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Identifying Subgroups of Patients with Depression Who Are at High Risk for Suicide

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Abstract

Objective—Although prior research has identified a number of separate risk factors for suicide among patients with depression, little is known about how these factors may interact to modify suicide risks. Using an empirically-based decision tree analysis for a large national sample of Veterans Affairs (VA) health system patients treated for depression, we identify subgroups with particularly high or low rates of suicide.

Method—We identified 887,859 VA patients treated for depression between April 1, 1999 and September 30, 2004. Randomly splitting the data into two samples (*primary* and *replication* samples), we developed a decision tree for the primary sample using recursive partitioning. We then tested whether the groups developed within the primary sample were associated with increased suicide risk in the replication sample.

Results—The exploratory data analysis produced a decision tree with subgroups of patients at differing levels of risk for suicide. These were identified by a combination of factors including a co-occurring substance use disorder diagnosis, male gender, African American race and psychiatric hospitalization in the past year. The groups developed as part of the decision tree accurately discriminated between those with and without suicide in the replication sample. The patients at highest risk for suicide were those with a substance use disorder, who were non-African American and had an inpatient psychiatric stay within the past 12 months.

Conclusions—Study findings suggest that the identification of depressed patients at increased risk for suicide is improved through the examination of higher order interactions between potential risk factors.

Keywords

suicide; depression; substance use disorders; decision trees; data mining

Introduction

Suicide is a major and potentially preventable public health problem¹. In the United States, over 30,000 people die by suicide every year, and suicide accounts for 4% of all deaths among adults aged 18–65². Depression is a major risk factor for suicide^{3, 4}. Two comprehensive meta-analyses estimated that 2–6% of individuals with affective disorders will die by suicide^{5, 6}.

However, the vast majority of patients with depression do not die by suicide, and more research is needed to better understand profiles of risk among patients with depression^{7, 8}. Typically, studies of suicide risk in individuals with depression have examined the independent effects of demographic factors, such as age and race, and of comorbid psychiatric conditions, such as substance use or personality disorders. Prior research has identified a number of risk factors, including a diagnosis of an alcohol or drug use disorder, male gender, white race/ethnicity, single marital status, unemployment, prior psychiatric hospitalization, and poor physical health^{9, 10, 11}. For example, Zivin and colleagues¹² found that among Veterans Affairs (VA) health system patients with depression, inpatient psychiatric hospitalizations in the year prior to their qualifying depression diagnosis and comorbid substance use were independent risk factors for suicide. Also, patients living in the southern or western United States were more likely to die by suicide. This approach is helpful for identifying general indicators of risk, but it does not provide information about how factors work together to influence this risk.

Suicide is a rare event and risk assessment requires the use of very large samples. It is therefore not surprising that few studies have evaluated interactions among risk factors. One report observed that problem drinking may increase risks differentially in whites compared to blacks¹³. Also, few studies have examined relationships between more than two risk factors. Standard logistic regression analyses typically examine interactions only between pairs of risk factors and their results are often difficult to apply in clinical practice.

An alternative approach uses exploratory techniques to identify subgroups of patients, characterized by clusters of specific risk factors, who are either at particularly high or low risk for suicide^{13, 15}. Data mining approaches identify the single strongest indicator of risk within the overall sample and certain subgroups in each sequential assessment point, taking into account the presence or absence of stronger predictors¹⁶. Baca-García and colleagues¹⁴ reported that a series of higher-order interactions among three or more variables developed through data mining could better predict rehospitalization among individuals with a prior suicide attempt than traditional multivariate analyses. However, to the best of our knowledge this approach has not been directly applied to examine suicide in individuals with depression.

In the present study, we conducted an exploratory analysis designed to derive an empirically-based set of interactions related to rates of suicide in a national sample of VA patients diagnosed with depression. This analysis was conducted with a randomly selected portion of our sample (i.e., 2/3 of the original sample) and a confirmatory analyses of the utility of these groups was conducted on the remaining 1/3 of the sample.

Method

Procedures and Participants

This study utilized data mining techniques to reanalyze data from a retrospective cohort study of suicide in VA patients with depression¹². Participants were drawn from the VA's National Registry for Depression (NARDEP) based at the VA Serious Mental Illness

Treatment Research and Evaluation Center, in Ann Arbor, Michigan¹⁷. The NARDEP includes data on demographic factors, diagnostic characteristics, pharmacy data and service utilization for VA patients with depression. The present study uses data from April 1, 1999 through September 30, 2004. Participants were included if they either (1) had been diagnosed with a depressive disorder and had been prescribed an antidepressant, or (2) were diagnosed with depression during two separate medical visits in the study period. Patients were excluded if they had bipolar I disorder, schizophrenia, or schizoaffective diagnoses recorded during the observation period or the year prior to the entry into the cohort. The use of these inclusion and exclusion criteria resulted in a sample of 887,859 patients.

To examine suicide risks in these patients, we linked treatment record data with information from the National Death Index (NDI). The NDI queries were submitted for the cohort of patients with a date of death in the VA Beneficiary Identification and Records Locator System (BIRLS) Death File during the study period. Because BIRLS data may not detect all individuals who died within a given year, we also initiated NDI searches for patients who did not use VA services in the year following the study period, even if there was no date of death for these patients in VA data. This comprehensive process identified 1,892 patients in the study cohort as having died from suicide using ICD-9 or ICD-10 codes specifically identifying suicide in NDI data (E950-E959 or ICD-10 codes X60-X84, Y87.0).

The sample was divided into *primary* and *replication* samples. A total of 589,825 (66.4% of the original sample) were randomly selected to be part of the primary sample and 298,034 (33.6% of the original sample) were selected to be in the replication sample. Characteristics of participants in the primary sample are presented in Table 1. The primary and replication samples did not significantly differ on any of these characteristics.

Measures

All analyses focused on predicting suicide as the primary outcome. As noted, suicide deaths were identified using NDI searches. The NDI is a national repository of data collected from state death certificates, and it is considered the “gold standard” of US mortality databases¹⁸.

The following candidate risk factors were derived from patient treatment records: age, race (White, African American, Other, Asian, American Native, Native Hawaiian or Pacific Islander, Multiracial or Unknown), gender (male or female), substance use disorder diagnosis (no or yes; i.e., a clinical diagnosis of any alcohol or drug use disorder), diagnosis of PTSD (no or yes), prior VA hospitalization (no or yes; for any psychiatric diagnosis in the year prior to cohort entry), service connection (no or yes; indicating some VA-recognized disability stemming from injuries or conditions that occurred or were exacerbated during military service), and baseline medical comorbidity reflecting the sum of all conditions in the past 12 months included in the Charlson Comorbidity Index¹⁹.

Analyses

The main set of data mining analyses was conducted on the primary sample. The replication sample was used to verify the original set of results using more traditional statistical methods. The data mining procedures used Bayesian Dirichlet Equivalent (BDE) methods to identify the strongest predictor. This data mining process examined possible higher-order relationships between predictors²⁰. For continuous variables, these determine the optimal cut points for splitting continuous predictors, such as age, into levels that maximally differentiate between levels of suicide risk²¹. This method has the advantage of using prior information to allow for the application of these methods to rare outcomes, such as suicide. In order to increase the potential utility of the results, we limited the results to a maximum of three cut points (similar to a three-way interaction). This process resulted in an

empirically derived decision tree with patients grouped at each level based on similarities in level of suicide risk. Additionally, for all cut points on the figures, we present rates of suicide per 100,000 person years. This information is provided for descriptive purposes and is not directly part of the decision tree analysis.

Following the development of the decision tree in the primary sample, we examined the extent to which the factors identified from the data mining approach could accurately discriminate between those with and without a suicide in the replication sample using chi-square analyses and odds ratios. A cut-off of $p < .01$ was used as an indicator of statistical significance.

Results

The overall rate of suicide was 89.55/100,000 person years (PYs) in the primary sample of depressed veterans. The data mining analysis identified a diagnosis of a substance use disorder as the strongest single risk factor for suicide (see Figure 1). The suicide rate for those with a substance use disorder was 128.27/100,000 PYs relative to 76.48/100,000 PYs for those without a substance use disorder. The data mining analysis split the sample into those with or without a substance use disorder and identified the most important remaining risk factors in these two separate groups.

Individuals with a substance use disorder

Depressed VA patients with a substance use disorder were subsequently divided based on their race. Specifically, African Americans were significantly less likely to die by suicide than individuals of any other race/ethnicity group (28.54/100,000 PYs vs. 157.11/100,000 PYs). In African Americans with a substance use disorder, no other variables reliably distinguished those who did versus those who did not die by suicide. In non-African Americans (who were predominately white), having been admitted to inpatient psychiatric treatment at least once in the prior 12-months conferred an additional risk for suicide. In the subgroup of depressed, non-African American veterans with a substance use disorder, the suicide rate was 247.21/100,000 PY among those with a prior inpatient psychiatric stay whereas it was 143.05/100,000 PY among those with no psychiatric admissions in the prior year.

Individuals without a substance use disorder

In those without a substance use disorder, gender was the strongest indicator of suicide risk. The suicide rate for men in this group was 82.08/100,000 PYs versus 26.22/100,000 PYs for women. In women, no other available risk factors reliably identified individuals at differing levels of risk. In men without a substance use disorder, race again was related to suicide risk. Specifically, African American men without a substance use disorder were less likely to die by suicide with a rate of 33.30/100,000 PYs compared to 86.78/100,000 PYs for non-African Americans.

Results from the replication sample

A series of comparisons were conducted in the replication sample to examine the extent to which more traditional analytic techniques would yield similar results. For these analyses, we reconstructed the prior steps in the decision tree in an *a priori* manner and examined the extent to which each additional step significantly distinguished between the groups. Table 2 presents the results of chi-square test of the groups generated by the data mining analyses in both the primary and replication samples. In all cases, the groups produced by the initial exploratory data mining analyses significantly discriminated those who died from suicide from those who did not.

Discussion

Using a large national database of VA patients with depression, a combination of factors including demographic characteristics, psychiatric disorders, and prior psychiatric hospitalizations discriminated between individuals with and without a suicide. Consistent with prior research on this sample¹², a substance use disorder was the single strongest indicator of suicide risk in depressed veterans. However, the sample could be further divided into smaller groups of high and low risk individuals. Depending on the constellation of risk factors, the risk of suicide in veterans with depression ranged from a low of 26.22/100,000 PY among women without a substance use disorder to a high of 247.21/100,000 PY among non-African American patients with a substance use disorder and an episode of inpatient psychiatric treatment within the past year. This substantial variability in level of risk highlights the need to better understand how risk factors interact and combine to influence risk for suicide.

The finding that a diagnosis of a substance use disorder was the strongest single predictor of suicide in depressed veterans is consistent with prior research in non-depressed samples indicating that presence of an alcohol or drug use disorder is one of the most potent risk factors for suicide mortality²². According to an empirical review of cohort studies, individuals with alcohol dependence are at almost ten times more likely to die by suicide compared to the general population⁶. However, this research has not generally focused on additional risks conveyed by substance use disorder in other psychiatric populations, including depressed individuals. The strength of the association in the present sample of depressed veterans reinforces the importance of substance use disorder as an additional risk factor even among depressed patients who are already at an elevated risk for suicide.

Examining interactions among risk factors yields other potentially important findings, including the implication that gender is less immediately relevant in determining suicide risk once substance use is determined to be present. Gender is one of the most potent risk factors for suicide, with men being four times more likely to complete suicide than women in the general population². The odds ratios for suicide associated with male compared to female gender are still high among depressed populations, although somewhat smaller than in the general population. The ordering of risk factors in this study emphasizes the need to remain alert for suicide among depressed women as well as men once substance use is identified. It is also important to note that among depressed patients, once substance use is determined to be present, the most important factor to consider next is race. Gender is not among the top three risk factors for suicide among patients with both depression and substance use. This finding has implications for clinicians completing suicide risk assessments of dual diagnosis patients. Among patients who do not have substance use, gender again clearly emerges as one of the strongest predictors of suicide, even greater than other potentially important indicators of illness severity such as prior inpatient stays. However, these findings also likely reflect the composition of the present sample. It is important to note that the sample is predominantly male and we may not have been able to detect the impact of gender on suicide risk in certain subgroups.

This was an exploratory data analysis and the decision tree was derived purely based on the ability to discriminate between participants on completed suicide. This decision process does not adhere to established theory of suicide risk and the associations are not necessarily causal. Instead, these factors are markers of risk. Thus, they may reflect a direct influence on suicide risk or the influence of other unmeasured variables²³. Also, even in our highest risk groups, the vast majority of participants did not die by suicide. These results highlight the difficulty in developing specific models of low base-rate outcomes like suicide. Similarly, the risk of suicide likely fluctuates over time and we do not have data on proximal risk

factors for suicide. Identifying individuals at immediate risk for suicide requires combination of knowledge of risk factors with attention to recent life events (losses, conflicts) and clinical judgment.

Several additional limitations of this study should be noted. The sample is comprised of depressed veterans receiving health services from the Department of Veterans Affairs. Thus, it is important to be cautious in generalizing these findings to other depression treatment populations. All predictors in these analyses were based on data derived from VA treatment records. The measurement of diagnostic features, including PTSD and substance use disorders, reflects the real-world utilization of these diagnoses and likely differs from gold-standard measurements of these disorders with structured clinical instruments. In this sample, no reliable data were available on prior suicide attempts. Future research in other samples would benefit from the inclusion of information related to prior suicidal behaviors. Also, designations of suicide mortality were obtained from NDI data and are therefore necessarily limited by the accuracy of information in death certificates.

Despite these limitations, this is the first study of which we are aware to use an empirically derived decision tree to segment the depression treatment population by suicide risk. Our results indicate that the association between a known risk factor and suicide in veterans with depression is clearly not independent of another risk factor. Unlike traditional logistic regression analyses that include only main effects or interaction terms specified *a priori* by researchers, these analyses allowed for the examination of more complicated interactions that may have not been hypothesized to be important based on the existing research. Additionally, the decision tree allows for the presentation of complicated interactions, such as the one found between substance use disorder status, race/ethnicity, and 12-month hospitalization among suicide risk factors in a manner that is likely to be readily understandable by clinicians and policy makers.

Patients at highest risk for suicide among depressed patients are those with a substance use disorder, non-African American race and an inpatient stay in the past 12-months. Among patients without substance use disorder, those who are male and non-African American are at the greatest risk of suicide. Providers treating patients with these characteristics should be aware of these risks and consider target strategies to screen for current suicidal thoughts and plans.

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Figure 1.

Table 1

Patient Characteristics of the Primary Sample (N = 589,825)

	N	%
Gender		
Male	542,109	91.9
Female	47,716	8.1
Race and Ethnicity		
White	450,704	76.4
Black	73,126	12.4
Other	12,803	2.2
Unknown	53,192	9.0
Hispanic	27,522	4.7
Substance Abuse	130,228	22.1
PTSD	130,124	22.1
Inpatient Psychiatric Stay in past 12 Months	21,047	3.6
Service Connection	186,261	31.6
	Mean	Standard Deviation
Age	58.63	14.38

Table 2

Associations between risk factors and suicide

Primary Sample				
Step	Group/subgroup	Predictor	Chi-square (p- value)	Odds Ratio (95% confidence interval)
1	Primary sample	Any substance use disorder (Yes versus No)	147.2 (p <.0001)	2.0 (1.8–2.2)
2a	Those with a substance use disorder	Non-African American (Yes versus No)	83.1 (p <.0001)	5.6 (3.7–8.6)
3a	Those with a substance use disorder who are not African American	Any inpatient treatment in the prior 12-months (Yes versus No)	35.0 (p <.0001)	2.0 (1.6–2.5)
2b	Those without a substance use disorder	Gender (Male versus Female)	32.7 (p <.0001)	2.9 (2.0–4.2)
3b	Those without a substance use disorder who were male	Non-African American (Yes versus No)	27.0 (p <.0001)	2.6 (1.8–3.8)
Replication sample				
Step	Group/subgroup	Predictor	Chi-square	Odds Ratio (95% confidence interval)
1	Full replication sample	Any substance use disorder (Yes versus No)	47.6 (p <.0001)	1.8 (1.5–2.1)
2a	Those with a substance use disorder	Non-African American (Yes versus No)	44.7 (p <.0001)	8.5 (4.0–18.1)
3a	Those with a substance use disorder who are not African American	Any inpatient treatment in the prior 12-months (Yes versus No)	25.6 (p <.0001)	2.3 (1.6–3.2)
2b	Those without a substance use disorder	Gender (Male versus Female)	16.7 (p <.0001)	2.9 (1.7–4.9)
3b	Those without a substance use disorder who were male	Non-African American (Yes versus No)	13.6 (p <.0001)	2.6 (1.5–4.5)