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Do Risk Factors for Suicidal Behavior Differ by Affective Disorder Polarity?

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Abstract

Background—Suicide is a leading cause of death and has been strongly associated with affective disorders. The influence of affective disorder polarity on subsequent suicide attempts or completions and any differential effect of suicide risk factors by polarity were assessed in a prospective cohort.

Methods—Participants with major affective disorders in the National Institute of Mental Health Collaborative Depression Study were followed prospectively for up to twenty-five years. A total of 909 participants meeting prospective diagnostic criteria for major depressive and bipolar disorders were followed through 4,204 mood cycles. Suicidal behavior was defined as suicide attempts or completions. Mixed-effects, grouped-time survival analysis assessed risk of suicidal behavior and differential effects of risk factors for suicidal behavior by polarity. In addition to polarity, the main effects of age, gender, hopelessness, married status, prior suicide attempts, and active substance abuse were modeled with mood cycle as the unit of analysis.

Results—After controlling for age of onset, there were no differences in prior suicide attempts by polarity though bipolar participants had more prior severe attempts. During follow-up, forty cycles ended in suicide and 384 cycles contained at least one suicide attempt. Age, hopelessness, and active substance abuse but not polarity predicted suicidal behavior. The effects of risk factors did not differ by polarity.

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Declaration of Interest

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Conclusions—Bipolarity does not independently influence risk of suicidal behavior or the influence of well-established suicide risk factors within affective disorders. Suicide risk assessment strategies may continue to appraise these common risk factors without regard to mood polarity.

Keywords

Adult; major depression; bipolar disorder; completed suicide; prospective cohort study; risk factors

Introduction

Unipolar and bipolar disorders differ with regard to several clinical and course of illness variables (Serretti *et al.*, 2002). The validity of the bipolar versus unipolar distinction for affective disorders is supported by a general diagnostic stability (Rice *et al.*, 1986; Coryell *et al.*, 1989; Rice *et al.*, 1992), familial aggregation (Coryell *et al.*, 1984; Endicott *et al.*, 1985; Rice *et al.*, 1987), and course of illness (Coryell *et al.*, 1989; Goldberg and Harrow, 2004). One important sequela of affective disorders is suicide. Suicide was the fifth leading cause of death when ranked by years of potential life lost before age 65 in the United States from 1999 to 2002 (C.D.C., 2005), and the majority of suicide victims have a unipolar or bipolar depressive disorder at the time of suicide (Rihmer, 1996; Mann *et al.*, 2005).

Several (Dunner *et al.*, 1976; Kupfer *et al.*, 1988; Tondo *et al.*, 1999) but not all (Cassano *et al.*, 1992) retrospective studies have suggested higher rates of suicide attempts among individuals with bipolar, particularly type II, versus unipolar disorders. Bipolar disorder was associated with greater risk of suicide attempts and completions in one prospective study of 2,826 Italian outpatients with affective disorders followed for a mean of 3.6 years, during which 27 completed suicides and 363 suicide attempts were recorded (Tondo *et al.*, 2007). However, bipolar disorder has not consistently been associated with greater risk of suicidality prospectively (Coryell *et al.*, 1987). For bipolar patients, suicide attempts appear most likely to occur in the setting of depressed states (Tondo *et al.*, 1999; Oquendo *et al.*, 2000; Valtonen *et al.*, 2005) though mixed states or cycling also been associated (Tondo *et al.*, 1999; Dalton *et al.*, 2003; Valtonen *et al.*, 2005). To our knowledge, there are no studies that directly test for differential effects of well-established risk factors for suicide by affective disorder polarity.

The Collaborative Depression Study (CDS) dataset provides a unique opportunity to assess differential effects of risk factors for suicide owing to its duration, size and scope. To enhance the accuracy of diagnosis and reduce the risk of misclassification from relying solely on cross-sectional diagnoses, we examined the risk of suicide outcomes based on a prospective rather than initial diagnosis. To effectively utilize our long-term prospective dataset, we further analyzed risk factors at the beginning of a mood cycle rather than simply at study intake. Given disparate findings in previous studies regarding risk of suicide outcomes by subtype of affective disorder, we sought to explore potential differential effects of previously identified risk factors by affective disorder polarity. With limited background research on this topic, we hypothesized that risk factors for suicide would not differ significantly by polarity. While a number of analyses of the entire CDS dataset have assessed suicide risk factors (Scheftner *et al.*, 1988; Fawcett *et al.*, 1990; Young *et al.*, 1994; Coryell *et al.*, 2001; Coryell *et al.*, 2002; Maser *et al.*, 2002), only one has looked at affective disorder type as a risk factor for suicide (Fawcett *et al.*, 1987). The Fawcett *et al.* (1987) study compared 25 patients who committed suicide by four year follow-up with those who did not over a variety of clinical variables. Diagnostic subcategories did not differentiate completers from non-completers as assessed by Fisher's exact test. No CDS analysis has utilized prospective diagnoses in the study of suicide risk or compared the differential effects (interaction) of risk factors by affective disorder polarity.

Method

Study Design

Patients with affective disorders were recruited for participation in the National Institute of Mental Health Collaborative Program on the Psychobiology of Depression from five academic centers: Massachusetts General Hospital and Harvard University in Boston, Rush Presbyterian – St. Luke’s Medical Center in Chicago, the University of Iowa in Iowa City, New York State Psychiatric Institute and Columbia University in New York, and Washington University School of Medicine in St. Louis. Participants were Caucasian, English-speaking, and knowledgeable regarding their biological parents. Participants further met Research Diagnostic Criteria (RDC) (Spitzer *et al.*, 1978) for major depressive disorder, schizoaffective disorder, or manic disorder. Intake diagnosis was used to identify 936 probands. This sample was further restricted to 909 participants with at least one follow-up assessment. Participants in this sample were followed for a mean of 15.4 (median: 19; SD: 8.8) years and for up to twenty-five years. Seventy-eight percent of participants were followed for a decade or more.

Follow-up assessments were completed using various forms of the Longitudinal Interval Follow-up Evaluation (LIFE) (Keller *et al.*, 1987), which categorizes severity of psychopathology and was administered semiannually in the first five years and annually thereafter. The LIFE tracked each RDC syndrome weekly and was utilized to prospectively diagnose participants into one of two groups: unipolar and bipolar. An initial diagnosis of bipolar disorder was based on an intake RDC diagnosis of bipolar II, bipolar I, schizoaffective manic, or schizoaffective depressed with a history of mania or schizoaffective-mania, mainly affective. The latter category was included as it is virtually identical to mania as defined by the 4th edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV). An initial diagnosis of unipolar depression was based on intake RDC diagnosis of major depressive disorder or schizoaffective-disorder, depressed, mainly affective. The latter category was included as it is analogous to major depression as defined by the DSM-IV. Follow-up ratings from the LIFE Psychiatric Status Rating (PSR) were used to reclassify participants diagnostically. Participants with unipolar depression on intake, who developed mania or hypomania during follow-up, were thus classified as having bipolar disorder. For consistency and to utilize the most accurate diagnoses, prospective diagnoses were utilized for all subsequent analyses.

Data Analytic Procedures

Baseline demographics and prior suicide attempts were compared between participants with unipolar and bipolar disorders. Age of onset was estimated using the earliest of age of first psychiatric treatment, onset of depressive symptoms, or onset of manic symptoms from the Schedule of Affective Disorders (SADS) (Endicott and Spitzer, 1978; Endicott and Spitzer, 1979). A retrospective analysis of suicide attempts was performed to explore differences in baseline suicidality prior to enrollment in this prospective cohort study. Separate analyses were conducted for suicide attempts and severe suicide attempts. Severity of attempt was determined from the SADS using previously utilized cutoffs, wherein a severe attempt was operationally defined as a SADS suicidal intent (item 249) or medical lethality (item 250) score ≥ 4 (Fiedorowicz and Coryell, 2007). These cut-offs require a “serious” level of suicidal intent to kill oneself or at least “moderate” medical lethality (i.e. “had brief unconsciousness”). Logistic regression was performed to control for age of onset in assessing suicide attempts prior to intake by polarity.

Descriptive statistics related to suicidal behaviors during follow-up and burden of depressive symptoms were compiled for those with prospective diagnoses of unipolar or bipolar disorder. Burden of depressive symptoms during prospective follow-up was obtained from the LIFE

Psychiatric Status Rating (PSR) scales, which were anchored to diagnostic thresholds for RDC disorders. Based on previously published criteria (Judd *et al.*, 2002), a week of depressive symptoms was operationalized as a PSR cutoff score of $\geq 3/6$ (moderate symptoms or impairment) on the major depression or schizoaffective depression scale or a score of $3/3$ (definite criteria) for minor or intermittent depression with a PSR of ≤ 2 on the major depressive scale. Differences in percentage of time depressed were assessed non-parametrically using the Wilcoxon rank sum test.

Any suicidal act was included in the survival analysis, regardless of intent or lethality and including those acts with minimal if any intent or no actual threat to life. Suicidal behaviors were broadly defined and encompassed suicide attempts or suicide completions. Time to suicide attempt or completion by prospective diagnosis was illustrated using Kaplan-Meier methods. Survival time represented the number of weeks from intake into the cohort study until the outcome of interest: suicide attempt or suicide completion. Cases lost to follow-up prior to suicide attempts or completions were censored. This analysis assumed that censoring and suicide attempts or completions were independent. Death indices from vital statistics were methodically searched, minimizing the risk that suicide completions went unrecognized in censored cases. When the cause of death was unknown, the death was not included as a suicide in our analysis. The above analyses were completed utilizing SAS version 9.1 (SAS Institute Inc, Cary, NC, 2003) and SPSS version 13.0.

The strength of the association between each of several previously established and *a priori* selected risk factors for completed suicide were examined in a grouped-time mixed-effects survival analysis (Hedeker *et al.*, 2000). Given that risk factors may change over time, the unit of analysis was changed from individual participant to mood cycle to best utilize the prospective data. The mood cycle included a mood episode and the subsequent period of recovery until next episode, if applicable. Cycle length was grouped as a grouped-time, ordinal variable into the following ten categories: ≤ 8 weeks (≤ 2 months), 9–16 weeks (2–4 months), 17–26 weeks (4–6 months), 27–36 weeks (6–9 months), 37–52 weeks (9–12 months), 53–104 weeks (1–2 years), 105–156 weeks (2–3 years), 157–208 weeks (3–5 years), 209–312 weeks (4–6 years), or more than 312 weeks (> 6 years). The beginning of a cycle was determined by study intake or the first week of any recurrence following a period of recovery. The end of a cycle was determined by the week prior to any recurrence following a period of recovery or the point at which the participant was lost to follow-up. A recovery was defined as eight consecutive weeks with no or only residual symptoms (PSR ≤ 2) on the major depressive, manic, schizoaffective depressive, or schizoaffective manic scales of the PSR with no symptoms on the hypomania, minor depression, or intermittent depression scales. A recurrence was defined as any PSR scale > 2 lasting one or two weeks, for (hypo)manic and depressive symptoms respectively.

Age at cycle onset was included as a continuous covariate in the assessment of the following risk factors: gender, feelings of hopelessness, history of suicide attempt, history of multiple suicide attempts, marital status (married versus others), and substance abuse. Data on hopelessness was collected only on intake. With the exception of hopelessness and gender, the most recent assessment prior to cycle onset was used for other main effects. The model containing main effects thus contained the following variables: age, male gender, hopelessness, married status, prior suicide attempts, current substance abuse, and polarity. A differential effect of these risk factors by polarity was then assessed. For each assessed polarity by main effect interaction, the likelihood ratio test compared the full model with an interaction term to the reduced model without the interaction term (main effects only). Each statistical test used a two-tailed alpha of 0.05. These mixed-effects grouped-time regression models were calculated using SuperMix software.

Results

Stability of Diagnosis

Diagnostic categories were stable during follow-up for the majority of participants though clinically meaningful rates of conversion from unipolar major depression to a bipolar disorder were observed during follow-up. Of the patients who entered the CDS with unipolar major depression, the prospectively observed conversion rate to a diagnosis of bipolar II or I was 10.6 % and 6.9 % respectively. Participants were followed for a mean of 799 (median: 988; SD: 460) weeks or 15.4 (19; 8.8) years of prospective follow-up. Comparisons of baseline and demographic variables between diagnostic groups are detailed in Table 1. Unipolar patients were significantly older at study intake and more likely to be married.

Suicide Attempts Prior to Intake into the Collaborative Depression Study (CDS)

Participants with bipolar disorder (38.4%) were somewhat more likely than those with unipolar disorder (28.7%) to have attempted suicide prior to intake, although bipolar participants were not at significantly greater risk for any prior suicide attempt (HR=1.14, 95% C.I. 0.95–1.38, $p=0.16$) or multiple prior suicide attempts (HR=1.08, 0.91–1.39, $p=0.38$) when age of onset was controlled for in logistic regression. However, participants with a bipolar disorder were 30% more likely than those with unipolar disorder to have had prior *severe* suicide attempts (HR=1.30, 1.09–1.38, $p<0.005$) controlling for age of onset in logistic regression.

Suicide Attempts and Depressive Morbidity after Intake into the CDS

The frequency of suicide outcome measures by diagnosis during follow-up is detailed in Table 2. Individuals with bipolar disorder had a greater frequency of suicide attempts during prospective follow-up than those with unipolar depression (34.0% vs. 27.2%). Bipolar participants were not more likely to complete suicide than their unipolar counterparts, however (4.4% vs. 4.2%). A total of 40 completed suicides were recorded in this study: 21 among those with unipolar depression, 19 with bipolar disorder. Consistent with previously published results (Judd *et al.*, 2003), significant differences in the percentage of weeks depressed for each diagnostic category were observed (Table 2), with bipolar disorder associated with a lower cumulative depressive burden. Kaplan-Meier survival curves illustrated suicide attempts and suicide completions (Figure 1) over the course of prospective follow-up in the CDS for individuals by prospective diagnosis.

Main Effect of Risk Factors on Suicidal Behavior: Unipolar vs. Bipolar

The effect of polarity on suicidal behavior, defined as suicide attempts or completions, was assessed in mixed-effects grouped-time survival analysis (Table 3). Age at cycle onset was included as a continuous covariate for analysis of main effects. A statistically significant linear protective effect of age was noted (HR=0.95, 95% C.I. 0.94–0.96, $p<0.001$). Independent statistically significant main effects were also seen for hopelessness (HR=3.00, 95% C.I. 1.97–4.51, $p<0.001$) and substance abuse (HR=2.28, 95% C.I. 1.64–3.15, $p<0.001$). The impact of male gender, married status, and prior suicide attempts did not reach statistical significance. Polarity did not independently predict risk of suicidal behavior.

Differential Effect of Risk Factors on Suicidal Behavior: Unipolar vs. Bipolar

Polarity by main effect interactions terms were individually added to the above model to assess for differential effects of risk factors on suicidal behavior by polarity. No statistically significant polarity by risk factor interactions were noted.

Discussion

The increased rate of suicide attempts prior to study entry in participants with bipolar disorder appears to largely reflect an earlier age of onset which has been previously noted with bipolar disorder (McMahon *et al.*, 1994). While a trend was noted in our retrospective analyses of increased prior suicide attempts with bipolar disorder compared with unipolar disorder, the differences observed were statistically significant, after controlling for age of onset, only for severe suicide attempts. These findings differ somewhat with an analysis of the Epidemiologic Catchment Area database which revealed an excess of suicide attempts in individuals with bipolar disorder even after controlling for age of onset (Chen and Dilsaver, 1996). While frequency data may have been suggestive of increased suicidal behaviors during follow-up in participants with bipolar disorder, polarity did not independently predict suicidal behaviors when modeled in a mixed-effects grouped-time survival analysis. Age at cycle onset, hopelessness at study intake, and active substance abuse did independently predict suicidal behavior during mood cycles. The likelihood ratio tests revealed no significant main effect by polarity interactions and therefore demonstrated no evidence of differential effects of risk factors for suicidal behavior by polarity.

Prior studies have contrasted risk of suicide between those with bipolar and unipolar disorders with mixed results. Several studies have assessed suicide risk factors in unipolar and bipolar disorders (Fawcett *et al.*, 1990; Krupinski *et al.*, 1998; Schneider *et al.*, 2001; Angst *et al.*, 2002; Oquendo *et al.*, 2007; Tondo *et al.*, 2007), and some have conducted separate analyses by polarity (Black *et al.*, 1988; Kallner *et al.*, 2000; Angst *et al.*, 2005a). An assumption of the former studies is that risk factors do not vary by diagnosis and the latter studies do little to validate this assumption. To date, the assumption that established risk factors do not vary by polarity has not been empirically tested in a well-defined prospective cohort. None of these studies have statistically assessed, using an interaction term, differential effects of risk factors by polarity. A community sample of registered admissions did assess for differential effects of risk factors by polarity using an interaction term, but given limitations in available data was not able to test for any traditionally established risk factors apart from age, instead focusing on variables related to time from hospital admission (Hoyer *et al.*, 2004). Another study assessed interactions though did not assess differential affects by diagnosis or polarity (Young *et al.*, 1994). Our study uniquely addresses this long-maintained assumption for some established suicide risk factors and supports the now empirically-validated assessment of risk factors independent of polarity in affective disorders.

Of the 4,204 cycles assessed, 40 ended in suicide and 384 contained suicide attempts. To ensure adequate power to assess the differential effect of risk factors for suicidal behavior by polarity, we utilized suicidal behavior, representing suicide attempts or completions, as an outcome. The inclusion of suicide attempts may nonetheless limit the generalizability of our findings to the prediction of risk for completed suicide. Those who complete suicide may represent an overlapping but not identical population from those who attempt suicide (Beautrais, 2001). Our focus on polarity further did not allow the assessment of a differential effect of risk factors by bipolar subtype. The lower cumulative depression burden in those with bipolar disorder reflects those with bipolar I, but not bipolar II spending less time depressed. Comparison by bipolar subtype would further allow assessment of other risk factors, such as mixed states or cycling. Our analyses controlled for a linear effect of age on suicide, which may not adequately control for a non-linear age effect. A significant linear effect of age was nonetheless revealed and analysis of the data did not suggest a non-linear age effect. The adjustment of our diagnosis for prospective changes in the psychiatric status of participants strengthens the comparison of these groups by reducing the risk of misclassification. Length of follow-up considered, our observed rate of conversion from unipolar to bipolar disorder is generally consistent with the previous literature (Akiskal *et al.*, 1983; Akiskal *et al.*, 1995; Goldberg *et al.*, 2001; Angst *et al.*

al., 2005b). Screening of vital statistics and obtaining death certificates reduces our risk of misclassification for suicide; however, it remains possible that those who died of unknown causes may have actually died of suicide and have been misclassified. The Collaborative Depression Study uniquely provides comprehensive demographic, diagnostic, and phenomenological data for a large clinical sample of individuals with affective disorders followed for an extended period of time. Other advantages of this sample include rigorous clinical evaluations and low rates of loss to follow-up.

The mixed-effects grouped-time models used in this analysis pose several advantages for the assessment of suicide risk factors in a longitudinal study of this duration. Many studies in psychiatry using survival analysis have utilized more traditional time-to-event approaches such as the logrank test or Cox proportional hazards models (Leon *et al.*, 1990). These approaches assume independence among observations and therefore cannot include repeated observations per participant. To accommodate changes in risk factors over time, we changed the unit of analysis to mood cycle, allowing risk factors to be re-assessed each cycle. The mixed-effects grouped-time survival method represents a modern approach to examine correlated observations, such as multiple mood cycles, in a single model (Hedeker *et al.*, 2000). This allows for correlation in within-subject mood cycles and for the number of mood cycles to vary widely. All prospectively observed mood cycles were able to be analyzed together, allowing us to assess polarity as a predictor of suicidal behavior and a differential effect of risk factors by polarity within a mood cycle. Many of these risk factors vary over time and our statistical modeling was able to account for this.

The lack of any independent or differential effects of polarity on suicide risk poses several clinical and public health implications. Previous research has suggested that suicide risk factors may differ between those with alcoholism and those without (Murphy *et al.*, 1992). Our data does not support any such differences by polarity in affective disorders. While the presence of an affective disorder shapes suicide risk assessment, polarity may be of limited relevance for suicidal risk or the effect of other suicide risk factors. This information may inform current efforts to develop standardized tools to augment the clinical suicide risk assessment. In the light of growing interest in the use of standardized suicide assessment psychometrics, it will be important to clearly delineate that suicide risk factors do not vary by diagnosis. While the current study suggests no differences in risk factors between the bipolar and unipolar disorders, these findings may not generalize outside of the affective disorders. Suicide risk remains difficult to predict (Goldstein *et al.*, 1991) and public health initiatives should continue to target the identification and appropriate treatment of affective disorders as a general preventative approach (Rihmer, 1996; Mann *et al.*, 2005).

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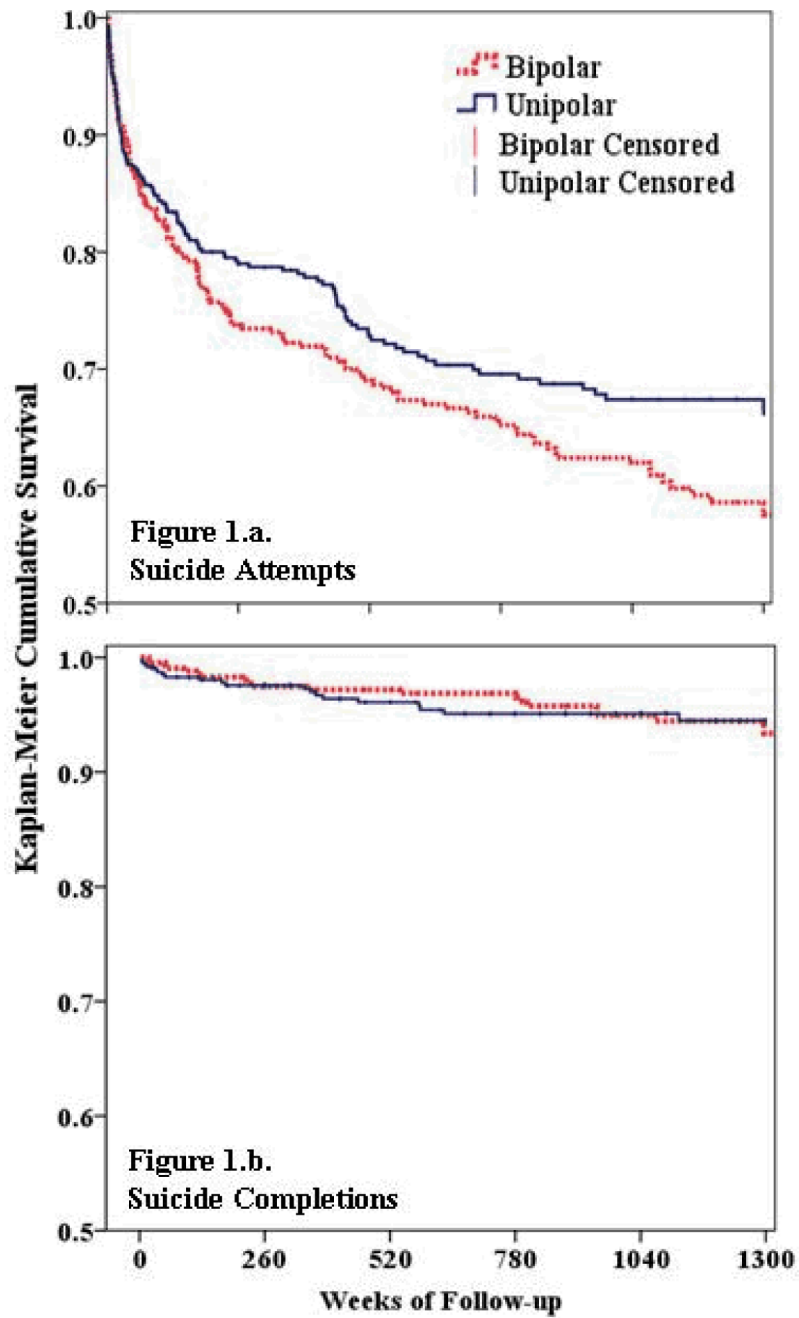


Figure 1. Survival by affective diagnosis
 Kaplan-Meier survival estimates for participants based on prospective diagnosis for time to:
 (a) suicide attempt and (b) completed suicide.

TABLE 1

Baseline Demographic and Clinical Characteristics of Participants by Polarity

	Unipolar	Bipolar
N	501	435
# (%) Female	294 (58.7%)	250 (57.5%)
Age, Mean (SD) ^a	39.9 (15.0)	36.3 (13.2)
Educational Level, # (%) ^b		
Without Diploma	100 (20.1%)	53 (12.2%)
High School Grad	141 (28.3%)	115 (26.4%)
Some College	137 (27.5%)	147 (33.8%)
College Graduate	120 (24.1%)	120 (27.6%)
Marital Status, # (%) ^c		
Married	240 (47.9%)	148 (34.0%)
Divorced/Separated	78 (15.6%)	99 (22.8%)
Never Married	158 (31.5%)	178 (40.9%)
Widowed	25 (5.0%)	10 (2.3%)
Prior Suicide Attempt ^d	144 (28.7%)	167 (38.4%)
Multiple Prior Attempts ^e	61 (12.2%)	79 (18.2%)
Prior Severe Attempt ^f	71 (14.2%)	107 (24.6%)

The above table outlines baseline and demographic information obtained from participants on intake from the Schedule for Affective Disorders and Schizophrenia (SADS) and Personal History of Depressive Disorders (PHDD). Differences in suicide attempts are not significant after controlling for age of onset.

^a $t=3.8$, $df=933$, $p<0.0001$

^b $\chi^2=13.2$, $df=3$, $p<0.005$

^c $\chi^2=27.4$, $df=3$, $p<0.0001$

^d $\chi^2=9.8$, $df=1$, $p<0.002$

^e $\chi^2=6.6$, $df=1$, $p<0.02$

^f $\chi^2=16.4$, $df=1$, $p<0.0001$

TABLE 2

Frequency of Suicidal Behavior and Proportion of Time Depressed During Follow-up by Polarity

	Unipolar	Bipolar
Any Suicide Attempt ^a	131 (27.2%)	148 (34.0%)
Multiple Suicide Attempts ^b	75 (15.6%)	87 (20.0%)
Severe Suicide Attempt ^c	79 (16.4%)	97 (22.3%)
Multiple Severe Attempts	35 (7.3%)	44 (10.1%)
Completed Suicide	21 (4.2%)	19 (4.4%)
Mean (Median: SD) % Weeks Depressed ^d	38.6 (27.2; 33.1) %	31.7 (22.1; 30.4) %

The above table outlines the rate of selected suicide outcomes by prospective diagnosis during a median prospective follow-up of 19 years. Severity of suicide attempt was determined by a previously utilized score of 4 or greater for intent or lethality on the SADS.

^a $\chi^2=6.9$, $df=1$, $p<0.01$

^b $\chi^2=4.1$, $df=1$, $p<0.05$

^c $\chi^2=6.5$, $df=1$, $p<0.02$

^dWilcoxon rank sum test, $p<0.001$

TABLE 3

Main Effects and Main Effect by Polarity Interactions on Suicidal Behavior

Main effect	Hazard Ratio	Likelihood Ratio
Male Gender	0.76	$X^2 = 0.42$
	0.55 – 1.04	df = 1
	$p = 0.87$	$p = 0.52$
Hopeless †	3.00	$X^2 = 0.01$
	1.97 – 4.57	df = 1
	$p < 0.001$	$p = 0.93$
Married	1.00	$X^2 = 0.53$
	0.76 – 1.31	df = 1
	$p = 0.98$	$p = 0.46$
Prior Suicide Attempts	1.25	$X^2 = 0.56$
	0.91 – 1.70	df = 1
	$p = 0.17$	$p = 0.45$
Substance Abuse †	2.28	$X^2 = 0.33$
	1.64 – 3.15	df = 1
	$p < 0.001$	$p = 0.56$
Bipolar polarity	1.16	
	0.85 – 1.58	
	$p = 0.34$	

The above table details the hazard ratios, 95% confidence intervals of the hazard ratio, and p -values for each main effect modeled in a mixed-effects, grouped-time survival analysis to predict suicide attempts or completions. Age at cycle onset was included as a covariate in the model. Interactions were individually compared utilizing the likelihood ratio test for comparing nested models where the interaction term was removed for the reduced model.

† Denotes a statistically significant main effect. There were no statistically significant polarity by risk factor interactions on risk of suicidal behavior.