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Mental Disorder Comorbidity and Suicide Among 2.96 Million Men Receiving Care in the Veterans Health Administration Health System

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Abstract

Comorbid mental disorders are common among suicide decedents. It is unclear if mental disorders in combination confer additive risk for suicide, in other words, if risk associated with two disorders is approximately the sum of the risk conferred by each disorder considered separately, or if there are departures from additivity such that the combined risk is less (i.e., subadditive) or

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The authors had full access to all of the data in the study and take full responsibility for the integrity of the data and the accuracy of the data analysis. Data were acquired for program planning and evaluation purposes. Input from the Veterans Affairs Office of Mental Health Services shaped the design and conduct of the study; the collection, management, analysis, and interpretation of the data; and the preparation, review, and approval of the manuscript. However, the views expressed in this report are those of the authors and do not necessarily represent those of the Department of Veterans Affairs.

more than additive (i.e., synergistic). Using a retrospective cohort design, all male Department of Veterans Affairs, Veterans Health Administration (VHA) service users who utilized VHA services in fiscal year (FY) 1999 and were alive at the start or FY 2000 (N= 2,962,810) were analyzed. Individuals were followed until death or the end of FY 2006. Using the VHA National Patient Care Database, diagnoses of mental disorders in FY 1999 were grouped into six categories (e.g., posttraumatic stress disorder). In proportional hazards models, 2-way interactions between disorders were used to examine departures from additive risk. There were 7,426 suicide deaths in the study period. Two-way interaction tests were nearly all statistically significant, indicating departures from additivity, and the results of these tests were consistent with subadditive risk. Sensitivity analyses examining the first year of follow-up showed similar results. Subadditive risk may be explained by factors that serve to lower the increased risk associated with a comorbid diagnosis, which may include common underlying causes of mental disorders, difficulties of differential diagnosis, the nature of etiological relationships between mental disorders, and intensive clinical care and monitoring of patients with comorbidity.

Keywords

suicide; comorbidity; veterans; cohort

In 2008, there were more than 36,000 suicides in the United States, making it the tenth leading cause of death and the fifth leading cause of years of potential life lost before age 65 (Centers for Disease Control and Prevention, 2011). The Department of Veterans Affairs health system, the Veterans Health Administration (VHA), is the largest integrated health care system in the United States. Each year, more than 1,600 VHA users die by suicide (McCarthy et al., 2009). Moreover, individuals who use VHA services, the large majority of whom are veterans, are at increased risk for suicide compared with the U.S. general population (McCarthy et al., 2009). Accordingly, suicide prevention among veterans is both a national and a VHA priority.

Mental disorders play a key role in suicide among users of VHA services (Ilgen et al., 2010) and other populations (Nock et al., 2008). Mental disorder comorbidity, defined as the presence of two or more mental disorders, is commonly present among suicide decedents (Cavanagh, Carson, Sharpe, & Lawrie, 2003; Yoshimasu, Kiyohara, Miyashita, & The Stress Research Group of the Japanese Society for Hygiene, 2008). Studies using psychological autopsy research designs (Conner, Beautrais, & Conwell, 2011) provide most of the descriptive data on comorbidity and suicide. A meta-analysis of case-control psychological autopsy studies (Cavanagh et al., 2003) showed that the combination of a substance use disorder (SUD) plus another mental disorder is more common in suicides (median = 38%, range 19% to 57%) than in nonsuicide controls (median = 6%, range 0% to 13%). Similarly, several individual psychological autopsy reports indicate that suicide decedents are more likely to have comorbidity than controls (Hawton et al., 2002; Kim et al., 2003; Lesage et al., 1994; Waern et al., 2002).

The general observation that mental disorder comorbidity is common among suicide decedents has generated interest in the potential that risk conferred by two disorders in

combination is greater than the sum of the risk conferred by each disorder considered separately, in other words, the combined risk is more than additive, which is also referred to as synergism (Gradus et al., 2010). SUD and depression are the most common disorders among suicide decedents (Cavanagh et al., 2003; Yoshimasu et al., 2008), and, accordingly, potential synergism between SUD and depression has received the greatest attention. Along these lines, investigations using case-control psychological autopsy designs have tested potential synergism using tests of interactions between SUD and depression, but these tests have not supported this idea (Cheng, Chen, Chen, & Jenkins, 2000; Conner et al., 2003; Zhang, Conner, & Phillips, 2012). The general lack of evidence for synergism between SUD and depression based on psychological autopsy studies may indicate that these disorders in combination do not confer greater risk than would be expected from risk associated with each disorder independently. Thus, their combined effects may be additive. Alternatively, with rare exception (e.g., Zhang et al., 2012), psychological autopsy studies have insufficient sample sizes for tests of synergism. Although we are not aware of a study illustrating synergism of SUD and depression per se in suicide, a case-control analysis of a national sample of 5.4 million individuals in Denmark showed that individuals who had been diagnosed with posttraumatic stress disorder (PTSD) and depression were at more than additive risk for suicide compared with those diagnosed with either of these disorders alone, providing evidence of synergism (Gradus et al., 2010). There are also some data to suggest that mental disorders in combination, regardless of the specific diagnoses considered, confer greater than additive risk (Beautrais et al., 1996).

Interestingly, recent studies of suicide (Flensborg-Madsen et al., 2009; Zhang et al., 2012) and nonfatal suicide attempts (Nock et al., 2009) raise the possibility that mental disorders in combination confer less than additive risk for suicidal behavior (i.e., subadditive risk). Nock and colleagues (2009) conducted an analysis of survey data from 21 countries participating in the World Mental Health Survey and showed that the lifetime risk for suicide attempt increased with the number of mental disorders, yet tests of interactions indicated that risk for an attempt associated with each additional disorder "decayed" (i.e., decreased) with each additional disorder, consistent with subadditive risk (Nock et al., 2009). A large cohort study in Denmark showed a statistical interaction between alcohol use disorder and other mental disorders in suicide risk. In a follow-up analysis stratified by the presence or absence of another psychiatric disorder, alcohol use disorder conferred higher risk for suicide in individuals without mental disorder than the group with a mental disorder (Flensborg-Madsen et al., 2009). These results suggest that the impact of alcoholism on suicide was decreased with the addition of another mental disorder, consistent with subadditive risk. Finally, in a large case-control psychological autopsy study of males in China, a statistically significant interaction between alcohol use disorder and major depression showed that the association between depression and suicide risk was weaker in men with alcohol use disorder, consistent with subadditive risk (Zhang et al., 2012).

In light of the high prevalence of comorbid mental disorders among suicide decedents and conflicting reports about synergistic and subadditive effects, clarifying if mental disorders in combination confer additive risk, subadditive risk, or act synergistically is essential to inform suicide prevention efforts. If risk conferred by mental disorders is additive, then clinicians should not assign more weight in risk formulations to a given diagnosis based

on the presence of comorbidity, for example, the contribution of depression to suicide risk may be judged without factoring in comorbid conditions. On the other hand, if risk between mental disorders is generally synergistic, it would be essential to consider comorbid conditions (e.g., SUD) in handicapping risk associated with a given disorder (e.g., depression). Finally, if risk conferred by disorders in combination is subadditive, it would suggest that one could reach a point of diminishing returns (for the purpose of suicide risk identification) with the uncovering of additional comorbidities.

Differences between veteran and nonveteran populations points out the critical importance of dedicated study of veteran groups. For example, veterans have higher rates of posttraumatic stress disorder (PTSD), largely a product of combat exposure, compared with the general population (Tanielian, & Jaycox, 2008; Kulka et al., 1990). Yet unlike other populations where PTSD may be presumed to confer risk for suicide, analyses of VHA service users show that this is not necessarily the case (Desai, Dausey, & Rosenheck, 2005; Zivin et al., 2007). A study of a large cohort of VHA patients discharged from inpatient psychiatric treatment showed that PTSD did not confer risk for suicide after adjusting for other comorbid mental disorders (Desai et al., 2005). A study of a large cohort of VHA patients, all with depressive disorders, showed that a diagnosis of comorbid PTSD *lowered* risk for eventual suicide (Zivin et al., 2007). To account for these results, it has been hypothesized that robust treatment services for PTSD in VHA may explain why comorbid PTSD may afford some protection (Desai et al., 2005; Zivin et al., 2007). These special considerations underscore the need for dedicated analyses of comorbidity and suicide among veterans.

The purpose of the current study was to examine mental disorder comorbidity and suicide in a large national cohort of users of VHA services over a 6-year follow-up (Ilgen et al., 2010), with a goal of determining if specific combinations of disorders were additive, subadditive, or synergistic in their impact on suicide risk. We also examined additivity, subadditivity, and synergism associated with the number of mental disorders, regardless of the type of disorder. There are significant sex differences in risks for suicide associated with mental disorders among users of VHA services (Ilgen et al., 2010), suggesting the importance of stratifying analyses of suicide in this population by sex. The current analysis was limited to male VHA patients because of the lower prevalence of female patients and the lower prevalence of suicide among women (Ilgen et al., 2010); thus, it was not feasible to conduct reliable tests of interactions between mental disorders among female patients.

Method

Study Population

The methods and sample have been previously described in detail (Ilgen et al., 2010). Briefly, the cohort included all male VHA patients who utilized VHA services in fiscal year (FY) 1999 and were alive at the start or FY 2000 (N= 2,962,810). Risk began at the start of FY 2000. These individuals were followed until death or the end of FY 2006, which ever came first. Fiscal years reflect the time period from October 1 of a given year until September 30 of the following year. Analyses received approval from the Ann Arbor VA Human Subjects Committee.

Data Sources

Data are based on linkage of the VA National Patient Care Database (NPCD) and the Centers for Disease Control and Prevention's National Death Index (NDI). The NPCD included demographic and diagnostic information for all treatment contacts of patients seen anywhere within the VHA treatment system. NDI provided information about vital status and cause of death for all U.S. residents from state vital statistics offices from the start of FY 2000 though the end of FY 2006. NDI searches were conducted on all individuals who utilized care during the index year but did not have any record of VHA care following FY 2006. Among population-level sources of mortality data, the NDI has the greatest sensitivity in determining vital status (Cowper, Kubal, Maynard, & Hynes, 2002). In instances where the NDI search yielded multiple records as potential matches, standard procedures guided conclusions of "true" matches (Sohn, Arnold, Maynard, & Hynes, 2006).

Measures

Demographic characteristics.—We examined age stratified into the following groups: 18 to 29 years, 30 to 39 years, 40 to 49 years, 50 to 59 years, 60 to 69 years, 70 to 79 years, 80+ years (reference group). With the exception of sex, reliable information on other demographic characteristics (e.g., race/ethnicity) was not available.

Diagnostic characteristics.—Mental disorder diagnoses were based on *International Classification of Diseases, 9th Revision, Clinical Modification* (World Health Organization, 1995) diagnostic codes given during a visit in FY 1998 or FY 1999. The six categories of diagnoses examined were (a) PTSD, (b) SUD, (c) depression, (d) bipolar disorder (Type I or II), (e) anxiety disorder apart from PTSD, and (f) and schizophrenia.

Suicide.—Using NDI data, we identified dates and underlying causes of death. Suicide deaths were identified using the International Classification of Diseases-10 codes X60-X84, Y87.0 (World Health Organization, 2004).

Analyses.—All calculations used the cohort of individuals who used VHA services in FY 1999 and were alive at the start of FY 2000. Time of observation began on the first day of FY 2000 and ended at the date of suicide or the last day of FY 2006, if alive. Individuals who died from causes other than suicide were censored on their date of death. Models were adjusted for age. Covariance sandwich estimators were used to adjust for the clustered nature of the data, with patients nested within VHA facilities. First, a series of proportional hazards regression models yielded hazard ratios (HRs) and 95% confidence intervals (CIs) to estimate risk of suicide for each diagnostic category, irrespective of comorbidity. Second, proportional hazards regression models examined the HR of suicides for each diagnostic category that occurred alone, without a comorbid diagnosis (e.g., pure PTSD). Third, we examined the HR for each two-way combination of diagnoses among individuals who did not have any other mental disorder diagnosis (e.g., PTSD and SUD only, without other comorbidity). In each of these models, we used a common reference group of individuals with no mental disorder diagnosis that allowed for comparison across disorders.

To examine hypotheses pertaining to synergism, we conducted 15 two-way interaction tests. In these models, we included the main effect for a diagnosis irrespective of comorbidity (e.g., SUD), the main effect for a second diagnosis irrespective of comorbidity (e.g., depression), and the two-way interaction term, along with adjustment for age. Statistically significant interaction tests were interpreted to indicate that the null hypothesis that the relationship between mental disorders was additive should be rejected (Greenland, Lash, & Rothman, 2008). Under these conditions, statistically significant interaction terms with a negative beta (β) were interpreted as evidence of subadditive risk, and significant interaction terms with a positive beta as evidence for synergism. Model fits were assessed using likelihood ratio tests. Alpha was set to .05. With time, mental disorders may remit with treatment or naturalistically. Therefore, in sensitivity analyses, we limited follow-up to FY 2000, the first year of observation, in order to determine if the results of the primary analyses held with a shorter follow-up.

Recognizing that some suicide decedents have more than two mental disorders, we described the number of suicide decedents with a total of 0, 1, 2, 3, 4, 5, and 6 (all possible) mental disorders. We also calculated the HRs and 95% CIs for suicide associated with each diagnostic group (e.g., one disorder, two disorders) in a multivariate model, adjusted for age. In this model each category was compared with a no-disorder reference group.

Results

Of male patients treated in VHA in FY 1999, a total of 7,426 individuals (0.25%) died by suicide between FY 2000 and FY 2006. Among suicide decedents, 3,456 (46.5%) had been diagnosed with one or more mental disorders and 3,122 (42.0%) had been treated in a mental health or SUD treatment setting. Descriptive results are shown in Table 1. Depression was the most common diagnosis category present among suicide decedents (n= 2,281; 30.7% of suicides), followed by SUD (n = 1,583; 21.3%), anxiety disorder (n = 1,080; 14.5%), PTSD (n = 869; 11.7%), schizophrenia (n = 660; 8.9%), and bipolar disorder (n = 638; 8.6%). A minority of suicide decedents with a mental disorder diagnosis had been diagnosed in only one category (i.e., pure diagnosis), including 562 of 2,281 (24.6%) suicides with depression, 402 of 1,583 (25.4%) suicides with SUD, 168 of 1,080 (15.5%) suicides with anxiety disorder, 117 of 869 (13.5%) suicides with PTSD, 129 of 660 (19.5%) suicides with schizophrenia, and 53 of 638 (8.3%) of suicides with bipolar disorder.

In Table 2, HRs for suicide are presented as associated with each disorder irrespective of comorbidity (other disorders allowed), each disorder with no other mental disorder (pure disorder), each two-way comorbid combination of disorders irrespective of comorbidity (other disorders allowed), and each two-way combination alone with no other mental disorder (pure two-way combination). In nearly all instances, each disorder or two-way combination conferred statistically significant risk for suicide. The lone exceptions were the pure two-way combination of PTSD plus schizophrenia and the pure two-way combination of bipolar disorder plus other anxiety disorder. However, these nonsignificant results are not interpretable, given the very small number of suicide decedents (n = 8 and n = 3, respectively) in these categories.

All of the two-way tests of statistical interaction between mental disorders showed adequate fit, with p < .001 for all likelihood ratio tests. With one exception, the two-way interaction tests had a negative beta (β) and reached statistical significance: PTSD × SUD ($\beta = -0.246$, p = .0003), PTSD × Depression ($\beta = -0.546$, p < .0001), PTSD × Bipolar Disorder $(\beta = -0.537, p < .0001)$, PTSD × Anxiety Disorder ($\beta = -0.161, p = .0038$), PTSD × Schizophrenia ($\beta = -0.522$, p < .0001), SUD × Depression ($\beta = -0.161$, p = .0038), SUD × Bipolar Disorder ($\beta = -0.487$, p < .0001), SUD × Schizophrenia ($\beta = -0.602$, p < .0001), Depression × Bipolar Disorder ($\beta = -0.500$, p < .0001), Depression × Anxiety Disorder $(\beta = -0.302, p < .0001)$, Depression × Schizophrenia ($\beta = -0.490, p < .0001$), Bipolar Disorder × Anxiety Disorder ($\beta = -0.415$, p < .0001), Bipolar Disorder × Schizophrenia (β = -0.666, p < .0001), and Anxiety Disorder × Schizophrenia ($\beta = -0.475$, p < .0001). These statistically significant interactions indicate that the null hypothesis that the relationship between disorders in suicide risk is additive should be rejected. The fact that the betas were universally negative in these models is consistent with subadditivity. The lone nonsignificant two-way interaction test was SUD × Anxiety Disorder ($\beta = -.0165$, p = .791), indicative of an additive effect.

We conducted further examination of the results by inspecting the first row of Table 2. Nearly all (14 of 15) comorbid combinations followed a pattern whereby two disorders in combination conferred higher risk for suicide than either disorder considered separately based on nonoverlapping 95% CIs (for example, PTSD plus SUD, HR [95% CI] = 3.81[3.40, 4.27], versus PTSD, HR [95% CI] = 2.60 [2.39, 2.82], or versus SUD, HR [95% CI = 2.98 [2.76, 3.21]), or two disorders in combination conferred similar risk for suicide compared with one, or the disorder considered separately, based on overlapping 95% CIs (for example, bipolar disorder plus schizophrenia, HR [95% CI] = 4.35 [3.76, 5.04], versus bipolar disorder, HR [95% CI] = 4.29 [3.91, 4.71]). In all of these cases, there was a statistically significant two-way interaction and a negative beta, interpreted to indicate that the risk associated with two disorders in combination was *less* than would be expected considering each disorder independently, consistent with subadditive risk. Uniquely, SUD plus anxiety disorder was the only comorbid combination to show additive risk. Specifically, risk associated with SUD plus anxiety disorder (HR [95% CI] = 4.82 [4.31, 5.39]) was greater than risk associated with either of these disorders considered separately (SUD, HR [95%] CI = 2.98 [2.76, 3.21]; anxiety disorder, HR [95% CI] = 2.79 [2.57, 3.02)]). Moreover, the nonsignificant two-way interaction test (provided previously) indicates the null hypothesis of additive risk should not be rejected.

Sensitivity analyses examining the first year of follow-up indicated that there were 1,203 suicides, and 633 (52.6%) had been diagnosed with one or more mental disorders. Diagnoses of depression (n = 420, 34.9%) and depression plus SUD (n = 198, 16.5%) were the most common mental disorder and comorbidity, respectively. Each mental disorder was associated with increased risk for suicide and risks were higher compared with the primary analyses, with HRs (95% CI) ranging from 3.41 (2.84, 4.09) for PTSD to a high of 6.25 (5.08, 7.69) for bipolar disorder. Each comorbid combination also conferred higher risk compared with the primary analyses, with HRs (95% CI) ranging from 3.89 (3.18, 4.77) for PTSD plus depression, to 9.21 (7.04, 12.04) for bipolar plus anxiety disorder. Thirteen of the 15 two-way interaction tests showed a negative beta and a statistically significant result,

consistent with subadditive risk, with the only exceptions being the combinations of SUD plus depression and SUD plus anxiety disorder, which showed additive effects.

Considering pure disorders and pure two-way combinations (row 2 of Table 2), the pattern of findings is generally consistent with the primary results presented here, although the magnitude of risk for suicide associated with the pure disorders and pure combinations are typically smaller.

The number of male veteran suicide decedents with 0, 1, 2, and so forth mental disorders is provided in Table 3, along with the HR (95% CI) associated with each category. The number of suicide decedents decreased as the number of diagnoses increased, for example 1,431 (19.3%) decedents had one diagnosis, versus 28 (0.4%) with all six diagnoses. Consistent with the primary results from the two-way interaction tests, the results in Table 3 appear consistent with subadditivity. For example, risk for suicide associated with three diagnoses, HR (95% CI) = 3.27 (2.98, 3.59), is increased but less than expected if it were additive given risk associated with two diagnoses, HR (95% CI) = 2.69 (2.51, 2.89), and one diagnosis, HR (95% CI) = 1.99 (1.87, 2.12).

We performed post hoc analyses to determine if there is a linear trend in the hazards ratios (HR) as the number diagnoses increases (as visual inspection of Table 3 suggests). We did this by approximating such a linear relationship using a fourth-degree polynomial in the predictor part of the proportional hazards model, which models the log function of HR. The latter yielded a reasonably straight line when transformed back to the original HR scale. We then used likelihood ratio test (Wilks, 1938) to compare this model with the one based on coding the number of diagnoses as a nominal variable. The chi-square test statistic was 3.38 (df = 2), p = .184, consistent with a linear trend.

Discussion

The present study examined the association between differing combinations of mental disorders and suicide risk in male veterans who used VHA services. These results indicate that almost half (46.5%) of men in the cohort who died by suicide in the 6-year follow-up period had at least one mental disorder diagnosed (e.g., depression) during the year prior to follow-up. Among those with a diagnosis, most had another comorbid condition. We conducted two-way tests of interaction between the disorders in order to determine if the presence of comorbidity was additive, synergistic, or subadditive. Nearly all (14 of 15) two-way combinations of disorders showed subadditive risk; in other words, the disorders in combination showed lower risk for suicide than would be expected by summing risk for suicide associated with each disorder considered separately.

Despite being placed in different diagnostic categories, many mental disorders have common underlying causes (Kendler et al., 2011; Rzhetsky, Wajngurt, Park, & Zheng, 2007). Subadditivity may occur when two disorders—for example, depression and anxiety disorders—share a common underlying cause that confers risk for suicide, such as neuroticism (Brezo, Paris, & Turecki, 2006). The challenges of differential diagnosis also likely played a role in subadditivity. For example, in the current study, a diagnosis of

schizophrenia did not contribute additional risk among individuals diagnosed with bipolar disorder. Schizophrenia and bipolar disorder are difficult differential diagnoses to make, particularly in their acute phases. Therefore, there is increased potential that these comorbid diagnoses were merely an artifact of different labels for the same clinical presentation. Under this scenario, a second diagnostic label would not be expected to contribute increased risk, consistent with the data. The etiological relationship between mental disorders may also contribute to the finding of subadditivity. For example, depression that is substance induced is overrepresented among individuals with SUD, and preliminary data suggest that substance-induced depression confers lower risk for suicidal behavior compared with depression that occurs independent of substance use (Preuss et al., 2002). If the substanceinduced subtype is indeed a less suicidogenic form of depression, then it would be expectable that the contribution to risk of a diagnosis of depression among individuals with SUD (much of which may be assumed to be substance induced) would be less than additive, consistent with the current findings. Finally, identification of comorbid mental disorders may lead to more intensive clinical care and monitoring, which may serve to lower risk for suicidal behavior among veterans treated in the VHA (Ilgen, Jain, Lucas, & Moos, 2007; Valenstein et al., 2009), potentially serving to lower the impact of comorbidities on suicide risk.

Interestingly, in the primary analyses, we did not replicate a previous finding that PTSD is associated with decreased risk for suicide among VHA patients with a depression diagnosis after controlling for other risk factors (Zivin et al., 2007). However, in the secondary analyses of pure disorders and pure two-way combinations (row 2 of Table 2), a nonsignificant trend was observed such that the risk associated with depression alone, HR (95% CI) = 2.41 (2.20, 2.64), approached being greater than risk associated with depression plus PTSD with no other diagnoses, HR (95% CI) = 2.03 (1.68, 2.44).

Sensitivity analyses examined the cohort during the first year of follow-up. These results revealed increased associations of mental disorders and comorbid disorders with suicide compared with the primary analyses, attributable to the closer time between diagnoses (i.e., active symptoms) and suicides. Importantly, 13 of the 15 interaction tests in the sensitivity analyses were consistent with subadditive risk, indicating that the primary results revealing subadditivity were not an artifact of the extended period of follow-up. Indeed, the only two-way interaction test that showed subadditivity in the primary analysis but not in the sensitivity analysis was SUD plus depression, a diagnostic combination that, given its high prevalence, warrants further study.

Limitations

Mental disorder diagnoses were based on clinical records with associated limitations of reliability and validity. The diagnoses were made prior to implementation of VHA-wide screening for alcohol use disorders, depression, and PTSD that could have served to improve the sensitivity to detect these disorders. About 46% of suicide decedents were diagnosed with a mental disorder, making it likely that some mental disorders were missed, although the extent to which veterans without a diagnosis were true negatives (no disorder) versus false negatives (missed disorder) is unknown. The analyses were not able to shed light on

the nature of the relationship between mental disorders, for example, between disorders that may be considered primary versus secondary to another diagnosis (e.g., substance-induced depression). The diagnoses were made in the first year that the cohort was observed, and analyses did not adjust for remission or recovery of disorders or the addition of new diagnoses in subsequent years. Other comorbidities, including physical illnesses, were not analyzed. The study population included men treated in VHA, with unclear relevance to other populations. Because a small percentage of male VHA users are not veterans, it was not strictly a veteran sample.

Conclusion

The results of the current study add to a small but growing literature suggesting subadditive risk of mental disorders in suicidal behavior (Flensborg-Madsen et al., 2009; Nock et al., 2009; Zhang et al., 2012). Subadditive risk is potentially explained by a variety of mechanisms, including common causes of mental disorders, difficulties of differential diagnosis, the etiological relationships between mental disorders, and patients with comorbid mental disorders receiving greater clinical care and monitoring. Analyses were based on a large population of male veterans and were responsive to growing public concern about suicide in military populations (Joshua Omvig Veterans Suicide Prevention Act, 2007). The present study was a rare analysis outside of Scandinavia (Gradus et al., 2010; Laursen, Munk-Olsen, Nordentoft, & Mortensen, 2007; Qin, Agerbo, & Mortensen, 2003; Qin & Nordentoft, 2005; Tidemalm, Elofsson, Stefansson, Waern, & Runeson, 2005) that examined mental disorders and suicide using a national registry of patients.

References

- Beautrais AL, Joyce PR, Mulder RT, Fergusson DM, Deavoll BJ, & Nightingale SK (1996). Prevalence and comorbidity of mental disorders in persons making serious suicide attempts: A case-control study. The American Journal of Psychiatry, 153, 1009–1014. [PubMed: 8678168]
- Brezo J, Paris J, & Turecki G (2006). Personality traits as correlates of suicidal ideation, suicide attempts, and suicide completion: A systematic review. Acta Psychiatrica Scandinavica, 113, 180– 206. doi:10.1111/j.1600-0447.2005.00702.x [PubMed: 16466403]
- Cavanagh JTO, Carson AJ, Sharpe M, & Lawrie SM (2003). Psychological autopsy studies of suicide: A systematic review. Psychological Medicine, 33, 395–405. doi:10.1017/S0033291702006943 [PubMed: 12701661]
- Centers for Disease Control and Prevention. (2011). Leading causes of death in the U. S., 2007. Retrieved from http://www.cdc.gov/nchs/fastats/lcod.htm/
- Cheng ATA, Chen THH, Chen CC, & Jenkins R (2000). Psychosocial and psychiatric risk factors for suicide: Case-control psychological autopsy study. The British Journal of Psychiatry, 177, 360–365. doi:10.1192/bjp.177.4.360 [PubMed: 11116779]
- Conner KR, Beautrais AL, Brent DA, Conwell Y, Phillips MR, & Schneider B (2011). The next generation of psychological autopsy studies. Part I. Interview content. Suicide & Life-Threatening Behavior, 41, 594–613. doi:10.1111/j.1943-278X.2011.00057.x;10.1111/j.1943-278X.2011.00057.x [PubMed: 22050639]
- Conner KR, Beautrais AL, & Conwell Y (2003). Moderators of the relationship between alcohol dependence and suicide and medically serious suicide attempts: Analyses of Canterbury Suicide Project data. Alcoholism: Clinical and Experimental Research, 27, 1156–1161. doi:10.1097/01.ALC.0000075820.65197.FD

- Cowper DC, Kubal JD, Maynard C, & Hynes DM (2002). A primer and comparative review of major US mortality databases. Annals of Epidemiology, 12, 462–468. doi:10.1016/S1047-2797(01)00285-X [PubMed: 12377423]
- Desai RA, Dausey DJ, & Rosenheck RA (2005). Mental health service delivery and suicide risk: The role of individual patient and facility factors. The American Journal of Psychiatry, 162, 311–318. doi:10.1176/appi.ajp.162.2.311 [PubMed: 15677596]
- Flensborg-Madsen T, Knop J, Mortensen EL, Becker U, Sher L, & Gronbaek M (2009). Alcohol use disorders increase the risk of completed suicide–irrespective of other psychiatric disorders. A longitudinal cohort study. Psychiatry Research, 167, 123–130. doi:10.1016/j.psychres.2008.01.008 [PubMed: 19359047]
- Gradus JL, Qin P, Lincoln AK, Miller M, Lawler E, Sorensen HT, & Lash TL (2010). Posttraumatic stress disorder and completed suicide. American Journal of Epidemiology, 171, 721–727. doi:10.1093/aje/kwp456 [PubMed: 20160171]
- Greenland S, Lash TL, & Rothman KJ (2008). Concepts of interaction. In Rothman KJ, Greenland S, & Lash TL (Eds.), Modern Epidemiology (3rd ed., pp. 71–86). Philadelphia, PA: Lippincott, Williams, & Wilkins.
- Hawton K, Simkin S, Rue J, Haw C, Barbour F, Clements A, ... Deeks J (2002). Suicide in female nurses in England and Wales. Psychological Medicine, 32, 239–250. doi:10.1017/ S0033291701005165 [PubMed: 11866319]
- Ilgen MA, Bohnert AS, Ignacio RV, McCarthy JF, Valenstein MM, Kim HM, & Blow FC (2010). Psychiatric diagnoses and risk of suicide in Veterans. Archives of General Psychiatry, 67, 1152– 1158. doi:10.1001archgenpsychiatry.2010.129 [PubMed: 21041616]
- Ilgen MA, Jain A, Lucas E, & Moos RH (2007). Substance use-disorder treatment and a decline in attempted suicide during and after treatment. Journal of Studies on Alcohol and Drugs, 68, 503–509. [PubMed: 17568953]

Joshua Omvig Veterans Suicide Prevention Act, Pub. L. No. 110-110 (2007).

- Kendler KS, Aggen SH, Knudsen GP, Roysamb E, Neale MC, & Reichborn-Kjennerud T (2011). The structure of genetic and environmental risk factors for syndromal and subsyndromal common DSM-IV Axis I and all Axis II disorders. The American Journal of Psychiatry, 168, 29–39. doi:10.1176/appi.ajp.2010.10030340 [PubMed: 20952461]
- Kim C, Lesage A, Seguin M, Chawky N, Vanier C, Lipp O, & Turecki G (2003). Patterns of co-morbidity in male suicide completers. Psychological Medicine, 33, 1299–1309. doi:10.1017/ S0033291703008146 [PubMed: 14580083]
- Kulka RA, Schlenger WA, Fairbanks JA, Hough RL, Jordan BK, Marmar CR, & Cranston AS (1990). Trauma and the Vietnam War generation: Report of findings from the National Vietnam Veterans Readjustment Study. New York, NY: Brunner/Mazel.
- Laursen TM, Munk-Olsen T, Nordentoft M, & Mortensen PB (2007). Increased mortality among patients admitted with major psychiatric disorders: A register-based study comparing mortality in unipolar depressive disorder, bipolar affective disorder, schizoaffective disorder, and schizophrenia. Journal of Clinical Psychiatry, 68, 899–907. doi:10.4088/JCP.v68n0612
- Lesage AD, Boyer R, Grunberg F, Vanier C, Morisette R, Ménard-Buteau C, & Loyer M (1994). Suicide and mental disorders: A case-control study of young men. The American Journal of Psychiatry, 151, 1063–1068. [PubMed: 7503818]
- McCarthy JF, Valenstein M, Kim HM, Ilgen M, Zivin K, & Blow F (2009). Suicide mortality among patients receiving care in the Veterans Health Administration health system. American Journal of Epidemiology, 169, 1033–1038. doi:10.1093/aje/kwp010 [PubMed: 19251753]
- Nock MK, Borges G, Bromet EJ, Cha CB, Kessler RC, & Lee S (2008). Suicide and suicidal behavior. Epidemiologic Reviews, 30, 133–154. doi:10.1093/epirev/mxn002 [PubMed: 18653727]
- Nock MK, Hwang I, Sampson N, Kessler RC, Angermeyer M, Beautrais A, ... Williams DR (2009). Cross-national analysis of the associations among mental disorders and suicidal behavior: Findings from the WHO world mental health surveys. PLoS Medicine, 6, e1000123. doi:10.1371/ journal.pmed.1000123 [PubMed: 19668361]
- Preuss UW, Schuckit MA, Smith TL, Danko GP, Buckman K, Bucholz KK, ... Reich T (2002). Comparison of 3190 alcohol-dependent individuals with and without

suicide attempts. Alcoholism: Clinical and Experimental Research, 26,471–477. doi:10.1111/j.1530-0277.2002.tb02563.x

- Qin P, Agerbo E, & Mortensen PB (2003). Suicide risk in relation to socioeconomic, demographic, psychiatric, and familial factors: A national register-based study of all suicides in Denmark, 1981–1997. The American Journal of Psychiatry, 160, 765–772. doi:10.1176/appi.ajp.160.4.765 [PubMed: 12668367]
- Qin P, & Nordentoft M (2005). Suicide risk in relation to psychiatric hospitalization: Evidence based on longitudinal registers. Archives of General Psychiatry, 62, 427–432. doi:10.1001/ archpsyc.62.4.427 [PubMed: 15809410]
- Rzhetsky A, Wajngurt D, Park N, & Zheng T (2007). Probing genetic overlap among complex human phenotypes. Proceedings of the National Academy of Sciences, 104, 11694–11699. doi:10.1073/ pnas.0704820104
- Sohn MW, Arnold N, Maynard C, & Hynes DM (2006). Accuracy and completeness of mortality data in the Department of Veterans Affairs. Population and Health Metrics, 4, 2. doi:10.1186/1478-7954-4-2
- Tanielian T, & Jaycox J (Eds.). (2008). Invisible wounds of war: Psychological and cognitive injuries, their consequences, and services to assist recovery. Santa Monica, CA: Rand Corporation.
- Tidemalm D, Elofsson S, Stefansson CG, Waern M, & Runeson B (2005). Predictors of suicide in a community-based cohort of individuals with severe mental disorder. Social Psychiatry and Psychiatric Epidemiology, 40, 595–600. doi:10.1007/s00127-005-0941-y [PubMed: 16091857]
- Valenstein M, Kim HM, Eisenberg D, Zivin K, McCarthy JF, Piette JD, ...Blow FC (2009). Service implications of providing intensive monitoring during high-risk periods for suicide among VA patients with depression. Psychiatric Services, 60, 439 – 444. doi:10.1176/appi.ps.60.4.439 [PubMed: 19339317]
- Waern M, Runeson BS, Allebeck P, Beskow J, Rubenowitz E, Skoog I, & Wilhelmsson K (2002). Mental disorder in elderly suicides: A case-control study. The American Journal of Psychiatry, 159, 450–455. doi:10.1176/appi.ajp.159.3.450 [PubMed: 11870010]
- Wilks SS (1938). The large-sample distribution of the likelihood ratio for testing composite hypotheses. The Annals of Mathematical Statistics, 9, 60–62. doi:10.1214/aoms/1177732360
- World Health Organization. (1995). International classification of diseases, Ninth Revision, Clinical modification (ICD-9-CM). Los Angeles, CA: Practice Management Information Corporation and World Health Organization.
- World Health Organization. (2004). International statistical classification of diseases, 10th revision (ICD-10). Geneva, Switzerland: World Health Organization.
- Yoshimasu K, Kiyohara C, Miyashita K, & The Stress Research Group of the Japanese Society for Hygiene. (2008). Suicidal risk factors and completed suicide: Meta-analyses based on psychological autopsy studies. Environmental Health and Preventive Medicine, 13, 243–256. doi:10.1007/s12199-008-0037-x [PubMed: 19568911]
- Zhang Y, Conner KR, & Phillips MR (2012). Case-control study in china of risk factors for suicide in men with alcohol use disorders. Journal of Studies on Alcohol and Drugs, 73, 15–20. [PubMed: 22152657]
- Zivin K, Kim HM, McCarthy JF, Austin KL, Hoggart KJ, Walters H, & Valenstein M (2007). Suicide mortality among individuals receiving treatment for depression in the Veterans Affairs health system: Associations with patient and treatment setting characteristics. American Journal of Public Health, 97, 2193–2198. doi:10.2105/AJPH.2007.115477 [PubMed: 17971541]

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Descriptive Data on Mental Disorders and Two-Way Combinations of Mental Disorders Among Male Suicide Decedents in the Veterans Health Administration

Diagnosis	Nature of disorder or comorbidity ^a	Disorder itself n (%)	Comorbid substance <i>n</i> (%)	Comorbid depression n (%)	Comorbid bipolar <i>n</i> (%)	Comorbid anxiety <i>n</i> (%)	Comorbid schizophrenia <i>n</i> (%)
PTSD	Any	869 (11.7%)	419 (5.6%)	618 (8.3%)	189 (2.5%)	320 (4.3%)	155 (2.1%)
	Pure	117 (1.6%)	54 (0.7%)	123 (1.7%)	8 (0.1%)	26 (0.4%)	8 (0.1%)
Substance	Any	1,583 (21.3%)		977 (13.2%)	330 (4.4%)	462 (6.2%)	281 (3.8%)
	Pure	402 (5.4%)		282 (3.8%)	19 (0.3%)	43 (0.6%)	35 (0.5%)
Depression	Any	2,281 (30.7%)			482 (6.5%)	792 (10.7%)	399 (5.4%)
	Pure	562 (7.6%)			68 (0.9%)	210 (2.8%)	72 (1.0%)
Bipolar	Any	638 (8.6%)				230 (3.1%)	229 (3.1%)
	Pure	53 (0.7%)			Ι	3 (<0.1%)	31 (0.4%)
Anxiety	Any	1,080(14.5%)					186 (2.5%)
	Pure	168 (2.3%)			I	Ι	12 (0.2%)
Schizophrenia	Any	660 (8.9%)					
	Pure	129 (1.7%)					I

or a given diagnostic combination excluding those with other comorbidities, for example, 117 (1.6%) had been diagnosed with PTSD only, and 54 (0.7%) had been diagnosed with PTSD plus substance use 869 (11.7%) of 7,426 suicide decedents had been diagnosed with PTSD, and 419 (5.6%) had been diagnosed with PTSD plus substance use disorder; (b) "Pure" refers to only those with a given diagnosis ^aNature of disorder or comorbidity refers to two groups of male suicide decedents: (a) "Any" refers to all those with a given diagnosis or diagnostic combination irrespective of comorbidity, for example, disorder but no other mental disorders. Author Manuscript

Table 2

Results of Cox Proportional Hazards Models of Mental Disorders and Two-Way Combinations of Mental Disorders in Suicide Among Men Treated in the Veterans Health Administration

		Disorder itself	Comorbid substance	Comorbid depression	Comorbid bipolar	Comorbid anxiety	Comorbid substance Comorbid depression Comorbid bipolar Comorbid anxiety Comorbid schizophrenia
Diagnosis	Nature of disorder or comorbidity ^a	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
PTSD	Any	2.60 (2.39, 2.82)	3.81 (3.40, 4.27)	3.07 (2.79, 3.37)	4.52 (3.87, 5.29)	3.26 (2.91, 3.65)	3.42 (2.88, 4.05)
	Pure	1.61 (1.34, 1.93)	2.79 (2.06, 3.78)	2.03 (1.68, 2.44)	3.09 (1.36, 7.00)	1.69 (1.18, 2.42)	1.56 (0.82, 2.97)
Substance	Any	2.98 (2.76, 3.21)		4.27 (3.89, 4.68)	5.19 (4.57, 5.90)	4.82 (4.31, 5.39)	3.68 (3.20, 4.24)
	Pure	1.85 (1.67, 2.07)	I	3.84 (3.36, 4.39)	3.33 (2.03, 5.48)	3.00 (2.11, 4.27)	2.14 (1.56, 2.93)
Depression	Any	3.01 (2.84, 3.19)			4.85 (4.37, 5.37)	3.48 (3.20, 3.78)	3.82 (3.38, 4.32)
	Pure	2.41 (2.20, 2.64)	I	I	4.05 (3.17, 5.18)	2.39 (2.07, 2.76)	3.42 (2.69, 4.33)
Bipolar	Any	4.29 (3.91, 4.71)				5.20 (4.46, 6.07)	4.35 (3.76, 5.04)
	Pure	3.41 (2.57, 4.51)	Ι	I		1.34 (0.44, 4.11)	3.51 (2.48, 4.96)
Anxiety	Any	2.79 (2.57, 3.02)					3.77 (3.22, 4.40)
	Pure	1.58 (1.34, 1.86)					2.02 (1.13, 3.63)
Schizophrenia	Any	3.04 (2.77, 3.32)					
	Pure	2.24 (1.86, 2.69)	I	I			I

²Nature of disorder or comorbidity refers to two groups of male suicide decedents: (a) "Any" refers to all those with a given diagnosis or diagnostic combination irrespective of comorbidity, for example, the HR (95% CI) for PTSD = 2.60 (2.39, 2.82), and that for the combination of PTSD plus substance use disorder = 3.81 (3.40, 4.27); (b) "Pure" refers to only those with a given diagnosis or a given diagnostic combination excluding those with other mental disorders, for example, the HR (95% CI) for PTSD alone = 1.61 (1.34, 1.93), and that for the combination of PTSD plus substance use disorder but with no other mental disorders = 2.79 (2.06, 3.78).

Table 3

Descriptive Data and Cox Proportional Hazard Models of the Number of Mental Disorders in Suicide Among Men Treated in the Veterans Health Administration

No. mental disorders	n (%)	HR (95% CI)
0	3,970 (53.5%)	1.00 (ref)
1	1,431 (19.3%)	1.99 (1.87, 2.12)
2	994 (13.4%)	2.69 (2.51, 2.89)
3	589 (7.9%)	3.27 (2.98, 3.59)
4	313 (4.2%)	4.46 (3.88, 5.14)
5	101 (1.4%)	4.74 (3.87, 5.82)
6	28 (0.4%)	6.70 (4.49, 10.00)

Note. N(%) refers to the number and percent of all male suicide decedents in the database who had a given number of mental disorder diagnoses. HR (95% CI) results are based on a common reference group of individuals with no psychiatric diagnosis, adjusting for age. CI = confidence interval; HR = hazard ratio.