

<b>FINAL REPORT</b>	GRANT NUMBER R01DA07939	
PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR Rumi Kato Price, Ph.D., M.P.E.	PERIOD COVERED BY THIS REPORT	
	FROM 05-01-93	THROUGH 07-31-96
APPLICANT ORGANIZATION Washington University School of Medicine		
TITLE OF PROJECT (repeat title shown in item 1 on first page) Vietnam Veteran Drug User Follow-Up: Feasibility Study		

- a. Human Subject (Complete Item 7 on the Face Page)  
 Use of Human Subjects  Change  No Change Since Last  
 Progress Report
- b. Vertebrate Animals (Complete Item 8 on the Face Page)  
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(SEE INSTRUCTIONS)

## VIETNAM VETERAN DRUG USER FOLLOW-UP: FEASIBILITY STUDY FINAL REPORT

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GENDER AND MINORITY INCLUSION					Study Title		
Provide the number of subjects enrolled in the study <i>to date</i> (cumulative since the most recent competitive award) according to the following categories (See Page 8 for definitions.) If there is more than one study, provide a separate table for each study. In addition report on the subpopulations which are included in the study.					Vietnam Veteran Drug User Follow-Up: Feasibility Study		
	American Indian or Alaskan Native	Asian or Pacific Islander	Black, not of Hispanic Origin	Hispanic	White, not of Hispanic Origin	Other or Unknown	TOTAL*
Female	0	0	0	0	0	0	0
Male	7	4	242	59	909	6	1,226
Unknown	0	0	0	0	0	0	0
<b>TOTAL</b>	7	4	242	59	909	0	1,226

\*The number of subjects in the target sample. VES-I was a feasibility study; and no enrollment for interview was attempted.



## 1. INTRODUCTION

The Vietnam Era Study (VES) is a long-term follow-up of the study conducted in 1972 and 1974 by the Washington University School of Medicine (WUSM). The overall follow-up consists of three phases. Phase I, the feasibility study, evaluated the locatability of the target sample after two decades of hiatus, and provided preliminary outcome assessment; Phase II consisted of instrumentation and pretesting (DA07939). In Phase III, in-person and telephone interviews is currently conducted with over 850 of 1,100 surviving members (DA09281, "Vietnam Drug Users Two Decades Later").

This Final Report concerns Phase I and Phase II. Phase I was initially supported for a total of 15 months from May, 1993 to July 1994; Phase II was subsequently supported for 12 months from August 1994 to July 1995 as a competitive continuation; a no-cost extension was given for an additional 12 months until July 1996. The no-cost extension period overlapped with the first year of Phase III. In so far as preliminary results from Phase III are significantly relevant to the findings drawn from Phase I and Phase II, they are included in this report. Results from Phases I & II presented in this Final Report are subject to revision since Phase III, the main interview study, are currently ongoing.

## 2. SPECIFIC AIMS

Three kinds of objectives were addressed in this study.

The feasibility assessment aims were:

Aim 1: To locate and contact the original study respondents, including the Vietnam War veteran general-sample respondents negative for urinalysis in 1971, the Vietnam War veteran drug-positives in 1971, and the civilian controls interviewed in 1974;

Aim 2: To provide detailed documentation on the tracing procedures used in the feasibility study;

Aim 3: To provide cost estimates for the main study using results from this feasibility study and the information available from the original study.

The instrumentation aims were:

Aim 4: To develop the questionnaire instruments for the main study (Phase III);

Aim 5: To pretest in-person and telephone interview versions in a local sample to further refine the instruments.

Lastly, the data analysis aims included:

Aim 6: Linking the 1972 and 1974 database to the tracing data obtained in Aim 1, including mortality and location outcomes, and contact efforts, and current and past VA medical records;

Aim 7: To examine medical utilization patterns of located subjects through VA hospitals' medical records;

Aim 8: To examine demographic and behavioral correlates of mortality, mobility, and tracing efforts.

The methods and results of the study subsequently presented are organized by phases of the activities (Phase I, Phase II); and also by specific aims in the Results and Data Analysis and Dissemination sections.

## 3. BACKGROUND

### 3.1. The Original Study

The Original Study was initiated by the White House Special Action Office for Drug Abuse Prevention (SAODAP) with concerns about a large number of returning veterans who had been addicted to illicit drugs while stationed in Vietnam. The interview study was conducted in 1972 and 1974 under the direction of Lee N. Robins, Ph.D.; the fieldwork was subcontracted to the National Opinion Research Center. One of the most significant findings of this study related to an extraordinary high remission rate from opiate addiction among the probability sample of returning veterans. Among the 1972 cohort, 97% of the sample tested positive for urinalysis at the time of departure, and 45% of the general probability sample admitted using opiates amphetamines, or barbiturates in Vietnam. About half of opiate users reported being addicted to them. The rate of opiate addiction among the general probability sample dropped from 20% to 1% at one year after Vietnam, and less than 10% of these addicted in Vietnam had become re-addicted to opiates in three years after returning from Vietnam (Robins, 1974; Robins, Helzer & Davis, 1975; Robins & Helzer, 1975).

The Original Study became a classic epidemiological study in the drug abuse field, although several other studies on drug abuse problems among Vietnam veterans were carried out at the time. (Stanton, 1972; Roffman & Sapol, 1970; Nace *et al.*, 1978). The scale of the study was one reason for its recognition, although the sample size is modest at best from the current trend of large-scale general-population studies. More important reasons, however, included a uniqueness sampling and longitudinal measurement design, low refusal rates and the importance of its findings. These reasons provided an unique scientific opportunity to a follow-up two decades later.

The Original Study included three samples. First, a probability sample of veterans was selected from the Army's active duty roster containing a list of all 13,760 September 1971 returnees. Second, "drug-positive" veterans were selected from the Surgeon General's list of 1,400 veterans who had positive urine at DEROS (Date Eligible for Return from Overseas) (Baker, 1972).<sup>1</sup> Third, a control sample of civilians matched to the general-sample respondents was added in 1974. Oversampling of the drug-positive veterans allowed for a detailed study of the causes and consequences of drug abuse among the veterans, while the drug-positive sample was weighted to the general-sample veterans to allow for the generalization of findings to all Army enlisted men returning from Vietnam in September 1971. In addition, inclusion of the matched civilians allowed for estimating expected use and addiction rates if men had not had the Vietnam experiences.

The measurement design of the Original Study combined retrospective and prospective design, since the 1972 interview utilized a catch-up design by including repeated measures for pre-service, in-Vietnam and after-Vietnam periods up to 1972; and the 1974 interview employed a prospective design measuring events between 1972 and 1974.

The Original Study was also known for low refusal and no-location rates. The response rate was 95.2% for the 1972 interview and 93.3% for the 1974 interview, despite high geographical mobility of the veteran sample at the time. The high cooperation rates were achieved in part because of unlimited access to VA records.

Finally, the surprising findings about the extraordinary high remission rate and continued abstinence contradicted a widely held belief at the time about irreversibility of opiate addiction. Such a high rate of remission had been unthinkable in U.S. treatment populations. The findings invited a number of speculations about sources of the inconsistencies, such as ascertainment differences, age of onset, route of administration environmental cues, availability and social influence (Price, 1993b, 1994; Robins, 1993; see **Appendix A, #1**).

### 3.2. Why A Long-Term Follow-Up?

There are several reasons that make the Original Study particularly suitable for a long-term follow-up study on the natural history of drug abuse. First, even though Vietnam veterans are a well-studied population (Figley, 1978; Egendorf *et al.*, 1981), there was not a longitudinal study of Vietnam veteran drug users, which included epidemiologic baseline information collected shortly after returning from Vietnam. Several large-scale studies have been conducted concerning Vietnam veterans, including the National Vietnam Veterans Readjustment (NVVR) Study (Kulka, Schlenger, Fiarbank, *et al.*, 1988), the Centers for Disease Control Vietnam Experience Study (CDC VES 1988a, 1988b, 1988c), and the Vietnam Era Twin Registry (Eisen *et al.*, 1991). While each study is unique, these large-scale studies were all retrospective with respect to their baseline information.

Second, although not a general-population sample,<sup>2</sup> the sample was a probability sample drawn from a known universe of Vietnam veterans. Further, the veteran population arguably can be considered to represent the general population of the same age group, weighted to slightly lower SES. There always is a cohort effect; however, Vietnam veterans' drug user patterns generally followed their civilian age cohort members (O'Donnell *et al.*, 1976).

Third, a number of large-scale prospective studies on drug use have largely drawn samples from student populations, (Jessor & Jessor 1977; Kandel, Simcha-Fagan & Davis, 1986; Johnston, O'Malley & Backman, 1994). These studies, while findings are highly generalizable, do not permit a detailed examination of the natural course of drug *abuse*. Existing long-term follow-up studies of drug abusers, on the other hand, have often been limited to clinical samples (O'Donnell, 1972; Vaillant, 1973; Hubbard, 1989) which are likely to introduce bias due to

1. Data on troop build-up in Vietnam yield a rough estimate that .2 to .4 million were stationed in Vietnam during the period around the height of heroin epidemic there (1969-1971). The 1971 returnees from the enlisted men are estimated at 150,000. About 15,700 men of these returnees, can be considered as the sample universe for our drug-positive veterans.
2. The Original Study did not include female veterans in its sampling frame; subsequently our follow-up focused only on males. A number of factors made this limitation justifiable: most female Vietnam veterans were nurses who would have been ineligible for the original study because the sample was drawn from the enlisted population, not from officers; female veterans represented only about 4% of U.S. veterans up to several years ago (US VA, 1988), although the trend is changing rapidly; the prevalence of drug abuse among female Vietnam veterans is significantly lower than for male Vietnam veterans (1.0 vs. 5.7%, lifetime), (Jordan *et al.*, 1991); and, the drug abuse rate among women in the general population of the same age group as the target sample is considerably lower than that in the male counterpart age group (5.1 vs. 8.4%, lifetime) (Anthony & Helzer, 1991).

selection factors in treatment (Price, Cottler & Robins, 1990) and consequently have only limited validity. The Original Study sample was a non-clinical and non-student sample, in which 50% were abusers of "hard" drugs. Thus, use of this sample, we hoped, will avoid sampling bias problems due to treatment selection, while developing cost-efficient follow-up protocols. Furthermore, the length of follow-up would be at least 24 years in our study. Such a long follow-up length is rarely available in existing non-clinical studies of drug abuse.

Fourth, the Original Study was one of few available at the time, which documented the wealth of psychiatric and substance abuse information with use of structured interviews. The database of the Original Study includes detailed information on use and abuse of six classes of psychoactive drugs, alcohol (Robins, Hesselbrok, Wish & Helzer, 1979; Wish, Robins, Hesselbrok & Helzer, 1979) and nicotine, measured for the pre-service and in-Vietnam periods, as well as during the one-year and three-year post-Vietnam periods. The database also includes measures of demographics, family history, childhood problems, war experience (Helzer, 1984), depressive syndrome (Helzer, Wish & Hesselbrok, 1979), and environmental risk factors such as drug availability and drug-using networks. This existing database, then, will allow us to prospectively examine the course of drug abuse, comorbidity with alcohol abuse, and long-term outcomes of involvement with drugs, as well as to assess the impact of both pre-service and in-Vietnam risk factors affecting the long-term outcomes.

Perhaps more important, a long-term follow-up of our cohort, we felt, may provide valuable information to develop an integrated theory of the course of drug abuse. Many advances have been made during the last decade in the area of developmental theories of substance use and abuse (Kaplan, 1980; Kandel & Logan, 1984; Huba & Bentler, 1982). To understand the complex underlying forces operating on the *course* of drug abuse requires a sufficiently large sample size, a high concentration of at-risk sample with a known ascertainment to allow for inferences to the population level, good baseline data, repeated measures which allow modeling over-time changes, and measures covering many domains. The proposed follow-up study utilizes a sufficiently large general-population sample, while including a large number of clinical and subclinical drug users. Thus, it will provide an adequate database to begin developing an integrated theory of the adult course of drug abuse.

## 4. METHODS

### 4.1. Samples

#### 4.1.1. The Original Study Sampling Design

The 1972 wave drew two samples: the general sample (N=470)--a random sample of all September 1971 returnees, and the DEROS-positive sample (N=494)--a sample from September 1971 returnees who showed positive urine at departure from Vietnam. Twenty-two respondents fell into both the general sample list and the DEROS-positive list; within the general sample, 17 were found to have been positive at departure (due to the incomplete Surgeon General's list). The response rate was over 95% for all categories (**Table 1**).

The target sample for the 1974 interviews from the 1972 cohort was chosen on the basis of the service induction date and the residence at induction. Those who were inducted before January 1969, or those who resided at induction in the states from which less than 10 interviewed veterans were inducted, were dropped from the 1974 target sample. The total of 571 veterans were reinterviewed in 1974. The 1974 wave added a non-veteran sample (N=302)--a sample selected from the Selective Service records who had never been in service, matched with the general-sample respondents interviewed in 1974. Matching with respect to draft eligibility, size and location of pre-draft residential area, age, and education, was achieved for 259 respondents of the interviewed non-veterans (N=284). Altogether, 855 respondents were interviewed in 1974, yielding the overall response rate of 93.3%.

#### 4.1.2. The Follow-Up Tracing Samples

Respondents were categorized into three groups for the Phase III follow-up sampling purpose. The first is an "ineligible" sample consisting of veterans in the original target sample who were never interviewed (N=44). This group was traced in part because effects of early attrition was of some interest given that they were part of the probability samples of the Original Study. Military records are still available, which will allow comparison of members of this group with those ascertained in the Original Study.

Table 1: Sampling Design of the Original Study

Sample in the Original Study	Urinalysis at Departure	1972 Interview: 1 Year after Vietnam		1974 Interview: 3 Years after Vietnam	
		Target Sample N	Interviewed f %	Target Sample N	Interviewed f %

<u>General Sample:</u>								
Selected from 13,760 Army enlisted men departed from Vietnam in Sept., 1971	negative	431	414	96.1%	278	<b>262</b>	94.6%	
	positive	17	15	88.2%	10	<b>9</b>	80.0%	
<u>In Both Samples:</u>								
	positive	22	22	100.0%	14	<b>13</b>	92.9%	
<u>DEROS-Positive Sample:</u>								
Selected from 1,400 Sept. returnees who had positive urine at departure	positive	472	447	95.0%	315	<b>287</b>	91.1%	
<u>Non-veteran sample:</u>								
Selected from Selective Service records: men who had never been in service	N/A	not interviewed in 1972			302	<b>259</b>	94.7%	
						(matched) 25 (non-matched)		
-----								
TOTAL N		942	898	95.2%	919	855	93.3%	

**Follow-Up "Pool 1" Target Sample: TOTAL N=830**

General sample drug-negative veterans: N=262; Drug-positive veterans: N=309; matched non-veterans: N=259.

Respondents eligible for inclusion in Phase III included two groups. The "Pool 1" sample consists of 830 subjects, including 571 veterans interviewed both in 1972 and 1974 and 259 nonveterans matched to the veteran sample and interviewed in 1974 (see Table 1, bottom). This sample was considered to be most useful with respect to maximizing the information available from the interviews in 1972 and 1974. The "Pool 2" sample included remaining respondents ascertained in the Original Study. Pool 2 totals 352 and consists of 327 veterans interviewed only in 1972 and 25 unmatched nonveterans interviewed in 1974. This group will augment some of the Pool 1 subjects, including the deceased, unlocated, refusals, or those who otherwise are unavailable to participate in the follow-up interview study. The probability sampling plan for the 1972 study was based on the total including Pool 1 and Pool 2 veterans. Unmatched Pool 2 veterans could still be matched with Pool 2 veterans. Thus, the "disadvantage" of the Pool 2 veteran sample could in effect be reduced only to the lack of information from 1974 interviews.

Our tracing sample size therefore was 1,226, including the "Ineligibles", Pool 1 and Pool 2 follow-up samples. The nonveterans in the target sample who were not interviewed were not traced because there was no clearly defined universe from which nonveterans were drawn and also no useful information was left about these non-ascertained nonveterans in the Original Study database. The whole sample was traced for death records; all veteran sample (N=942) was traced for VA utilization. Of those interviewed at least once in the Original Study (N=1,182), those who have not deceased after the initial death search were traced for location assessment.

#### 4.1.3. Sample Characteristics

Overall, 19.7% of the whole VES sample (Ineligible, Pool 1 & Pool 2) are African Americans, 4.8% are Hispanics, and 74.2% are whites. Because the sample for the Original Study was drawn from enlisted men, African Americans are over-represented in the proposed study, compared to the general veteran population (8%), as well as to the U.S. population as a whole (11%) (Bureau of the Census, 1988). The percentage of Hispanics is about the same as for the veteran population (4.0%), and about two-thirds of the representation in the U.S. population as a whole (7%). The drug-positive sample includes 34.1% African Americans, four times as high a representation as for the veteran population (**Table 2**).

The target sample was reaching an average of 44 years of age in 1993, the start of Phase I. In 1972, 17.2% of the general-sample drug-negatives and 15.7% of the drug-positives were still on active duty. At that time, 14.2% of the general sample and almost 30% of the drug-positives were unemployed, indicating that a considerable portion of the drug-positive respondents was still experiencing adjustment problems in one year after their return home. By 1974, only 3.8% of the general-sample drug-negatives and 1.6% of the drug-positives were still on active duty in 1974. Of those interviewed in 1974, 14% of the general sample and 25% were unemployed (not shown). In comparison, about 10% of the civilian sample were unemployed.

Table 2: Demographic Characteristics of Phase I Tracing Sample

Demographic characteristics		Veterans:	Veterans:	Comparison
		General-sample drug-negatives (N=431)	Drug-positives (N=511)	Civilians (N=284)
AGE:	expected mean age in 1993 (SD)	45.2 yrs (4.9)	43.5 yrs (3.2)	43.6 yrs (1.6)
RACE:	% whites	81.7%	59.9%	88.4%
	% African Americans	11.6%	34.1%	6.3%
	% Hispanics	4.9%	5.7%	3.2%
EMPLOYMENT STATUS:				
	% active duty*	17.2%	15.6%	0.0%
	% unemployed*	14.2%	29.9%	10.1%

\* The veterans' employment status was based on the 1972 interviews (N=898); nonveterans' employment status was based on the 1974 interviews (N=284). See text for veterans' employment status in 1974.

The unweighted prevalence of drug use and abuse is provided for each sampling category and for three periods: before-Vietnam, in-Vietnam, and the after-Vietnam period from 1971 to 1974. Data on Pool 1 sample is presented because comparisons of drug use in 1974 is only available for Pool 1 sample. It also allows comparison of drug use between the general-sample and civilians, because they were "matched" (**Table 3**).

Table 3: Drug Use and Abuse History of Pool 1 Sample.  
Pre-, In-, and Three Years after Vietnam

Drug use and abuse		Veterans:	Veterans:	Civilians:
		General-sample drug-negatives (N=263)	Drug-positives (N=308)	Matched controls (N=259)
BEFORE VIETNAM:*				
	% marijuana use only	12.2%	17.9%	16.2%
	% hard drug** use	27.4	43.8	12.0
	% narcotic§ dependence, 1+ sxs <sup>†</sup>	.4	6.2	1.5
IN VIETNAM:				
	% hard drug use	45.3%	95.5%	-
	% narcotic dependence, 1+ sxs	27.0	86.4	-
THREE YEARS AFTER VIETNAM (1972-74):				
	% marijuana use only	22.1%	23.7%	22.0%
	% hard drug use	33.8	64.6	18.9
	% narcotic dependence, 1+ sxs	3.8	14.9	1.5

\* The non-veteran's drug use "before Vietnam" was assessed using the induction date of his matched veteran;

\*\* Hard drugs includes narcotics, stimulants and sedatives; § narcotics means heroin and other opiates;

<sup>†</sup> The measure of narcotic dependence is a 5-point scale.

Among the drug-positive sample, the rate of opiate dependence syndrome, measured as experiencing at least one dependence symptom, was still 14.9% for the 1972-74 period, three years after return from Vietnam, although it was reduced to 17% of the in-Vietnam level. The rate was still more than twice as high as the pre-Vietnam level. During this two-year period, 64.6% of the drug-positive veterans used hard drugs, i.e., at least one of the opiates, stimulants or sedatives. The prevalence of hard drug use among the general-sample veterans was still almost twice as high as that among their civilian counterpart.

#### 4.2. Phase I Protocols

At the onset of Phase I, several implementation changes were made. These included sample size increase (see above), expanded death search and VA search, and streamlined contact procedures. These changes resulted in an expansion to multiple tracing sources, including four death searches, several computer searches of VA users, and two on-line services (Trans Union and PhoneDisc). Another consequence of these changes was reliance of location based on our "single exact match" criteria without confirmation with our respondents, because contact was attempted only if computer and record search tracing did *not* yield a reasonable certainty of identity.

#### 4.2.1. Tracing Procedures

Available tracing information from the Original Study include social security number (SSN), full name, date of birth, 1972 or 1974 interview completion, and address and telephone numbers of the respondent and of relatives or friends. Information on 1,268 original subjects was obtained from tracing files. Because of inconsistent information about social security information, a total of 1,261 social security numbers were traced which included 35 dual and invalid social security numbers as well as several dual names (**Table 4**).

Table 4: Social Security Number Information Available from the Original Study

	<u>Veterans</u>	<u>Non-Veterans</u>	<u>Total</u>
Total number of subjects with some information	942	326	1,268
Number SSN's with no interview	40	40	80
Number SSN's with 1972 interview only	344	N.A.	344
Number SSN's with 1972 and 74 interview	566	N.A.	566
Number SSN's with 1974 interview only	N.A.	286	286
Number of subjects traced	945*	281	1,226
Number duplicate SSN's	30	5	35
Number total number SSN's traced	975	286**	1,261

\* Included three additional names and associated SSN's due to name changes and/or SSN changes prior to the 1972 interviews.

\*\* Excludes 40 non-veterans who were not interviewed.

We relied heavily on technologies that only recently became available. Multiple tracing sources were utilized for both tracing and early outcome assessment purposes. Death search included Equifax death search (Decoufle, Holmgren, Calle & Weeks, 1991), VA Beneficiary Identification and Recorded Location System (BIRLS), National Death Index (NDI) and obtaining death certificate. Medical records were searched through VA archives and the Patient Data Exchange (PDX), and other location search using VA benefit files. Two commercial on-line services, Trans Union and PhoneDisc, were also utilized.<sup>3</sup>

The general principle was adapted to employ methods that use unique identifiers whenever possible. Cost consideration nevertheless outweighed logical considerations in some areas. In the interest of time, a few sources were used simultaneously to quickly identify difficult-to-locate subjects. For example, death search was designed to eliminate the deceased from the pool of tracing. However, VA medical utilization and benefit search were performed simultaneously with death search.

A respondent was considered "located" only if a single exact match was obtained for the subject's SSN or exact name with a single accompanying address. This meant that a living respondent was considered "located" with: SSN and address identification through VA tracing; single exact matches via Trans Union with accompanying single addresses; or, single exact matches via PhoneDisc with accompanying single addresses and telephone numbers (Price, Copeland & Murray, 1993).

##### 4.2.1.1. Death Search

Equifax maintains its own database compiled through sources including the Social Security Administration Office. Advantages of Equifax death search included speedy processing and inexpensive fees. Search covered the period from 1955 to 1993. All SSNs (N=1,261 SSNs) were submitted to Equifax. The Identification and Recorded Location System (BIRLS) maintains the records of all veterans for whom death benefits were claimed. ALL SSNs of veterans (N=975 SSNs) were submitted. The National Death Index (NDI) search was used in a different way. NDI's application procedures are complicated, which led to a delay in submission of search cases. Also, fees were expensive, as they are charged per year of search. For these reasons, NDI was used after the results from Equifax and BIRLS were obtained and preliminary location assessment was completed. The cases submitted to NDI included known dead cases with no death certificate, non-located subjects, VA-located subjects with no addresses. Together, 118 SSN's including dual SSNs were submitted. Search was available from 1979 to 1992.

3. Search through the Internet was introduced at the onset of Phase III (Price, Ji & Cooper, 1996).

For each subject identified as dead by any of the above three methods, we requested a death certificate. Some copies of death certificates for those identified by BIRLS were conveniently stored in the Federal Archives Records Center located in St. Louis; others were requested to states where deaths occurred.

#### **4.2.1.2. VA tracing**

The national VA medical records database is located at the Austin Data Processing Center in Austin, Texas. VA researchers have access to this database for research purposes. This tracing source was chosen because it provides information on the location of the hospital the subject utilized most recently. This information in turn was used to request the subject's last known address. In addition, the database contains detailed information on VA medical services utilization nationwide, thus allowing for some outcome assessment for VA medical care users nationwide.

The inpatient service utilization database was available from 1974 to 1992 during Phase I. Output included location of services received, service type and data of admission and discharge. The outpatient service utilization data was available from 1986 to 1992. Date and place of treatment, type of clinic used were among the data available from this database. All veteran SSN's (N=975) were submitted including dual SSNs. VA PDX address search was used in addition to obtain the subjects' last known address individually by accessing on-line to patient records through the VA PDX system. Information was obtained for a total 125 VA patients.

The VA benefit database contains information on veterans who have drawn any benefit during the past three months. The database is updated every three months and the previous database is deleted. An address accompanies each match. This method is more efficient in obtaining current addresses than is the VA medical utilization search.

#### **4.2.1.3. Commercial Tracing**

The SSNs are matched through on-line linkage to the Trans Union national network to obtain names, addresses and telephone numbers. We utilized Trans Union Trace search. A list up to six names and addresses may appear on the Trace report. If the SSN has not been issued by the Social Security Administration, a warning is given. Most names that are different from the subjects' tended to be their relatives. All SSNs of alive veterans and nonveterans eligible for Phase III were submitted.

PhoneDisc search had become available by the time of Phase I start-up when CD-ROM became one of common accessories for personal computer. Two compact disks provided a current telephone directory for the entire United States. Individual names are keyed one at a time to obtain addresses and telephone numbers. Unfortunately, matching criteria include middle or first name initials as well as full names, so that a common last name produced a list of up to several hundred names.

#### **4.2.2. Contact Procedures**

Due to a uncertain prospect for Phase III funding at the time, merits of contacting in Phase I was debated over. Benefits of contact seemed obvious. Contact is the best way to identify the subject. It also permits assessment of cooperation rates. In fact, in certain cases, contacting may be the only way to identify the subject. Nevertheless, disadvantages of premature contact were also several-fold. Some respondents will back off if given time to reflect. This would result in an increased refusal rate or under-reporting to sensitive questions. Another reason against contacting prematurely was that waiting longer than anticipated due to a funding delay will dampen the enthusiasm of cooperative subjects. We could even lose credibility with the subjects if there were a prolonged delay in recontacting. Since contact in Phase I does not guarantee contact at the time of in-person interview in Phase III, it seemed that potential negative impacts of premature contact should be given more weight. After considerable discussion, we have decided to contact the subject only if other tracing sources did not yield reasonable identity, and to proceed contacting subjects within a 10% random sample at a time (Price & Murray, 1994).

A total of 162 fell in the category of "unlocated" according to our criteria. We examined the information obtained from on-line tracing and other tracing data such as the respondents' address and telephone numbers in 1972 and 1974, and addresses and telephone numbers of relatives and friends. Two mailings were attempted, which asked respondents to contact us. Mail contact was followed by telephone contact attempts, and more intensive tracing such as DMV record search and U.S. Postal Services search based on the 1972 and 1974 information were performed if no other leads were available.

#### **4.3. Phase II Protocols**

While Phase I focused on location feasibility, Phase II concentrated on instrumentation and pretest, and further preparation for Phase III, in-person interviews.

### **4.3.1. Instrumentation**

#### **4.3.1.1. Focus Group**

At the onset of Phase II, we held three focus group meetings. Two meetings were held with clients of St. Louis VET Centers (N=9). These clients had varying degrees of problems in the areas of substance abuse, post-traumatic stress disorder (PTSD), interpersonal relations, and employment, among others. The participants were limited to those with demographic characteristics similar to those for our sample veterans. All were male Vietnam veterans between 35 and 50 years of age. A Vietnam veteran who returned from Vietnam in September 1971 will be excluded to avoid the slight chance that the person might be one of the subjects of the original study. Third meeting was held with representatives of veterans' organizations (N=5).

The focus group discussed three topics: substance use and psychiatric problems, perceptions of research, and perceptions about the Vietnam War. These three topics were selected to help guide the instrument development and the procedures for the Phase III main study subject contact and interviewing (Gaebelein, Collins & Price, 1996; **Appendix A, #2**).

#### **4.3.1.2. Measures Used from the Original Study**

The measure used in the original study covered several domains, including substance use and other drug-related variables, war and military service experiences, adjustment problems, and background variables. Four repeated measures are available to span the respondent's life up to the average age of 24 (**Table 5**).

#### **4.3.1.3. Domains and Measures**

Several factors were considered in selecting measures for the main study. The measures available from the original study should be retained as much as possible. However, we needed to incorporate new assessment techniques, as well as update language with contemporary terminology. **Table 6** lists domains, measures and names of instruments.

#### **4.3.1.4. Existing Assessment Instruments**

Several "parent" instruments were selected to adapt and modify for the instruments for the main study.

Substance use and abuse: *The Substance Abuse Module* (SAM) (Robins & Cottler, 1990) allows for a detailed examination of substance use and abuse patterns, including the frequency and quantity of use, route of administration, and onset and recency of each symptom of abuse or dependence for each of 10 classes of psychoactive substances. The reliability of this instrument has been established (Cottler, Robins & Helzer, 1989). The alcohol use section of the NIMH DIS-III-R (Robins, Helzer, Cottler & Goldling, 1989) will be expanded to assess quantity and frequency of alcohol use and abuse.

One challenge we faced was how to best incorporate time dimension to symptom-oriented assessment of the established lay instruments such as SAM and DIS-III-R. When tracing history of episodes of drug use and abuse over two decades, it seems more cognizant to drug user's organization of memory to ask about each specific class of drugs. A disadvantage of type-of-drug oriented assessment, on the other hand, includes repetition of questions, and the length of the instrument.

Table 5: Measures Available from the Original Study

Measures		<u>Pre-Vietnam</u>	<u>In-Vietnam</u>	<u>Up to 1 year after Vietnam (1971-2)</u>	<u>1-3 years after Vietnam (1972-4)</u>
<b>DRUGS:</b>					
Drug use and abuse:	Narcotics	x	x	x	x
	Stimulants	x	x	x	x
	Sedatives	x	x	x	x
	IV use	x	x	x	x
	Marijuana	x	x	x	x
	Other illicit drugs				x*
Alcohol problems		x	x	x	x
Cigarette smoking			x		x*
Urinalysis	Tests		x	x	x
	Knowledge about testing		x		
Treatment		x	x	x	x
Drug availability			x	x	
Drug user networks		x	x	x	x
Attitudes about illicit drug use		x	x	x	x
Drug charges		x	x	x	x
<b>VIETNAM WAR/MILITARY SERVICES:</b>					
War experience			x		
Attitudes about veterans					x
Attitude about Vietnam War					x
Disciplinary actions		x	x	x	
Enlistment		x	-	x	x
VA use		-	-	x	x
<b>ADJUSTMENT PROBLEMS:</b>					
Psychiatric	Depression	x	x	x	x
	Nervous problems	x	x	x	x
Arrest/legal troubles		x	-	x	x
Material possessions					x
<b>BACKGROUNDS:</b>					
Race (invariant)		-	-	x	x
Age		-	-	x	x
Residence		x	-	x	x
Family history		x	-	-	-
Childhood behavioral problems		x	-	-	-
Education		x	-	x	x
Marital status		x		x	x
Employment			-	x	x
Income					x
Children					x*

\* lifetime & last 2 years; - Not asked, but unnecessary information for that particular period.

Post-traumatic stress disorder (PTSD): The prevalence of combat experience as meeting two of three questions (combat patrols or other dangerous duties, surrounded by the enemy and enemy fire) was 59% among the 1974 follow-up veteran cohort (Helzer, 1984). Given this high prevalence, the Phase III follow-up will be suitable for examining the causal relationship between drug abuse and PTS symptoms, as PTSD has been found to be associated with drug and alcohol abuse (Cottler, Compton, Mager, *et al.*, 1992; Breslau & Davis, 1987; CDC VES, 1988a), family history (Davidson *et al.*, 1985), depression (Hendin & Hass, 1991) and social networks (Escobar *et al.*, 1983; Card, 1987). Because PTSD diagnostic criteria were not operationalized until 1980, the Original Study did not assess PTS symptoms. However, incidence of PTS symptoms that originated from combat, or developed after other traumatic events before service or after coming home can be estimated. In addition to PTSD assessment for diagnostic and event purposes, we also plan to use the Mississippi Scale for Combat-Related PTSD, widely used for veteran populations (Keane, Caddell & Taylor, 1988).

Other psychiatric: We planned to use portions of the DIS-III-R created by members in our Department (Price, 1993a). This interview is well validated (Helzer, *et al.*, 1985) and has been used in numerous epidemiological re-

search studies. We exclude sections on somatization, eating disorders, obsessive compulsive disorder, mania, schizophrenia from consideration because the prevalence rates of these disorders are expected to be low among the target sample, based upon reports on general-population epidemiologic studies (Robins & Regier, 1991).

Table 6. In-Person Interview Domains and Measures

<u>Domains</u>	<u>Measures</u>
<u>Substance Use and Abuse:</u>	Marijuana, stimulants, sedatives, prescription stimulants, prescription sedatives, prescription opioids, cocaine, heroin, opioids, PCP, hallucinogens, inhalants, alcohol use, cigarette/tobacco use, other IV use/method of use, level or length of use, recency/onset, withdrawal symptoms, drug charges, attitude about illicit drug use, attitude about drug laws.
<u>Post-Traumatic Stress: Vietnam War/ Military Experiences:</u>	Combat, traumatic and stressful events, PTS symptoms, PTS scale, PTSD. Enlistment, disciplinary actions, service/reserves, attitudes about Vietnam war, attitudes about veterans, affect of war experiences.
<u>Other Psychiatric: Health Care Utilization: Physical Health:</u>	Somatic symptoms, depression, antisocial personality. Recency, type of service, health insurance, drug/alcohol treatment, mental health treatment, VA use, VA program, hospitalization, visit to doctors, doctor's specialty, practice setting, preventive services. General health, physical symptoms, somatic symptoms, alcohol-related symptoms, drug-related symptoms, recency-onset, injury, disability, impairment, hypertension, cardiovascular disorders, cancer, cirrhosis, digestive disorder, skin condition, diabetes, respiratory diseases, vision, deafness, nutrition, infectious diseases, occupational health, skin problems.
<u>Family History:</u>	Family background, siblings, spouses, children, family illness history, family's history of substance abuse/mental health problems.
<u>Social Networks: Life Adjustment:</u>	Drug availability, drug user networks, social relations, influence, support. Education, marital status, employment history, income, material possessions, residential mobility, marital history, parenting history, work adjustment
<u>Crime:</u>	Arrest, conviction, alcohol/drug related arrest, violent actions, alcohol/drug-related offenses, arson, disorderly conduct, motor vehicle violation, theft/fraud, incarceration, concealed weapon, violent crime.
<u>Demographics:</u>	Race, age, current residence.
<u>"Parent" Instruments:</u>	Original Study 1972 Interview; Original Study 1974 Interview; Substance Abuse Module, 1990 (Robins & Cottler 1990; Cottler, Robins & Helzer 1989); Mississippi Scale for Combat-Related PTSD, circa 1987 (Keane, Caddell, Taylor 1988; Kulka et al., 1991); National Survey of the Vietnam Generation, 1987 (Kulka & Schlenger 1986); NIMH Diagnostic Interview Schedule-Version III, Revised, 1989 (Robins et al 1989; Helzer et al 1985); Health Services Questionnaire, 1981 (Shapiro et al. 1985); National Medical Expenditure Survey, 1989; (Edwards & Berlin 1989); Health Interview Survey, 1991 (NCHS 1992); St. Louis Health Study Wave II, 1982; Baltimore Health and Mental Health Study, 1993; National Crime Survey, 1990 (U.S. Department of Justice 1990); National Youth Survey, Wave V, 1989 (Elliot, 1989).

Health care utilization: The original study included a number of questions about drug abuse treatment as well as about VA use for medical and other purposes. We intended to use similar questions for the follow-up. In addition, questions from *Health Services Questionnaire* (HSC) developed for ECA (Shapiro, *et al.*, 1985) and the *National Medical Expenditure Survey* developed by the National Center for Health Services Research (Edwards & Berlin 1989) will also be compared.

Physical health: In conjunction with the health care utilization section, physical illness and symptoms will be assessed. Of interest are outcomes regarding cancer, heart disease and other chronic illnesses associated with heavy cigarette smoking, as well as physical illness associated with alcoholism and drug abuse. We also planned to include questions regarding sexually-transmitted diseases such as hepatitis and HIV.

Family history: Several questions were asked about substance abuse history of the subject's parents in the 1972 interview. For the follow-up main study, we will also include substance use and psychiatric history of the subject's siblings, spouse and children. A section from the *St. Louis Health Study Wave II Questionnaire* (St. Louis ECA, Wave 2) provided a good starting point. Questions were extended to ascertain symptoms about *each* family member.

Social networks: To test the social influence and social support hypotheses, we planned to assess the subject's social relations in addition to family history. We will include questions similar to those asked in 1972 and 1974 to measure drug availability and drug-user networks. We planned to extend previous social network instrumentation protocols (Price 1992, 1994).

Adjustment problems: Measures of other types of life adjustment include education, marital relations, employment income, residential mobility, and work adjustment. Given time-independent nature of these measures,

we planned to incorporate these measures in the life chart assessment.

#### **4.3.1.5. Life History Assessment**

The literature is generally positive about assessment of life history over a long period of time. Three strategies have been examined:

**A chart method:** This is used routinely in medical examination. Using memorable events as clues, such charts help the patient reconstruct the past history. The Baltimore follow-up of the Epidemiologic Catchment Area (ECA) survey extends this method to chart landmark events, marital status and employment (Johns Hopkins University School of Hygiene and Public Health, 1993).

**Year-by-year assessment:** In the St. Louis ECA follow-up, some symptoms were assessed year by year (Washington University Department of Psychiatry, 1993). This strategy is suitable for event history analysis.

**Extended-recency method:** This method extends the recency assessment built into the DIS flow chart (WHO, 1993). The question can be asked starting from the most recent past to the next recent, and so on.

We have decided to employ a chart method similar to the life chart section of the John's Hopkins' ECA follow-up instrument. The chart will be used at the beginning of the interview to elicit major events since 1974 and responses will then be used to increase recall accuracy in subsequent sections. By pairing responses from the chart, we planned then to use the year-to-year assessment methods only for critical dependent variables such as remission and recurrence of drug use. It was unknown, however, if such an assessment can be extended to a duration over a decade. We therefore expected a significant amount of pilot testing on life chart methods.

#### **4.3.2. Pretest Interviews**

##### **4.3.2.1. Pretest subject recruitment**

The pretest subjects were drawn from Metropolitan St. Louis area residents. For clinical samples, we initially planned to ascertain cases from the St. Louis VA Medical Center outpatient clinics. However, with on-going collaboration with St. Louis VET Center initiated first by our focus group meetings, we obtained a majority of clinical cases from St. Louis VET Center, and additionally from East St. Louis VET Center.

To obtain non-clinical veteran samples, several local chapters of veterans organizations were contacted, including American Regions, Disabled American Veterans (DAV), Veterans of Foreign Wars of the United States (VFW), and Vietnam Veterans of America (VVA). Recruitment was facilitated by attending chapter meetings, putting flyers in chapter newsletters and word of mouth. It was decided that pretest of nonveterans was not necessary, as they should not be much different from the general population of this age group.

##### **4.3.2.2. Sample**

We attempted to match the demographic composition of the pretest sample as closely as possible to that of the target sample. The inclusion criteria were: Vietnam veterans, ages 40 years or older, clinically significant drug abuse or psychiatric problems if recruited from VET Centers. The exclusion criteria were current unstable psychiatric conditions, and those who returned from Vietnam in September 1971 to avoid possibly drawing a respondent from the original sample. Altogether 75 subjects were recruited from May 1995 to April 1996. Several more pretests were conducted as part of Phase III, after the instrument was nearly complete.

##### **4.3.2.3. Pretest Procedures**

Each module was developed pretested sequentially as the module development and pretest proceeded. After the Demographic Module was completed, much time was spent on the development and pretesting on the Life Chart Module, the PTSD Module, and the Military Experience Module. The development of the Physical Health Module and Health Care Utilization followed. Family history assessment was divided into the Family History I and Family History II. In addition to PTSD, psychiatric assessment included only depression and antisocial personality due to the length of the interviews. The Substance Use History Module included sections on cigarette, alcohol and each class of drugs specified in DSM-IV.

We decided not to perform extensive data analysis of the pretest material, as numerous revisions of each module made it impossible to draw quantitative results with sufficient power. Instead, focused analyses were carried out to answer conceptual and methodological questions on-going at the pretest stage. For example, the reliability of life chart assessment was examined by test-retest with several subjects; different layout of life chart was tried out to examine the order of questions and grouping of years of assessment. Some of these analyses are presented in the Results section.

## **5. RESULTS**

## 5.1. Phase I

### 5.1.1. Location Feasibility (Aim 1)

#### 5.1.1.1. Assessment of Tracing Sources

Phase I tracing activities took place between June 1993 and January 1994. For the tracing purposes, we considered that matching was "exact" only if the exact SSN, or exact first name, middle initial and last name was matched (a variation of reasonable degree on the first name was allowed). The subject was considered "located" only if a single exact match was obtained for the subject with a single accompanying address. For each of multiple tracing sources we used, the percent of exact match, and the percent of single exact match given an exact match was obtained are presented (**Table 7**).

Table 7: Efficiency of Each Tracing Utilized

	<u>Trans Union</u>	<u>PhoneDisc</u> †	<u>VA inpt.</u>	<u>VA outpt.</u>	<u>VA benefit</u>	<u>Equifax death</u>	<u>VA BIRLS</u>
SSN Sample Size*	1,102	1,099	975	975	975	1,261	975
% Exact match	77.3	64.8	22.8	28.8	9.4	5.4	8.1
% Single exact match out of exact matches**	91.6	27.1	100.0	100.0	100.0	100.0	100.0
% identified or confirmed***	DK	DK	DK	DK	DK	74.0	88.0

\* Sample size different depending on the inclusion criteria; \*\* Percent of exact matches which meets the criteria of single exact match; \*\*\* the denominator is the number that could have been identified, given the search interval and timing of search; † Only procedure by name match.

Of the seven tracing sources tried out, all but PhoneDisc used social security number as the identifier. The results show methods that used social security number are much more efficient than PhoneDisc, which uses names as an identifier, which can be aided by address. With the Trans Union search, the percentage of exact match where the name is identical is 77.3%, although 86.2% of SSNs were matched. A majority of the names different from our subjects appear to be their relatives. Further, more than one exact match was obtained for a small portion in which both SSNs and names were identical. This is possible if the subject had two addresses or if errors were made in entry by a credit company. PhoneDisc results were discouraging given this is one of more commonly used methods to obtain telephone numbers. A major problem with PhoneDisc was overmatching, in particular, for common names.

VA medical records tracing produced records of 222 patients of our sample who were admitted to a VA hospital between 1974 and 1992, and 281 patients who used VA outpatient clinic at least once between 1886 and 1992. The total number of VA medical care users was 329, or 34.9% of the veteran sample after removing dual SSNs. As for VA benefit tracing, 93 of our veterans were matched with the list of benefit receipts for a three-month period prior to September, 1993. The percent of match is lower given the short duration of search.

For death search, we found VA BIRLS death search had a higher success rate than Equifax death search. Nevertheless, about 10% of the dead we know about by now were missed by VA BIRLS. This suggests death search should be pursued with multiple sources. In Phase I, it was not possible to assess the accuracy of addresses or telephone numbers of those identified with the single exact match, because we decided to postpone direct contact for those considered "located".

#### 5.1.1.2. Contact attempts

Further tracing and direct contact attempts were made for 162 "unlocated" subjects between January and July 1994, while additional search for addresses continued into 1995 for those not contacted by July 1994. Of them, 97 (59.9%) were contacted and their identity confirmed. Of confirmed, only a few were hostile or indicated refusals to be interviewed. This Phase I confirmation already showed difference in difficulty of tracing and confirmation: 50.7% of unlocated drug-positive veterans were contacted, compared to 70.7% of drug-negative veterans and 64% of nonveterans (Price, Ji & Cooper, 1996). We felt that the contact rate of 60% was satisfactory, given that these respondents represented a harder-to-locate segment of the sample and tracing at this stage did not involve laborious case-by-case tracing.

#### 5.1.1.3. Overall Location Results

Subjects eligible for inclusion in the Phase III in-person interviews form two groups. The first, Pool 1, consists

of 830 subjects: veterans interviewed in 1972 and 1974 and nonveterans matched with veterans interviewed in 1974. The second, Pool 2, totals 359 and consists of veterans interviewed only in 1972 and unmatched nonveterans interviewed in 1974 (see 4.1.2.). In **Table 8**, 93.8% of the eligible sample of 1,184

**Table 8: Phase I Location Results by Sampling Status**

Phase III Sample	Original Study Sample Status							
	Veterans Interviewed 72 & 74:				Nonveterans:		Total	
Pool 1: N=830	Drug -		Drug +		Matched		N	%
	N	%	N	%	N	%		
Dead	8	(3.0)	35	(11.4)	4	(1.5)	47	(5.7)
Locate (Single Exact Match)*	223	(84.8)	214	(69.5)	208	(80.3)	645	(77.7)
Direct Contact**	22	(8.4)	31	(10.1)	27	(10.4)	80	(9.6)
Total Expected§	262	(100.0)	309	(100.0)	259	(100.0)	830	(100.0)
Pool 2: N=354	Veterans Interviewed 72 only:		Drug +		Nonveterans:		Total	
	Drug -		Drug +		Non-Matched		N	%
N	%	N	%	N	%	N		
Dead	12	(7.9)	31	(17.6)	0	(0.0)	43	(12.1)
Locate (Single Exact Match)*	126	(83.4)	119	(67.6)	23	(85.2)	268	(75.7)
Direct Contact**	10	(6.6)	13	(7.4)	5	(18.5)	28	(7.9)
Total Expected§	152	(100.0)	175	(100.0)	25	(100.0)	352	(100.0)
Ineligible Sample: N=44¶	Veterans Not Interviewed 72:		Drug +				Total	
	Drug -		Drug +				N	%
N	%	N	%			N		
Dead	3	(17.6)	4	(14.2)			7	(15.6)
Alive	11	(64.7)	21	(75.0)			33	(73.3)
Total Expected§	17	(100.0)	27	(100.0)			44	(100.0)
<b>Grand Total</b>	431	(100.0)	511	(100.0)	284	(100.0)	1,226	(100.0)

\* Based on several tracing sources including VA benefits, VA hospital use, Trans Union, and PhoneDisc tracing.

\*\* Includes mailing and telephone contact attempts which resulted in confirmed contact with respondents.

¶ In the veteran target sample for the 1972 study but not interviewed, or interviews not kept (N=2); also includes a drug-status unknown (N=1).

§ The total number of cases expected from the original 1972 and 1974 studies. The data compiled in September 1994, at that time, several misclassification still persisted.

(Pools 1 and 2) have been identified as dead or located with an address through direct contact or according to the single exact match criteria. Of these, 90 were known to be dead at the time of data compilation (September 1994). Of the 1,099 subjects known or presumed at that time to be alive, 92.9% have been located. Excluding known dead cases, location rates for drug-negative veterans is 96.7%, the drug-positive veterans' rate is 90.2%, and the nonveterans' is 93.3%.

Thus, Phase I activities seemed to have yielded results showing the feasibility of successfully conducting in-person interviews. Uncertainties nevertheless existed. These included the accuracy of addresses obtained through the single exact match; availability of the subject's telephone number from a given address; mobility of subjects; and, finally cooperativeness of the subjects once contact is made.

### 5.1.2. Documenting Tracing Procedures (Aim 2)

The Phase I tracing and contact procedures were compiled in two technical reports: one for tracing (Price, Copeland & Murray 1993; see **Appendix A, #3**), and the other for contacting (Price & Murray, 1994; see **Appendix A, #4**). These results shown in these reports were combined with Phase III tracing efforts up to the start of in-person interview fieldwork in June 1996 and were presented at the Annual Meetings of the Problems of Drug Dependence in Puerto Rico, June, 1996 (Price, Ji & Cooper, 1996).

### 5.1.3. Cost Estimates for Phase III (Aim 3)

An obstacle for Phase III in-person interviews rested in the fact the sample members, while modest in size, were distributed in all states of the nation in 1972, since a random sample was drawn from a list of the 1971 returnees at the time of departure from Vietnam. Our preliminary zipcode analysis of addresses obtained from Phase I location assessment showed that 94.9% of the total 873 zipcodes included only one respondent. It would be impossible, therefore, to apply cost estimate formula similar to those based on a typical cluster sampling derived from primary sampling units.

The state information of the addresses of located subjects (N=1,017) was also analyzed to assess the current geographical distribution at the state level (**Figure 1**). The respondents were indeed scattered in all states; however, 86% of fell into 25 of the 50 states. Thus, it appeared that in-person interviews would be financially and logistically feasible. Furthermore, cross-tabulation by sample status showed 93.9% of the Pool 1 respondents resided in these 25 states, and 81.4% of Pool 2 respondents were in the 25 states. Among located drug-positive veterans, 92.9% in the Pool 1 sample resided in the 25 states, compared to 69.3% in the Pool 2 sample. These results indicated that supplementing Pool 1 respondents to reach 830 completed interviews would be minimized without sacrificing cost efficiency. It seemed by allocating telephone interviews to these least dense states will maximize the yield of in-person interviews.

Further analyses of geographical distribution using zipcodes were performed by the National Opinion Research Center, assuming that no new major mobility trends would apply in the Phase III period so that aggregate geographical distribution remains the same. This resulted in dividing the sample into four categories: **a**) "local" cases requiring a maximum of 100 miles round trip; **b**) "circuit" cases requiring an average 200-mile round trip; **c**) long-distance cases requiring a carefully planned trip averaging 500 miles round-trip; and **d**) cases requiring air travel. The *direct* costs for the main study field work was estimated at approximately \$468,000, which, at the time, included completed in-person interviews with 830 original study respondents, hair sample collection for drug testing from all interviewed who consent to collection, and data delivery (Price, 1994).<sup>4</sup>

The Phase III in-person interviews appeared to be financially feasible. Cost considerations for the follow-up main study may have been given more weight than was actually necessary. Our results suggest certain sampling strategies, such as limiting geographical areas for follow-up ascertainment and minimizing interviewer's travel time, may sufficiently curtail the costs for data collection.

## 5.2. Phase II

### 5.2.1. Instrument Development (Aim 4)

The instrument package was completed in Spring 1996. It then underwent cognitive appraisal and final formatting by the Research Triangle Institute (RTI). **Appendix B** includes the VES-III Main Questionnaire, "the Vietnam Era Study Phase III (VES-III). Modules to Assess the Longitudinal Course of Substance use, Psychiatric Syndrome and Health Outcomes", the Supplemental Questionnaire, and Showcard Booklet (Price, Cooper, Virgo, *et al.*, 1996).<sup>5</sup> A Training Manual was also completed at that time. There are a total of 14 modules. Each is described briefly below.

4. At the time of the subsequent funding of VES Phase III (DA09281), the proposed budget was severely cut, which led to substantial rebudget, revision of protocols and reopening the bid for the fieldwork subcontractor. We eventually employed services by Research Triangle Institute.
5. The VES-III Instruments were really the result of collective work. Acknowledgments are due to: Lee N. Robins, Ph.D., Washington University School of Medicine; Constantine Lyketos, M.D., Johns Hopkins University School of Medicine; Gary Collins, LPC, LCSW, St. Louis VET Center; Robert Bellar, M.A., VA Regional Office; John R. Piepho, J.D., Vietnam Veterans of America, Chapter 265; Andreas Muller, Ph.D., University of Arkansas at Little Rock; Monika L. Pohle, B.S., Johns Hopkins University School of Public Health; Wanda Abernathy, Washington University School of Medicine; and Timothy K. Smith, M.A., Research Triangle Institute.

Figure 1. State Distribution of Locates Subjects

Section A. Demographics: This short module ascertains age, race, education, and technical training.

Section B. Family History I: This module ascertains main mother figure, main father figure, age, care and general welfare, their education and work status, parental military experience; each of siblings, age, sex, their age, their living situations; marital status, each of spouses, their education; each of children, sex, age, their living situations. The section overviews most family members of importance. Family Chart is introduced where information about each of the family members is coded. This section fills the first half of the chart. Information in this section is carried into the Family History II. This section also provide some clues to the Life Chart assessment. Some questions were taken from the St. Louis Epidemiologic Catchment Area (ECA) Study.

Section C. Life Chart: This module assess year-to-year history between 1972 and 1996 (present time) of residence (rough address, number of moves); landmarks; memorable events and subjective assessment; relationships (spouses/surrogates; name of spouse, marital status); employment (status, name of employer, industry, occupation). This module is intended for enhancing memory over the period since 1972; to obtain codable information relating to changes in major sphere of their lives; and obtain qualitative information of life events for future event pattern analysis. The module is designed to be least structured of all VES-III modules. The module question portion is used for script purpose. Answers are coded on Life Chart or Work History Chart. The assessment technique is modeled after the Baltimore ECA Follow-up.

Section D. Military Experience: This module assesses experiences in the U.S. Armed Forces. Most questions relate to the Vietnam War. Measures include: active duty, start of duty, enlistment status, branch, duration serving in Vietnam, military occupation, release date, highest rank, discharge status, disciplinary action, places toured in Vietnam, exposure to hostility and dangerous missions, assessment of competency of unit, and trusting people in unit. The module first asks general experience in military, specific experience in Vietnam, then subjective reflection about comrades and effect on their lives. A majority of questions were modified from the National Readjustment Study. Nonveteran matched samples who did not served in military after 1972 will skip out after

one question.

The Mississippi Scale is administered by the respondent after Section D is completed for a in-person interview. The scale consists of 35 five-point items assessing PTSD syndrome developed by Keane. The scale is slated toward assessing PTS related to war experiences.

Section E. Post-Traumatic Stress Disorder (PTSD): The module is designed to assess stressful life events and ask specifically about two worst events for which PTSD symptoms are asked. Measures include: nine types of extraordinary upsetting or frightening events, their connection to war; details of the worst events - description, time, consequences, other victims; assessment of criteria for PTSD for each of two events: four symptom criteria; duration, impairment, and exclusions. The module is a mixture of Kulka's PTSD section and DIS-III-R, with extensive modifications made to suit for our sample. The current version assesses PTSD for only two worst events, one prior to 1972, the other since 1972. All criteria for the new DSM-IV are assessed except exclusion of psychiatric disorders.

Section F. Family History II: This module is used to assess psychiatric history of each of the family members ascertained in Family History I. Measures include depression, alcoholism, psychiatric hospitalization, impairment, suicide attempt, arrest; respondent's living with the person at the time. The Family Chart used in Family History I is used again to code answers to all questions in Family History II. Some questions were derived from the St. Louis ECA.

Section G. Social Networks: This module is intended to assess the respondent's support networks and characteristics of those at the core. Four most important people are ascertained from the spheres of childhood, school, military, veterans' organizations, civic organizations, clubs, work, religious activities, neighbors, social gatherings or leisure activities, other gathering places like bars, pool halls, street, treatment facilities and others. Measures for each of four network members include: gender, age, how long known, when met last time contact, frequency contact, status, what did, illicit drug use, drinking and arrest. This module was modified from Price's Risk Network Assessment (Price & Tayler, 1994).

Section H. Substance Use History: This module assesses use and symptom patterns of nicotine, alcohol and other drugs including marijuana, stimulants, sedative, cocaine, PCP, hallucinogens, inhalants, and others. The module was revised from DIS-III-R and DIS-IV to be more suitable for assessment of over-time patterns, as well to assess the criteria for DSM-IV substance dependence or abuse. The nicotine section includes: ever use, onset, recency, quantity, quitting attempt, withdrawal, and dependence symptoms. Non-users and experimenters will skip out after two questions. The alcohol section includes use since 1972: largest amount, frequency, worst year, social/interpersonal problems, physically hazardous, role obligations, legal problems, increased amount, secure alcohol, forfeit important activities, tolerance, cut down/quit withdrawal, use despite physical/psychological problems, and help seeking. Non-drinkers and sporadic drinkers will skip out after a few questions. The drug section includes ever use, first use, 5+ times use since 1972, years using most, frequency use when most, route of administration, social/interpersonal problems, legal problems, hazardous, craving, tolerance, efforts for drug, increased amount, quite or cut down, withdrawal, reduced important activities, role obligations, physical/psychological problems, and use despite problems. A Drug Chart is used to organize the classes and various names of drugs used. Never-users and 5 or less users since 1972 will skip out for the particular class of drugs. Use patterns and symptoms of dependence or abuse are assessed separately for each class of drugs once meeting the "inclusion" criteria.

Section I. Antisocial Personality (ASP): The module consists of "adult" antisocial behavior questions after age 15. The childhood questions prior to age 15 were omitted since several measures are available from the 1972 interviews. The adult questions include: alias, forfeit role obligations, neglect, vagrancy, recklessness, child neglect, property damage, sealing, weapon, physical assault, remorse, arrest. The onset and recency are coded in the questionnaire, and clusters of behaviors over-time are assessed in chart. The module is revised from DIS-IV to be more suitable for assessing adult antisocial behaviors over-time that might be event-related.

Section J. Physical Health: This module assesses current general health and takes broad medical history. Measures include: current general health and limitation in activities; problems in activities in past 4 weeks; 16 medical illnesses - existence before/in/after Vietnam, last 12 months, use of medication, and hospitalization. The first half of the module was adapted from the SF-36 Survey (Ware & Sherbourne, 1992), a self-administered questionnaire to assess general health conditions; and, the latter half consists of medical charts relating to disorders common among substance abusers.

Section K. Depression: This module assesses symptoms and criteria for major depression according to DSM-IV. Measures include: gateway questions - depressed 2 weeks, lost interest, duration of episode; seven symptom groups - appetite, sleep problems, fatigue, slowness/restlessness, worthless/guilt, death ideation, starting and

ending, worst year; and exclusion and grieving. Our version was modified from the DIS-IV. If symptoms are not met, R will be skipped out for assessment of timing.

Section L. Health Care Utilization: This module is designed to assess recent hospitalization, outpatient visits, and health care and related issues. Measures include: hospitalization in last five years - time, length, condition, operation, location, type of hospital, substance abuse treatment, treatment for psychiatric problems; outpatient visits in past six months - conditions, treatment for substance use, treatment for psychiatric problems, surgery, location, doctor speciality; usual health care - place, type of doctor, how far, waiting time; health care coverage - insurance, smoking program, alcohol program, drug program, mental health program, income; VA related questions - VA contact, disability, pension. Two charts are utilized: one relating to hospitalization and the other relating to outpatient visits. Answers are coded in these charts if the duration criteria are met.

Section M. Hair Sampling: This section describes hair sampling procedures from the head or from other parts of the body. Supplies and procedures are described. The material is adopted from the Psychemic's procedures.

Section N. Interviewer Observations: This section is completed by the interviewer right after the interview or during the editing time. The standard questions are chosen from several sources, including the Composite International Diagnostic Schedule, DIS-III-R, the St. Louis ECA, and instruments used in 1972 and 1974 surveys.

### **5.2.2. Pretest (Aim 5)**

The pretest analyses were conducted as needs for decision making rose to inform the direction of revision. Several examples of such analyses are listed below.

#### **5.2.2.1. Life Chart**

One of the most difficult tasks of instrumentation was to develop the life chart method that can accurately and succinctly capture the respondent's life since 1972. Constantine Lyketsos, M.D., was invited to consult with us on a number of issues (Lyketsos, *et al.*, 1994). The pretest results aided us in making decisions. Some issues resolved by pretest results are as follows:

Year-to-year assessment vs. 5-year block: In addition to a "year-to-year" life chart dated from 1972 to 1995, we also used a "five-year block" version to see if there would be any time saving. We found that time saving was negligible, and that in many cases there was a significant loss of detail in the number of recorded landmark events.

Forward vs. backward assessment: Many of our forward vs. backward pretest subjects have found it easier to talk about landmark events and residences from 1972 forward, as they have Vietnam as a major event in their life histories. Moving linearly backwards in time, the earlier dates have been harder for them to pinpoint. We thus allowed Phase III interviewers to go either way.

Landmark events: We tried a two-column method asking both negative and positive events, and a one-column method letting the respondent elicit the most "memorable" events. Separating to two-columns biased the type of events solicited. We settled on the one-column method with 5-point scale for each event judged by the respondent.

#### **5.2.2.2. Mississippi Scale**

Although our PTSD module assesses all symptoms included in the DSM-IV diagnostic criteria, we felt it was also important to use a simple questionnaire which is widely used for the veteran's populations. The Mississippi Scale and a subscale of MMPI (Keane, Malloy & Fairbank, 1984) were chosen based on their use in earlier Vietnam veteran studies. Because of time constraints, only one could be used. Results of 13 pretests which completed both scales were examined. Between the two scales, 13 symptoms overlapped and there was a consistent agreement between the two scales. Furthermore, remaining symptoms of the MMPI subscale did not appear to be symptoms as defined by DSM-IV criteria. Therefore, we decided to use the Mississippi scale only.

#### **5.2.2.3. PTSD**

One important issue was the number of events solicited for which to diagnose PTSD. It would appear that the more events solicited, the more likely that one of them will lead to a diagnosis. On the other hand, it may be equally likely that if the most traumatic event does not lead to a PTSD, a less traumatic one certainly would not. In the beginning, we ascertained three most traumatic events. Using 10 pretest interviews, a list was compiled which included the number of symptoms for each criteria across three events. We found that adding a third event did not change the diagnosis for all 10 cases. There were a few atypical cases where the symptom number was higher for Event 2 and/or Event 3 than it was for Event 1. However, Event 3 still did not reach the criterion level for the diagnosis in any case. Thus we dropped the third event. Eventually, two events were sequenced so that Event 1 assess the most traumatic event before 1972; Event 2 since 1972.

#### **5.2.2.4. Year-to-Year Symptom Assessment**

We attempted to assess symptom clustering by charting appearance of symptoms between 1972 and 1995. However, we were concerned about the respondent's ability to recall the existence of a specific symptom in a particular year. We found that respondents had difficulties in answering specific years in which specific symptoms of depression occurred. However, respondents rarely had difficulties remembering when their substance abuse problems flared up. The Depression section was therefore reverted back to the recency-onset format; while we pursued year-to-year assessment for the Substance Use History.

## **6. Data Analysis and Dissemination**

### **6.1. Tracing (Aim 6 & 8)**

As mentioned, two technical reports were produced for tracing and contact efforts in Phase I. In March 1996, we began updating the tracing information collected in Phase I. First, WUSM began the new tracing based on the Trans Union, PhoneDisc, 1972-74 information and other sources. Second, the Telephone Survey Unit at RTI began additional searches through their own database and other sources. By May, 1996, we obtained over 1,000 updated addresses, and completed about 720 confirmation calls with the respondents. Power of electronic tracing was even more evident in Phase III than Phase I two years ago. We started an Internet search which was not possible in Phase I. However, as Phase III unfolded, we discovered confirmation was much more difficult than locating whereabouts of the subjects. The results combining Phase I and Phase III tracing were presented at the Annual Meetings of the College of the Problems of Drug Dependence, June, 1996 (see **Appendix A, #5**). The manuscript is currently under revision for a journal publication.

### **6.2. VA Medical Utilization (Aim 6 & 7)**

We examined the utilization patterns of VA inpatient and outpatient services among our 329 veterans who used VA inpatient medical service at least once since 1974, or outpatient clinic since 1986. About 51% of them last visited the VA between 1990 and 1992. We focused on the analysis of utilization of mental health and substance abuse services. The results of inpatient utilization show that 12.4% and 33.8% of all admissions were treated primarily by substance abuse and psychiatric specialists, respectively (**Table 9**); over 52% of admissions treated by substance abuse specialists occurred between 1985 and 1989 (average age over 35 years); and that the cumulative death rate up to 1992 is 15.8% in this subsample. These results were presented at the American Sociological Association Meeting in August, 1993 (Price, Virgo & Copeland, 1993). Outpatient utilization data available between 1986 and 1992 included over 13,000 clinic "stops", which represent approximately 7,400 days of patient visits. In this subsample, over 3,600 clinic stops (27.1%) were made to substance abuse or mental health units over the seven-year period.

Utilization is higher among Pool 2 VA users than among Pool 1 VA users. The mean number of hospitalizations is 1.8 vs. 1.2; the mean number of clinic stops is 53.1 vs 39.6. It appears that utilization for substance use treatment and psychiatric services among our subsample is high, although data are lacking to make exact comparisons with the corresponding age-specific male population, the general veteran population, or the Vietnam veteran population (US Department of Veterans Affairs and Bureau of the Census, 1989).

Table 9: VA Medical Utilizers (N=329) - Number of Services Used by Follow-Up Status

VA Services	Pool 1		Pool 2		All cases	
	Inpt. admss. (N=113)	Outpt. stops (N=142)	Inpt. admss. (N=99)	Outpt. stops (N=130)	Inpt. admss. (N=222)	Outpt. stops (N=281)
Substance abuse	30 (12.1)	793 (14.1)	22 (12.6)	331 (4.8)	55 (12.4)	1,201 (9.0)
drugs	2	544	3	115	5	659
alcohol	18	105	11	49	31	225
unclassified	10	144	8	167	19	317
Psychiatry	78 (31.4)	896 (15.9)	66 (37.7)	1,075 (15.6)	149 (33.8)	2,064 (15.4)
Psychology*	-- --	72 (1.3)	-- --	159 (2.3)	-- --	330 (2.5)
Homeless outreach*	-- --	2 (0.03)	-- --	28 (0.4)	-- --	30 (0.02)
Other <sup>†</sup>	140 (56.6)	3,861 (68.7)	87 (49.7)	5,311 (76.9)	237 (53.7)	9,755 (72.9)
ALL SERVICES	248 (100.0)	5,624 (100.0)	175 (100.0)	6,904 (100.0)	441 <sup>¶</sup> (100.0)	13,380 <sup>‡</sup> (100.0)

( ) Percentages; \* Outpatient services only; <sup>†</sup> Not yet analyzed.

<sup>¶</sup> Total number of admissions for 222 patients.

<sup>‡</sup> Total number of clinic stops made by 281 patients representing 7,378 days of clinic visits.

In March, 1996, Katherine Virgo, Ph.D., VA Consultant, completed updating VA medical utilization for the period of 1993 to 1995 and benefit receipt searches from the most recent VA compilation period. Of all veterans in the Original Study target sample (N=975), 22 were newly admitted to VA hospitals; 59 were new outpatient clinic users. There were 237 hospital admissions during the most recent three-year period, compared to 441 during the previous 19-year period (1974 to 1992); the number of outpatient visit days were 6,500 during the three-year period, compared to 7,400 from the previous seven-year period (1986-1992). These results show VA medical use is increasing rapidly among a subsample of veterans (Price, Ji & Cooper, 1996).

VA utilization data is now being analyzed further in conjunction with the Original Study database. A modified Anderson's model is used to predict inpatient and outpatient VA use from the measures available in 1972 and 1974. The variables measuring the domain of characteristics of population at risk (predisposing, enabling and need factors) were used as independent variables to predict types and quantity of VA services use. Dr. Virgo's analyses show that self-reported substance abuse (alcohol and drug problems) are predictive of both inpatient and outpatient contacts with VA. However, among utilizers, the associations with substance use problems are less significant or nonsignificant. Thus, it appears that early substance use problems significantly predict entry to the VA health care system, but they do not appear to affect how much care they have received. (**Appendix A, #6**). Currently, other confounding variables are examined in the multivariate logistic and linear regression analyses.

### 6.3. Mortality (Aim 6 & 8).

#### 6.3.1. Preliminary Findings

A total of 97 of the original study target samples are known to have died as of December 1993. Differences in death rates across three sampling statuses of the Original Study (Pool 1, Pool 2 and Ineligible combined) are striking. The cumulative death rate since 1971 and 1993 is 13.5% for drug-positive veterans and 5.4% for drug-negative veterans. The cumulative death rate since 1974 is 1.4% for nonveterans. In the veteran target sample, the rate is highest for the ineligible group and lowest for the Pool 1 sample, with the rate for the Pool 2 sample in the middle. This in part reflected initial deaths that occurred after return from Vietnam but before interviews could be conducted. Over 70% of deaths were confirmed by death certificates obtained individually from states of death as of June 1994. No false positives were found. Examination of causes of death from death certificates showed 37% of the drug-positive veterans had alcohol or drug-related causes of death and 14% were found to be homicide victims; results are consistent with other reports showing increased mortality of Vietnam veterans due to drug- and alcohol-related deaths. (CDC VES 1986; Fett *et al.*, 1987) For drug-positive veterans, the hazard rate was found to increase during the mid-30s (Washington University in St. Louis, 1994; Price, Eisen, Virgo, *et al.*, 1994; see **Appendix A, #7, #8**).

#### 6.3.2. Causes of Death

Seth Eisen, M.D., the VA Component P.I., began analysis of causes of death using the MANSON program, provided by a Harvard University School of Public Health. The software utilizes ICD-9 codes for causes of death and compute cause-specific standard mortality rate adjusted for basic demographics (age, race and gender). The analyses show that veterans are not at higher risk for most causes of death compared to the general population, once demographics are adjusted. However, subgroups are significantly at higher risk for dying from causes that are known to be associated with substance abuse, such as cirrhosis of liver among white drug-positive veterans (C.I.=5.43-32.39), infective and parasitic disease for non-white veterans (C.I.=1.43-10.33), and external causes of death among veterans (white C.I.=1.10-2.32, nonwhite C.I.=1.01-2.69) (**Appendix A, #9**). Unfortunately, the number of cases for a specific cause is generally small so that the confidence interval is generally very wide. We are combining causes of death currently and certain categories to produce more stable estimates of odds ratios.

### 6.3.3. Early Predictors of Mortality

Earlier, we had difficulties in solving inconsistencies between the Phase I dataset and the database from the 1972 and 74 studies. Solving these inconsistencies was a laborious but important process because errors in linking wrong individuals between the 1972 & 74 period and the VES follow-up period would be so damaging for any analysis using the combined database. Because no conclusive evidence was available for a few respondents in the Pool 2 and Ineligible samples with multiple names and multiple social security numbers obtained from 1972 study, other pieces of information were needed to resolve inconsistencies. We were able to link all cases finally in late 1995.

We have since then examining the predictive utility of substance use and psychosocial information gathered in the early 1970's for mortality over more than two decades. We introduced the Receiver Operating Characteristic (ROC) method in the logistic and Cox regression to assess the predictive utility of "distal" epidemiologic measures. Five variables were available with minimum missing cases for the target sample of veterans (N=942) and interviewed nonveterans (N=285): age, veteran v.s. nonveteran status, "drug-positive" v.s. general-sample sampling status, enlistment status and race. The ROC analysis with logistic regression yielded the value of the Area Under Curve (AUC) .68 with these five variables, which is considered to fall in a "good" but not an "excellent" range. The predictors in the logistic regression are all significant except the enlistment status. The odds ratios are large: age (metric), O.R.=1.07, C.I.=1.02-1.13; veteran status (vet=1), O.R.=3.39, C.I.=1.10-10.47; drug-positive sampling status (D+=1), O.R.=3.34, C.I.=1.87-6.00; race (black=1), O.R.=2.15, C.I.=1.33-3.48.

The variables from in and after-Vietnam periods were added to the ROC analysis to improve the prediction. However, only veterans could be used for this set of analysis due to availability of measures. Among veterans, no significant predictor from the in-Vietnam period remained in the logistic regression when all periods were pooled, with assessment of ROC area under the curve (AUC) predicting mortality. Overall, in- and after-Vietnam predictors did not contribute much in improving the value of ROC AUC. In fact, the value of ROC AUC was slightly lower than that of the five-variables prediction using the whole sample, owing to the loss of information about nonveterans. It could be that much of variance in the data are captured by the pre-Vietnam predictors, or, that while individual drug use was increased, it added little to long-term mortality. Alternatively, it can be argued that veteran sample was homogeneous with respect to major risk variables such as age, drug and alcohol use. It should be noted that the measures available in the in-Vietnam and after-Vietnam periods were limited to substance use and related peer-influence variables, except in Vietnam period in which combat experience variables were available (**Appendix A, #10**).

### 6.4. Methodological Developments.

The P.I. obtained an Independence Scientist Award (ISA, K02) in October 1994, at the time the one-year continuation was also funded. In conjunction with her K02 methodological enhancement component, the P.I. therefore began pursuing methodological developments using the 1972 and 1974 database and Phase I tracing data. In the below, preliminary work in this area is described.

#### 6.4.1. General Equation Estimation (GEE) Modeling

GEE is an extension of generalized linear models developed specifically for the analysis of longitudinal data. It is a flexible estimation technique that can handle dependent variables of recurring events as well as repeated data points. GEE nevertheless is more suitable for capturing a causal mechanism that is robust over time, since individual changes over time are estimated but treated as a nuisance factor (Andrade, Eaton & Chilcoat, 1994). A workshop was held in the Department of Psychiatry Epidemiology Seminar to get hands-on experience with GEE. Howard Chilcoat, D. Sc., a GEE Consultant currently at Henry Ford University Department Psychiatry, was invited to lead the workshop. We estimated effects on drug problems using measures on alcohol problems, availability of drug using associates, combat experience, and "fixed" measures of adolescent antisocial behavior, military status, age

and race. Since VES-III interview data is not yet available, measures used involved pre-Vietnam, in-Vietnam, post-Vietnam up to 1972, and simulated “current-time” measures assuming a monotonic decay function since 1972. We found that the in-Vietnam “time” variable--which is considered a collection of unmeasured time-specific effects--had the largest effect on drug problems (OR=15.1, CI=7.5-30.5).

The GEE program and SAS IML were installed at that time and we are waiting for an arrival of the Phase III data.

#### 6.4.2. Analyses using Neural-Network (NN) models and Genetic Algorithms (GA)

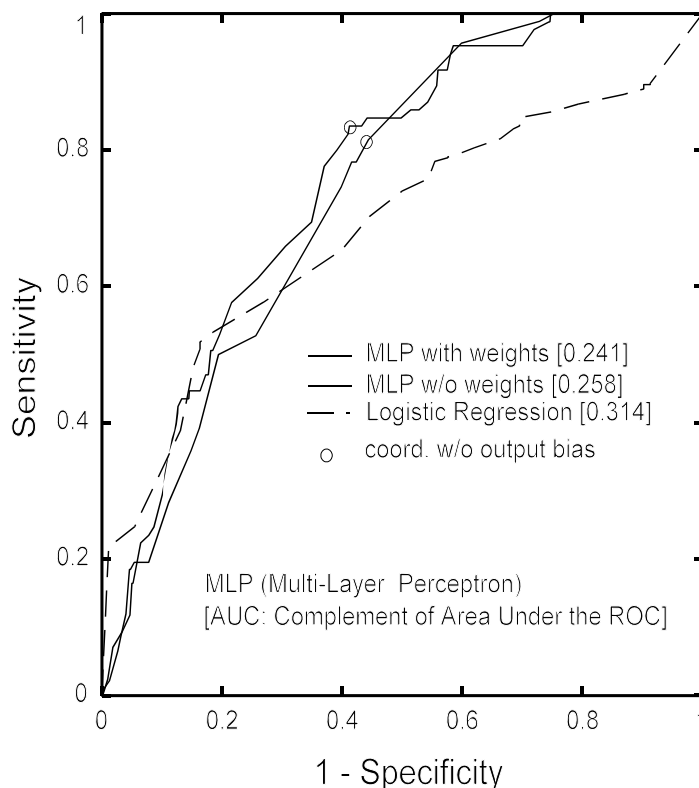
To improve epidemiologic prediction by distal measures, we began introducing more “novel” techniques. These techniques are typically known as “nonparametric”, although models can be considered as quasi-parametric in certain instances. The techniques are widely employed in engineering, computer science and neuroscience with their origin in the development of artificial intelligence. We began experimenting with Neural-network Models (NN) and Genetic Algorithm (GA), because they seem particularly relevant to epidemiologic problems we often encounter such as prediction improvement, and improvement of criteria for variable selection.

**Figure 2** provides results for mortality prediction of produced by the Multi-Layer Perceptron (MLP), the most commonly used NN method, compared to logistic regression using five variables (age, veteran status, urinalysis status, enlistment status and race), which was earlier described (See “Early Predictor of Mortality”). Both MLP and logistic prediction were validated with tenfold cross-validation to avoid biased estimates (if test cases were included in the prediction dataset, the result would be an biased estimate).

The MLP without pattern weighting of errors to propagate back to the iteration process produced the complement of AUC value of .258; with pattern weighting, .241. The logistic regression yielded .314. The value of AUC varies from 0 to .5, therefore, .07 difference of AUC between the MLP and logistic can be interpreted as 14% improvement in prediction. Parametric estimates such as logistic regression’s beta estimates still provide vital information because weights (coefficients) in MLP are uninterpretable beyond one or two hidden neurons.

Several experiments with GA used a subset including veterans’ information (N=898) only. GA was utilized as a search technique for variable selection. An advantage of GA is flexibility for fitness function. In our application, it is defined as the complement of the ROC AUC. From over 1,000 variables in the 1972 database to start, a reduced set of 61 variables was chosen and recoded by reviewing bivariate analyses out of the 123 variables chosen first to evenly encompass three periods of pre-Vietnam, in-Vietnam and post-Vietnam, up to 1972. We performed a series of logistic regressions separately for each time period and picked the best 16 variables (7 pre-V, 5 In-V, 4 post-V) with evaluation of ROC. GA picked the best 16 variables with MLP evaluation for the AUC criteria; MLP was further trained using the best 16 to improve the AUC. We repeated logistic regression on this set of 16 variables. Another experiment consisted of replacing GA with backward elimination with MLP to see which 16 variables would be selected.

**Figure 1**  
Predicting Mortality from 5 variables (N=1227)



**Table 10** shows the variables picked by GA-MLP, and overlaps with the best variables using the backward elimination BE-MLP and those from independent logistic analyses. BE-MLP picked 7 of the GA-MLP's 16 best variables; 5 variables overlapped between GA-MLP and the independent logistic analyses. The significance levels of the logistic  $\beta$  estimates on the 16 variables chosen by the GA-MLP show that several informative variables would have been eliminated, if a narrow significance level had been used for variable selection. IQ, antisocial behavior and arrest are among those which emerged with GA-MLP. These results were presented at the Annual Meetings of the College of the Problems of Drug Dependence in Puerto Rico, June, 1996 (see **Appendix A, #11**).

Newer parametric methods such as GEE and quasi-parametric to nonparametric models such as NN and GA add to the utility of existing standard statistical techniques.

When the causal structure is expected to be complex and of nonlinear nature, these techniques provide additional insights into understanding the data. We have shown that they can also improve prediction considerably, if careful analyses are carried out with a rigorous assessment of outcome prediction. Selection of variables is an important aspect of data analysis. Variables chosen by linear modeling techniques such as backward elimination and forward selection may be substantially different from variables chosen from nonlinear optimization techniques such as GA.

## 7. SUMMARY AND FUTURE DIRECTION

This Final Report focused on activities during the Phase I and Phase II of the Washington University Vietnam Era Study. The report described the specific aims of the first two phases, background of the overall follow-up including the significance of the Original Study, and of the VES follow-up. Phase I and Phase II sample and methods were described, followed main results for each specific aim. The on-going work with respect to data analyses and dissemination efforts included also an expanded effort in the area of methodological enhancement, which utilized the VES database.

The VES-III, in-person interview study, was judged feasible by the Phase I location study. The end product of Phase II, the instrumentation study, was a set of complex interviews. At this time of writing, the Phase III fieldwork is still incomplete. However, enough data, systematic and anecdotal, are available to reflect on the conclusions we have drawn for the Phase I and Phase II activities. Choosing not to contact most sample members in Phase I is still judged appropriate. However, we did find a significant portion of the location information we collected in Phase I became quickly outdated by the time Phase III tracing started. In particular, telephone contact proved challenging than we anticipated. Difficulties in contacting in Phase III were in part responsible for cost over-run resulted in the fieldwork, and for the necessity to continue fieldwork beyond Fall, 1996, to achieve our goal of 850 completed cases.

The instruments have been field-tested in Phase III. As we anticipated, obtaining accurate information about life history over two decades proved to be a challenge for interviewers. However, life chart taking enabled not only rapport building with the respondent, but also understanding of trajectory of the respondent's life, prior to

**Table 10: Variables Selected by GA (N=898)**

Variable	BE's pick with ML	PI's pick With Logistic	Prob. level Logistic $\beta$ 's
Race	X	X	.025
Residence while teens	X		.046
Lived with parents 'til 16		X	.048
GT score (IQ)	X		.483
Pre-Vietnam antisocial behavior			.333
Pre-Vietnam arrest	X		.868
Pre-Vietnam morning drinking	X		.602
Pre-Vietnam drinking binges			.736
Pre-Vietnam drinking need to cut down		X	X
.011			
In-Vietnam Combat scale			.552
In-Vietnam Drinking pattern		X	.443
Post-Vietnam Married			
/live with girlfriend			.797
Post-Vietnam Drug dependency			.937
Post-Vietnam Continued narc use	X	X	.044
Post-Vietnam Used heroin			.855
Post-Vietnam Used codeine			.787

assessment of substance use and psychiatric history. With the combination of life chart and family history sections, the interviewer was able to scan the life of the respondent prior to other assessments. This was attested by several interviews conducted by the P.I. and her coordinator (Cooper, Price, Rivera & Collins, 1996; see **Appendix C, #1**). We speculate that our successful hair sampling (estimated 90 to 95% cooperation rate) may be in part attributable to the nature of our instruments. The respondent, after life chart taking, pretty much opened himself up and did not attempt to conceal information afterwards.

We were also pleased that year-to-year assessment for substance use history has worked well. Our assessment about the respondent's ability to cluster substance use symptoms over two decades appears to still hold, although the judgement must await the completion of Phase III data analysis.

We are still facing a number of challenges. Although the data collection had unanticipated challenges, we feel that we can still meet our ascertainment goal. One of findings that are emerging from the fieldwork is huge differences we are seeing between veterans and nonveterans now that they are at the prime time of their adult life. Our veteran sample turned out to be at a higher-risk than we anticipated perhaps due to the high level of combat experiences of this cohort and the high level of substance abusers at the time of their departure from Vietnam. It appears that even drug-negative veterans may be at higher-risk for alcoholism and psychiatric symptoms than the level expected from general-sample studies of Vietnam veterans, which include older cohorts as well as non-theater veterans.

It may be that substance abusing veterans with significant psychiatric problems including PTSD requires assistance tailored specifically to the type of problems they have. It may be that the available system has not been able to reach this segment of population, even if the established mechanism of care through VA is sufficiently available. Our analysis of PTSD, substance use and health care utilization from the Phase III data will be a first step to confirm speculated unmet needs of our sample and the population this sample represents -- veterans with at a higher risk of substance abuse and psychiatric problems.

As expected, PTSD appears to hold a critical place in the adult course of substance abuse among this population. The P.I. and Naomi Breslau, Ph.D., who has published extensively in the area of PTSD among the general population, are organizing a symposium titled "PTSD and Substance Abuse" for the Annual Meetings of the College of Problems of Drug Dependence, to be held in June, 1997. The symposium will include topics on clinical description, comorbidity, timing issues, genetics and neurobiology. The VES data on 270 cases completed and put in SAS format thus far will be analyzed for this symposium (see **Appendix C, #2**).

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APPLICANT ORGANIZATION Washington University School of Medicine		FROM 5-01-93	THROUGH 7-31-96
TITLE OF PROJECT <i>(repeat title shown in item 1 on first page)</i> Vietnam Veteran Drug User Follow-Up: A Feasibility Study			

(SEE INSTRUCTIONS)

## APPENDICES

### Appendix A: VES Phase I & II Selected Articles and Reports

1. Robins LN. Vietnam veterans' rapid recovery from heroin addiction: A fluke or normal expectation? *Addiction* 1993; 88:1041-1054.
2. Gaebelein C, Collins G, Price RK. Follow-up study tracks veterans after 25 years. *Voice* 1996; 17, 1:32.
3. Price RK, Copeland R, Murray KS. Washington University Vietnam Era Study Phase I (VES-I). Tracing procedures and results to date, 1993 (unpublished technical report).
4. Price RK, Murray KS. Washington University Vietnam Era Study Phase I (VES-I). Contact procedures, 1994 (unpublished technical report).
5. Price, RK, Ji THC, Cooper MH. A follow-up of a national sample two decades later: Tracing in the information age. Presented at the College of Program of Drug Dependence Meetings, San Juan, Puerto Rico, June, 1996.
6. Virgo KS, Ji THC, Price RK. Predictors of VA medical utilization among Vietnam veterans with an oversample of drug abusers. Manuscript under preparation.
7. Washington University in St. Louis. Study finds high mortality rate among Vietnam veterans. *Record*, 1994: vol. No.9.
8. Price RK, Eisen SA, Virgo KS, Copeland R, Murray KS, Robins LN. Vietnam drug users two decades later. I. Mortality results. *Problems of Drug Dependence 1994, Vol II.. NIDA Research Monograph Series 153* (DHHS-NIH95-3883). Washington DC: U.S. Government Printing Office, 1995:204.
9. Eisen SA, Price RK, Lin N. Vietnam drug users two decades later. II. Causes of death. Manuscript under preparation.
10. Price RK, Ji THC. Predicting mortality over two decades: A report based on Vietnam veterans with an oversample of drug users and civilian men. Presented at the Epidemiology Seminar, Department of Psychiatry, Washington University School of Medicine, April 1996 (under preparation).
11. Price RK, Downey TJ, Mayer DJ, Ji THC, El-Ghazzawy OG, Spitznagel EL. Applying the neural-network models to epidemiologic data in substance abuse research. Presented at College of Program of Drug Dependence Meetings, San Juan, Puerto Rico, June, 1996.

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## APPENDICES

### Appendix B: VES Phase III Instruments

Price RK, Cooper MH, Virgo KS, Eisen SA, Kinsey, SK. *The Vietnam Era Study Phase III (VES-III). Modules to Assess the Longitudinal Course of Substance Use, Psychiatric Syndrome and Health Outcomes*, Department of Psychiatry, Washington University School of Medicine, June, 1996

1. Main Questionnaire
2. Questionnaire Supplement
3. Showcard Booklet

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## APPENDICES

### Appendix C: VES Phase III Dissemination Efforts

1. Cooper MC, Price RK, Rivera E. Collins G. Interviews begin for 25-year follow-up study. *Voice* 1996; 17, 3:14-15.
2. Price RK, Breslau N. 1977 CPDD Annual Meeting Symposium Proposal, August, 1996.