

# Post-traumatic stress disorder, drug dependence, and suicidality among male Vietnam veterans with a history of heavy drug use

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## Abstract

This study examines the roles of post-traumatic stress disorder (PTSD) and drug dependence in non-fatal suicidality, i.e., suicidal ideation and suicide attempt, among Vietnam veterans in their adult years. The sample includes male veterans deployed to Vietnam, including an oversample of those who tested positive for opiates at their return ( $n = 642$ ). PTSD, substance abuse, suicidality, and other psychopathology are analyzed using three waves of survey and military data covering the time period from early adolescence to middle adulthood. Measures include the onset and recency of each of the lifetime DSM-IV PTSD symptom criteria, and yearly symptom measures of DSM-IV dependence for alcohol and eight classes of psychoactive substances. Survival and hazard models are applied to assess the effects of drug dependence, PTSD, and other psychopathology on the duration of suicidality. Longitudinal models estimate the casual relationships among PTSD, drug dependence, and suicidality over a 25-year period. Results show evidence of strong continuity of PTSD, drug dependence, and suicidality over time. The causal role of drug dependence on PTSD and suicidality is limited to young adulthood. Evidence is stronger for self-medication in later adulthood. The results indicate that a life course perspective is needed for the combined treatment of PTSD and drug dependence for severely traumatized populations.

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## 1. Introduction

Suicide and suicidal behavior have become major public health issues in the United States (Department of Health and Human Services, 1999) and elsewhere (Leenaars et al., 2002). More attention has recently been given to the prevention of adolescent suicide (Gould et al., 2003; Novick et al., 2003) as well as to suicide in the elderly (Ron, 2002; Waern et al., 2003) than to suicide in mid-life. According to recent statistics from the Centers for Disease Control (2003), the suicide rate among the 40–60 age group in 2001 was 6.89 for females (per 100,000) and 23.14 for males, and the suicide rate for middle-aged men has remained stable over the past

three decades (Riggs et al., 1996). Compared to the suicide rate for males ages 40–60 in 2001, the younger males (ages 15–24) had a suicide rate of 16.63 while the elderly (ages 70+) had a rate of 35.29. These rates indicate that the suicide rate in middle-aged men has been actually higher than that of men in the younger age groups. A critical gap exists in knowledge about the epidemiology and prevention of suicide in middle-aged men, perhaps reflective of the reluctance of males in this age group to seek help (Moller-Leimkuhler, 2003).

Certain experiences put a definable group at increased risk for suicide. Although the estimates of suicide among Vietnam veterans vary widely among reports (Pollock et al., 1990), speculation has persisted about an increased risk of suicide among Vietnam veterans as compared to that of the general population of the same age group (Bullman and Kang, 1995), or to veterans as a whole (Baker, 1984). Our own investiga-

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tion of the suicidal risk of Vietnam veterans confirmed an increased risk of both suicide and suicide attempt among male Vietnam veterans compared to non-Vietnam veteran males in the same age group (Price et al., unpublished).

Building on earlier findings (Price et al., 1998), this paper examines why the risk of suicidality is higher among male Vietnam veterans by focusing on the role of trauma, subsequent post-traumatic stress disorder (PTSD), and substance abuse. Such an examination has a practical and clinical significance not only for the well-being of veterans but also for the family members and the healthcare system at large, because Vietnam veterans currently constitute 8.0% of the adult U.S. male population (U.S. Census Bureau, 2003) and about 23% of men in the age group of 40–60 years (Price et al., unpublished). Furthermore, the comorbidity of substance abuse and PTSD is well documented for veterans and other populations (Regier et al., 1990; McFall et al., 1992; Brown and Wolfe, 1994). The burden on the health care system is even larger when comorbid substance abuse exists (Virgo et al., 1999; Piette et al., 1997). At a time when citizens of many countries are living in fear of global terrorism, an understanding of the long-term consequences of PTSD on behavior, including suicidality, may help in educating others about the mental health consequences of war and global conflict.

### 1.1. Trauma, PTSD, and suicidal behavior

Different types of trauma result in the syndrome of PTSD. A substantial body of research supports evidence for the significant impact of family violence, sexual abuse, and physical abuse on adolescent suicide (Marttunen et al., 1994; Krupinski et al., 1998) and suicidal behavior (de Wilde et al., 2001; Wagner, 1997). For adult populations, however, the research on suicidal outcomes appears to be limited to extraordinary trauma such as rape and war trauma (Resick et al., 1988; Kilpatrick et al., 1985). An elevated risk for suicide and non-fatal suicidality among veterans is often attributed to PTSD (Kramer et al., 1994; Farberow et al., 1990) as well as to general psychiatric disorders (Fontana and Rosenheck, 1995), rather than to the exposure to trauma per se. Several reports indicate that survivor guilt (Hyer et al., 1990; Hendin and Hass, 1991), being an agent of killing (Fontana et al., 1992), and the intensity of an injury resulting from combat (Bullman and Kang, 1996) are the core reasons for suicidality among veterans with PTSD. These results also appear to be generalizable beyond the Vietnam veteran population. For example, the effect of trauma exposure for developing PTSD appears greatest among those who are already vulnerable, either by earlier environmental assault (Cordray et al., 1992), or by psychiatric (McFarlane, 1988) or biological predispositions (True et al., 1993). However, the severity and type of trauma exposure appear to have an independent effect on the probability for developing PTSD, the magnitude of the disorder's symptom expression (Goldberg et al., 1990; Snow et al., 1988), and also on the levels of associated outcomes such as suicidality (Kramer et al., 1994; Farberow et al., 1990).

### 1.2. PTSD and substance abuse

A significant proportion of those with PTSD have comorbid substance abuse problems (Regier et al., 1990; McFall et al., 1992; Brown and Wolfe, 1994). Other related risk and protective factors associated with PTSD are similar to those factors for suicide and non-fatal suicidality. PTSD has been found to be associated not only with substance abuse (both alcohol and illicit drugs) but also with family history (Davidson et al., 1985), social support, and social networks (Boscarino, 1995; Card, 1987). The literature on PTSD indicates several underlying mechanisms governing the relationship between PTSD and substance use. First, predisposing psychopathology that leads to high-risk behaviors, such as early conduct problems and adult antisocial behaviors, appears to put some individuals at risk for exposure to stressful or traumatic events (Breslau and Davis, 1991; Helzer et al., 1987). A second hypothesis also argues for exposure, but the exposure is considered to be a direct consequence of substance abuse (Cottler et al., 1992). A third perspective is that psychoactive substances may be used by those with PTSD symptoms as self-medication to mask their symptoms (Lacoursie et al., 1980). Since both trauma and substance use could conceivably alter neurological mechanisms, a variety of subtle neurological deficits may be a link for the high comorbid rate between PTSD and substance abuse (van der Kolk, 1993; Folli et al., 1992; Friedman and Yehuda, 1995).

### 1.3. PTSD, substance abuse, and suicidality

In both the PTSD and drug abuse literature, particularly the literature involving opiate addiction, involvement of the hypothalamic–pituitary–adrenal (HPA) axis has repeatedly been demonstrated or suggested (Yehuda, 1997; van der Kolk, 1993). Although not as well replicated as the finding of lower levels of 5-hydroxyindoleacetic acid (5-HIAA) in the cerebrospinal fluid (CSF) (Winchel et al., 1990), the HPA axis hypothesis for suicidality is further supported by the fact that the stress-induced elevation of cortisol and corticotropin-releasing hormone (CRH), which causes the over-reactivity of the HPA axis, paradoxically reduces the basal level of CRH concentrations over time (Brunner et al., 2001). A common biological mechanism, such as decreased basal CRH level as a consequence of prolonged over-sensitization of the HPA axis (which may itself be a consequence of gene expression (Arango et al., 2003)) may be involved in the association among PTSD, drug dependence, and suicidality.

Alternatively, an argument can be made that the impact of psychiatric comorbidity adds up over time to put those with comorbid conditions on a socially disadvantageous position beyond reasonable hope. The cumulative effect, regardless of specific psychiatric comorbidity, is then responded to by suicidality. This idea is consistent with that of “cumulative disadvantage” which is used to explain a wide range of inequalities such as gender and racial/ethnic inequality (O’Rand, 1996). The concept of “cumulative disadvantage” is therefore use-

ful in addressing suicidality as a response to the cumulative impact of psychiatric comorbidity (Hertzman, 1999).

Unfortunately, little systematic longitudinal data exist that document the time sequence and causal role of PTSD and substance abuse affecting the outcome of suicidality over time, even though much knowledge exists about the associational nature of PTSD with suicidality on one hand, and substance abuse with PTSD on the other. Our 25-year follow-up of a Vietnam Era cohort (Washington University Vietnam Era Study Phase III (VES-III)), provides an opportunity to examine the nature of associations among PTSD, drug dependence, and suicidality over time with relative economy, owing to a concentration of veterans with a history of heavy combat experience and substance abuse. We attempt first to describe the association of PTSD and drug dependence with non-fatal suicidality, then model over-time causal relationships among PTSD, drug dependence, and suicidality.

## 2. Methods

### 2.1. Sample

The VES cohort of 1227 men originated from surveys in 1972 and 1974, which were initiated by the White House Special Action Office for Drug Abuse Prevention (Robins, 1974). A total of 943 veterans was tagged to the database in 1971. About half of the veteran sample were randomly drawn from a list of Army servicemen (pay grades E1–E9) who had positive urine tests for opiates, amphetamines, or barbiturates at the time of their departure from Vietnam in September 1971. This sampling frame represents the drug-positive population, which is an estimated 10.5% of the 13,760 Army enlisted returnees in September 1971. The other half, the “general” sample of the 1972 survey, was randomly drawn from the total population list of Army enlisted returnees leaving Vietnam in September 1971. For simplicity, 39 drug-positive members who also appeared in the “general” sample (Robins, 1974) are included here only in the drug-positive sample. Thus, drug-positive (D+) veterans ( $n = 512$ ) and drug-negative (D–) veterans ( $n = 431$ ) are mutually exclusive. For the 1974 survey, nonveteran controls ( $n = 284$ ) were recruited from Selective Service registrations and individually matched to those in the “general” sample (Robins and Helzer, 1975). The response rates for the two follow-ups reflected design attrition, deaths, failure to locate, and interview refusals. For VES-III, more than 93% of the surviving members ( $n = 1024$ ) were located.

By the time of the 1996–1997 survey (VES-III), 10.5% ( $n = 129$ ) of the entire cohort was lost through death: 17.4% of drug-positives, 7.4% of drug-negatives and 2.8% of the nonveterans (Price et al., 2001a). The urine drug status at departure was an excellent discriminator for mortality and morbidity in part because this one-shot test was a very good indication of the inability of the narcotic-using servicemen to abstain from use even for several days. Nine death certificates confirmed suicide and all were from the veteran samples.

Since the number of suicides was small, only a descriptive analysis is provided.

The fieldwork was discontinued after 841 had been interviewed (82.1% interview rate), exceeding the recruitment goal. For this paper, nonveterans are excluded from the analysis because trauma experiences were different from veterans for the obvious reason that they were not deployed to Vietnam (Price et al., 2001b). The unweighted lifetime non-fatal suicidality rate is 8.6% among nonveterans compared to 19.3% among veterans. Separate analyses only for nonveterans were judged unfruitful given the sample size ( $n = 198$ ). The main analyses thus included 641 veterans.

### 2.2. Measures

For each type of analysis completed, the Appendix table lists the measures, variable definitions, timing, and how the variables were used. For the period prior to 1972, available predictive measures varied according to respondents' inclusion in the 1972 and 1974 surveys (details of the data structure and time periods of prior surveys are described elsewhere (Price et al., 2001a). For the period covering 25 years since 1972, we retrospectively obtained measures from the 1996–1997 survey with the aid of a detailed life history chart (Lyketsos et al., 1994). Measures obtained from the latter period constitute most of the measures used for this study.

#### 2.2.1. Suicide and non-fatal suicidality

Death certificates were used to identify those who committed suicide. The external causes of death (E codes) qualifying for suicide (World Health Organization, 1977) were coded by an expert cause-of-death coder. Consistent with established mortality statistics rubrics, one underlying cause was determined for each veteran's death. The measures of non-fatal suicidality were obtained from responses to a question regarding “ever having frequent thoughts of committing suicide,” and additional questions regarding “making a suicide plan” or “attempted suicide.” The onset and recency of non-fatal suicidality ascertained in the 1996–1997 survey for the surviving respondents were used to create lifetime and duration measures of non-fatal suicidality. Yearly point estimates of suicidality covered the period from 1971 to 1996.

#### 2.2.2. Trauma and PTSD

During the 1996–1997 follow-up survey, respondents were asked to recall major traumas (accidents, fires, assaults, witnessing acts of violence, life threatening situations, deaths of loved one, or natural disasters). After completing the list, they were asked to choose the most traumatic event for the period before 1972 and for the period after 1972. DSM-IV PTSD symptoms were obtained for each of the two most traumatic events. We ascertained the time from the trauma to onset of each symptom cluster, as well as the duration since the onset. The respondent was considered positive for PTSD in year  $i$  if he was positive for each symptom cluster in year

*i*, and he met the lifetime DSM-IV criteria. The final yearly PTSD diagnosis measures combined the diagnoses for the pre-1972 and post-1972 most traumatic events.

### 2.2.3. *Drug use and dependence*

The 1972 survey questions were used to create measures for years prior to 1972. The resulting measures included self-reported dependence on “uppers,” “downers,” and “narcotics” for the period before deployment to Vietnam, and self-reported dependence on narcotics for the period of deployment in Vietnam. The 1996–1997 survey questions were used to obtain the measures of drug use and problems for the time period after 1972. Respondents who reported illicit drug use five times or more since 1972 were asked to verify the years in which they had each DSM-IV dependence symptom for a specific class of drugs (sedatives, stimulants, marijuana, cocaine, opiates, PCP, hallucinogens, and inhalants). We obtained the point estimate of the DSM-IV drug dependence for each year from 1972 based on the symptoms endorsed each year. Each respondent thus was assigned a yearly DSM-IV diagnosis of drug dependence between 1972 and 1996.

### 2.2.4. *Covariates and exogenous measures*

The measures that were not central to the relationships among PTSD, drug dependence, and suicidality were considered “covariates” or “exogenous” (outside of the over-time relationship consideration). From the 1972 survey, such exogenous measures included race (African-American versus others), age, enlistment status (volunteered versus drafted), urine drug status at discharge (D+ versus D–), a military aptitude test score, and a measure of childhood antisocial personality. Education status was taken from the 1996–1997 survey, because many went to school after their service in Vietnam. Yearly measures were obtained from the 1996–1997 survey in a similar fashion as yearly PTSD and drug dependence measures. We obtained yearly diagnostic measures of alcohol dependence if respondents reported drinking more than seven drinks in one day, drinking at least one drink everyday for two weeks, or drinking six drinks a day at least once a week for several weeks. They were asked to verify the years in which they had each DSM-IV alcohol dependence symptom. Time-dependent covariates of major depression and adult antisocial personality since 1972 were computed from recency and onset data reported for each DSM-IV symptom. The questions on suicidality were removed from the computation of the DSM diagnostic measure of depression.

### 2.2.5. *Measures for analyses over four discrete time periods*

To assess the causal roles of PTSD and drug dependence in suicidality over time, summary measures were constructed for four time periods: pre-Vietnam (before 1971), in-Vietnam (around 1971), 10 years after return (1972–1981), and the subsequent 15 years (1982–1996). The in-Vietnam period covers the duration of deployment to Vietnam, which was about one year on average in this sample. Different durations

chosen for each time period reflect behavior influx in the in-Vietnam period and gradually increasing stability over the subsequent 25 years. We assessed PTSD and suicidality retrospectively from the 1996–1997 survey. For the pre-Vietnam and in-Vietnam periods, the measures were the presence or absence of PTSD or suicidality anytime prior to the departure to Vietnam and during the deployment, respectively. For the “1972–1981” and “1982–1996” time periods, the measures were the total number of years that the respondent met a PTSD diagnosis and the total number of years with suicidality, respectively. The summary measures of alcohol dependence and major depression were obtained in a similar fashion.

The drug dependence measure for the pre-Vietnam period was a 4-point scale (0–3) based on self-reported dependence on narcotics, uppers, and downers. For the in-Vietnam period, the measure was a 2-point scale: one point for a self report of narcotic dependence while in Vietnam and a point for being drug-positive. This measure was considered optimal because self-reported dependence on uppers and downers was unavailable for the in-Vietnam time period and the drug-positive servicemen were only a portion of those who have reported narcotic dependence while in Vietnam. For the 1972–1981 and 1982–1996 time periods, each measure in the time period represented a sum of the number of years of the number of DSM-IV drug dependence diagnoses over the eight drug categories for each year.

## 2.3. *Analyses*

The standardized mortality ratios (SMRs), the ratios of observed to expected deaths of the population adjusted for race and age (Lai et al., 1996), were estimated for each specific cause of death (Monson, 1974). We used descriptive analyses to show the patterns of associations among non-fatal suicidality, demographic measures, PTSD, drug dependence, and other psychopathology (alcohol dependence, depression, and adult antisocial personality). Prevalence rate comparisons in bivariate analyses are adjusted for oversampling of drug-positive veterans. Annual prevalence rates of PTSD, drug dependence, and suicidality are presented using the yearly measures obtained from the 1996–1997 survey. But the estimate of drug dependence in 1971 was obtained from self reports on narcotic dependence for the in-Vietnam period. We present the point estimates without weights for yearly measures because subsequent multivariate analyses were carried out without weight adjustment. This was justifiable since our main interest in this set of analyses was to determine the causal roles of PTSD and drug dependence in suicidality, and not to arrive at generalizable estimates of prevalence rates (Robins and Price, 1991).

We obtained Kaplan-Meier survival estimates for the sub-sample of respondents who reported suicidality in the 1996–1997 survey to assess the effect of PTSD and drug dependence on the duration of suicidality. The observation was considered censored if the last year of suicidality occurred in the year of the interview. The respondent was coded positive

for PTSD if he met both the lifetime DSM-IV PTSD diagnosis and all three symptom criteria simultaneously for at least one year during the period of suicidality. The respondent was coded positive for drug dependence, if he met the DSM-IV drug dependence diagnosis for any of the eight classes of illicit drugs for any year after 1972 during the period of suicidality, or if he had suicidality prior to 1972 that overlapped with a pre-Vietnam or in-Vietnam self report on dependence on narcotics, uppers or downers. Both the log-rank test and the Wilcoxon test are reported to determine whether PTSD or drug dependence significantly prolonged suicidality.

We used the yearly measures in time-dependent Cox regression analyses to assess whether alcohol dependence, major depression, and antisocial personality were confounding factors for the association of PTSD or drug dependence with the duration of suicidality. Cox regression could produce biased results if an effect of a covariate varies systematically over time. Therefore, Cox regression analyses were rerun five times including an interaction term between a covariate and the log of time. An interaction term between each of the major predictive variables (alcohol dependence, major depression, adult antisocial personality, PTSD, and drug dependence) was entered one at a time so as to avoid producing overly complex models. Standard errors for hazard ratio parameters were adjusted by a robust sandwich estimator (Huber, 1967; White, 1980) to take into account repeated observations over time per case. When the clustering structure does not involve a complex survey stratification scheme, the sandwich estimator provides estimates slightly more conservative than those estimated by the Taylor series method (Cohen, 1997).

Because Cox regression analyses do not provide causal inferences about the relationships among PTSD, drug dependence, and suicidality, we carried out a series of path analyses using the summary measures for the four time periods: pre-Vietnam (before 1971), in-Vietnam (around 1971), the following 10 years (1972–1981), and the most recent 15 years (1982–1996). The main measures of interest (i.e., endogenous variables) are metric summary measures of PTSD, drug dependence, and suicidality for each time period except for the measures for the in-Vietnam period (see Section 2.2.5). These analyses controlled for demographic characteristics and the childhood antisocial scale, as well as for PTSD, drug dependence, and non-fatal suicidality for the pre-Vietnam period.

We used path analyses to provide a relatively simple interpretation of causality among PTSD, drug dependence, and suicidality. Four time periods were constructed:  $T_0$ , pre-Vietnam (before 1971);  $T_1$ , in-Vietnam (1971);  $T_2$ , 1972–1981; and  $T_3$ , 1982–1996. Effects of background measures (age, race, enlistment, high school education, and aptitude test in military), and measures of PTSD, drug dependence, and suicidality in the pre-Vietnam period ( $T_0$ ) were simultaneously estimated as exogenous measures. For the relationship over time from  $T_1$  to  $T_3$ , models initially included only two constructs: drug dependence and suicidality, and PTSD and suicidality. Based on the results of the best two-

construct models, we built three-construct models including PTSD, drug dependence, and suicidality over the three time periods, plus background and pre-Vietnam measures. For simplification, the effects of exogenous ( $T_0$ ) measures were estimated on the in-Vietnam ( $T_1$ ) measures of PTSD, drug dependence, and suicidality. In turn, the effects of PTSD, drug dependence and suicidality in one time period were estimated only on the measures of the next time period ( $T_1$ – $T_2$ ,  $T_2$ – $T_3$ ) or within the same time period. Coefficients were estimated using a generalized least square (GLS) estimator, which corrects for unequal variances of error terms and adjusts for auto-correlations of error terms over time (Hanushek and Jackson, 1977).

### 3. Results

#### 3.1. Associations of demographics and other psychopathology with PTSD, drug dependence, and suicidality

Respondents were in their early 20's at the time of their return from Vietnam. They reached their middle to late 40's at the time of their VES-III surveys in 1996–1997. Nine veterans committed suicide between 1971 and 1996 (Table 1, far right column). All but one of the suicides were Caucasian and were those who enlisted voluntarily. The standard mortality ratios (SMRs) for the most common causes of death among drug-negative veterans fell within the ranges expected for a general population of middle-aged men (not shown). However, suicide was the only cause of death for which the SMR among drug-negative veterans was higher than for the drug-positive veterans (2.0 versus 1.5, respectively).

Of the 641 veterans interviewed (Table 1, the middle two columns), 15.7% (weighted) reported suicidality (frequent thoughts of suicide, plans of suicide, or suicide attempts) sometime in their lives. In our sample, African-American veterans were more likely than Caucasians to report suicidality (21.7% versus 13.8%, respectively). Those who had enlisted voluntarily were more likely than draftees to report suicidality (23.7% versus 6.9%, respectively), as were those with drug-positive urinalysis status in 1971 as compared to drug-negative veterans (23.6% versus 15.1%, respectively).

Of the interviewed veterans, 20.7% met the lifetime diagnosis of DSM-IV PTSD while 17.2% met the drug dependence diagnosis. Demographic and sampling characteristics, alcohol dependence, major depression, and antisocial personality were associated with PTSD and drug dependence (Table 2). Being African-American, voluntarily enlisted, and drug-positive at the time of departure from Vietnam, as well as meeting the DSM-IV criteria for alcohol dependence since 1972, lifetime major depression, and adult antisocial personality since 1972, were all significantly associated with having a DSM-IV drug dependence since 1972. Most of these measures were also significant with the lifetime DSM-IV criteria

Table 1  
Non-fatal suicidality and completed suicide by demographic characteristics<sup>a</sup>

	Interviewed in 1996–1997 ( <i>n</i> = 641)		Completed suicide (1971–1996) ( <i>n</i> = 9)	
	No lifetime non-fatal suicidality ( <i>n</i> = 517)	Non-fatal suicidality reported <sup>b</sup> ( <i>n</i> = 124)		
<b>Race</b>				
Caucasian	392	(86.3)	87	(13.8)
African-American	98	(78.4)	26	(21.7)
Other	27	(70.1)	11	(29.9)
<b>Enlistment<sup>c</sup></b>				
Draftee	218	(93.1)	23	(6.9)
Volunteered	288	(76.3)	97	(23.7)
<b>Drug urinalysis status in 1971<sup>d</sup></b>				
Drug-negative	271	(85.0)	48	(15.1)
Drug-positive	246	(76.4)	76	(23.6)

<sup>a</sup> Percentages are weighted to adjust for oversampling of drug-positive veterans.

<sup>b</sup> Includes frequent thoughts of committing suicide, planning suicide, or suicide attempt; lifetime assessment.

<sup>c</sup> Excluding missing cases.

<sup>d</sup> Sampling status based on urinalysis testing at the time of departure from Vietnam.

for PTSD. Only the associations of race and enlistment status with PTSD were insignificant. Lifetime PTSD and drug dependence since 1972 were also associated significantly with each other.

### 3.2. Effects of PTSD and drug dependence on the duration of non-fatal suicidality

The annual prevalence rates (unweighted) of PTSD, drug dependence, and suicidality show differences from 1971 to 1996 (Fig. 1). PTSD was the most stable over the 25-year-period, hovering around 12–14% each year. Drug dependence was the highest at 45.1% in 1971 when opiates were abundant in Vietnam. The rate decreased from 16.4% in 1972 to 5.9% by 1996. The rate of suicidality, on the other hand, increased monotonically from 1971 until around 1985 and continued to hover between 7 and 8% (the dip in 1996 was due to truncated durations for those interviewed in 1996).

In Fig. 2A and B, survival curves for those who reported suicidality in their lives are shown separately depending on the status of PTSD and drug dependence. Both PTSD and drug dependence prolonged the duration of non-fatal suicidality. Remission from suicidality occurred more rapidly for respondents without concurrent PTSD ( $P < .01$  for both the log-rank test and Wilcoxon test for the differences of two strata). Remission from suicidality occurred more slowly among those with concurrent drug dependence than those without. However, the two groups began to reach equal remission rates after 20 years (by the early 1990's). This is attested to by a significant Wilcoxon test ( $P = .04$ ), which tends to be more sensitive than the log-rank test to differences in remission rates in the earlier years; the log-rank test was non-significant ( $P = .17$ ), since it assumes an exponential distribution. The differences in the stratified survival curves suggest that concurrent PTSD and drug dependence prolonged the duration of suicidality. The role of PTSD on the duration of suicidal-

Table 2  
Associations of demographic characteristics and selected psychopathology with PTSD and drug dependence<sup>a</sup>

Covariate categories	% DSM-IV PTSD, lifetime <sup>b</sup>	% DSM-IV drug dependence since 1972 <sup>b</sup>
African-American	26.8	30.5**
Volunteered for service	23.5	21.2**
Drug-positive for urinalysis status	33.5*	44.7**
Positive for DSM-IV alcohol dependence since 1972 <sup>b</sup>	36.0**	39.9**
Positive for DSM-IV depression, lifetime <sup>b,c</sup>	71.2**	35.7**
Positive for DSM-IV adult antisocial personality since 1972 <sup>b</sup>	35.9**	44.4**
Positive for DSM-IV PTSD, lifetime <sup>b</sup>	–	32.1**
Drug dependence since 1972 <sup>b</sup>	38.8**	–

<sup>a</sup> Percentages shown are for the category listed and are weighted to adjust for the oversampling of drug-positive veterans. To obtain a *P*-value for the prevalence differences between the two categories of a covariate, a normalized weighted logistic regression was used which adjusts for the oversampling of drug-positive veterans. Bivariate logistic regression was run separately for each covariate with the outcome being lifetime PTSD diagnosis or lifetime alcohol dependence. \* $.01 < P < .05$ , \*\* $P < .01$ .

<sup>b</sup> The measures were obtained from the 1996–1997 survey and did not incorporate information from earlier surveys to maintain consistencies across covariates.

<sup>c</sup> Removed the question of suicidality from computation of the DSM-IV diagnostic variables.

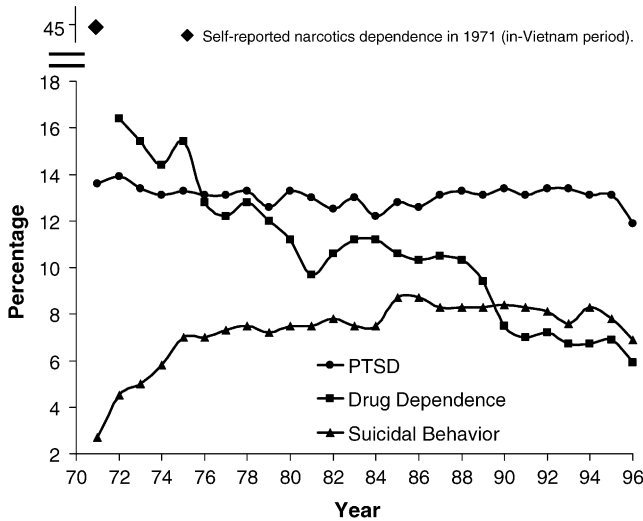


Fig. 1. Percentage of sample with PTSD, drug dependence, and suicidal ideation from 1971 to 1996.

ity appears fairly substantial except for the first few years; the role of concurrent drug dependence appears to diminish by the time these men reached their early to middle 40's.

Table 3 shows the results of the time-dependent Cox regression analysis applied to 25 years of information over all veterans interviewed in the 1996–1997 survey. The effects of PTSD and drug dependence are examined controlling for alcohol dependence, major depression, adult antisocial personality, and demographic characteristics (age, race, enlistment status, and education). Suicidality was excluded from the algorithm for the DSM-IV diagnosis of major depression. As expected, the hazard ratio for major depression was the largest at 3.21, but the hazard ratio for drug dependence was the next largest, 2.06. Adult antisocial personality had an effect that is somewhat weaker than that of drug dependence (hazard ratio = 1.88). Although a somewhat conservative ro-

Table 3  
Effects of PTSD, drug dependence, and other psychopathology on non-fatal suicidality over a 25-year period since 1972 ( $n = 637$ )<sup>a</sup>

	Hazard ratio	P	Risk limits
Alcohol dependence	1.18	.343	.84 – 1.68
Major depression <sup>b</sup>	3.21	<.001	1.93 – 5.34
Adult antisocial personality	1.88	.002	1.25 – 2.81
PTSD	1.51	.339	0.65 – 3.48
Drug dependence	2.06	.002	1.31 – 3.24
PTSD × log(time) <sup>c</sup>	1.31	.049	1.00 – 1.70

<sup>a</sup> Results of time-dependent Cox regression allowing recurrence of events over time. The person-year sample size is 15,925 for the period from 1972 to 1996. Excludes cases without timing information on non-fatal suicidality. The measures were obtained from the 1996–1997 survey and did not incorporate information from earlier surveys to maintain consistencies of measures across covariates. For depression and PTSD, information prior to 1972 and after 1996 was excluded from the analyses. The hazard ratios were adjusted for effects of demographic measures (as fixed variables) including age, race, enlistment status, and education. Variances were adjusted for repeated observations over time using a robust sandwich estimator.

<sup>b</sup> Removed the question of suicidality from the computation of the DSM-IV diagnostic variables.

<sup>c</sup> The PTSD × log(time) interaction term was included because the hazard ratio associated with PTSD on suicidal ideation was not constant over time. The hazard ratio associated with alcohol dependence, major depression, adult antisocial personality, and drug dependence did not vary over time (results not shown).

bust estimator was applied to adjust standard errors, the hazard ratio was significant for drug dependence ( $P = .002$ ). Each log(time) interaction term involving alcohol dependence, depression, adult antisocial personality, or drug dependence was not significant, and its corresponding hazard ratio was close to one (0.94–1.16), indicating that the major predictive variables were not unduly influenced by the timing in which they occurred. The hazard ratio for PTSD was non-significant when an interaction term PTSD × log(time) was simultaneously entered, but the latter was significant (hazard ratio = 1.31,  $P = .05$ ). Further analyses showed that the PTSD hazard ratio increased from 1.51 to 3.56 over 25 years. Yearly interaction

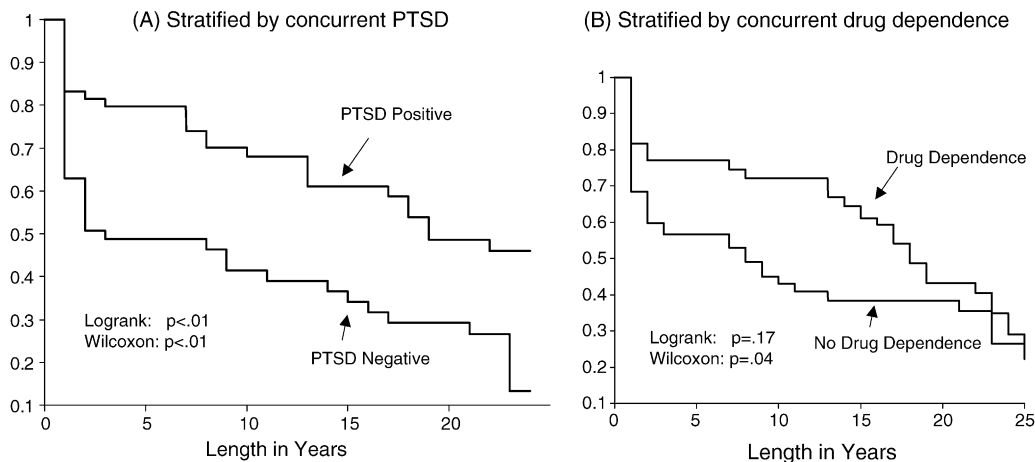


Fig. 2. Length of lifetime suicidal ideation stratified by concurrent PTSD or drug dependence ( $n = 120$ ). Subjects with missing timing information are excluded from these analyses. Concurrent PTSD and drug dependence is defined as meeting DSM-IV diagnostic criteria during the time period that suicidal ideation lasted.

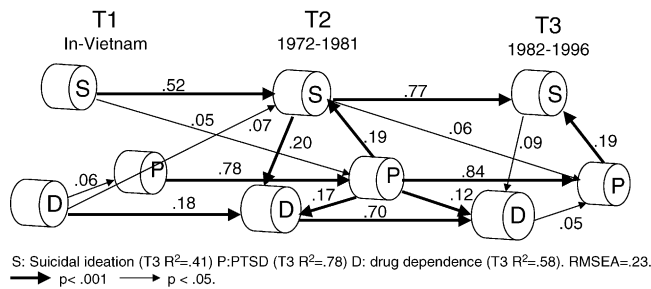


Fig. 3. Path analysis for suicidal ideation, PTSD, and drug dependence (only endogenous variables shown).

effects indicate that PTSD became significant around 1974 when the time dimension was simultaneously taken into account. Alcohol dependence, when other measures were simultaneously controlled for, was not a significant covariate of suicidality for this sample. The results affirm that the large differences by PTSD and drug dependence strata in the survival curves shown in Fig. 2 are unlikely to be reduced to effects by other psychiatric measures.

### 3.3. Causal roles of PTSD and drug dependence in non-fatal suicidality over time

Final path models included only those which were significant at  $P < .05$ . Background measures had significant effects on the in-Vietnam ( $T_1$ ) drug dependence ( $p = -.24$  for each year increase in age,  $p = .21$  for being an African-American, and  $p = .21$  for being a volunteer enlistee). Their effects on  $T_1$  PTSD and suicidality were non-significant. Childhood antisocial personality had effects on both  $T_1$  PTSD ( $p = .19$ ) and  $T_1$  drug dependence ( $p = .22$ ) (data not shown).

Final path analysis results for endogenous relationships ( $T_1$  to  $T_2$  to  $T_3$ ) are diagrammed in Fig. 3. The strengths of the path coefficients ( $p$ 's) are represented by thickness of the arrows. The values of the path coefficients are shown along the arrows. Not surprisingly, each condition was very stable over time. From the pre-Vietnam period ( $T_0$ ) to in-Vietnam ( $T_1$ ) and subsequent 10 ( $T_2$ ) and 15 years ( $T_3$ ), path coefficients for PTSD, drug dependence, and suicidality were all substantial. The magnitude of coefficients increased over time. For suicidality,  $p = .34$  from pre-Vietnam ( $T_0$ ) to in-Vietnam ( $T_1$ ) period,  $p = .52$  from the in-Vietnam ( $T_1$ ) to the 1972–1981 ( $T_2$ ) period, and  $p = .77$  in the 1982–1996 ( $T_3$ ) period. Relatively small coefficients on drug dependence covering the first three time periods ( $p = .15$  from  $T_0$  to  $T_1$ ,  $p = .18$  from  $T_1$  to  $T_2$ ) reflect rapid changes in drug use patterns in and out of Vietnam that were uniquely experienced by respondents in this sample.

The most interesting finding is perhaps the directional changes of effects among PTSD, drug dependence, and suicidality from youth to mid-life. The effect within the same time period of  $T_1$  drug dependence on  $T_1$  PTSD was small but significant ( $p = .06$ ); and  $T_1$  drug dependence on  $T_2$  suicidality was also significant ( $p = .07$ ). However,  $T_2$  PTSD and  $T_2$  sui-

cidality both had significant effects on  $T_2$  drug dependence ( $p = .17$  and  $p = .20$ ).  $T_2$  suicidality significantly affected  $T_3$  PTSD, and  $T_2$  PTSD had a relatively large effect ( $p = .12$ ) on  $T_3$  drug dependence.  $T_2$  drug dependence, on the other hand, did not significantly affect  $T_3$  PTSD nor  $T_3$  suicidality. For the last 15 years up to 1996 ( $T_3$ ), the effect of suicidality on drug dependence ( $p = .09$ ) and that of drug dependence on PTSD ( $p = .05$ ) were much weaker than the effect of PTSD on suicidality ( $p = .19$ ). However, considerable collinearity was observed which was likely to have affected the estimates of path coefficients.

Similar path analytic models were constructed replacing drug dependence for alcohol dependence to examine if the over-time effects of drug dependence on PTSD or on suicidality can be replicated; similarly replacing depression for suicidality to examine if suicidality is just an indicator of the association of major depression with drug dependence and PTSD. Although the path coefficients of alcohol dependence and depression over time ( $T_1$  to  $T_2$  to  $T_3$ ) were all large, the effects between the two constructs (e.g., alcohol dependence on suicidality, and major depression on drug dependence) were much weaker. These results are consistent with the results of the time-dependent Cox regression.

## 4. Discussion

Of the 943 Vietnam veterans in the cohort database, nine veterans committed suicide between 1971 and 1996. Although the number is too small to make any generalization, it should be noted that all but one of the suicides were Caucasian and were those who enlisted voluntarily. The standard mortality ratio (SMR) for suicide was higher among the drug-negative veterans than the drug-positive veterans, contrary to other most common causes of death.

The main strength of this study is the approach of combining information on PTSD, drug dependence, and non-fatal suicidality over time for surviving veterans. Of the 641 veterans interviewed in 1996–1997, 15.7% reported suicidality. Unlike most data showing a decreased risk for suicidality in African-Americans, African-American veterans were more likely than Caucasians to report suicidality in our sample, in part because race is associated with drug-positive status in this sample. Over 20% of the veterans met the lifetime diagnosis of DSM-IV PTSD, and 17% met the diagnosis of drug dependence. Being African-American, voluntarily enlisted, and drug-positive at the time of departure from Vietnam, as well as meeting the DSM-IV criteria for alcohol dependence since 1972, lifetime major depression, and adult antisocial personality since 1972, were all significantly associated with having a DSM-IV drug dependence since 1972. Most of these measures were also significant with the lifetime DSM-IV criteria for PTSD.

Over the 25-year-period, the annual prevalence rate for PTSD was stable, but the rate of drug dependence decreased from over 16% in 1972 to under 6% in 1996, and the

rate of suicidality increased monotonically from 1971 until around 1985. The survival curves showed that remission from suicidality occurred more slowly for respondents with concurrent PTSD or with concurrent drug dependence. Results of time-dependent Cox regressions showed that major depression had the largest effect, and drug dependence had the next largest effect on the timing of suicidality. Further analyses also indicated that PTSD began to have a significant effect on suicidality around 1974. Alcohol dependence did not have a significant effect on suicidality for this sample.

Discrete-time path models demonstrated that younger age, being African-American, and being a volunteer enlistee had significant effects on the in-Vietnam drug dependence, but not on the in-Vietnam PTSD and suicidality. Childhood antisocial personality affected both in-Vietnam PTSD and drug dependence. Not surprisingly, PTSD, drug dependence, and suicidality were quite stable over time. Drug dependence appeared to exacerbate both PTSD and suicidality in young adulthood; however, once the patterns of association were set, PTSD and suicidality appear to lead to continuation of drug dependence in middle adulthood. This suggests the likelihood of illicit drug use as self-medication (Chilcoat and Breslau, 1998) perhaps because of their familiarity with drug experience, or their learning from the effects experienced in the past. This spiral process appears to strengthen the associations over time. We found that drug dependence was a stronger factor for suicidality than alcohol dependence. PTSD had a larger time-dependent effect on suicidality, controlling for depression, once suicidality was removed from the diagnostic criteria for major depression.

Common vulnerability, such as a genetic propensity to PTSD, drug dependence, and suicidality certainly can contribute to the behavioral expression in all areas once trauma is experienced and drug use initiated. The results of this study show a stronger association over time and the evidence of self-medication once the person experiences drug dependence. It may not be coincidental to observe the high level of co-occurrence of PTSD, drug dependence, and non-fatal suicidality in this cohort of Vietnam veterans, owing to their history of short but intensive use of opiates in Vietnam. From our study, we are not able to ascertain whether the spiral process was dictated by the biological or the social processes. Future longitudinal studies may consider incorporating promising endophenotypes (such as endocrinological measures of the HPA axis activities) within a traditional epidemiologic framework.

Design and analysis limitations need to be noted. The results are not generalizable to the entire population of Vietnam veterans, as our cohort is represented by a relatively late cohort of Army Vietnam veterans and did not include officers. The unique experiences of this cohort, i.e., high exposure to war trauma and high exposure to illicit drugs, provide an economical sample to investigate the association of PTSD and drug abuse and their impacts on suicidal behavior. Further

replications are therefore necessary to see if similar patterns are observed for veterans of other wars as well as victims of non-war related traumas of similar intensity. More than 10% of the original cohort was lost to premature death, but the number of completed suicides was too small to examine in detail. For the most part, the measures used were based on retrospectively obtained self reports over 25 years. Selective recall may have influenced patterns of association to appear more stable than if prospective follow-ups had been carried out annually. However, it would have been nearly impossible to carry out such a study retaining the near identical measures for annual repeated assessment over two decades.

In the current examination, varying durations of suicidality could potentially have biased the results of the survival curves stratified by PTSD and drug dependence, since the opportunity to be classified by one or the other category depended on the duration of suicidality. The Cox regression analyses were confined to the measures since 1972 to maintain consistencies across measures, thus over-time variations prior to 1972 were not reflected in the results. With the abundance of opiates, many soldiers deployed in Vietnam at that time did not consume as much alcohol as they had in the U.S. A lack of strong association between alcohol dependence and suicidality over time may reflect the unique changes of alcohol use patterns in this sample. The Cox regression analysis could produce biased results if an effect of a covariate varies systematically over time, due to its proportional hazard assumption. In addition to addressing this issue by using interaction terms with "time," we examined time dependency by replicating the results using the generalized estimation equation (GEE) (Diggle et al., 1994). The GEE results confirmed the results obtained from Cox regression using a user-defined correlation matrix over time. This suggests that the over time correlation of suicide ideation was unsystematic in this sample. The path analytic models were successively constructed from two- to three-construct models. Some paths that were eliminated in an earlier stage could potentially have some importance when three constructs were combined. We did not conduct exhaustive searches of all combinations of paths. Our experience, however, indicates hierarchical modeling is sufficient for most multivariate analyses. Lastly, we obviously did not include all potentially causally important measures in the path analytic models, which is reflected in a relatively high RMSEA (.23). Since we specifically wanted to address causal roles of PTSD and drug dependence in suicidality, inclusion of additional measures were considered a detraction. Given the relatively small sample size and high collinearity involved in estimating path coefficients, replications are needed to further support the inferences we made about the causal mechanism among PTSD, drug dependence, and suicidality over time.

In summary, this article has documented the potentially causal roles involving PTSD, drug dependence, and suicidality over time. Prevention of and treatment for suicidality for this age group of men with trauma experience should include intervention and prevention of drug use as well as

treatment for depression. Once PTSD is well developed, it may be more difficult to intervene in drug dependence and suicidality. Therapies to enhance coping strategies and alternatives to drug use may reduce the duration of suicidality (Oquendo et al., 2003; Johnson et al., 2004). At a time when global terrorism is spreading to many parts of the world (NYT, 2004), early detection of PTSD and substance abuse could save many lives that would be lost to suicide and reduce health care burdens for the treatment of suicidality in years to come.

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## Appendix A

Measures used in three types of analyses:

(A) Survival analyses: this set of analyses were used to determine the factors that prolonged non-fatal suicidality. All measures were lifetime assessment.

Measure	Variable definition	Used as
Duration of non-fatal suicidality	Years of ideation	Outcome
PTSD	DSM-IV (0,1)	Strata
Drug dependence <sup>a</sup>	DSM-IV (0,1)	Strata

<sup>a</sup> Includes information from both the 1972 and 1996 surveys.

(B) Cox regression analyses: this set of analyses were used to determine the factors that affect non-fatal suicidality using time-dependent person-year data.

Measure	Variable definition	Timing	Used as
Suicidality	(0,1)	Yearly repeated (1972–1996)	Outcome
PTSD	DSM-IV (0,1)	Yearly repeated (1972–1996)	Covariate of interest
Drug dependence	DSM-IV (0,1)	Yearly repeated (1972–1996)	Covariate of interest
Alcohol dependence	DSM-IV (0,1)	Yearly repeated (1972–1996)	Control covariate
Major depression <sup>a</sup>	DSM-IV (0,1)	Yearly repeated (1972–1996)	Control covariate
Adult antisocial personality	DSM-IV (0,1)	Yearly repeated (1972–1996)	Control covariate
Age in 1971 <sup>b</sup>	Age in years	Fixed <sup>c</sup>	Control covariate
Race <sup>b</sup>	African-American = 1 Other = 0	Fixed <sup>c</sup>	Control covariate
Enlistment status <sup>b</sup>	Volunteer = 1 Draftee = 0	Fixed <sup>c</sup>	Control covariate
High school education	H.S. diploma = 1 No diploma = 0	Fixed <sup>c</sup>	Control covariate

<sup>a</sup> Removed the question of suicidality from computation of the DSM-IV diagnostic variables.

<sup>b</sup> Based on information from the 1972 survey. All other variables are from the 1996–1997 survey.

<sup>c</sup> Fixed variables are invariant or are measured only once.

(C) Path analyses: this set of analyses were used to determine associations among drug dependence, PTSD, and non-fatal suicidality over time.

Measure	Variable definition	Timing	Used as <sup>c</sup>
Age in 1971 <sup>a</sup>	Age in years	Fixed <sup>b</sup>	Exogenous
Race <sup>a</sup>	African-American = 1 Other = 0	Fixed <sup>b</sup>	Exogenous
Enlistment status <sup>a</sup>	Volunteer = 1 Draftee = 0	Fixed <sup>b</sup>	Exogenous
Drug urinalysis status in 1971 <sup>a</sup>	Drug-positive = 1 Drug-negative = 0	Fixed <sup>b</sup>	Exogenous
High school education	H.S. diploma = 1 No diploma = 0	Fixed <sup>b</sup>	Exogenous
Military aptitude test <sup>a</sup>	(0–10)	Fixed <sup>b</sup>	Exogenous
Childhood antisocial scale <sup>a</sup>	Based on truancy, fights, and arrests (0–10)	Pre-Vietnam	Exogenous
Suicidality, $T_0$	(0,1)	Pre-Vietnam	Exogenous
PTSD, $T_0$	(0,1)	Pre-Vietnam	Exogenous
Drug dependence, $T_0$ <sup>a</sup>	Based on self-report of uppers, downers, and narcotics (0–3)	Pre-Vietnam	Endogenous
Suicidality, $T_1$	(0,1)	In-Vietnam	Endogenous
PTSD, $T_1$	(0,1)	In-Vietnam	Endogenous
Drug dependence, $T_1$ <sup>a</sup>	Based on self-report of narcotics and urinalysis (0–2)	In-Vietnam	Endogenous
Suicidality, $T_2$	One point for every positive year (0–10)	1972–1981	Endogenous
PTSD, $T_2$	One point for every positive year (0–10)	1972–1981	Endogenous
Drug dependence, $T_2$	One point for every positive year (0–10)	1972–1981	Endogenous
Suicidality, $T_3$	One point for every positive year (0–15)	1982–1996	Endogenous
PTSD, $T_3$	One point for every positive year (0–15)	1982–1996	Endogenous
Drug dependence, $T_3$	One point for every positive year (0–15)	1982–1996	Endogenous

<sup>a</sup> Based on information from the 1972 survey. All other variables are from the 1996–1997 survey.

<sup>b</sup> Fixed variables are invariant or are measured only once.

<sup>c</sup> Exogenous variables are the variables whose causes are not listed explicitly in the model. The exogenous variables in our path analyses are either fixed and not subject to change, or represent the pre-Vietnam period ( $T_0$ ). In our path analyses, the endogenous variables are the variables that are affected by earlier time periods as well as by other variables in the same time period. The endogenous variables cover three time periods: in-Vietnam time period ( $T_1$ ), 1972–1981 ( $T_2$ ), and 1982–1996 ( $T_3$ ).

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