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Acute risk factors for suicide attempts and death: prospective findings from the STEP-BD study

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Abstract

Objectives—Suicide is unfortunately common in psychiatric practice, but difficult to predict. This study sought to assess which clinical symptoms increase in the months before suicidal behavior in a sample of psychiatric outpatients with bipolar disorder.

Methods—Data from the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) trial were used. A total pf 103 participants who attempted suicide or died by suicide during the trial were included; a 15% random sample of the remaining participants (n = 427) was used as a comparison sample. Linear mixed models in the six months before suicidal behavior were conducted for each of five proposed acute risk factors for suicidal behavior. Participants were assessed using the Clinical Monitoring Form (CMF) at each visit for the following potential acute risk factors for suicidal behavior: suicidal ideation, loss of interest, anxiety, psychomotor agitation, and high-risk behavior.

Results—Each of the five symptoms was elevated overall in individuals who engaged in suicidal behavior (p < 0.05). The severity of both suicidal ideation and loss of interest significantly increased in the months before suicidal behavior (p < 0.001). Anxiety demonstrated comparable effect sizes across multiple models. Psychomotor agitation and high-risk behavior were not significantly elevated before suicidal behavior.

Conclusions—Suicidal ideation, loss of interest and, to a lesser extent, anxiety may represent acute suicide risk factors up to four months before suicidal behavior in outpatients with bipolar

Disclosures

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CAZ is listed as a co-inventor on a patent for the use of ketamine and its metabolites in major depression and has assigned his rights in the patent to the U.S. government but will share a percentage of any royalties that may be received by the government. EDB, JLVV, DAL, RM-V, and MT report no conflicts of interest, financial or otherwise.

disorder. Further investigation of these potential acute risk factors in prospective analyses is warranted.

Keywords

anhedonia; anxiety; bipolar disorder; suicidal ideation; suicide

In 2012, over 40,000 Americans died by suicide (1). With over eight million adults thinking about suicide, and one million attempting suicide each year in the United States (2), suicide risk assessment is an essential skill for all mental health clinicians. However, suicidal behavior remains very difficult to predict (3), as it is a low base rate phenomenon that occurs across psychiatric diagnoses, ethnicities, and most age groups (4). Death by suicide is even more difficult to predict, as few studies are sufficiently powered to detect its relatively low base rate (5). Careful suicide assessment is essential for psychiatric diagnoses such as bipolar disorder (BD), which has been associated with particularly high rates of suicidal behavior and death (6–8).

Predicting suicidal behavior often relies on identifying and monitoring both long-term and acute risk factors. Risk assessments include factors that may lead to a suicide death sometime in the patient's lifetime (long-term) and those variables that signal a more transient, dynamic state indicating near-term risk (acute). In short, when completing a comprehensive risk assessment, a clinician may collect data on a number of factors that indicate elevated lifetime risk; history of suicide attempts is a commonly cited example (9). However, these static variables do not tell the clinician *whether the patient in her office will kill himself in the next week to month.* Such a distinction has implications for treatment, including psychiatric hospitalizations and watch status.

While research on acute suicide risk factors are critical and a focus of the Suicide Research Prioritization Task Force (10), empirical data on acute risk factors in particular are limited. Techniques that have been used to recreate the time before a suicide attempt or death include follow-back interviews (11) and psychological autopsies (12). Another potential method is examining large naturalistic studies and clinical trials where the suicidal behavior occurs prospectively in the context of clinical assessment. For example, data regarding suicide attempts and deaths over the course of the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) study have been previously reported, and baseline predictors of future suicidal behavior (long-term risk factors) have already been published (13–17). Those studies suggested that lifetime history of suicidal behavior is a significant predictor of future suicidal behavior. In addition to long-term risk factors, the STEP-BD dataset also provides an opportunity to evaluate acute risk factors for suicidal behavior in patients with BD.

This analysis sought to evaluate potential acute risk factors in the six months before a suicide attempt or death in the STEP-BD sample. Acute risk factors in this context are described as symptoms that significantly increased in the months before suicidal behavior, as these variables would be most helpful to clinicians in determining whether a patient is experiencing a suicidal crisis. The time period differs from the framework around suicide warning signs proposed by Rudd and colleagues (18), in which specific symptoms such as

increased ideation or giving away belongings are thought to signal imminent suicide risk in the following minutes, hours, or days. It should be noted, however, that more recent critical reviews of the literature have stated that there are little to no data on the specific symptoms or time frames associated with imminent risk of suicidal behavior (19, 20).

Available data in the STEP-BD study included information about overall mood states (depression, mania, or irritability), substance abuse, and headaches/migraine in addition to DSM-IV symptoms of depression and mania. From these options, we were interested in specific symptoms that might signal an acute suicidal crisis (18). Consequently, we concentrated on suicidal thoughts and symptoms such as anxiety/agitation rather than overall mood effects (i.e. whether the patient was in a depressed, manic, or mixed episode), although such analyses of mood were completed post-hoc due to the relationship between BD mood states and suicide attempts (7, 21). In total, the five symptoms included in the analysis were: 1) suicidal thoughts, due to the relationship to later suicide attempts and death (22, 23); 2) loss of interest as a measure of anhedonia, which has been linked to acute suicide risk (24); 3) anxiety, due to its relationship to the transition from suicidal thoughts to suicidal behavior (25); 4) psychomotor agitation, because of its relationship to death by suicide in psychiatric inpatient samples (26); and 5) high-risk behavior, as a proxy for impulsivity or recklessness, both of which have also been associated with suicidal behavior (27).

Patients and methods

Participants

All data were drawn from the STEP-BD study (28), which followed 4,360 patients with BD across 22 academic psychiatry centers over seven years. The prospective study used comparable assessments over the course of both naturalistic treatment and randomized clinical trials. All clinicians were trained and certified in assessment and evidence-based treatments. The study was reviewed and approved by the institutional review board (IRB) of each participating institution.

Suicidal behavior outcome

Over the course of the STEP-BD study, data on prospective suicidal behavior were collected via the serious adverse events report [(SAE) reviewed by an independent safety officer and committee for serious adverse events], which recorded deaths by suicide and suicide attempts, and the Care Utilization form (CU) in which all participants were asked whether they had attempted suicide in the last three months. In the sample of 4,360 patients participating in the STEP-BD study, eight suicide deaths and 44 attempts were reported on SAE forms, and 244 attempts were reported on CU forms. Previous analyses of suicidal behavior in the STEP-BD trial calculated a suicide rate of 0.014 per 100 person years (15). Additional data regarding suicide attempts and deaths in this sample have been reported using similar methods of determining suicidal behavior (13, 15). In the present study, data from the CU and SAE forms were collapsed, as detailed in the *Statistical analysis section* and in Supplementary Figure S1.

Affective Disorder Evaluation (ADE)

Upon baseline entry into the original STEP-BD study, all patients were assessed using the Affective Disorder Evaluation (ADE) for clinical assessment (28, 29). This assessment evaluated the intensity of suicidal ideation, loss of interest, abnormal anxiety, psychomotor agitation, and high-risk behavior. Each of these symptoms, with the exception of anxiety, was rated on a scale from +2 to -2, with +2/-2 signifying 'much more' or 'much less' than usual, +1/-1 signifying 'clearly present and fulfills SCID criteria', and 0 signifying 'none or usual' for the past week. These symptoms were assessed in the same manner on every clinic visit using the Clinical Monitoring Form (CMF). Specifically, suicidal ideation was assessed using the questions: "Were there times when you were feeling so bad that you felt your life was not worth living? What about actually thinking about suicide or harming yourself?". Loss of interest was assessed using the question: "Have you been able to enjoy pleasant *things that happened?*, and then reverse-coded to facilitate comparison to other variables. Psychomotor agitation was assessed using the question: "Were there times you were so fidgety or agitated it was hard for you to stay still?". High-risk behavior was assessed using the questions: "Did you do anything that was unusual for you or that other people might think was excessive, foolish, or risky? Did you do anything which would have caused a problem if you were caught?".

Anxiety was assessed differently; patients were asked how many days they had experienced abnormal anxiety over the past two weeks on the ADE and then what percentage of the last 10 days they experienced abnormal anxiety on the Clinical Monitoring Form (CMF) (resulting in a scale from 0 to 100). Data from the ADE were used to analyze baseline data, and results from the CMF were used to analyze symptom trajectories during the study.

Statistical analysis

Patients with suicidal behavior—Data on suicidal behavior were collected from the SAE and CU forms, including the date of suicidal behavior compared to the date of consent (resulting in a *days from consent* variable). One hundred and eighty-six patients with prospective suicidal behavior were included in baseline univariate analyses.

In order to track clinical symptoms across time and reduce overall missing data, the analysis was limited to patients who had at least two clinic visits, in two different months, before the suicidal behavior. The resulting sample comprised 103 participants (Supplementary Fig. S1 describes this process). This group will hereafter be referred to as the *prospective suicidal behavior* group.

Comparison sample—For comparison, a 15% random sample was selected from the patients with BD who did not attempt suicide during the study in order to obtain a sample roughly three to four times greater than the sample with prospective suicidal behavior. The full sample was not used in order to avoid problems with heterogeneous variances that can occur with substantial differences in group sample sizes. No attempt was made to match the samples. The random selection procedure from SPSS provided a pseudo-random sample using no replacement in a Mersenne Twister algorithm. Five hundred and sixty-four individuals were selected for this group and all were included in the baseline univariate

analysis. In order to assess trajectory of symptoms, the comparison group was limited to the first six months of participation in STEP-BD. These patients were limited to those who had at least two clinic visits in this timeframe, resulting in 427 patients for analysis. This group will be referred to as the *no* prospective suicidal behavior group.

Univariate analysis—Demographic and baseline characteristics of individuals who did and did not engage in suicidal behavior over the course of the STEP-BD study were evaluated using *t*-tests and chi-squares. Age, suicide attempt history, and scores on the Personality Disorders Questionnaire (PDQ) (30) were included in these models, as these variables were shown to predict prospective suicide attempts in previous multivariate analyses of the dataset (13). In addition, Spearman correlations were used to evaluate the relationship between the five symptoms of interest in the month before suicidal behavior. Significance was considered at p < 0.05, two-tailed. Supplemental analyses were conducted to compare participants included in linear mixed model analysis and those who did not have at least two clinic visits before exhibiting suicidal behavior.

Time analysis—The six months before suicidal behavior (or the first six months of participation in the comparison sample) was coded in relation to the time of attempt (Month -1 is the latest month and occurred closest to the time of suicidal behavior). If a patient had multiple visits within the same 30-day period, their scores were aggregated using median score. Therefore, each patient had up to six time points recorded for each clinical variable.

Linear mixed models—Separate linear mixed models were run using each clinical symptom as the dependent variable. Suicidal behavior (whether or not the patient engaged in prospective suicidal behavior) was a fixed between-subjects factor, and time (months before suicide attempt) was included as a fixed within-subjects factor. The interaction between time and suicidal behavior was also included in the model, as was a fixed intercept. According to Schwarz's Bayesian criteria, a compound symmetry covariance structure had the best fit for the data. Models were run with quadratic codings for time, with similar fit for the results; the linear models are thus reported. Missing data were accounted for using restricted maximum likelihood estimation. Due to the five clinical symptoms of interest, all linear mixed models were run using a Bonferroni correction for multiple analyses, p < 0.01, two-tailed. Effect sizes were calculated using Cohen's *d*. Due to the use of linear mixed models, all figures include estimated marginal means and standard errors of these mean estimates.

Global functioning and mood effects—Because many other potential suicide risk factors were not included in the initial analysis, supplemental models were run assessing global functioning, mood effects, substance abuse, and headaches in the six months before suicidal behavior to describe general clinical functioning. Clinical functioning was assessed using the Clinical Global Impression (CGI) and Global Assessment of Functioning (GAF) rating scales. Mood effects were measured by items assessing mood elevation and abnormal irritability (which was assessed similarly to abnormal anxiety, on a scale from 0 to 100) as well as depressed mood (which was assessed similarly to the other potential acute risk factors, on a scale from -2 to +2). Substance use, alcohol use, headaches and migraine

headaches were assessed using a dichotomous variable. Results across these analyses were compared using effect sizes.

Supplemental analyses

Because of the high rate of missing data in the overall model (36%), secondary analyses were run that collapsed clinical ratings using medians across two-month intervals. Thus, linear mixed models were run across three, instead of six, time points. While this approach did not allow for fine-grain analysis of the month before suicidal behavior, missing data were reduced to 3%. This approach also limited the analysis to patients with visits throughout the six month timeframe (i.e., patients who only had visits in the two months before the suicidal behavior were excluded).

Due to concerns about differences in reporting methods between the SAE report and CU form, the models were also run using only suicidal behavior reported on the SAE form. Models were also run excluding suicide deaths. Similarly, in order to adjust for baseline levels of symptoms, all models were run for the five months before suicidal behavior, adjusting for symptoms reported in the sixth month. In addition, due to the importance of age, history of suicide attempt, and PDQ score noted in previous analyses by Antypa (13), models were run adjusting for these variables.

All statistics were conducted with IBM SPSS 21.

Results

Baseline demographic and clinical characteristics of the sample are presented in Table 1. Prospective suicidal behavior was associated with past history of suicide attempts; younger age; higher PDQ and CGI scores; lower GAF score; increased suicidal ideation, loss of interest, abnormal anxiety, psychomotor agitation, high-risk behavior, and irritability; and a more prevalent history of migraine headaches at baseline (p < 0.05). In comparing participants with (n = 103) and without (n = 83) two clinic visits before suicidal behavior, no significant differences were found for baseline clinical symptoms, age, or gender. Individuals who were excluded from the linear mixed model analysis due to number of clinic visits were more likely to report a past history of suicide attempts (X^2 = 6.87, p = 0.009).

A correlation matrix of selected CMF variables at Month -1 is presented in Table 2. Each prospective suicide risk factor was significantly correlated with the others (p < 0.05) with the exception of high-risk behavior with suicidal ideation and loss of interest. Significant correlations ranged from r = 0.13 to 0.48. With regard to mood effects variables, each was significantly correlated with the prospective suicide risk factors with the exception of high-risk behavior due to 0.48. With regard to mood effects variables, each was significantly correlated with the prospective suicide risk factors with the exception of high-risk behavior with depressed mood, and elevated mood with suicidal ideation and loss of interest.

Proposed acute suicide risk factors

From the linear mixed models, a main effect for prospective suicidal behavior was found for suicidal ideation, loss of interest, and abnormal anxiety (p < 0.001), with values higher in the

group with prospective suicidal behavior (Table 3). A significant time by suicidal behavior interaction was observed for suicidal ideation and loss of interest (p < 0.001). For suicidal ideation, a significant difference was noted between the groups at all time points with the exception of Month -5 (the fifth month before suicidal behavior). For loss of interest, a significant difference was observed from Months -4 to -1. The main effect or time by suicidal behavior interaction for abnormal anxiety and psychomotor agitation were not significant after adjusting for multiple comparisons. The time by behavior interaction for suicidal ideation was still significant when adjusting for depressed mood (p < 0.001).

Trajectories of clinical symptoms in the six months before suicide attempt are presented in Figures 1A–1E. Overall effect sizes between groups ranged from 0.18 (high-risk behavior) to 0.66 (suicidal ideation). In order to compare the symptom trajectories across the same scale, the effect sizes for all symptoms by month before suicidal behavior are presented in Figure 2.

Global functioning and mood effects

For a general picture of clinical functioning and mood effects, additional models were run with the CGI scale, the GAF scale, elevated mood, irritability, depressed mood, substance/ alcohol use, as well as headaches and migraine headaches, not adjusting for multiple comparisons. Both CGI and GAF scores demonstrated a significant main effect and time by suicidal behavior interaction (p < 0.001). Elevated mood, abnormal irritability, alcohol use, substance use and headache demonstrated a significant main effect, but there was no time by behavior interaction. For depressed mood, the main effect was significant, but the interaction did not reach significance (p = 0.08) although effect sizes were comparable to those for loss of interest and anxiety. Additional data regarding potential acute suicide risk factors adjusted for mood effects, as well as age, history of suicide attempts, and PDQ score are presented in the Supporting Information.

Supplemental analyses

As noted previously, ratings were collapsed over two-month, instead of one-month, intervals in a post-hoc model due to concerns about missing data. Using linear mixed models with these intervals, similar effect sizes were noted for suicidal ideation, loss of interest, and anxiety. Models also found similar effect sizes when only SAE form-reported suicidal behaviors were included and when models were run excluding suicide deaths (see Supplementary Tables S1A and S1B).

Symptoms in the five months before suicidal behavior were run, adjusting for symptoms in the sixth month (see Supplementary Table 1C). Across the supplemental analyses, similar effect sizes were found for the loss of interest and anxiety variables.

To ensure that these findings were not due to variables in the comparison sample, the same models were run with a new, distinct 15% random sample of non-attempters. Overall effect sizes for main effects and interactions were comparable.

Discussion

In this sample of patients drawn from the STEP-BD study, suicidal thoughts were elevated for up to four months before suicide attempt or death. Loss of interest was also moderately elevated before suicidal behavior, while anxiety was not significantly elevated before suicidal behavior after adjusting for multiple comparisons. Psychomotor agitation and high-risk behavior were associated with prospective suicidal behavior overall, but did not demonstrate a similar trajectory in the months just before suicidal behavior. Taken together, our findings suggest that suicidal ideation and loss of interest may represent acute risk factors for suicidal behavior in patients with BD in outpatient settings.

These results reinforce the role of suicidal ideation as an acute risk factor for suicidal behavior (22, 23). The post-hoc finding that suicidal ideation was elevated in the months before suicidal behavior independent of changes in depressed mood further underscores the importance of regular direct assessment of suicidal thoughts in order to observe possible fluctuations. Measures such as the Columbia Suicide Severity Rating Scale (C-SSRS) (31), the Scale for Suicide Ideation (SSI) (32), and the Suicide Status Form (SSF) (33) were developed for this purpose. In addition, it is possible that suicidal thoughts increased in intensity during the time before suicidal behavior, although this is difficult to interpret from the CMF item. Further investigations of factors that lead to increased severity of suicidal thoughts may have important implications for the treatment of suicidal patients.

Loss of interest (often referred to as anhedonia) and, to a lesser extent, anxiety, also emerged as acute risk factors for suicide; nevertheless, inconsistent results on supplemental analyses underscore the need for additional replication. Fawcett and colleagues previously identified anhedonia as a clinical warning sign for suicide (24) and, more recently, changes in anhedonia were shown to correlate with suicidal thoughts independent of depression in a sample of psychiatric inpatients (34). Anxiety has commonly been assessed as an acute risk factor for suicide and has been associated with the transition from suicidal thoughts to suicidal behavior (25). In addition, anxiety sensitivity has been the focus of cognitive behavioral treatment to reduce suicidal thoughts and behavior (35). Because these symptoms are closely related to depressed mood, further work is needed to examine whether each symptom independently predicts acute risk or whether it represents an underlying suicidal 'process' or 'mode' comprising multiple related symptoms as part of a suicidal crisis (36).

In the present study, psychomotor agitation and high-risk behavior showed no statistically significant increase in symptoms right before suicide attempt/death. Non-significant findings may reflect the inadequacy of a single item to capture a phenomenon as complex as agitation or impulsivity, which may also depend on clinical context such as mood state or substance abuse. Nevertheless, the results suggest that these symptoms may be useful as long-term, but not acute, risk factors in the months before suicidal behavior. For example, aggressive impulsivity is a proposed suicide endophenotype (37), but whether it functions as an underlying risk factor for suicidal crisis or "impulsive attempt" remains to be seen (38). Such a discussion highlights the difficulties inherent in suicide research and the need for innovative approaches to better categorize the time period before suicidal behavior.

Despite the importance of these preliminary findings, this study is also associated with several limitations that reinforce the need for further investigation and replication. First, participants in a research trial may not generalize to assessment and care received in the community. As noted in a previous STEP-BD analysis (15), the suicide rate in the STEP-BD trial may be lower than what would be seen in the community due to the regular clinical visits, standardized assessments, and evidence-based treatments associated with the trial. In addition, we excluded potentially high-risk participants with less than two visits during the time frame of interest from analysis, which may have led to an incomplete picture of acute suicide risk in this sample. As follow-up with suicidal patients is often difficult, new technologies such as text messaging and smartphone applications could be beneficial in future studies of symptom monitoring in suicidal patients.

Second, the use of single items from the CMF, which often used a 'none or usual' score, may not have captured the complexity of symptoms. Future analyses will need to use assessments comprising multiple items, such as the C-SSRS, SSI, or SSF—all of which can independently capture both symptom intensity and change from baseline—for a more comprehensive suicide risk assessment.

Third, it is possible that these symptom trajectories, or the impact of mood state, would differ if weekly or daily data were available. Fourth, many other possible clinical symptoms could have been evaluated as acute risk factors, such as sleep disturbance, more in-depth assessments of the symptoms of borderline personality disorder, or other types of physical pain. Fifth, the time period for the comparison sample may not have been comparable to the time frame used in the participants with suicidal behavior. Lastly, data presented here were reported by the patient to a clinician. Multimodal investigation of these acute risk factors, including implicit measures, biomarkers, and behavioral paradigms (39), is indicated.

Conclusions

This study found that increased suicidal ideation, loss of interest and, to a lesser extent, anxiety, may represent acute risk factors for later suicidal behavior in patients with BD. High-risk behavior and increased psychomotor agitation were confirmed as longer-term risk factors; however, patients may not report increased intensity of these symptoms in the months before suicide attempt or death.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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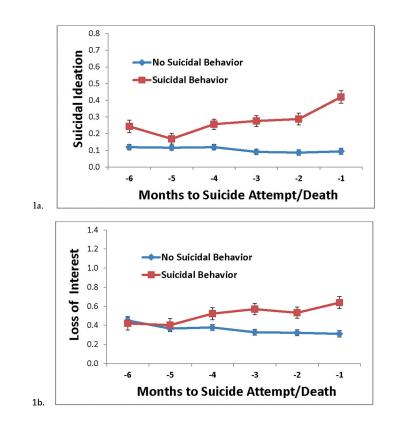
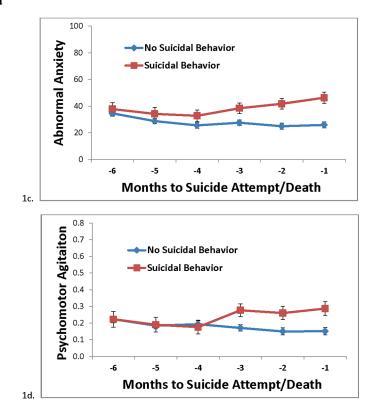


Figure 1a



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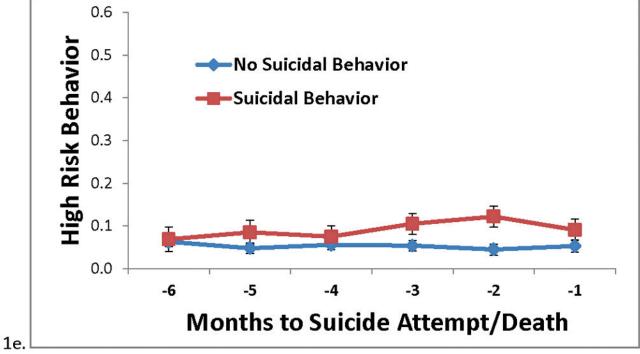


Figure 1c

Figure 1b

Figure 1.

1A-1E. Median clinical symptoms in the six months before suicide attempt/death, compared to random sample of non-attempters. All assessments were taken from the Clinical Monitoring Form (CMF). Due to the use of linear mixed models, all figures include estimated marginal means and standard errors of these mean estimates.

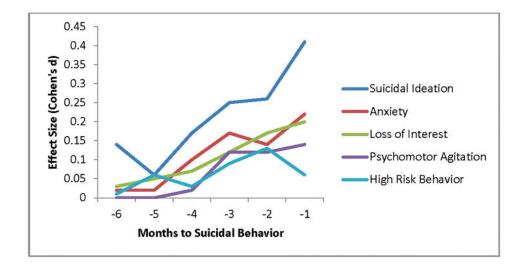


Fig. 2.

Differences in symptom trajectories in the six months before suicidal behavior in patients with versus without prospective suicidal behavior.

Table 1

Baseline demographic and clinical characteristics of suicide attempters compared to random sample of nonattempters

	No prospective suicidal behavior	Prospective suicidal behavior	χ^2 or t	p-value
Demographics and clinical characteristi	cs			
Gender, male, n (%)	232 (45)	59 (36)	3.53 ^a	0.06
Past suicide attempt, n (%)	171 (31)	131 (73)	96.82 ^a	< 0.01
Age, years, mean (SD)	39.00 (12.90)	35.46 (12.05)	-3.08	< 0.01
PDQ score-, mean (SD)	36.86 (18.40)	48.07 (16.92)	6.57	< 0.001
Proposed acute suicide risk factors, mea	nn (SD			
Suicidal ideation	0.16 (0.34)	0.34 (0.48)	5.61	< 0.01
Loss of interest	0.45 (0.64)	0.71 (0.78)	4.49	< 0.01
Abnormal anxiety	4.74 (5.49)	5.89 (5.54)	2.47	0.01
Psychomotor agitation	0.24 (0.40)	0.38 (0.54)	3.63	< 0.01
High-risk behavior	0.08 (0.27)	0.13 (0.35)	2.32	< 0.01
Global functioning, mean (SD)				
CGI overall	2.92 (1.26)	3.61 (1.17)	6.58	< 0.001
GAF in last month	61.07 (12.09)	55.99 (12.03)	-4.95	< 0.001
Mood effects, mean (SD)				
Elevated mood	1.76 (3.37)	2.00 (3.54)	0.82	0.41
Abnormal irritability	3.87 (4.87)	5.98 (5.75)	4.89	< 0.001
Depressed mood	0.43 (0.70)	0.52 (0.84)	1.07	0.29
Alcohol/substance abuse and headaches	/migraines			
Alcohol use (drinks per day), mean (SD)	0.74 (1.92)	0.82 (2.90)	0.44	0.66
History of substance use, n (%)	93 (16)	40 (22)	2.56 ^a	0.11
History of migraines, n (%)	149 (26)	66 (35)	6.17 ^a	0.01

Suicidal ideation, loss of interest, psychomotor agitation, high-risk behavior, and depressed mood are rated on a scale from -2 to +2. Abnormal anxiety, elevated mood, and abnormal irritability were rated as days in the last two weeks.

PDQ = Personality Disorders Questionnaire; CGI = Clinical Global Impression rating scale; GAF = Global Assessment of Functioning rating scale.

^aChi-square.

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Snearman correlations of Clinical Monitoring Form (CMF) outcome variables at Month - 1

Proposed acute suicide risk factors Suicidal ideation		•	I SYCHIMINUM AGUAUNI	Suicidal ideation Loss of interest Abnormal anxiety Psychomotor agriation High-risk behavior
I				
	0.48^{a}	0.32 ^a	0.27 ^a	0.11
Loss of interest	I	0.36 ^a	0.21 <i>ª</i>	0.01
Abnormal anxiety		I	0.21 <i>a</i>	0.13^{b}
Psychomotor agitation			I	0.22 ^a
High-risk behavior				Ι
Mood effects				
Elevated mood 0.05	0.02	0.16^{a}	0.26 ^a	0.34 <i>a</i>
Abnormal irritability 0.20^a	0.25 ^a	0.46^{a}	0.28^{a}	0.23 ^a
Depressed mood 0.50^{a}	0.58^{a}	0.37 ^a	0.21 <i>ª</i>	0.06

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Table 3

Fixed effects for clinical symptoms in time before suicide attempt/death

		Main effect for suicidal behavior	Time by sui	Lime by suicidal behavior interaction	Overall effect size between groups	Effect size at Month -1
	F	p-value	${f F}$	p-value	Cohen's d	Cohen's d
Proposed acute suicide risk factors	e risk factors					
Suicidal ideation	58.57	$< 0.001^{f}$	7.31	$< 0.001^{f}$	0.67	0.41
Loss of interest	13.28	$< 0.001^{f}$	4.00	0.001^{f}	0.31	0.22
Abnormal anxiety	12.91	$< 0.001^{f}$	2.39	0.04	0.31	0.20
Psychomotor agitation	4.22	0.04	2.64	0.02	0.18	0.14
High-risk behavior	6.20	0.013	0.86	0.51	0.22	0.06
Global functioning						
CGI ^a	53.28	<0.001	5.84	<0.001	0.63	0.38
${ m GAF} b$	30.51	<0.001	4.84	<0.001	0.48	0.33
Mood effects						
Elevated mood $^{\mathcal{C}}$	9.89	0.002	0.51	0.12	0.28	0.08
Abnormal irritability $^{\mathcal{C}}$	13.01	<0.001	0.72	0.61	0.31	0.11
Depressed mood ^d	13.62	<0.001	1.99	0.08	0.38	0.24
Alcohol/substance abuse and headaches/migraines $^{\mathcal{C}}$	ise and heada	iches/migraines ^e				
Alcohol abuse	4.46	0.035	1.66	0.14	0.19	0.05
Substance abuse	12.31	<0.001	1.49	0.19	0.30	0.06
Headaches	4.30	0.039	1.01	0.41	0.18	0.09
Migraine headaches	0.61	0.44	1.17	0.32	0.07	0.00

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 $b_{GAF} = Global$ Assessment of Functioning. Higher scores represent higher levels of functioning. Average GAF in the last month before suicidal behavior was 56.3 (SE = 1.2). Average GAF in last month for controls was 65.1 (SE = 0.7).

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 d Depressed mood was assessed on the same scale as suicidal thoughts, loss of interest, psychomotor agitation, and high-risk behavior, that is, on a scale from -2 to +2.

 e^{a} Alcohol/substance abuse and Headaches/migraines were measured on a dichotomous scale of 'Yes/No'.

 f_{s} Significant after correcting for multiple comparisons, Bonferroni, p = 0.01, two-tailed.