

## Gender Differences in Suicidal Risk Factors among Individuals with Mood Disorders

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### Abstract

**Objective:** Suicide is a leading cause of death, especially for individuals who have a diagnosed mood disorder. There is conflicting evidence regarding factors that may heighten risk for suicide and whether they differ for men and women. The aims of this study were to identify the degree to which gender influences suicide risk among patients with mood disorders, or moderates the effects of other demographic and clinical suicide risk factors.

**Methods:** The sample included 268 women and 154 men who were part of a geographically diverse, multi-center registry of the National Network of Depression Centers. Measures of depression, anxiety, childhood adversity, psychiatric diagnosis, living arrangement and employment status were analyzed, along with gender, to determine their association with suicidal risk.

**Results:** Multiple regression analysis indicated that men had greater suicide risk than women. In addition, factors that predicted suicide risk differed by gender. Childhood adversity was more strongly associated with suicide risk for women ( $\beta=0.22$ ,  $p<0.000$ ) than for men ( $\beta=0.04$ , NS) while anxiety predicted suicide risk for men ( $\beta=0.25$ ,  $p<0.000$ ) but not for women ( $\beta=0.05$ , NS). Severity of depression was the primary predictor for both sexes ( $\beta=0.79$ ,  $p<0.000$ ). Specific mood diagnosis, living arrangement and employment status did not predict suicide risk.

**Conclusions:** Findings indicate the importance of regularly assessing severity of depressive and anxiety symptoms, with attention to anxiety as a key factor that may heighten suicide risk for men. Results suggest a profound role for early cumulative trauma in exacerbating later suicide risk for women, indicating a need to also screen for childhood adversity. Further research is warranted to identify the gender-specific effect of different adversities and types of anxiety in development of suicidal ideation and suicide completion.

**Keywords:** Depression; Anxiety; Sex differences; Childhood adversity; Social determinants

### Introduction

Suicide is the 10th leading cause of death in the U.S. and the 2<sup>nd</sup> leading cause of death among individuals between the ages 10-24 years old [1]. Most individuals who demonstrate suicidal behavior have a diagnosed mood disorder such as major depressive disorder (MDD) and bipolar disorder [2,3], increasing their risk of suicide by 10 fold compared to the general population [4]. Although the nature of suicide attempts appears more severe for individuals with bipolar disorder, the NIMH Collaborative Depression Study found no difference in the number of suicide attempts between individuals with bipolar disorder and major depression [5].

Consistent gender differences in suicide risk have not emerged. A large national study of patients with mood disorders found that women had more suicide attempts than men [6], supporting other findings that female gender is associated with suicide attempts [7,8]. Research also indicates that women are nearly twice as likely as men to report moderate difficulty with suicidal feelings or behaviors [9]. However, the NIMH collaborative study found no gender differences in number of suicide attempts [5] and a recent cohort study found that male sex predicted risk for suicide [10]. Another prospective study of stress and depression also demonstrated that, under conditions of stress, male sex was a significant predictor of suicidal ideation [11]. This lack of consensus across studies may reflect various sociodemographic or clinical factors that differ for men and women. Our study sought to examine these factors in order to better understand gender-related differences in suicide risk among individuals with mood disorders.

### Sociodemographic factors

Disconnection from social resources has featured prominently in theoretical models of suicide [12]. Lower levels of social support and smaller social networks appear to predict suicide attempts among patients with MDD [13]. Likewise, decreased social support has been linked to increased suicidal ideation [14]. Living alone is often a reflection of decreased social support and diminished social networks. Studies have shown that living alone is a strong predictor of suicide ideation or completion [10,15-17]. However, other research has not found that living alone is a significant predictor of suicide [18]. There is little evidence that living alone imparts differential risk for suicide in men and women, although research suggests that men are more likely to live alone without other social supports which in turn may increase their likelihood of suicide [19].

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Previous studies also indicate that prolonged economic downturns are associated with an increase in deaths caused by suicide, even when controlling for mental illness [20-22]. Although unemployment contributes to elevated risk for suicide in both men and women, there is evidence that the relationship is stronger in women [23].

### Severity of depression

Studies demonstrate that suicide risk is greatest for men and women during a depressive episode [24]. Compared to those in remission, patients experiencing a unipolar depressive episode have shown a 21-fold greater risk for a suicide attempt [13] while those in a bipolar depressive episode had an 18-fold increase in risk [25,26]. Prospective studies across psychiatric and primary care settings also show that the severity of a depressive episode is a risk factor for a suicide attempt or completion among patients with major depression [26-32].

However, it is less clear whether there are gender differences in the role that severity of depressive symptoms may play for suicide risk. In a longitudinal study of over 300 patients with depression, women with higher severity ratings for depression were at greater risk for suicide attempts, compared to men [33]. Still, other research has found no gender differences [34]. Differences in clinical settings, study design, and assessment of depressive symptoms may account for the conflicting findings.

### Anxiety

A few studies have demonstrated an association between anxiety symptoms and an increased risk of suicide [35-38], with one study finding anxiety to be more significant than depression as a predictor of suicidal ideation [39]. Data is conflicting regarding an independent association between anxiety disorders and suicidal behavior [9,40-43]. Results of one study indicate that the association between anxiety and suicidal behavior is no longer significant once comorbid disorders are controlled for in aggregate [8]. However, other research, which controlled for a variety of comorbid psychiatric illnesses, reported a significant relationship between anxiety disorders and suicidal ideation/attempts [44,45].

Despite growing evidence of an association between anxiety and suicidality, gender differences have rarely been investigated. Some studies report that a wider range of anxiety disorders is associated with increased suicidal risk in women compared to men [46,47] while other research shows no gender differences [48].

### Childhood adversity

Childhood adversity and suicidal behavior in adulthood have been strongly linked [49-52], even when controlling for demographic risk factors [53]. Having seven adverse events or more in childhood appears to increase the risk by 30-fold for a suicide attempt [54]. The impact of child abuse on suicidality in adulthood is greater in individuals meeting diagnostic criteria for depression [52] and bipolar disorder [55], possibly because these conditions may increase risk for suicidal behaviors as well.

Among abuse categories, research indicates that childhood sexual abuse is the strongest predictor of suicide attempts [56,57]. Emotional abuse and neglect also predict suicidal behaviors [58], with Puzia et al. finding emotional abuse to be a stronger predictor of suicidal ideation than sexual or physical abuse [59]. A few large studies report higher prevalence of suicidal ideation in children of parents with psychopathology or addiction [60,61], and confirm that suicidality rates vary by the type of parental psychopathology. Parental divorce has also been linked to increased suicidality [62], especially in combination with

other types of childhood adversity [63]. Lastly, research has shown that loss of a parent at a young age [64] and exposure to domestic violence [65] predict suicidal behavior in adulthood.

In spite of the important role that childhood experience appears to play in later suicide risk, research on gender differences regarding the effects of different adversities is limited and inconclusive. One large study reported an increased rate of suicide attempts in abused women compared to men, although investigators questioned whether the findings reflected higher abuse prevalence in women rather than differential susceptibility to the abuse [66]. However, Isohookane et al. also found that early sexual abuse predicted suicidal behavior among adolescent girls but not boys [67]. In contrast, Fergusson and colleagues reported that teen boys who had been sexually abused displayed more suicidal behaviors than sexually abused girls [68].

### Study Aims

The aims of this study were:

- 1) To identify the degree to which gender, along with selected demographic and clinical factors, may influence suicide risk among patients with mood disorders;
- 2) To determine whether gender moderates the effect of these demographic and clinical factors on suicide risk.

We sought to address limitations of previous research by compiling a sample from multiple clinical sites across a broad geographic region and who represented a wide age range. In addition, we examined a number of potentially important factors together to account for their mutual effects.

### Methods

#### Procedures

Data for this study came from a prospective, observational, multi-center registry of patients with mood disorders who received routine clinical care at the participating centers of the National Network of Depression Centers (NNDC). The NNDC is a 501(c)(3) nonprofit organization comprised of leading depression centers and academic medical centers in the U.S. who are dedicated to advancing research, treatment and public education regarding depression and bipolar disorder through comprehensive, multidisciplinary collaboration and national-scale networking of resources. The Depression Centers reflect a broad geographic distribution of patients from various regions of the U.S., including the north, south, west, east and middle of the country. Seventeen centers contributed patient data for this study.

Patients receiving healthcare at participating centers of the NNDC were approached to join the registry. Eligible participants for the registry were adults age 18 or older, with the diagnosis of a mood disorder, who were English-speaking and able to provide informed consent. All eligible patients were approached for consent at their initial clinic visit. Participating sites and patients had the option of completing measures via an electronic data capture system or as paper-based surveys. The web-based system allowed patients to enter information from any location, using a secure, password-protected sign-on. All information was de-identified prior to inclusion in the centralized registry. Protocols were approved by the Institutional Review Boards for Human Research Protection at each participating Center.

#### Measures

All measures were part of a larger standardized battery employed

by the NNDC. The measures consisted of self-report scales that could provide a broad picture of symptoms and functioning for those diagnosed with mood disorders. Measures were selected based on their established validity as well as feasibility of administration and utility in tracking symptoms in psychiatric patients. Participants were asked to report on the following demographic characteristics: gender, racial and ethnic background, marital/relationship status, living situation (i.e. living alone or with others), educational attainment, occupational and employment status, and whether or not English was the primary language spoken in the home. In addition to the self-report data, a psychiatric diagnosis for each patient was determined through a diagnostic interview conducted by clinicians at each site.

The Concise Health Risk Tracking Scale (CHRTS-SR; Self Report Version) was used to quantify the severity of active suicide risk [69]. The CHRTS-SR includes 7 items assessing current suicidal thoughts and plans during the preceding week and rated on a 5-point Likert scale ranging from strongly agree to strongly disagree. The CHRTS-SR has shown good internal consistency ( $\alpha=0.78$ ), high agreement with clinician ratings of the scale items, and convergent validity with the Positive and Negative Suicide Ideation Inventory.

The Patient Health Questionnaire (PHQ-9) was used to measure depressive symptoms. It is a nine-item self-report questionnaire based on the DSM criteria for major depression [70]. Scores range from 0-27, with higher scores indicating more severe depression. Meta-analyses of the PHQ-9 validity have concluded that it is equal or superior to other established depression measures. The performance of the PHQ-9 is good across different modes of administration as well as across sex, age and racial/ethnic groups [71]. Item 9 (assessing suicidal ideation) was not included in the score used for analysis to eliminate the potential for confounding with the measure of suicide risk.

Anxiety was assessed using the Generalized Anxiety Disorder Assessment (GAD-7) [72]. The GAD-7 is a 7-item scale assessing the degree of anxiety experienced by the patient. Scores can range from 0-27, with different cut-points to indicate mild-severe anxiety. The GAD-7 has shown good psychometric properties as a screening tool. Using a cut-point of 10 for various anxiety disorders, sensitivities for the GAD-7 range from 0.66 to 0.89 and specificities range from 0.80 to 0.82.

Adverse Childhood Experiences (ACE) were assessed with a 10-item self-report scale that has been widely used [73]. The ACE scale measures the number and type of difficult and potentially traumatic experiences a person may have experienced in childhood. Content validity was described in initial development of the measure and its predictive validity has been supported in numerous studies [54,73,74].

### Data analysis

Descriptive statistics were used to identify sample characteristics. Pearson correlations or ANOVAs were computed to identify preliminary relationships of predictors to suicide risk. Predictors showing a significant bivariate relationship to suicide risk were entered simultaneously into a multiple regression model to examine Aim 1. In a second model, predictors showing a significant main effect in the first model were entered along with interaction terms that examined their relationship to gender. In looking at the contributions of these interaction terms, we assessed the moderating effects of gender (Aim 2). Separate regression models also were computed for men and women to better understand any gender-specific predictors of suicide risk. Finally, correlations were computed to determine specific associations that might underlie significant interactions. Aims were analyzed using SPSS version 21.

## Results

### Sample characteristics

The sample included 268 (63%) women and 154 (37%) men, ranging in age from 19-90. Mean age of the men was 49 (SD=15.2); mean age of the women was 46 (SD=14.7). The sample was primarily Caucasian (86%), with 4.7% of these patients being Hispanic or Latino. 6.4% of participants were of African heritage and 3.3% were Asian. The educational level of the sample was high, with 24% having a bachelors degree, 25% having an advanced graduate or professional degree, and 25.7% having some college education. The remainder had a high school diploma or less than an 8<sup>th</sup> grade education (25.3%). Table 1 shows the distribution of mood disorders by gender. Table 2 presents their relationship status, living arrangement (living alone or with someone), and employment status. Means for suicide risk and all predictor variables with continuous scores are shown in Table 3.

### Predictors of suicide risk

Bivariate analyses between suicide risk and each of the potential predictors revealed that all predictors were associated with risk except for living alone. Living alone was not associated with suicide risk ( $F=1.06, p<0.35$ ). All other predictors were entered into a regression model to examine Aim 1.

**Aim 1:** In this initial model looking at main effects of the predictors (Table 4), diagnosis of depressive versus bipolar disorder was not a significant predictor of suicide risk ( $\beta=-0.03, NS$ ). Similarly, unemployment had no significant effect ( $\beta=0.04, NS$ ). Gender was a significant predictor (0.08,  $p<0.03$ ), with men showing greater suicide risk. Severity of depression emerged as the strongest predictor ( $\beta=0.56, p<0.000$ ), but childhood adversity ( $\beta=0.17, p<0.000$ ) and anxiety ( $\beta=0.18, p<0.001$ ) were also significant predictors. The model accounted for 56% of the variance in suicide risk.

**Aim 2:** To examine Aim 2 (moderating effects of gender), predictors

Diagnosis*	Women	Men
Major Depressive Disorder	59.7	58.4
Dysthymic Disorder	6.7	5.8
Bipolar Disorder I	14.9	30.5
Bipolar Disorder II	14.9	6.5

Note: \* Patients may have more than one diagnosis

Table 1: Percent of patients with selected mood disorders.

	Women	Men
Live Alone	24.6	24.0
Divorced/Separated	22.0	12.3
Widowed	2.2	2.6
Single/Never Married	23.5	30.5
Married/Committed Relationship	50.4	50.6
Unemployed	13.4	17.5

Table 2: Percent of patients with selected relationship, living arrangement and employment situations.

	Women	Men
Suicide Risk	32.45 (0.64)	36.27 (0.92)
Childhood Adversity	3.54 (0.15)	2.39 (0.19)
Depression	12.24 (0.26)	12.44 (0.37)
Anxiety	10.23 (0.24)	9.01 (0.34)

Note: Means are adjusted for other variables in the model

Table 3: Means and standard errors for suicide ideation/behavior, childhood adversity, depression and anxiety by gender.

Predictor	B	SE	Beta	p
Diagnosis	-0.72	0.95	-0.03	0.452
Unemployment	1.51	1.21	0.04	0.216
Gender	1.98	0.93	0.08	0.033
Childhood Adversity	0.83	0.17	0.17	0.000
Depression	1.03	0.09	0.56	0.000
Anxiety	0.36	0.10	0.18	0.001

Table 4: Initial regression model for predictors of suicide risk.

Predictor	B	SE	Beta	p
<b>Step 1</b>				
Gender	3.53	1.96	0.13	0.070
Childhood Adversity	1.84	0.51	0.37	0.000
Depression	1.45	0.28	0.79	0.000
Anxiety	-0.21	0.31	-0.10	0.509
<b>Step 2</b>				
Gender x Adversity	-0.79	0.37	-0.22	0.029
Gender x Depression	-0.28	0.19	-0.25	0.146
Gender x Anxiety	0.42	0.21	0.33	0.050

Note: F = 72.37 (df = 7), p < 0.000

Table 5: Final regression model for predictors of suicide risk and their gender interactions.

Predictor	B	SE	Beta	p
<b>Women</b>				
Childhood Adversity	1.06	0.19	0.22	0.000
Depression	1.18	0.10	0.70	0.000
Anxiety	0.11	0.12	0.05	0.395
<b>Men</b>				
Childhood Adversity	0.24	0.29	0.04	0.422
Depression	0.92	0.13	0.56	0.000
Anxiety	0.52	0.16	0.25	0.002

Note: Women: F = 104.98 (df = 3), p < 0.000; Men: F = 63.90 (df = 3), p < 0.000

Table 6: Differential regression models for predictors of suicide risk by gender.

Type of Adversity	Women	Men
Humiliation/Fear	0.30*	0.01
Physical Abuse	0.23*	0.01
Sexual Abuse	0.18	0.04
No Love/Support	0.31*	0.06
Neglect	0.16	0.13
Parent Separation/Divorce	0.13	0.15
Domestic Violence	0.14	-0.12
Parent Alcohol/Drugs	0.26*	0.03
Family Mental Illness	0.10	0.06
Family Incarceration	0.07	0.04

Table 7: Correlations between specific adversities and suicide risk scores for women and men.

showing significant effects in the initial model were entered along with their interaction terms into the final model. As shown in Table 5, gender appeared to have no moderating effect on the relationship between severity of depression and suicide risk (beta=-0.25, NS). However, it did moderate the effect of anxiety (beta=0.33, p<0.05), suggesting different effects of anxiety for men and women. Gender also moderated the effect of childhood adversity on suicide risk (beta=-0.22, p<0.03). These differential gender effects for depression, anxiety and childhood adversity can be seen in Table 6. For women, depression (beta=0.70, p<0.000) and childhood adversity (beta=0.22, p<0.000) were significant predictors of risk while anxiety was not significant (beta=0.05, NS). For

men, depression (beta=0.56, p<0.000) and anxiety (beta=0.25, p<0.002) were significant predictors of suicide risk while childhood adversity was not significant (beta=0.04, NS). Table 7 shows the association of each type of adversity with suicide risk. After controlling for multiple comparisons with a Bonferroni adjustment (0.05/10), women's childhood experiences of humiliation/fear, physical abuse, lack of love/support, and exposure to parental alcohol/drug abuse were significantly associated with greater suicide risk at p<0.005. For men, no childhood adversity showed any significant association with suicide risk.

## Discussion

Results indicate that, among this sample of individuals currently in treatment for a mood disorder, men were at somewhat greater risk for suicide than women. Our findings are in contrast to a number of previous studies that have found women to have more suicidal ideation and attempts [6-9]. However, our findings are supported by two prospective studies that found men to have greater suicide risk [10-11]. Sample differences in size, age, race/ethnicity, overall mental health status, geographic distribution, and other factors may account for some of the gender differences across studies. In addition, specific measures of suicide risk may capture dimensions of suicidal ideation or behavior that are more salient to men versus women. It will be important for these issues to be examined in future research.

Depression severity was the strongest predictor of suicidal risk for both men and women. This finding is consistent with previous studies in both psychiatric [27,28,30-31] and primary care populations [24,32]. In a prospective study conducted over 50 years, Bradvik et al found that the long-term risk of a completed suicide was 3.1-3.7% for those with moderate depressive symptoms, compared to 11.4-13.8% for those with severe depressive symptoms [75].

Our results do not suggest that gender moderates the relationship between depression severity and suicide risk. Although some studies show gender differences in the effect of depression severity on suicide attempts or completions [33,75], our findings are consistent with research that has also used a standardized assessment scale to measure suicide risk [69]. Inconsistencies in the literature regarding relationships among gender, depression severity and risk of suicide may be due to variability in how risk is defined as well as the heterogeneity of populations being studied.

Results indicate that childhood adversity was a significant predictor of suicide risk for women but not for men. The fact that women in our sample experienced significantly more childhood adversity than men could have contributed to its more profound impact in their lives, including a stronger association between adversity and suicide risk. Only 14% of the women reported no adversity in their childhood whereas 26% of the men reported no adverse events. 15% of the women had actually experienced 7 or more adverse events as children, in contrast to only 7% of the men in our sample. Having 7 or more adverse childhood experiences has been linked in previous research to a 30-fold increase in suicide risk [54]. Over time, the cumulative load of traumatic stress may foster suicidal ideation among women.

Perceived lack of love and support as well as humiliation and fear showed the strongest correlations with suicide risk for women. In line with these findings, Ehnvall et al., reported that feeling rejected by parents was a significant predictor of lifetime suicide attempts for women, although not for men [76]. Being deprived of love and emotional security represent the core of emotional abuse, which has been noted in previous research to more strongly predict suicidal ideation than either sexual or physical abuse [59,77].

Results regarding the effects of anxiety were unexpected. Some research to date suggests that anxiety is more strongly associated with suicidal risk in women than men [46-47]. However, we found that anxiety was a more important risk factor for men. Our finding is in concert with a large cohort study that showed a significantly greater effect of self-reported anxiety and nervousness on subsequent suicide attempts of men than of women [78]. Those investigators proposed that men may be less capable of dealing with feelings of anxiety than women, placing them at greater suicidal risk from distress they experience.

It is important to note that we found no differences in suicidal risk between individuals with diagnoses of depression versus bipolar disorder. These results support other research with a large sample of patients in the NIMH Collaborative Depression Study [5]. In addition, living alone and unemployment did not emerge as significant contributors to suicide risk. However, the influence of these factors may be mediated through the development of depression or through anxiety, which was a significant predictor of risk for men in our study.

### Limitations of the Research

Strengths of this research include a standardized data collection system that engaged a sample representative of multiple clinical sites, geographic regions and a broad age range. However, the advantages of using a patient data collection system that is integrated with routine clinical care must be evaluated against study limitations. Because the registry used as few assessments as possible to enhance clinical utility and integration with work flow, only one measure of suicide risk was included. Similarly, no data was available about patients' current stressors, losses or adversities or about their ongoing treatment. These variables could have accounted for some of the variance in suicide risk. In addition, all data on affective symptoms and adverse childhood experiences is self-reported. Lastly, the cross-sectional nature of the data precluded examination of any change in suicide risk over the course of treatment.

### Conclusions

Findings of this research indicate the importance of regularly assessing the severity of depression among patients with mood disorders and giving special attention to the assessment of anxiety in men. Symptom severity clearly heightens suicide risk. A number of suicide prevention protocols recommend that special attention be paid to men because they are often reluctant to engage in treatment [79]. In addition, screening for early childhood adversity among women is critical since our results confirm prior support for a link between child abuse and suicidality in individuals meeting diagnostic criteria for depression and bipolar disorder. Our findings implicate the profound role of multiple adversities for women in potentially fostering suicidal ideation and behavior over time.

Previous research has shown that the majority of individuals who are victims of suicide experience problems in the coordination and continuity of their care prior to the suicide [80]. Models of care that include a care manager who provides improved care coordination and support for the patient's management of his/her symptoms have shown positive outcomes for patients with complex mental health profiles [81,82]. In light of our findings, such models should be tested for their effects in reducing suicide risk and completion.

More focused studies of specific adverse experiences and types of anxiety also are needed to clarify their differential effects on men and women. In addition, longitudinal research is essential to understand developmental trajectories that may underlie progression to suicidal

risk and how anxiety, depression or other mental health problems may mediate risk in different ways for women versus men. Knowledge of important mechanisms and time points in these trajectories can inform early gender-specific interventions that could prevent later suicide.

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