

Clinical Predictors of Suicide in Primary Major Depressive Disorder

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Objective: Follow-up studies of patients with depressive disorders have identified only a few replicable predictors of suicide and have not explored possible interactions between them. The following analysis takes advantage of a large cohort of depressed patients given detailed, structured interviews 2 decades ago.

Method: The data set on which this analysis is based was collected between 1976 and 1990. Research personnel administered the Schedule for Affective Disorders and Schizophrenia to 785 adults who had major depressive disorder (Research Diagnostic Criteria) but who lacked other Axis I disorders. The current analysis used the National Death Index to determine mortality status as of 2003.

Results: One in 4 of the 134 deaths were by suicide for an overall suicide rate of 4.2%. In comparison to the remaining 752 patients, the 33 who died by suicide were more likely to have been inpatients and to have had a history of suicide attempts at the time of baseline assessment. They had also expressed more hopelessness and had higher ratings of suicidal tendency. The last of these variables was the most robust by far and, when tested with other predictors in regression analyses, was the only one to retain significance ($p < .0001$). No interactions between predictors emerged. As in an earlier, similar study, the suicidal tendency rating was predictive of suicides that occurred after the first year of follow-up, which suggests that suicidal tendencies comprise a trait that persists across episodes.

Conclusion: A global rating of suicidality appears to be the single most important predictor of eventual suicide in patients with major depressive disorder.

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Suicide is currently the tenth leading cause of death in the United States and was carried out by more than 30,000 individuals in 2003.¹ Psychological autopsy studies have shown that up to 86% of those who commit suicide are in episodes of major depression at the time² and that substantial proportions of these individuals had been recognized by a health care professional as having a depressive disorder within 6 months of death. Although there has been a marked increase over the past 15 years in the recognition of depressive disorder, and in the use of antidepressants in the United States,³ there has been only a modest decline in suicide rates, and this decline has been confined to females.⁴

Health care providers and, in particular, psychiatrists must often weigh risks for suicide in their patients with depressive disorders to determine what steps should be taken to protect that person until the depressive illness resolves, or at least until it improves substantially. Such steps extend from an increase in the frequency of outpatient contacts to voluntary or involuntary hospitalization. When admission is necessary, the physician must then decide when discharge is appropriate and may be required to do this under pressure from the patient, from his or her family, or from third-party payers.

Unfortunately, research on the prediction of suicide has produced little consensus on how suicidal risk is best determined in such circumstances. Simply questioning patients as to whether they are currently planning suicide is apparently inadequate. A recent study described 76 patients who committed suicide while hospitalized or immediately after discharge and found that 78% had denied suicidal ideation when they were last questioned.⁵

Conclusions from the existing literature are limited by a number of factors. First, nearly all suicide prediction studies have derived the risk factors they tested from a medical record review. This approach lessens the likelihood that robust predictors will be identified, because a given clinical feature may be missing either because the patient did not have it or because the clinician did not inquire about it. Second, the samples described by most predictor studies have been diagnostically mixed, though it is intuitively likely that the factors predisposing to suicide in patients with anorexia nervosa or antisocial personality disorder, for instance, will differ from those predictive of suicide in uncomplicated major depressive disorder (MDD). Direct evidence for this difference de-

METHOD

rives from a psychological autopsy study in which the immediate antecedents of suicide in individuals with alcoholism had little in common with the antecedents of suicide in individuals with a primary depressive disorder.⁶

Third, those studies that have confined their subjects to those with uncomplicated depressive disorders have described relatively small samples, and no two tested the same array of predictors. Surprisingly few factors have emerged as significant predictors in 3 or more of these reports. Individuals who completed suicide were significantly more likely to be male in 7 studies.⁷⁻¹³ In 2 others,^{14,15} though, the sexes were equally represented among suicides and nonsuicides, and in yet another,¹⁶ females were significantly overrepresented. Five studies^{7,8,17-19} have found those who committed suicide to be more likely to have been separated, divorced, or living alone, but 1 study⁹ found the opposite. At least 9 reports have found that suicidal ideas or recent attempts were significantly more common among depressed patients who went on to commit suicide.^{7,11,14,17,19-23} Several of these found the severity of past attempts to be important.^{17,23}

Such studies have rarely tested for interactions among those variables shown to be predictive of suicide in univariate analyses, though important interactions may exist. For instance, if men are less likely to communicate suicidal thoughts than are women,²⁴ and if men with depression are more likely to commit suicide than women with depression, the predictive importance of expressed suicidal ideas may differ by sex.

Finally, nearly all of these studies have pooled suicides that occurred shortly after the baseline clinical assessment with those that occurred substantially later. It is intuitive that some variables are likely to be associated with an imminent risk for suicide while others reflect a liability to suicide that will extend across depressive episodes. Fawcett et al.²⁰ separately ascertained the predictors of those suicides that occurred within the first year after baseline assessment and those that occurred later in a 10-year follow-up. They found little overlap. Suicides in the near term were associated with alcohol abuse, anhedonia, psychic anxiety, diminished concentration, and global insomnia, while later suicides were associated with hopelessness and suicidal ideas.

To avoid these limitations, we took advantage of a data set collected at the University of Michigan over 20 years ago. These data describe a large cohort of depressed patients who, as part of their participation in research protocols in a depressive disorders unit, underwent fully structured and detailed clinical interviews. Because baseline descriptions included demographics and social security numbers, individuals who died any time before 2002 could be reliably identified through the National Death Index.

Subjects

Between the years 1976 and 1990, the University of Michigan Affective Disorders Unit conducted a series of research protocols designed to characterize the pathophysiology underlying the various types of affective disorder. Because protocols varied, so did the inclusion and exclusion criteria applied to potential participants. For inclusion in the following analyses, we required subjects to have been at least 18 years old at the time of their baseline assessment, to have met Research Diagnostic Criteria (RDC)²⁵ for MDD, and to lack a history of schizophrenia, alcoholism, drug dependence, somatization disorder, panic disorder, obsessive-compulsive disorder, or antisocial personality disorder. These criteria yielded a sample of 785 subjects.

Procedures

Clinically experienced interviewers administered the full Schedule for Affective Disorders and Schizophrenia (SADS)²⁶ to each subject, and senior clinicians reviewed the resulting diagnoses. Raters used the 17-item Hamilton Rating Scale for Depression (HAM-D)²⁷ to quantify the severity of depressive symptoms. Many patients underwent serial assessments, and HAM-D scores were determined for each of these.

The National Death Index, a service provided by the Division of Vital Statistics at the Centers for Disease Control and Prevention, used the name, sex, birth date, and social security number for each subject to determine if a death certificate existed anywhere in the United States for that individual. ICD codes of E950-E958 were taken to indicate death by suicide.

We selected 2 sets of potential predictors for testing. The first 3 predictors derived from the aforementioned studies^{7,11,17,19-23} that focused on MDD: sex, marital status, and the presence or absence of suicidal ideas or of prior attempts. The last of these reflected suicide attempts both during and preceding the current episode. Current marital status was dichotomized as separated or divorced versus all others, and the latter category included individuals who were married and those who had never married. Suicidal tendencies were quantified according to SADS item 246, a 7-point scale that ranged from absent to very extreme, e.g., suicide attempt with definite attempt to die or potentially medically harmful. In accord with the SADS conventions, this rating pertained to the week in the current episode when suicidal ideas were most intense. In addition to the 3 principal variables of interest, we also considered polarity, the presence or absence of current delusions, whether or not the patient was hospitalized, hopelessness (assessed with SADS item 244 on a scale of 1-6; 1 = not at all discouraged about the future, 6 = extreme), and overall depressive severity as measured by the HAM-D.

Table 1. Patients With Primary Major Depressive Disorder by Suicide During Follow-Up: Baseline Measures^a

Variable	Suicide (N = 33)	No Suicide (N = 752)
Age, mean (SD), y	36.0 (13.1)	38.9 (14.9)
Female, N (%)	18 (54.6)	512 (68.1)
Separated or divorced, N (%)	8 (26.7)	115 (16.4)
Inpatient status, N (%) ^b	22 (66.7)	350 (47.5)
Diagnosis, N (%)		
Unipolar	26 (79.8)	578 (78.2)
Bipolar II	5 (15.2)	101 (13.7)
Bipolar I	2 (6.1)	60 (8.1)
HAM-D score, mean (SD)	18.5 (6.6)	18.0 (7.1)
Suicidal tendencies rating, mean (SD) ^c	4.7 (1.6)	3.5 (1.6)
No. of attempts among attempters, mean (SD)	3.7 (2.8)	2.6 (2.5)
History of suicide attempt, N (%) ^d	9 (27.3)	97 (12.9)
Delusions, N (%)	4 (12.9)	64 (8.9)
Hopelessness rating, mean (SD) ^e	4.5 (0.8)	4.2 (1.0)

^aDenominator varies by row because of missing values.

^b $\chi^2 = 4.7$, $df = 1$, $p = .05$.

^cSchedule for Affective Disorders and Schizophrenia item 246, on which a score of 1 = absent, 7 = suicide attempt with high intent; $t = -4.6$, $df = 780.0$, $p < .0001$.

^d $\chi^2 = 5.6$, $df = 1$, $p = .018$.

^eSchedule for Affective Disorders and Schizophrenia item 244, on which a score of 1 = not at all discouraged about the future, 6 = extreme; $t = -2.4$, $df = 37.3$, $p = .0211$.

Abbreviation: HAM-D = Hamilton Rating Scale for Depression.

The other set of predictors was selected to replicate the findings of Fawcett et al.,²⁰ who also used the SADS for baseline assessment and who described a sample of similar size, though with a shorter follow-up of 10 years. In that study, the predictors of suicides that occurred within 1 year of study intake differed substantially from the predictors of later suicides. Table 4 lists the variables that were associated with early and late suicides in the Fawcett et al. study.

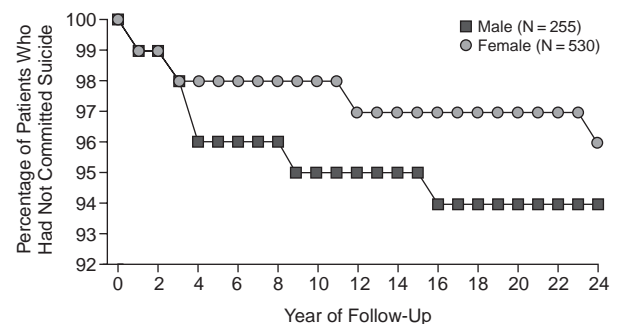
Data Analysis

Univariate analyses were used to compare those who committed suicide at any time during follow-up with those who did not by each of the previously specified baseline variables. Groupings by sex, marital status, inpatient status, presence or absence of any prior suicide attempt, presence or absence of delusions in the index episode, and polarity (nonbipolar versus bipolar II versus bipolar I) were compared by time to suicide using non-parametric Kaplan-Meier survival analyses.²⁸ Logistic procedures tested for interactions between those variables that reached a .05 level of significance in the univariate analyses. Age and sex were also tested in this way because of their importance in the epidemiology of suicide.

Finally, the baseline SADS variables described by Fawcett et al.²⁰ as predictors of early or late suicide were likewise tested. Patients who committed suicide within 1 year of study intake and those who committed suicide after 1 year were separately compared with the remaining patients.

Table 2. Suicide Methods in Men and Women, N (%)

Method	Men (N = 15)	Women (N = 18)
Poisoning	3 (20.0)	10 (55.6)
Hanging	4 (26.7)	4 (22.2)
Carbon monoxide	4 (26.7)	3 (16.7)
Jumping from height	2 (13.3)	0
Firearms	1 (6.7)	1 (5.6)
Cutting self	1 (6.7)	0

Figure 1. Proportion of Patients Who Had Not Committed Suicide by Sex and Year of Follow-Up^a

^aWilcoxon $\chi^2 = 3.1$, $df = 1$, $p = .0786$.

RESULTS

Of 785 individuals submitted to the National Death Index, death certificates were matched to 134 individuals (17.1%) with a mean (SD) interval between intake and follow-up of 20.7 (3.6) years. The cause of death was determined to be suicide in 33 cases (24.6%). Nine (27.3%) of the suicides occurred within 1 year of the study intake, 19 (57.6%) occurred within 5 years, and the median time to suicide was 3.2 years. Of the 3 principal variables of interest, history of suicide attempts was present significantly more often among those who eventually committed suicide (Table 1). Patients who went on to commit suicide were somewhat more likely to be male and to be separated or divorced at the time of their baseline assessment, but group comparisons were not significant. Of the other 5 variables tested, inpatient status and degree of hopelessness were both significantly predictive of eventual suicide.

Men and women did not differ significantly by suicidal method when this was grouped in 6 categories (Table 2). Women, however, were more than twice as likely to use poisoning than were men ($\chi^2 = 4.3$, $df = 1$, $p = .05$). A higher proportion of the suicides among men occurred after the first year following intake (12 of 15, 80.0%) than among women (6 of 18, 33.3%; $\chi^2 = 7.2$, $df = 1$, $p < .01$) (Figure 1).

Table 3. Suicidal Tendencies Ratings at Study Intake, N (%)^a

Rating	Suicide (N = 33)	No Suicide (N = 749)
1—Absent	1 (3.0)	98 (13.1)
2—Morbid, but no suicidal thoughts	3 (9.1)	113 (15.1)
3—Occasional thoughts of suicide, no plans	4 (12.1)	154 (20.6)
4—Often thinks of suicide or has thought of specific method	5 (15.2)	202 (27.0)
5—Has plan or has made gesture	7 (21.2)	122 (16.3)
6—Has made preparations for a potentially serious suicide attempt	9 (27.3)	28 (3.7)
7—Suicide attempt with definite intent to die or potentially medically harmful	4 (12.1)	32 (4.3)

^aRatings made according to Schedule for Affective Disorders and Schizophrenia item 246.

Table 4. Logistic Regression Models of Suicide Prediction

Independent Variable	Wald χ^2	p
Suicidal tendency	20.30	< .0001
Sex	0.05	.82
Suicidal tendency	1.99	.16
Age	0.19	.67
Suicidal tendency	13.04	.0003
Marital status	0.02	.90
Suicidal tendency	15.2	< .0001
Patient status (inpatient vs outpatient)	0.88	.35
Suicidal tendency	6.08	.0137
Hopelessness ^a	0.09	.77
Suicidal tendency	15.8	< .0001
Any previous attempt	0.38	.54
Suicidal tendency	5.67	.02
Nonbipolar vs bipolar I	0.13	.72
Suicidal tendency	7.82	.005
Nonbipolar vs bipolar II	0.09	.77

^aSchedule for Affective Disorders and Schizophrenia item 244, on which a score of 1 = not at all discouraged about the future, 6 = extreme.

While a history of suicide attempts was significantly more common in the suicide group, the overall rating of suicidal tendencies was much more predictive (Table 1). A breakdown showed that a threshold rating of 5 or 6 best characterized those who would die by suicide (Table 3). A rating of 5 or more was given to 20 (60.6%) of the 33 patients who committed suicide but to only 182 (24.3%) of the 749 remaining patients for whom a rating was available. With a threshold of 6, these figures were 39.4% and 8.0%, respectively.

A series of logistic regression analyses tested for interactions between baseline suicidal tendencies and the other variables that were predictive in the univariate comparisons (Table 4). No interactions emerged between suicidal tendencies and marital status, inpatient status, hopelessness, or history of suicide attempt. Although sex, age, and polarity were not predictive of suicide in the univariate analyses, these variables were also tested with suicidal tendencies. With 1 exception, suicidal tendency was a sig-

Table 5. Potential Predictors of Early and Late Suicide

Variable	Suicide Within 1 y (N = 9)	Suicide After 1 y (N = 24)	No Suicide (N = 752)
SADS score, mean (SD)			
Hopelessness	4.2 (1.0)	4.5 (0.8)	4.6 (0.7)
Anhedonia	4.9 (1.0)	4.1 (1.5)	4.5 (1.3)
Psychic anxiety	3.4 (1.5)	4.2 (1.2)	3.6 (1.4)
Suicidal tendencies	4.3 (1.9)	4.9 (1.6) ^a	3.5 (1.5)
OCD features	1.8 (1.3)	1.8 (1.2)	1.5 (1.0)
Indecisiveness	4.1 (1.4)	4.3 (1.2)	3.7 (1.4)
Diminished concentration	4.2 (1.3)	4.5 (1.1)	4.4 (1.2)
Global insomnia	4.4 (1.0)	3.4 (1.7)	3.8 (1.5)
Separated or divorced, N (%)	3 (33.3)	5 (23.8)	115 (16.4)
Any suicide attempt, N (%)	2 (22.2)	7 (29.2) ^b	97 (12.9)

^aCompared with "no suicide," $t = 4.4$, $df = 771.0$, $p \leq .0001$.

^bCompared with "no suicide," $\chi^2 = 5.3$, $df = 1$, $p = .021$.

Abbreviations: OCD = obsessive-compulsive disorder, SADS = Schedule for Affective Disorders and Schizophrenia.

nificant predictor in each of these models. None revealed significant interactions between suicidal tendencies and the other variable, nor were clear trends apparent; the Wald χ^2 value for each interaction term was less than 0.1.

With age in the model, the measure of suicidal tendencies ceased to be a significant predictor (Table 4). Further exploration revealed a significant and negative correlation between age and suicidal tendency (Pearson correlation coefficient = -0.1640 , $p = .0001$). This relationship was similar for men ($r = -0.1946$, $p = .0019$) and women ($r = -0.1537$, $p = .0004$). When the sample was divided into young and old subgroups by the median age of 36 years, the suicidal tendency measure was more strongly predictive of a suicide outcome in the older group. Mean (SD) suicidal tendency ratings for those who did and did not commit suicide in the older group were 5.1 (1.3) and 3.3 (1.6) ($t = -3.98$, $df = 381.0$, $p = .0001$), respectively; for younger patients, they were 4.5 (1.9) and 3.6 (1.4) ($t = -2.37$, $df = 383.0$, $p = .0182$).

Of the SADS variables listed by Fawcett et al.²⁰ as significantly predictive of either early or late suicide, none were significantly associated with the 9 suicides that occurred within 1 year (Table 5). Only suicidal tendencies at intake and a history of suicide attempts significantly predicted suicides that occurred 1 or more years after assessment. The suicides in this sample were somewhat less likely to occur within the first year (27.2%) than were those in the Fawcett et al. sample (40.6%), and the statistical power for comparisons with nonsuicidal subjects was consequently less.

DISCUSSION

A search of the literature confined to studies of suicide among patients with depressive disorders identified 3 variables that had significantly predicted suicide in at least 3 studies. Our 21-year follow-up of 785 individuals

with RDC major depressive disorder found only 1 of these features, suicidal tendencies or a history of attempts, to be significantly associated with subsequent suicide.

Our finding that men were not significantly overrepresented among those who committed suicide probably does not reflect a lack of statistical power. The median number of suicides identified in the 16 studies we reviewed was 31, and none of the studies that identified sex as a significant risk factor reported a risk ratio for male sex as low as the one described here. Even in those studies in which males were at significantly greater risk, the ratio of males to females among those who died by suicide was 2 or less,^{7,9,11-13} a figure far smaller than the 4-to-1 ratio evident in the overall vital statistics on suicide for the United States. Likewise, vital statistics data show a robust age-by-sex interaction in which the risk for males, but not for females, climbs sharply after age 65. No significant age-by-sex interaction was noted in this cohort, though it should be emphasized that only 15% of the sample was 60 years of age or older when they entered the study. These results show that risk factors derived from vital statistics do not generalize well to patients who have sought treatment for a depressive disorder.

The 7-point SADS item that rated suicidal tendencies on the basis of professed planning or past behaviors in the current episode was, by far, the most robust predictor of eventual suicide. The fact that other variables such as marital status, age, and a history of attempts did not substantially alter this measure as a predictor in regression models suggests that these other measures added little predictive power despite statistically significant associations with suicide in univariate analyses. Moreover, the lack of significant interactions in most of these models further suggests that a simple quantification of suicidal tendency applies across clinically meaningful subgroups. Therefore, suicidal tendency as measured here appears to be as important in women as in men, in bipolar depression as in nonbipolar depression, and among patients who profess hopelessness as among those who do not.

Although age itself was not associated with suicide risk, its presence in a regression model diminished the predictive effect of suicidal tendency. Relationships between these variables proved complex. Older age was strongly correlated with lower ratings of suicidal tendency, yet eventual suicide was no less likely in older individuals, and ratings of suicidality were somewhat more predictive than they were for younger persons.

The results of our attempts to replicate the findings of Fawcett et al.²⁰ are difficult to interpret because of the relative lack of early suicides in this sample. In comparison to the no suicide group, ratings for anhedonia and for global insomnia indicated greater severity for early suicides but lesser severity for late suicides. These were among the 4 variables identified by Fawcett et al. as predictive of early, but not late, suicide. Also notable is the

fact that both the current results and those of Fawcett et al.²⁰ showed suicidal ideation to be a predictor of late suicide. This implies that a propensity to consider suicide is a relatively stable feature that extends across time and episodes. Indeed, a recent analysis of the cohort described by Fawcett et al.²⁰ found that suicide attempts rated as being of high intent or as high in lethality were at least as predictive of eventual suicide if they occurred before the index episode as they were if they occurred during the follow-up period nearer to the time of death.²³

Even patients rated at the highest 2 levels of the most predictive variable had only a 1 in 5 probability of completing suicide during the ensuing 21 years. It is doubtful that any clinical or biological predictor of suicide will ever approach the sensitivity or specificity demanded of most laboratory tests in medicine. This does not mean that attention to replicable predictors, however imperfect, will not save lives. The principal finding here is that a single item that quantifies the intensity of suicide thoughts together with the seriousness of suicidal behavior, if any, can estimate the risk for eventual suicide. The robustness of this predictor in comparison to other variables may result from the fact that all of these patients were given a structured interview that required the rating of this item. Clinicians who care for patients with depressive disorder should be likewise consistent.

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