



Twenty-five year mortality of US servicemen deployed in Vietnam: predictive utility of early drug use[☆]

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Abstract

Large numbers of young men were exposed to high-quality opiates for a relatively short time period during military service in Vietnam. This study examined the relationships of opiate and other drug abuse before, during, and shortly after their time of service in Vietnam with the subsequent 25-year mortality among the cohort of 1227 US Army enlisted returnees and their matched civilians previously studied in 1972 and 1974. Composite factor scores of a variety of drug use measures and other individual behavioral measures were selected separately for three time periods around service in Vietnam from over 120 measures associated with mortality. Results of path analytic models applied to selected significant measures showed that both in-Vietnam and post-Vietnam drug use factors were large and significant predictors of mortality, controlling for pre-service drug use, continuity to later drug use, and demographic and other behavioral measures. The magnitude of the direct effect of drug use on mortality was larger than those of the covariates that were entered in the path analyses, except age. Notwithstanding the high remission rate from opiate addiction, drug use in Vietnam had considerable predictive utility for premature death in this cohort. In light of the re-emergence of increased heroin use since the mid-1990s, the findings point to the importance of early intervention of drug use and comorbid problems for today's youth now initiating heroin use. © 2001 Elsevier Science Ireland Ltd. All rights reserved.

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1. Introduction

Although treatment of heroin and other opiate addiction is a scientifically well-advanced area in the history of drug abuse research, formidable methodological and logistical challenges face studies that aim to examine the long-term natural history of opiate abusers who were epidemiologically ascertained from the community. Long-term follow-ups of opiate abusers ascertained either through treatment systems (Vaillant, 1973;

Maddux and Desmond, 1986) or criminal justice systems (Nurco et al., 1981; Prendergast et al., 1998) frequently portrayed a recalcitrant nature of opiate addiction, in part owing to selective ascertainment (Graeven and Graeven, 1983; Rounsaville and Kleber, 1985). However, other studies have found that natural recovery from opiate addiction is actually common in the community (Winick, 1962; Biernacki, 1986). Among them are a few epidemiologic studies that documented rapid recovery from heroin addiction among Vietnam veterans after returning to the United States (Robins et al., 1975; O'Brien et al., 1980), leading to the notion that heroin addiction can be reversed quickly even in a natural setting — a view still considered controversial today (United States General Accounting Office, 1998).

Utilizing mortality data from a 25-year follow-up project of a Vietnam veteran cohort studied in the early

[☆] A fuller description of the variable selection process and supplemental data on significant drug use and other measures described in this report is available on the journal home page at <http://www.elsevier.com/locate/drugalcddepsuppmat/>.

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1970s, this article examines the relationships of drug use before, during and shortly after their service in the Vietnam war with subsequent premature death to assess whether or not brief but intensive use of drugs, mostly opiates, could predict long-term adverse consequences such as premature death. Such an inquiry is relevant in forecasting the future course of today's opiate users, given the appearance of potent heroin in the mid-1990s and the subsequent re-emergence of local heroin epidemics in the US (Community Epidemiology Work Group, 1998; United States Department of Health and Human Services, 1999). Other predictors of premature death, as well as drug use patterns over the adult life of surviving members from the 25-year follow-up project are reported elsewhere (Price et al., 2001a,b).

1.1. Historical background

Opiates were used extensively by American servicemen deployed in Southeast Asia during the latter part of the Vietnam War. The availability of high-potency heroin increased suddenly in the spring of 1970 (Baker, 1972). Drug-related hospitalizations and deaths among servicemen in Vietnam sharply increased in the months following (Alonso, 1973). A concurrent US drug use epidemic accelerated in the late-1960s and continued through the mid-1970s (O'Donnell et al., 1976), with heroin use incidence peaking in 1971 (Gfroerer and Brodsky, 1992). The dire prospect of large numbers of returning Vietnam veterans addicted to opiates spurred the fear that the heroin epidemic would further spread in the United States (Zinberg, 1972). In June President Nixon declared the 'War on Drugs'; 'Operation Golden Flow', as facetiously termed by soldiers, commenced at departure locations in Vietnam where soldiers were tested for drugs by urinalysis through the Date Eligible for Return from Overseas (DEROS) program (Stanton, 1976). The soldiers whose urine was positive for opiates, amphetamines, or barbiturates were provided 5–7 days of detoxification and treatment prior to their return to the United States (Baker, 1972).

The scale of this 'natural experiment' — large numbers of young men exposed to high-quality opiates for approx. 12 months — was unprecedented in US drug abuse history. However, the then large-scale Vietnam Drug User Returns (VDUR) project documented remarkable remission rates from opiate addiction among Army returnees from Vietnam in September 1971. While the addiction rate increased to 20% in Vietnam from 0.4% prior to arrival among the 'general' probability sample, it dropped to 1.0% for the 8–12 month period after departure (Robins et al., 1975). Subsequent relapse was also found to be uncommon in the 1974 follow-up (Robins and Helzer, 1975). Noteworthy, nonetheless, are other reports of this cohort and other veterans, which showed an excess of alcohol abuse

(O'Brien et al., 1980; Boscarino, 1981) and poor social adjustment (Mintz et al., 1979) among those with a history of opiate use in Vietnam, as well as the appearance of a depressive syndrome associated with combat experience (Helzer et al., 1976; Nace et al., 1977). Questions thus remain about the long-term outcomes for Vietnam veterans who began using opiates in Vietnam.

1.2. A 25-year follow-up

By taking advantage of the oversampling of opiate abusers in the VDUR project, the ongoing Washington University Vietnam Era Study (VES), a 25-year follow-up of the VDUR cohort, was aimed at assessing long-term psychiatric and medical consequences of drug abuse and war participation in Vietnam. This article utilizes mortality data coupled with interview and other record data from the earlier surveys of the VDUR cohort. In cross-sectional surveys, predictors of mortality are frequently inferred from cause-of-death information in death certificates (Centers for Disease Control Vietnam Experience Study, 1987; Fett et al., 1987a). In the current study, interview and records data collected while respondents were in their 20s were searched to identify predictors of death, thus attempting to overcome such methodological problems as inaccuracy and inconsistency of death-certificate coding across states (Kircher and Anderson, 1987) and the validity of the coding systems (Mackenbach et al., 1995). More importantly, the availability of self-report information during youth from both the deceased and surviving members can more accurately establish the utility of early drug use to predict long-term mortality. Drug use measures assessed separately for three periods around the time of service in Vietnam further enable documenting the relative importance of drug use in three time periods while controlling for continuity of drug use in successive periods.

2. Methods

2.1. Sample

The VDUR cohort of 1227 men consisted of three samples. About half of the veterans in the target sample were randomly drawn from the list of Army enlisted returnees with pay grade E1–E9 whose urine tested drug-positive at the time of their departure from Vietnam in September 1971 (DEROS-positive or D+). The DEROS-positive population comprised an estimated 10.5% of the total 13 760 Army enlisted returnees in that month. The other half, the 'general' sample of the 1972 survey, was randomly drawn from the same total Army enlisted returnees leaving Vietnam in September

1971. For this article, 39 D+ members who also appeared in the 'general' sample (Robins, 1974) were included only in the D+ sample for simplicity. Thus, DEROS-positive ($n = 512$) and DEROS-negative (D-) veterans ($n = 431$) are mutually exclusive (Table 1). The nonveteran control sample ($n = 284$) was ascertained from Selective Service registrations and individually matched to those in the target general sample for the 1974 survey with respect to draft eligibility, draft board location, age, and education completed by the time of the veteran's entry into service (Robins and Helzer, 1975).

All 1227 respondents were male and averaged 23.5 years of age at the time of the 1972 interviews. Racial composition reflected that of the US population at the time, except that African Americans constituted a higher percentage in the D+ veteran sample (34% in D+ sample vs. 11% in the United States as a whole). The veterans surveyed in 1972 numbered 898; 571 veterans were reinterviewed in 1974. Nonveteran respondents were interviewed only in 1974. Thus, 855 veterans and nonveterans participated in the 1974 survey.

The response rates for the 1974 and 1996–97 follow-ups reflected design attrition, deaths, no location, and interview refusals. For the 1974 survey, career soldiers who had been in the military for longer than 3 years and those living in sparsely populated states were dropped from the veteran samples. The interview rates of the target sample exceeded 95% in the 1972 survey and 92% in the 1974 survey. For the VES 1996–97 survey, 10.5% of the sample was lost by death. A location rate of over 93% for the surviving members ($n = 1024$) was achieved after two decades of hiatus.

The fieldwork was discontinued after the ascertainment goal of 830 interviews was surpassed, resulting in an 82.1% interview rate ($n = 841$).

2.2. Determination of death and causes of death

The Equifax Nationwide Death Search and the Department of Veteran Affairs Beneficiary Identification and Records Location System were utilized to identify the deceased. The National Death Index was employed to search for and verify additional deaths among unlocated respondents or those reported as dead by informants during fieldwork. The procedures were repeatedly applied in the 1993–94 VES location study and in the 1996–97 interview study (Fig. 1). Death certificates were requested from the Federal Archives Records Center or from the state vital statistics offices. Informant interviews were carried out to verify death status and causes of death for the deceased cases without death certificates. Together, 129 deaths were verified as having occurred by the end of 1996.

Causes of death were determined for 126 (97.7%) cases, 122 from causes of death listed on death certificates and four based on detailed informant interviews. Underlying causes of death were coded using the International Classification of Diseases, Ninth Revision (World Health Organization, 1977), by an expert cause-of-death coder who was blinded to DEROS status. Coding results were further verified by a physician and another vital statistics coding specialist. To examine if attrition from the 1972 or 1974 survey was likely to have biased the results derived from self-report information, drug-related causes of death were coded from death certificates, defined as deaths by intoxication,

Table 1
Washington University Vietnam era study samples ($n = 1227$)^a

Survey	DEROS-positive (D+) veterans ($n = 512$) ^b	DEROS-negative (D-) veterans ($n = 431$) ^c	Nonveteran controls ($n = 284$) ^d	Total ($n = 1227$)
1972	484 (94.5%)	414 (96.1%)	Not included	898 (73.2%)
1974	309 (60.4%)	262 (60.8%)	284 (100%)	855 (69.7%)
1996–97	323 (63.1%)	320 (74.3%)	198 (69.7%)	841 (68.5%)
Cumulative deaths by 1996	89 (17.4%)	32 (7.4%)	8 (2.8%)	129 (10.5%)

^a All percentages in parentheses are based on the target sample total for each sampling category.

^b DEROS-positive veterans were those whose urine tested positive for opiates, amphetamines, or barbiturates at the Date Eligible for Return from Overseas (DEROS) program. This sample consisted of those who were drawn randomly from the D+ veteran pool of 1400 army enlisted men with pay grade E1–E9 who departed from Vietnam in September 1971 and includes 39 who were also included in the general sample.

^c Selected randomly from the total 13 760 Army enlisted men departed at the same time, excluding those who also were selected in the D+ sample.

^d Selected from the Selective Service records of men who had never been in service and matched to the 'general' sample surveyed in 1974. Because a series of replacements was allowed, the exact number of potential interview candidates who were traced/contacted could not be clearly determined at the start of the 25-year follow-up; therefore only the interviewed sample of nonveterans were included in the target sample for the latest follow-up.

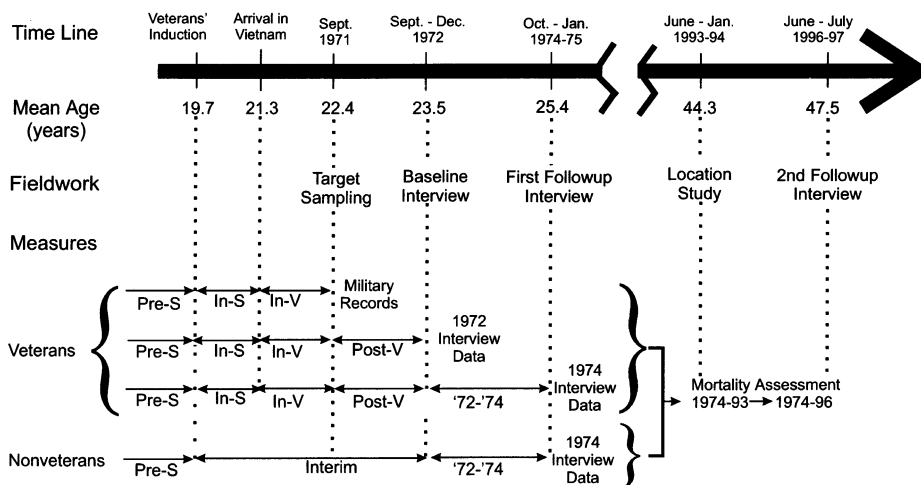


Fig. 1. Vietnam drug user returns project and Washington University Vietnam era study: study design and measures. Pre-S (pre-service), In-S (in-service), In-V (in-Vietnam), and Post-V (post-Vietnam) up to the 1972 interview. Measures from the in-service period for veterans prior to their arrival in Vietnam were not used in the subsequent analyses.

poisoning, overdose, addiction, or abuse for which drug use was specifically mentioned (ICD9 304–305, E850–858, E950, E980), or deaths among those with a history of opiate injection whose causes of death were judged to be a medical consequence of opiate abuse, including HIV and hepatitis B and C (ICD9 042, 070.3, 070.5; National Institute on Drug Abuse, 1997).

2.3. Selection of predictive measures

Available predictive measures varied according to respondents' inclusion in the 1972 and 1974 surveys (Fig. 1). Military records were available for all veterans in the target sample; self-report measures up to 1972 were available for all interviewed veterans. For veterans interviewed in both 1972 and 1974 and for nonveterans, measures were available for the periods through 1974.

The measures from each interview and record data were initially analyzed separately for three periods using two subsamples: pre-service, in-Vietnam, and post-Vietnam periods up to 1972 for the veteran sample ($n = 898$); and pre-service, interim, and 1972–1974 periods for the combined veteran and nonveteran sample ($n = 855$). The interim period covered the time from induction to two years prior to the 1974 interview, with each nonveteran's 'induction' date set to that of his matched veteran. For the period in service prior to arrival in Vietnam, measures were available only for veterans. Preliminary analyses showed that none of the variables confined to this short period reached a significant level of association with mortality. Thus, we considered that omission of this period could only slightly underestimate the predictability of 'interim' drug use on mortality.

Because thousands of variables could potentially be examined, several steps were taken to systematically

reduce the number of 'candidate' measures to a manageable level. Eleven domains were identified for the purpose of organizing measures including: demographics, socioeconomic status, military experience, family history, psychiatric symptoms, antisocial behavior, crime, social networks, drug use, alcohol use, and residual measures. Bivariate analyses, coupled with a review of findings from earlier published articles of 1972 and 1974 surveys and published reports on predictors of mortality from several at-risk populations, resulted in a list of over 120 'candidate' variables for each of the two subsamples that were spread over the 11 domains.

Multiple logistic regressions were subsequently employed as a primary means for identifying predictive measures for each time period, with backward elimination using the significance level of $P < 0.05$ as the variable inclusion criterion. Ordinary least-square regressions with leaps-and-bounds (Furnival and Wilson, 1974) augmented logistic regressions to select additional variables with substantial effects but with larger P values by identifying the combination of variables that maximized the explained variance of the mortality measure. Preliminary Cox proportional hazard analyses and logistic regressions yielded similar estimates of coefficients on covariates. In addition, estimating the effects of drug use on the timing of death was not a central concern for this article. Thus, use of logistic regressions at this stage was considered justifiable. These series of analyses resulted in 50 significant predictors of mortality across the 1972 and 1974 datasets, which became the basis for the subsequent path analyses. Further details of variable selection steps and a description of the 50 variables are available in an appendix at: <http://www.elsevier.nl/homepage/sab/drugalcdep/supmat.htm>.

2.4. Assessing the predictive utility of early drug use

To assess the relative importance of drug use in the periods before, during and shortly after Vietnam service in predicting mortality, we first pursued structural equation models (SEM; Jöreskog and Sörbom, 1979). Preliminary SEM analyses of saturated structural models, estimated from polychoric matrices of drug measures as indicators of the drug abuse liability for each of the three time periods and observed mortality outcome, produced unstable results which required relatively large ridge factors (SAS Institute, 1989) to obtain positive definite matrices. Such a solution was considered unsatisfactory (Wothke, 1993). Alternatively, three summary factors of drug abuse liability were derived using standardized factor scores obtained from the maximum likelihood (ML) factor analyses applied to Pearson correlations of drug use measures for each time period (McDonald and Burr, 1976). This approach was considered justifiable, given that factor loadings of Pearson correlations obtained from dichotomous measures empirically have been shown to be correlated very highly with those obtained using tetrachoric correlations (Shrout and Parides, 1992), even though standard errors of factor loadings obtained by the former method are known to be biased downward (Babakus et al., 1987). The summary factor scores (pre-Vietnam, in-Vietnam/interim, and post-Vietnam/1972–74), with the means of zero and the variances of one, approximately, are then interpreted as the predicted standardized composite scores which take into account the variations of all selected drug use measures and relative importance of these measures to the underlying factors.

Path analyses were subsequently performed on polyserial correlations among the three summary factors, demographic and individual non-drug behavioral measures, and the mortality outcome. The analyses allowed simultaneous estimation of the direct effects of drug use for the three time periods on mortality while controlling

for the effects of drug use on successive periods, as well as confounding effects of other covariates. To correct for standard errors, estimates were obtained by weighted least-squares (WLS) using LISREL8 (Scientific Software International, 1993), which produces asymptotically distribution-free estimates of standard errors of path coefficients (Browne, 1984).

All analyses were performed without sampling weights because the effects of weights in a complex multivariate analysis are sometimes unclear (Robins and Price, 1991). The DEROS status was used as a behavioral indicator of drug use in the in-Vietnam or interim periods in part to adjust factor loadings on self-reported drug use measures for oversampling of D+ veterans. Potential bias in the estimates of drug use effects due to inclusion of DEROS status was examined by creating artificial summary factors for the in-Vietnam/interim periods, in which D- veteran observations were inflated by the ratios of the weights to D+ veterans. The correlation coefficients were near unity. We thus judged that inclusion of DEROS status did not alter the summary factors in any discernible way.

3. Results

3.1. Mortality rates

The mortality between 1971 and 1996 was 17.4% (95% CI, 14.2–20.9%) among D+ veterans and 7.4% (95% CI, 5.1–10.3%) among D- veterans; the nonveteran sample experienced 2.8% mortality (95% CI, 1.2–5.5%) for the period from 1974 through 1996 (Table 1, bottom section). The cumulative mortality rates also differed by interview status. Among veterans, those who were in the target sample but were not interviewed in 1972 ($n = 45$) had the highest death rate at 22.3%, in part because six deaths occurred between the Septem-

Table 2
Drug-related deaths from cause-of-death information on death certificates^a

	Interviewed in 1972	Interviewed in 1974	Mean age at 1974 interview ^b	Total deceased by 1996 (%)	Drug-related deaths by 1996 (%)
Veterans ($n = 943$)	No ($n = 45$)	No ($n = 45$) ^{c,d}	26.1 years	10 (22.3%)	3 (6.7%)
	Yes ($n = 898$)	No ($n = 327$) ^c	27.9 years	50 (15.3%)	10 (3.1%)
		Yes ($n = 571$)	25.5 years	61 (10.7%)	7 (1.2%)
Nonveterans ^f ($n = 284$)	No ($n = 284$)	Yes ($n = 284$)	25.8 years	8 (2.8%)	2 (0.7%)

^a Drug-related deaths were defined as those deaths by intoxication, poisoning, overdose, addiction, or abuse for which 'drug' was specifically mentioned (ICD9 304–305, E850–858, E950, E980), or those deaths judged to be a medical consequence of opiate abuse, including HIV and hepatitis B and C (ICD9 042, 070.3, 070.5) among those with a history of opiate injection.

^b Mean age expected at the mid-point of the 1974 interview fieldwork duration (November 1974).

^c Not included in subsequent analyses for the 1972 veteran sample ($n = 898$).

^d Drug use history prior to death was unavailable.

^e Not included in subsequent analyses for the 1974 combined veteran and nonveteran sample ($n = 855$).

^f Mortality was assessed for the period from 1974 to 1996.

Table 3
Significant drug use measures for each time period^a

1972 sample (D+ veterans and D- veterans; n = 898 ^b)			1974 sample (D+ veterans, D- veterans, and nonveterans; n = 855)		
Measures	Factor loadings	Standardized scoring coefficients	Measures	Factor loadings	Standardized scoring coefficients
Pre-service:			Pre-service:		
Injected opiates	0.348	0.012	Injected opiates	0.796	0.425
Marijuana use	0.713	0.046	Marijuana use level	0.401	0.093
Extent of opiate experience	0.672	0.039	Use of heroin	0.821	0.493
Use of opiates once a week	0.356	0.013	Use of Robitussin (A-C) without prescription	0.330	0.072
Variety of drugs used	0.983	0.917			
In-Vietnam:^c			Interim:^d		
Significant withdrawal from opiates	0.794	0.382	Significant withdrawal from opiates	0.928	0.336
Opiate use soon after arriving	0.760	0.319	Injected opiates	0.545	0.039
More than half of unit used opiates regularly	0.423	0.091	Opiate use 1+ times a week	0.948	0.471
DEROS-positive at departure ^e	0.758	0.315	Use of downers	0.746	0.084
			Use of uppers	0.560	0.041
			DEROS-positive at departure ^e	0.791	0.106
Post-Vietnam:^f			1972–1974:^g		
Knows place to buy opiates	0.446	0.242	Significant withdrawal from opiates	0.572	0.411
Feels heroin use in US is OK	0.148	0.066	Offered opiates	0.517	0.341
Opiate use since return	0.706	0.610	Downers interfered with life	0.423	0.249
Treated for drugs at VA	0.199	0.090			

^a Variables included were drug-use measures with factor loading significant at $P < 0.001$, among 50 selected predictors of mortality across the three time periods and two surveys. (Details of measure selection are described in an appendix available at: <http://www.elsevier.com/inca/publications/store>.) Factor loadings were obtained from the principal factors estimated by ML factor analyses of Pearson correlations; standardized scoring coefficients are regression coefficient estimates of the 'true' factor scores on observed standardized measures. These factors were included in the subsequent path analyses shown in Fig. 2 and Table 4.

^b Effective sample size varied across three time periods for the 1972 sample due to different numbers of missing cases.

^c From the date of arrival in Vietnam to September 1971.

^d For a veteran, the induction date to two years prior to his 1974 interview; for a nonveteran, the induction date is set to that of his matched veteran. The most predictive drug-use measures for veterans listed in Table 3 covered the period from arrival to Vietnam to September 1971.

^e Nonveterans were given zero value.

^f Approximately 12 months from September 1971.

^g For two years prior to the respondents 1974 interview.

ber 1971 departure and the 1972 interviews (Table 2). Similarly, among veterans interviewed in 1972, the death rate was 15.3% among those who were not interviewed in 1974 ($n = 327$), which included eight deaths between the 1972 and 1974 interviews. This compared to 10.7% among those interviewed in 1974 ($n = 571$). The difference may also reflect a design attrition criterion of dropping older career soldiers from the 1974 interviews, although the difference in the mean expected ages between the two groups was statistically insignificant. Drug-related deaths were highest at 6.7% among veterans in the target sample who were not interviewed in 1972, and second highest at 3.1% among veterans who were interviewed in 1972 but not in 1974, compared to 1.2% among veterans interviewed both in 1972 and 1974. Out of 22 drug-related deaths, only four occurred before the 1974 interview time. Although the numbers are small, these results suggest self-report measures of drug use shown could have predicted mortality

at a higher level if these measures had been available for the veterans attrited prior to 1974.

3.2. Significant measures predictive of mortality for three time periods

Fifty measures were significant predictors of mortality across the 1972 and 1974 surveys when predictors were assessed for each of the three time periods separately: 28 variables were selected from the 1972 veteran sample ($n = 898$); 28 were from the 1974 combined sample ($n = 855$); and six variables were predictors in both sets of analyses. To construct drug use factor scores, 13 drug use measures for the 1972 veteran sample and 13 from the 1974 combined veteran and nonveteran sample were chosen (Table 3). Factor loadings on these 26 drug use measures were all significant at $P < 0.001$ when ML factor analyses were run separately for each time period and dataset. (The appendix

which is available on the Journal's website describes the details of the selected measures.) A majority of the variables were based on questions about opiates, but eight unique measures involved questions including other classes of drugs. Although factor loadings varied considerably, eigenvalues indicated that the one factor solution was optimal for each time period.

The value of a standardized scoring coefficient, estimating the measure's contribution to the summary factor, depended upon relative strengths of factor loadings of other measures. The factor loading was 0.983 for 'variety of drug used' in the pre-service period from the 1972 sample, and the corresponding scoring coefficient was 0.917. The value of this coefficient was large because all other factor loadings were much smaller than this loading. For other factors, however, no single measure produced such a large contribution to the factor. For example, the factor loading for 'significant withdrawal from opiates' in the interim period from the 1974 sample was 0.928 but the corresponding scoring coefficient was 0.336, because the factor loading for 'opiate use 1 + times a week', another measure for this factor, was a larger 0.948.

For the subsequent path analyses, individual covariates covering several domains (demographics, SES, antisocial personality, crime, alcohol use, military experience, and psychiatric problems) were added from the pool of the 50 predictive measures. Multi-collinear measures and the measures with t -ratios < 2 were subsequently removed in a sequential fashion at a preliminary stage, resulting in a subset of significant measures. These included age, race, pre-service antisocial behavior, heaviest drinking in Vietnam, disobeyed orders in service after Vietnam, and depression in the post-Vietnam period for the veteran only sample; and race, pre-service antisocial behavior and depression in the 1972–74 period for the veteran and nonveteran combined sample.

3.3. Predicting mortality from self-reported early drug use

The final path analysis models (Fig. 2) show results for the associations among three drug use factors and mortality, while controlling for other significant covariates described above. The path from pre-service drug use to mortality outcome was dropped for both 1972 and 1974 samples. Both models were reasonably well fit: for the 1972 dataset, the adjusted goodness of fit index (AGFI) was 0.944, and the root mean square residual (RMR) was 0.076; and for the 1974 sample, AGFI = 0.971, and RMR = 0.065. With the continuity of drug use from one time period to another partialled out, the direct effects of drug use on mortality were still all significant at $P < 0.05$: $b = 0.109$ and 0.101 for the direct effects of in-Vietnam and post-Vietnam drug use,

respectively, from the 1972 sample; $b = 0.117$ and 0.144 for the direct effects of drug use in the interim and 1972–74 period, respectively, from the 1974 sample. The minimum fit function χ^2 s indicate that the effect of pre-service drug use on mortality was negligible for both samples (for the 1972 sample, $\chi^2 = 0.148$, $df = 1$, $P = 0.700$ for dropping this path; for the 1974 sample, $\chi^2 = 1.813$, $df = 1$, $P = 0.178$).

The unstandardized regression coefficient of 0.040 (corresponding standardized $b = 0.109$) for the path from in-Vietnam drug use to mortality in the 1972 sample is the increase in probability of death per

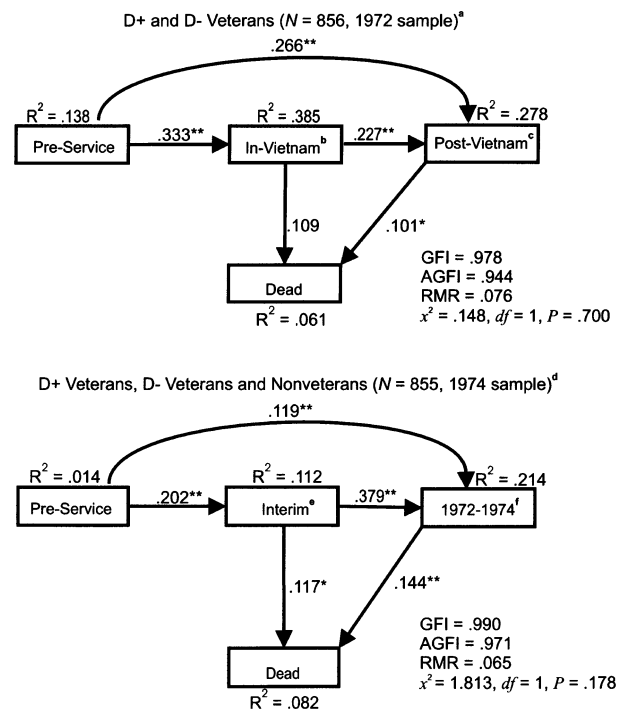


Fig. 2. Path analysis models used polyserial correlations of cumulative mortality and summary factors obtained from ML factor analyses of drug use measures listed in Table 3, controlling for demographics and other behavioral covariates. The path coefficients were estimated using the WLS method. The number indicates the value of the standardized path coefficient; * $P < 0.01$, ** $P < 0.001$, GFI = goodness of fit index; AGFI = adjusted goodness of fit index; RMR = root mean square residual. The χ^2 statistic is the minimum function χ^2 compared to the saturated model, which included the path from 'pre-service' to 'dead'. The effective sample size excluded missing cases. ^aDemographic covariates (direct and indirect effects) included age and race. Individual measures of behavioral covariates (direct effects) included antisocial behavior in pre-service, heaviest drinking in-Vietnam, disobeying orders in service and depression in post-Vietnam period. ^bFrom the date of arrival in Vietnam to September 1971. ^cApproximately 12 months from September 1971. ^dDemographic covariates included race (direct and indirect effects). Individual measures of behavioral covariates (direct effects) included antisocial behavior in pre-service and depression in the Post-Vietnam period. ^eFor a veteran, from induction date to two years prior to his 1974 interview; for a nonveteran, the induction date is set to that of his matched veteran. The drug-use measures for veterans listed in Table 3 covered the period from arrival in Vietnam to September 1971. ^fFor two years prior to the respondent's 1974 interview.

standard deviation difference in the drug use liability scale for this time period. The cumulative mortality in this sample is 12.7%, thus, an approximately 32% increase (0.040/0.127) in mortality in the subsequent 25 years can be inferred, with a one standard-deviation increase (roughly 35% above average) in drug use in Vietnam. Similarly, the path coefficient of 0.117 for the interim direct effect on mortality in the 1974 sample leads to the inference of a 40% increase for a one standard deviation increase in drug use during that time, given the cumulative mortality of 8.1% from the 1974 sample.

Age was the only variable that showed an effect ($b = 0.136$) on mortality larger than those of drug use factors for the veteran only sample, even after partialling out the effects through drug use and other behavioral measures. This indicates simply that, the older, the more likely to die, with other things being equal. Smaller direct effects on mortality were shown for all other behavioral covariates including race, anti-social behavior, heaviest drinking, disobeying in service, and depression.

Even though the direct effect was negligible, pre-service drug use could still have exerted an influence indirectly, given the strong continuity of drug use over time. The total effects of pre-service drug use on mortality were non-negligible (0.071 for the 1972 sample and 0.052 for the 1974 sample; Table 4). Nonetheless, the total effects of in-Vietnam/interim drug use were the largest, followed by those of the post-Vietnam/1972–74 periods.

4. Discussion

The processes leading to death in contemporary society are complex. Lacking a unified theory of death, this article has taken a data-driven approach to identify significant early predictors of premature death in this cohort. We found considerable predictive utility of drug use measures for the mortality outcome after 25 years, while controlling for other significant predictors. That 'drug abuse kills' is known from studies showing high follow-up mortality rates among drug abusers (Vaillant, 1973; Engström et al., 1991; Hser et al., 1993). We demonstrated more specifically that self-reported drug use up to respondents' mid-20s can predict subsequent death over 25 years. The direct effects of in-Vietnam/interim and post-Vietnam/1972–74 drug use were found to be larger than those of the pre-service period. The model fit indices indicated that the direct effect of pre-service drug use on mortality was negligible. Furthermore, the total effects involving the path from in-Vietnam/interim drug use to mortality were largest. For vulnerable youth, exposure to abundant opiates during their service in Vietnam appeared to have in-

Table 4
Total effect of drug use of each time period on mortality^a

1972 sample (D+ and D- veterans; $n = 856^b$)			
	Drug use in		
	Pre-service	In-Vietnam ^c	Post-Vietnam ^d
Total effect on mortality	0.071**	0.132*	0.101*
95% confidence interval	(0.034–0.107)	(0.046–0.217)	(0.027–0.174)
1974 sample (D+ veterans, D- veterans, and nonveterans; $n = 855$)			
	Drug use in:		
	Pre-service	Interim ^c	1972–1974 ^f
Total effect on mortality	0.052**	0.172**	0.144**
95% confidence interval	(0.031–0.073)	(0.105–0.238)	(0.073–0.215)

^a Based on the results of path analysis models shown in Fig. 2. The direct effect for the path from pre-service drug use to mortality was constrained to be zero. The standardized total effects are listed with the 95% confidence intervals in parentheses, * $P < 0.01$, ** $P < 0.001$.

^b Effective sample size excluding missing cases.

^c From the date of arrival in Vietnam to September 1971.

^d Approximately 12 months from September 1971.

^e For a veteran, the induction date to two years prior to his 1974 interview; for a nonveteran, the induction date is set to that of his matched veteran.

^f For two years prior to the respondent's 1974 interview.

creased the risk for premature death, over and above the increased risk of mortality accounted for by earlier drug use, later continuation, and other at-risk behaviors. It should be noted, however, that several other behavioral measures were also found to be significant predictors of mortality, even though early drug use was most predictive, aside from age, of the 25-year mortality. The significant individual behavior predictors identified here are consistent with those found using logistic regression models (Price et al., 2001b). This article, however, has focused on the predictive utility of self-reported early drug use alone for premature death, and the relationship of drug use in each of three time periods to mortality, given that drug use levels fluctuated enormously over this short period.

Behaviors after 1974, potential confounders of the observed associations of early drug use and mortality, are not available for the deceased because of two decades of hiatus before the VES follow-up. The finding of considerable statistical 'effects' of drug use from the in-Vietnam period and up to three years afterwards could mean that these measures were surrogates for

more recent drug use. Opiate use among the surviving members in this cohort assessed in the 25-year follow-up showed a continuous decline since 1972 (Price and Risk, 2000). Thus, although it is possible that opiate use patterns of the deceased were very different from those who survived, later relapse to opiate addiction appears as a minor reason for increased risk of premature death. Indeed, drug-related causes of death determined from death certificates accounted for only 16.0% of the deaths of those interviewed in 1972 or 1974. Even acknowledging that drug involvement is understated in death certificates, it is clear that our respondents died of a variety of other reasons as well.

A complex intervening process is more likely to have been involved, as drug use in Vietnam and shortly afterwards was correlated with other problems, which are also associated with premature death, such as alcohol abuse (Wish et al., 1979; Fett et al., 1987b), depression (Helzer et al., 1976; Nace et al., 1977), post-traumatic stress disorder (PTSD; Keane and Wolfe, 1990), and suicidality (Kramer et al., 1994). Among our cohort members, these problems appear to have taken a cumulative toll on the well-being of veterans, particularly those with a history of opiate use in Vietnam (Price et al., 1998, 2001a). Understanding the mechanism of environmental factors exacerbating these comorbid conditions would help reduce the long-term adverse consequences of early vulnerabilities well marked by illicit drug use.

Design and analysis limitations need to be noted. The results are not generalizable to the entire population of Vietnam veterans as our cohort represented a relatively late cohort of Army Vietnam veterans, and did not include officers. The study results, however, are more generalizable than are long-term follow-ups of illicit drug abusers obtained from treatment (Wahren et al., 1997; Ghodse et al., 1998) or criminal justice systems (Hser et al., 1993). Not all deaths were included in the assessment of the predictive utility of self-reported early drug use for mortality, as the measures were unavailable for deaths that occurred prior to the VDUR surveys (see Table 2, footnotes). However, analyses of causes of death obtained from death certificates showed that drug-related deaths were higher in the attrited veteran groups than among those included in the path analyses. Our results on the 'effects' of early drug use on mortality should be taken as conservative estimates.

The analysis scheme used in this article, comprising a combination of factor analysis and path analysis, is somewhat unorthodox. Because a variety of drug use measures were collinear, logistic regression analyses of all variables by combining the three time periods would have provided erroneous odds ratios without careful attention to multi-collinearity. Use of composite observed measures of drug use with mutually exclusive categories would have resulted in intended and unintended loss of information. Therefore, construction of summary factors

was considered optimal. Another alternative, the Cox regression approach with time-dependent covariates (Allison, 1995) was infeasible, given that 90% of the deaths occurred after the previous assessment in 1974. Hence the advantages of the current scheme outweighed the alternative approaches considered above.

In summary, this article has documented the relative importance of opiate and other drug use in each of the pre-, in- and after-Vietnam periods in predicting cumulative mortality among a cohort of Vietnam veterans and nonveteran controls followed up 25 years later. These and other findings from the VES follow-up demonstrate that, although the Vietnam era's heroin epidemic subsided by the mid-1970s, its shadow has extended across more than two decades in this cohort. It appears that drug use during service in Vietnam was a marker of conditions that adversely affected survival since then, even though opiate abuse alone may have been short-lived. In light of the re-emergence of increased heroin use since the mid-1990s (Community Epidemiology Work Group, 1998), the findings point to the importance of early intervention of drug use and comorbid problems for today's youth now initiating heroin use.

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References

- Allison, P.D., 1995. *Survival Analysis Using the SAS System. A Practical Guide*. SAS Institute, Cary, NC.
- Alonso, M.K., 1973. The scope of illicit drug use in a Vietnam combat unit. *South. Med. J.* 66, 245–248.
- Babakus, E., Ferguson, C.E., Jöreskog, K.G., 1987. The sensitivity of confirmatory maximum likelihood factor analysis to violations of measurement scale and distributional assumptions. *J. Market. Res.* 24, 222–228.
- Baker, S.L., 1972. US Army heroin abuse identification program in Vietnam: implications for a methadone program. *Am. J. Publ. Hlth* 62, 857–860.
- Biernacki, P., 1986. *Pathways from Heroin Addiction. Recovery without Treatment*. Temple University Press, Philadelphia, PA.
- Boscarino, J., 1981. Current excessive drinking among Vietnam veterans: a comparison with other veterans and non-veterans. *Int. J. Soc. Psychiat.* 27, 204–212.
- Browne, M.W., 1984. Asymptotically distribution-free methods for the analyses of covariance structures. *Br. J. Math. Stat. Psychol.* 37, 62–83.

- Community Epidemiology Work Group, 1998. Epidemiologic trends in drug abuse, vol. 1. Highlights and executive summary. National Institute on Drug Abuse, Rockville, MD (NIH No. 98-4300).
- Centers for Disease Control Vietnam Experience Study, 1987. Postservice mortality among Vietnam veterans. *J. Am. Med. Assoc.* 257, 790–795.
- Engström, A., Adamsson, C., Allebeck, P., Rydberg, U., 1991. Mortality in patients with substance abuse: a follow-up in Stockholm County, 1973–1984. *Int. J. Addict.* 26, 91–106.
- Fett, M.J., Adena, M.A., Cobbin, D.M., Dunn, M., 1987a. Mortality among Australian conscripts of the Vietnam conflict era. I. Death from all causes. *Am. J. Epidemiol.* 125, 869–877.
- Fett, M.J., Nairn, J.R., Cobbin, D.M., Adena, M.A., 1987b. Mortality among Australian conscripts of the Vietnam conflict era. II. Causes of death. *Am. J. Epidemiol.* 125, 878–884.
- Furnival, G.M., Wilson, R.W., 1974. Regressions by leaps and bounds. *Technometrics* 16, 499–511.
- Gfroerer, J., Brodsky, M., 1992. The incidence of illicit drug use in the United States, 1962–1989. *Br. J. Addict.* 87, 1345–1351.
- Ghodse, H., Oyefeso, A., Kilpatrick, B., 1998. Mortality of drug addicts in the United Kingdom 1967–1993. *Int. J. Epidemiol.* 27, 473–478.
- Graeven, D.B., Graeven, K.A., 1983. Treated and untreated addicts: factors associated with participation in treatment and cessation of heroin use. *J. Drug Issues* 13, 207–217.
- Helzer, J.E., Robins, L.N., Davis, D.H., 1976. Depressive disorders in Vietnam returnees. *J. Nerv. Ment. Dis.* 163, 177–185.
- Hser, Y.I., Anglin, M.D., Powers, K., 1993. A 24-year follow-up of California narcotics addicts. *Arch. Gen. Psychiat.* 50, 577–584.
- Jöreskog, K.G., Sörbom, D., 1979. *Advances in Factor Analysis and Structural Equation Models*. Abt Books, Cambridge, MA.
- Keane, T.M., Wolfe, J., 1990. Comorbidity in post-traumatic stress disorder: an analysis of community and clinical studies. *J. Appl. Soc. Psychol.* 20, 1776–1788.
- Kircher, T., Anderson, R.E., 1987. Causes of death. Proper completion of the death certificate. *J. Am. Med. Ass.* 258, 349–352.
- Kramer, T.L., Lindy, J.D., Green, B.L., Grace, M.C., Leonard, A.C., 1994. The comorbidity of post-traumatic stress disorder and suicidality in Vietnam veterans. *Suicide Life Threat. Behav.* 24, 58–67.
- Mackenbach, J.P., Kunst, A.E., Lautenbach, H., Bijlsma, F., Oei, Y.B., 1995. Competing causes of death: an analysis using multiple-cause-of-death data from the Netherlands. *Am. J. Epidemiol.* 141, 466–475.
- McDonald, R.P., Burr, E.J., 1976. A comparison of four methods of constructing factor scores. *Psychometrika* 32, 381–401.
- Maddux, J.F., Desmond, D.P., 1986. Relapse and recovery in substance abuse careers. In: Tims, F.M., Leukefeld, C.G. (Eds.), *Relapse and Recovery in Drug Abuse*. NIDA Research Monograph 72. US Government Printing Office, Washington, DC, pp. 49–71.
- Mintz, J., O'Brien, C.P., Pomerantz, B., 1979. The impact of Vietnam service on heroin-addicted veterans. *Am. J. Drug Alcohol Abuse* 6, 39–52.
- Nace, E.P., Meyers, A.L., O'Brien, C.P., Ream, N., Mintz, J., 1977. Depression in veterans two years after Viet Nam. *Am. J. Psychiat.* 134, 167–170.
- National Institute on Drug Abuse, 1997. *Heroin abuse and addiction. Research Report Series*. National Institute on Drug Abuse, Rockville, MD (NIH No. 97-4165).
- Nurco, D.N., Cisin, I., Balter, M.B., 1981. Addict careers, II. The first ten years. *Int. J. Addict.* 16, 1327–1356.
- O'Brien, C.P., Nace, E.P., Mintz, J., Meyers, A.L., Ream, N., 1980. Follow-up of Vietnam veterans. I. Relapse to drug use after Vietnam service. *Drug Alcohol Depend.* 5, 333–340.
- O'Donnell, J.A., Voss, H.L., Clayton, R.R., Slatin, G.T., Room, R.G.W., 1976. *Young Men and Drugs — A Nationwide Survey*. NIDA Research Monograph 5. US Government Printing Office, Washington, DC.
- Prendergast, M.L., Hser, Y.I., Gil-Rivas, V., 1998. Ethnic differences in longitudinal patterns and consequences of narcotics addiction. *J. Drug Issues* 28, 495–515.
- Price, R.K., Breslau, N., Triffleman, E., Chilcoat, H., True, W., Kosten, T., 1998. PTSD and substance abuse. *Problems of Drug Dependence 1997*. NIDA Research Monograph Series 178. (NIH No.98-4305). US Government Printing Office, Washington DC, pp. 48–51.
- Price, R.K., Risk, N.K., 2000. Substance abuse in adulthood: natural history over a 25-year period. Paper presented at the 62nd Scientific Meeting of the College on Problems of Drug Dependence. San Juan, Puerto Rico, June.
- Price, R.K., Risk, N.K., Spitznagel, E.L., 2001a. Remission from drug abuse over a 25-year period. I. Patterns of remission and treatment use. *Am. J. Publ. Hlth*, in press.
- Price, R.K., Risk, N.K., Stwalley, D., Murray, K.S., Eisen, S., Virgo, K.S., et al., 2001b. A 25-year followup of U.S. servicemen deployed in Vietnam: patterns and predictors of mortality. *Am. J. Publ., Hlth.*, submitted for publication.
- Robins, L.N., 1974. *The Vietnam Drug User Returns*. Special Action Office Monograph, Series A, No.2. US Government Printing Office, Washington, DC.
- Robins, L.N., Helzer, J.E., 1975. Drug use among Vietnam veterans—three years later. *Med. World News-Psych.* 16, 44–49.
- Robins, L.N., Helzer, J.E., Davis, D.H., 1975. Narcotic use in Southeast Asia and afterward: an interview study of 898 Vietnam returnees. *Arch. Gen. Psychiat.* 32, 955–961.
- Robins, L.N., Price, R.K., 1991. Adult disorders predicted by childhood conduct problems: results from the NIMH Epidemiologic Catchment Area Program. *Psychiatry* 54, 116–132.
- Rounsaville, B.J., Kleber, H.D., 1985. Untreated opiate addicts: how do they differ from those seeking treatment? *Arch. Gen. Psychiat.* 61, 182–192.
- SAS Institute, 1989. *SAS/STAT User's Guide*, Version 6, 4th edn., vol. 1 [Computer software]. SAS Institute, Cary, NC, 245–365.
- Scientific Software International, 1993. *LISREL 8 User's Reference Guide* [Computer software]. Scientific Software International, Chicago, IL.
- Shrout, P.E., Parides, M., 1992. Conventional factor analysis as an approximation to latent trait models for dichotomous data. *Int. J. Meth. Psychiat. Res.* 2, 55–65.
- Stanton, M.D., 1976. Drugs, Vietnam and the Vietnam veteran: an overview. *Am. J. Drug Alcohol Abuse* 3, 557–570.
- United States Department of Health and Human Services, 1999. New data show opiates take lead over cocaine in treatment admissions. *HHS News*, August 26.
- United States General Accounting Office, 1998. Drug abuse — research shows treatment is effective but benefits may be overstated. Report to congressional requesters. US General Accounting Office, Washington, DC (GAO/HEHS-98-72).
- Vaillant, G.E., 1973. A 20 year follow-up of New York narcotic addicts. *Arch. Gen. Psychiat.* 29, 237–241.
- Wharen, C.A., Brandt, L., Allebeck, P., 1997. Has mortality in drug addicts increased? A comparison between two hospitalized cohorts in Stockholm. *Int. J. Epidemiol.* 26, 1219–1226.
- Winick, C., 1962. Maturing out of narcotic addiction. *Bull. Narc.* 14, 1–7.
- Wish, E.D., Robins, L.N., Hesselbrock, M., Helzer, J.E., 1979. The course of alcohol problems in Vietnam veterans. In: Galanter, M. (Ed.), *Currents in Alcoholism*, vol. 6. Grune & Stratton, New York.
- World Health Organization, 1977. *Manual of the international statistical classification of diseases, injuries, and causes of death: based on the recommendations of the 9th Revision Conference, 1975, and adopted by the 29th World Health Assembly*. WHO, Geneva.
- Wothke, W., 1993. Nonpositive definite matrices in structural modeling. In: Bollen, K.A., Long, J.S. (Eds.), *Testing Structural Equation Models*. Sage, Newbury Park, CA, pp. 256–293.
- Zinberg, N.E., 1972. Heroin use in Vietnam and the United States: a contrast and a critique. *Arch. Gen. Psychiat.* 26, 486–488.