatment for the current episode of illness.

Müller-Oerlinghausen et al.¹⁶ followed 68 patients receiving lithium prophylaxis in a specialized lithium clinic for an average of 8 years. Inclusion criteria included taking lithium for at least 12 months and attempting suicide at least once before starting lithium. Fifty-five patients took lithium regularly, and 13 discontinued lithium. Four of those who stopped lithium died from suicide. One of these was a lithium-responder, and 3 were apparent nonresponders; all 4 had stopped lithium on the advice of their treating psychiatrist. Suicidal behavior occurred in 85% of those who stopped lithium and in only 11% of those taking lithium regularly. Two suicides occurred in those on regular

lithium treatment, but one of these had a plasma lithium level of 0 mmol/L 3 weeks prior to the suicide. A dramatic drop in parasuicides (suicide attempts) occurred in those on regular lithium prophylaxis. Only 6% of patients made suicide attempts during lithium treatment compared with 84% before lithium therapy, suggesting that lithium has a suicide-preventative effect. A comprehensive review of the efficacy of lithium prophylaxis can be found in Baldessarini et al.¹⁷ and Tondo et al.^{18,19}

CONCLUSION

The risk of suicide associated with affective disorders may have been overestimated as a result of selection biases, such as studying severely ill inpatients; however, the risk of suicide in bipolar patients remains substantial. The group of bipolar patients at highest risk of suicide are young men who are early in the course of the illness, especially those who have made a previous suicide attempt, those abusing alcohol, and those recently discharged from hospital. The risk of suicide is greatest in bipolar depression and mixed states. Lithium appears to provide some protection against suicidal behavior.

In recent years, there has been a trend toward using anticonvulsants as the first line of treatment for bipolar disorder, although not much is known about the effect of anticonvulsants on suicide risk. While considerably more is known about the effects of lithium on suicide rates, particularly when it is taken for at least 2 years, noncompliance rates with lithium are high, up to 50%, especially in those bipolar patients most likely to respond well to lithium, namely young men with euphoric mania early in the course of their illness. Studies are needed of the efficacy and acceptability of the combination of lithium and an anticonvulsant to compare with trials of lithium alone and anticonvulsants alone. It is possible that a lower (and more tolerable) level of lithium may be sufficient when it is used in combination treatment. A combination of mood stabilizing medications and psychotherapy is another strategy to be tested in the highest risk group of bipolar patients, although noncompliance will undoubtedly again be a major

complicating factor. Another clinical concern in this era of managed care is that patients are being released into the community in a very vulnerable condition after only a few days of treatment. Historically, this postdischarge period has been shown to be a time of high suicide risk, and many of these patients are in mixed states, which further increases their risk for impulsive suicidal behavior.

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