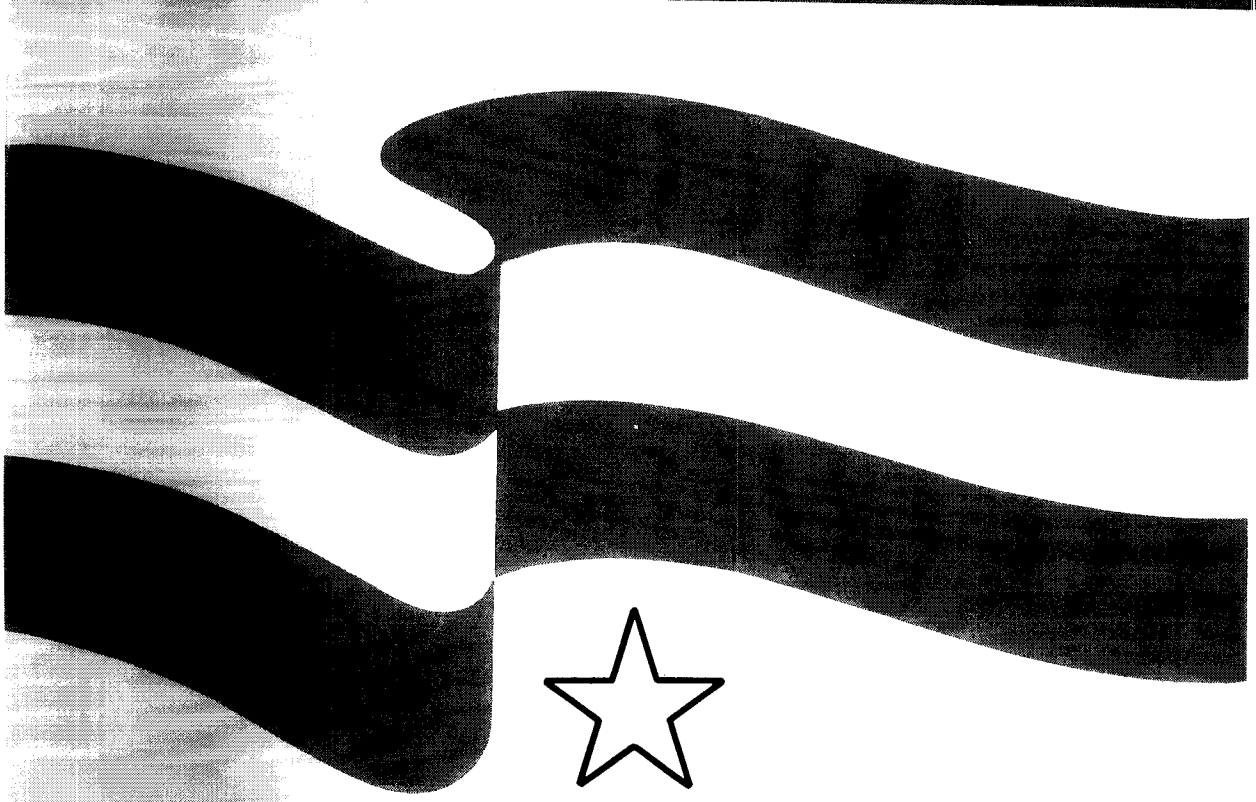

HEALTH STATUS OF VIETNAM VETERANS

VOLUME III
MEDICAL EXAMINATION

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
Centers for Disease Control

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The Centers for Disease Control
Vietnam Experience Study
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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
Centers for Disease Control
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CHAPTER 1

Introduction

1. INTRODUCTION

1.1 BACKGROUND

Many Vietnam veterans believe that they may be at increased risk for a wide variety of diseases as a result of their military service in Vietnam. Until now, little objective evidence has been available on the health of Vietnam veterans relative to the health of other veterans of similar ages and backgrounds. To address the concerns of Vietnam veterans Congress passed two laws mandating the conduct of studies of health effects related to service in Vietnam. In 1979, Public Law 96-151 (Veterans Health Programs Extension and Improvement Act of 1979, [HR 3892], 93 STAT 1092-1098) required that the Veterans Administration (VA) conduct an "epidemiological" study of U.S. veterans to assess the possible health effects of exposure to herbicides and dioxin during the Vietnam conflict. In 1981, Public Law 97-72 (Veterans' Health Care, Training, and Small Business Loan Act of 1981, [HR 34997], 95 STAT 1047-1063) expanded this mandate to include the study of other environmental exposures that may have occurred in Vietnam. In 1983, the Centers for Disease Control (CDC) became responsible for the design, conduct, and analysis of studies responsive to these laws.

The study protocol that CDC developed called for three distinct but related studies (Centers for Disease Control, 1983). The first study, the "Vietnam Experience Study" (VES), is the subject of this monograph, which is entitled Health Status of Vietnam Veterans. The monograph contains five volumes, of which this is Volume III (Medical Examination).

The purpose of the second study, the "Agent Orange Study," was to assess whether adverse health effects could be attributed to herbicide exposure in Vietnam. An initial evaluation of methods for assessing exposure, however, raised questions about proceeding with the study. When we used current levels of dioxin in serum as an indicator of exposure, we found that few Army ground troops had been heavily exposed to herbicides in Vietnam or elsewhere (Centers for Disease Control, 1987). As a result, the proposed Agent Orange Study was not conducted.

The third study, the "Selected Cancers Study," was designed to evaluate Vietnam veterans' risks of contracting six cancers—non-Hodgkin's lymphoma, Hodgkin's disease, soft tissue sarcoma, primary liver cancer, nasal carcinoma, and nasopharyngeal carcinoma—that some investigators have suggested may be related to phenoxyherbicide or dioxin exposure. The results of this study will be published in 1990.

The purpose of the VES is to evaluate the health effects that may have resulted from the "general experience" of having served in Vietnam. Although the major concern about the health of Vietnam veterans has focused on exposure to herbicides, particularly Agent Orange and its dioxin contaminant, the possibility remains that factors in the Vietnam service experience other than herbicide exposure could have affected the subsequent health of Vietnam veterans. Furthermore, Vietnam veterans who did not see active combat in Vietnam may, nonetheless, have been subjected to health-influencing events that were not part of the experience of those who served elsewhere. Thus, the Vietnam "experience' comprises numerous factors in addition to Agent Orange exposure, many of which are unknown, poorly defined, or not quantifiable.

The VES was designed as a retrospective cohort study in which the health of a group of male U.S. Army veterans who served in Vietnam would be compared with the health of a group of male Army Vietnam-era veterans who did not serve in Vietnam. The study has four

major components: (1) a mortality follow-up; (2) a telephone interview; (3) a medical and psychological examination; and (4) an evaluation of reproductive outcomes and child health.

The purpose of the mortality follow-up was to compare the rate of death among Vietnam veterans with the rate among a group of veterans who served elsewhere. The results of the mortality follow-up have been published in a separate monograph (Boyle *et al.*, 1987) and summary article (Centers for Disease Control Vietnam Experience Study, 1987). In brief, over the entire follow-up period through 1983, the postservice mortality in Vietnam veterans was 17% higher than for other veterans. The excess mortality occurred mainly in the first 5 years after discharge from active duty, during which time the excess was about 45% and involved motor vehicle crashes, suicide, homicide, and unintentional poisonings. After the first 5 years, mortality among Vietnam veterans was similar to that of other Vietnam-era veterans, except for the rate of drug-related deaths, which continued to be elevated.

The results of the other three components of the VES are the subject of this monograph, Health Status of Vietnam Veterans. The titles and contents of the five volumes are as follows: Synopsis (Volume I)—a summary of the VES results; Telephone Interview (Volume II)—a comparison of the past and present health status of Vietnam and other Vietnam-era veterans, in terms of various self-reported health outcomes; Medical Examination (Volume III)—the results of the physical health examinations; Psychological and Neuropsychological Evaluation (Volume IV)—the findings from the psychological and neuropsychological evaluations; and Reproductive Outcomes and Child Health (Volume V)—the data on veterans' reproductive outcomes and their childrens' health.

The purpose of the medical and psychological examination component was to provide an objective evaluation of the current health status of Vietnam veterans. The medical, or physical health, evaluation consisted of a comprehensive series of examinations and tests. This broad approach was adopted in order to evaluate the diverse health concerns that Vietnam veterans have expressed and to examine the many health conditions that have been suggested as being associated with Agent Orange or dioxin exposure. A high quality, comprehensive examination was also provided as a service to the veterans, with the view that it would encourage them to participate.

In addition to providing an extensive screening evaluation of the overall health status of the veterans, results of the medical tests also provided a detailed evaluation of certain organ systems that have been suggested as being most affected by dioxin—that is, the dermatologic, hepatic, neurologic, cardiovascular, and immunologic systems.

The many tests performed and the numerous factors that make up the Vietnam "experience" present an almost limitless number of associations that could be evaluated. Before we did the analysis, however, we selected several health outcomes of primary interest. These outcomes, or conditions, have been suggested as being associated with herbicide or dioxin exposure or as being sequelae of other components of the Vietnam service experience, such as combat and stress. The factors in the Vietnam experience are numerous, and many are not well defined. Therefore, we can identify, to only a limited extent, the reasons for any differences in health between the Vietnam veterans and the comparison group.

1.2 OVERVIEW OF PRESENTATION

In the following chapters in this volume (III), we compare the results of the VES medical examination for a group of 2,490 male Army veterans who served in Vietnam with results for

a group of 1,972 Vietnam-era Army veterans who served elsewhere. The contents of the chapters are as follows: Chapter 2—the general study procedures, including selection of the sample and the study design, conduct, and analysis; Chapter 3—the participation rates and characteristics of the study participants. Chapter 4—a broad overview of the general health history of the two groups; Chapters 5 through 13—the detailed findings according to specific organ systems; Chapter 14—a summary of the results of the individual organ system analyses and the key findings from the psychological and neuropsychological examinations (described in detail in Volume IV). In tables in the appendixes to this volume, findings for all medical examinations and tests for both groups of veterans are summarized and compared. Three supplements (A, B, and C) to this monograph contain more detailed information on specific study procedures and the quality of the data. In Supplement A (Laboratory Methods and Quality Control), the procedures and quality control results for all of the laboratory tests are presented. Supplement B (Medical and Psychological Data Quality) contains the results of our analyses of the quality of the data obtained from the medical and psychological examinations and tests. Supplement C (Medical and Psychological Procedure Manuals and Forms) contains copies of the procedures manuals, questionnaires, and data collection forms used in the medical and psychological examinations.

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CHAPTER 2

Study Procedures

2. STUDY PROCEDURES

In this chapter we describe the design, conduct, and analysis methods for the medical examination component of the Vietnam Experience Study (VES). The procedures and methods described are those generally applicable to most, or all, of the organ-specific analyses. Specific study procedures and methods for the examination of a particular organ system are described in the chapter dealing with the organ system.

2.1 COHORT DEFINITION

The primary objective in defining the study and reference groups was to obtain two cohorts that were as similar as possible with regard to major health-influencing factors other than Vietnam service. To increase the likelihood that any differences between the cohorts in mortality or morbidity after discharge were the result of service in Vietnam rather than the result of differences in preexisting health-related factors, we sought the highest degree of comparability. To achieve this objective, we included only veterans who met the following criteria:

a) ***U.S. Army veterans.*** Most military personnel who served in Vietnam were in the Army. Air Force and Navy personnel involved in the conflict were often stationed in other parts of Southeast Asia near Vietnam. Marine Corps personnel were deployed in ways very similar to Army troops, but in smaller numbers, and a high proportion of all Marine Corps personnel of the Vietnam era spent time in Vietnam, thus making it difficult to find an adequately large comparison group of Marines who had not served in Vietnam.

b) ***Male veterans.*** On the basis of the sample size and the selection process described below, too few women would be included for any meaningful conclusions to be drawn about the health of female Vietnam veterans.

c) ***Military occupational specialty (MOS) other than "duty soldier" or "trainee."*** During the early stages of the study, we found that men with behavior or conduct problems were given the military occupational specialty of "duty soldier" (MOS 57A10). The probability of assignment to Vietnam for someone with this MOS may have been based more on the individual's personal characteristics than on his specific training. A military occupational specialty of "trainee" (09B00) indicates that the individual never left basic or advanced training in the United States

d) ***Single term of enlistment in the Army.*** The background characteristics of veterans who reenlisted may be very different from those of veterans who did not reenlist. Further, reenlistment carried with it more opportunity to serve in the country of one's choice. Again, these characteristics may be associated with subsequent health. Because of the method of sample selection, the few men who entered another branch of the military after their Army duty could be included in the study cohort.

e) ***Minimum of 16 weeks of active service time.*** Army regulations stated that servicemen could not be sent to duty stations such as Vietnam until they had completed at least 16 weeks of active service time (U.S. Department of the Army, 1967).

f) ***Pay grade E-1 to E-5 at discharge.*** These paygrades correspond to the ranks of private through sergeant (or specialist 5th class). In many combat specialties the

vast majority of career soldiers had at least one tour of duty in Vietnam This restriction excluded most career soldiers for whom it would have been difficult to identify a comparison group of soldiers who had not served in Vietnam.

g) ***Entered military service for the first time between January 1, 1965 and December 31, 1971.*** This corresponds to the period when a substantial number of single-term volunteer or drafted soldiers were assigned to duty in Vietnam. Before and after this period, most U.S. servicemen in Vietnam were advisors (career enlisted men and officers), who were few in number and who are disqualified for one or more of the criteria given above.

h) ***Duty stations for men in the comparison group limited to the United States, Germany, and Korea.*** On the basis of a pretest conducted by the Centers for Disease Control (CDC) in May 1983, the vast majority of draftees and single-term volunteers who did not serve in Vietnam were assigned to these locations. More importantly, we believed that the assignment process for other countries worked differently than for Vietnam, the United States, Germany, and Korea. Therefore, the background characteristics of those who served elsewhere may be quite different from the background characteristics of those who served in Vietnam, the United States, Germany, or Korea.

To be included in the study cohort of Vietnam veterans, an individual had to have served in Vietnam at any time during his term of enlistment. Although the Army designated 12 months as the normal maximum tour in Vietnam (U.S. Department of the Army, 1967), we placed no minimum time on the actual number of months a veteran had to have served in Vietnam to be included in the study. For example, if a veteran was wounded and served only 4 months of his 12-month tour in Vietnam, he was still included in the Vietnam cohort. A small number of men managed to serve two tours of duty in Vietnam within their term of enlistment. A non-Vietnam veteran had to have served at least one tour of duty in the United States, Germany, or Korea, and to have never served in the Army in Vietnam.

The determination of an eligible veteran's cohort status was based entirely upon information contained in Army personnel files; these records listed the countries in which a veteran had served. Two circumstances led to a recheck of the personnel files of some veterans. This resulted in a change in the original cohort designation of a few medical examination participants. In the first circumstance, the records of 15 veterans originally placed in the Vietnam cohort were rechecked because, when asked questions about their Vietnam service experience during the telephone interview, these veterans stated that they had not served in Vietnam. After their military records were reviewed, one medical examination participant had his cohort designation changed from Vietnam to non-Vietnam; for the other 14, the records indicated that they had served in Vietnam. In the second circumstance, the records of 254 veterans originally placed in the non-Vietnam cohort were rechecked because during the psychological examinations they reported at least one symptom of combat-related post-traumatic stress or at least one combat experience This resulted in six medical examination participants having their cohort designation changed from non-Vietnam to Vietnam. The military records of the other 248 veterans contained no evidence that they had ever served in Vietnam.

Two other independent reabstractions of military records were also performed to determine the accuracy of cohort classification for the study. In the first, all 446 deceased men in

the VES mortality study were found to be correctly classified. In the second, a blind recheck of a systematic sample of records indicated that misclassification of place of service was not a substantial problem.

2.2 SELECTION OF EXAMINATION PARTICIPANTS

Vietnam-era veterans were randomly selected from a set of computer tapes containing "accession numbers," each of which refers to a unique military personnel record on file at the National Personnel Records Center (NPRC) in St. Louis, Missouri. NPRC supplied CDC with a restricted range of about five million accession numbers for U.S. Army veterans whose service records NPRC received between September 1964 and June 1977. NPRC estimated that the vast majority of discharged U.S. Army Vietnam-era veterans would be included in this set.

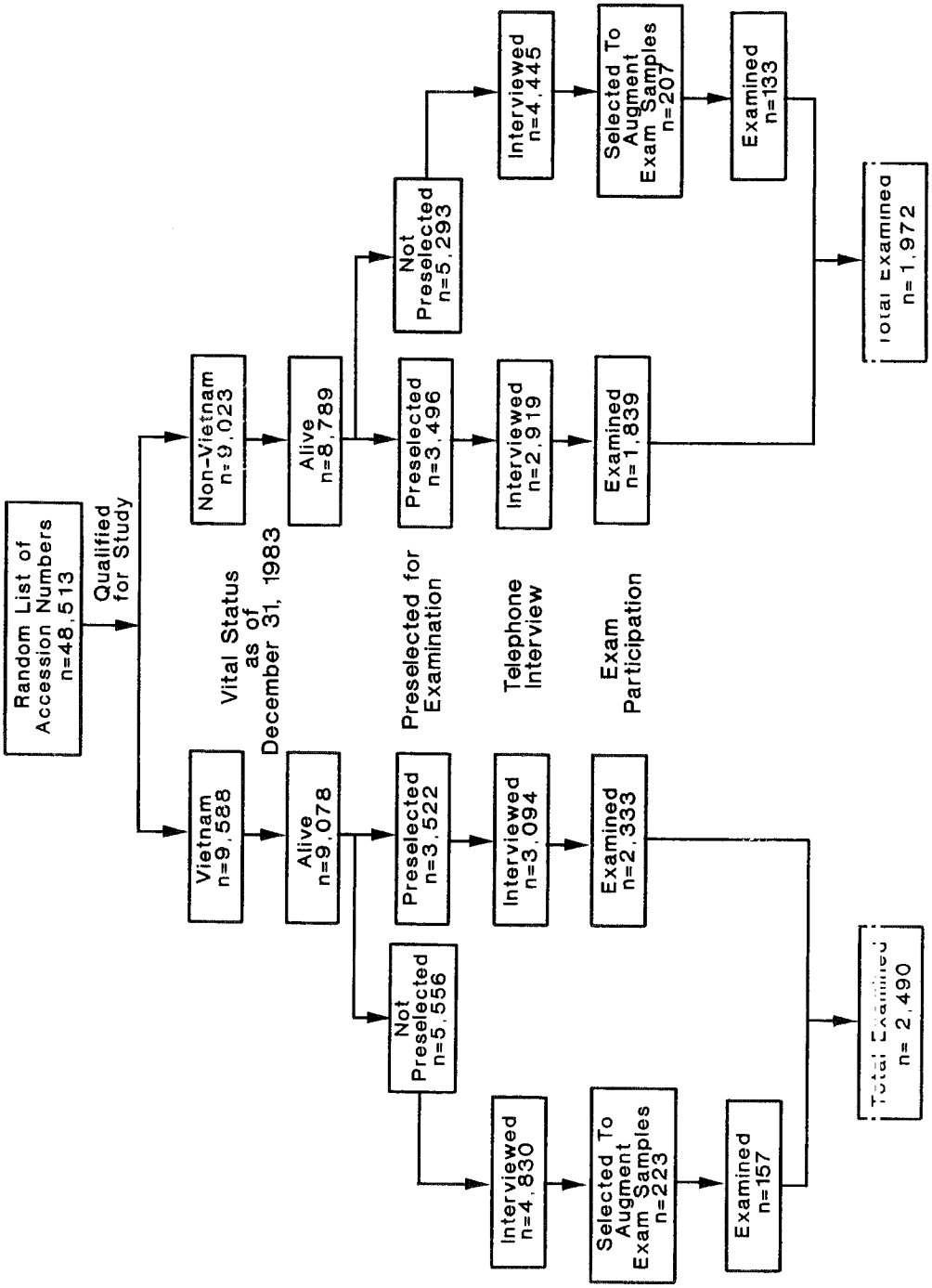
From a pilot test conducted in September 1983, we estimated that about 40% of Army veterans randomly selected from the NPRC files would meet the eight eligibility criteria outlined above and that about half of these would have served in Vietnam. Thus, to identify 16,000 to 17,000 qualified veterans, the required starting sample size was about 43,000 veterans.

A random number-generating program was used to select the sample of about 43,000 accession numbers from the larger group of numbers on file. The sample was split into 12 equal random samples for ease of processing. The decision to disqualify "short-term men" (less than 16 weeks of active service time), "trainees," and "duty soldiers" was made after the original sample had been drawn. To make up for these losses, we added two additional random samples of about 3,500 each to the list originally drawn. Personnel records corresponding to these numbers were pulled and reviewed for the inclusion criteria listed above.

As outlined in Figure 2.1, 99% (N = 48,513) of the random numbers generated corresponded to a unique accession number on the NPRC computer tapes. Of these, 1,355 referred to records that could not be located after several attempts. Apparently, many of these records were missing because of the veteran's subsequent reenlistment after an earlier discharge. Of the 47,158 veterans whose records were located and reviewed, 61% were excluded because they did not meet one or more of the inclusion criteria outlined above, and less than 1% were excluded because information necessary to determine study eligibility or to categorize them with respect to critical factors, such as duty station, was missing. Thus, 18,581 men qualified for the study (9,558 Vietnam and 9,023 non-Vietnam veterans).

Each month for 14 consecutive months, lists containing 3,500 accession numbers were sent to NPRC. NPRC located the corresponding military records (201 files) and sent them to the Army Reserve Personnel Center, formerly known as the Reserve Component Personnel and Administration Center (RCPAC), also located in St. Louis, Missouri. Each file was reviewed there for certain eligibility criteria, and a data abstraction form was initiated. Data abstraction forms and files of veterans who appeared to meet the criteria for the study were forwarded to the U.S. Army and Joint Services Environmental Support Group (ESG) in Washington, D.C., where a second qualification process was completed. Detailed information was then abstracted from the files of those veterans found to be qualified for the study.

Figure 2.1 Flow Diagram of Medical Examination Participation From Sample Selection to Examination



Most of the data for the study were taken from the Department of Defense Form 2314 and Department of the Army Form 20. All data abstraction forms were then sent to CDC for data entry and editing.

The first phase of the tracing and recruitment of eligible study participants was to determine each veteran's current vital status and his most recent address of residence. Several sources were used to determine vital status. In-service deaths were identified during the review of military personnel files to determine study eligibility. Deaths occurring after separation from active duty and the most recent address for veterans not known to have died were identified with the assistance of several Federal agencies. Computer tapes containing the names, social security numbers, and dates of birth of all veterans not known to have died in service were submitted simultaneously to the following agencies:

1. Veterans Administration—Beneficiary Identification and Record Locator Subsystem (BIRLS).
2. Social Security Administration.
3. Internal Revenue Service (through special arrangement with the National Institute for Occupational Safety and Health).
4. National Center for Health Statistics (NCHS)—National Death Index.

Each of these agencies receives notifications (in different degrees of completeness) of deaths and maintains this information in computer-based files. The most recent known address for veterans not known to have died was usually obtained through the files of the Internal Revenue Service.

The next phase in the participant recruitment process was to locate the eligible participants and invite them to participate in a telephone interview. The process of locating, contacting, and interviewing veterans was conducted by Research Triangle Institute (RTI). The details of these procedures are presented in Volume II (Telephone Interview) of this monograph. In brief, to trace the veteran RTI used the following information sources and methods: telephone directory assistance; telephone contacts with veterans; searches of automated credit bureaus; State motor vehicle records; city and town directories, public records and utility records; and contacts with relatives, neighbors, and employers.

In the next phase, a random sample of veterans was selected for the medical examination component of the VES from among those eligible to participate in the telephone interview. The overall goal was to have about 4,000 veterans undergo medical examinations. Names of veterans eligible for the interview component of the VES were grouped at random into 12 lists of about 1,430 each; the final list contained about 700 names. Beginning in January 1985, a new list was sent to RTI on the first day of each month. From each list provided to RTI, some veterans were preselected to be invited to participate in the medical examinations. The number of veterans preselected from each month's list varied, depending on the number needed to reach the target goal of 4,000 examinations. The proportion preselected was adjusted to account for the concurrent interview and examination success rates. On the average, 42% from each list was preselected for examination, with a range from 35% to 50%.

Subsequently, veterans preselected for the examinations who were successfully located and who participated in the telephone interview were invited to participate in the medical examination component. Each eligible veteran was informed at the end of his telephone interview that he had been selected for this examination and that he would soon be receiving more information about it.

Further recruitment and scheduling of participants selected for examinations was conducted by Lovelace Medical Foundation (LMF). On about a monthly basis, CDC provided LMF with a list of names and current locating information on the group of veterans who had been preselected for the medical examination component and who had completed the telephone interview during the previous month.

The information on veterans selected for examination who completed the telephone interview was transmitted electronically from RTI to CDC. Because of technical errors in the transmission process, CDC never received the names of 181 veterans eligible for examination. Since these veterans were not given an opportunity to participate in the examinations, they were, for analytic purposes, considered "not preselected" for examination.

Finally, in addition to the monthly lists of veterans who had been preselected for the examination, in June 1986 an additional 430 names of telephone interview participants who had not been originally preselected for examination were provided to Lovelace. These names were provided to achieve an adequate sample size for an additional test battery, semen analysis, added toward the end of the study (see Chapter 13). The 430 veterans were randomly selected from the last two lists, stratified by cohort status, of eligible veterans provided to RTI for telephone interview.

2.3 SAMPLE SIZE AND POWER

The goal of the examination component was to examine about 2,000 veterans in each of the two cohorts. This sample size was selected to provide good power (beta-error = alpha-error = 0.05, one sided) to detect a twofold increase in relative risk for health outcomes that ordinarily occur at a rate of 1.5%-2.0%. On the basis of Health Interview Survey (HIS) and Health and Nutrition Examination Survey (HANES) data, these outcomes should include such important conditions as ischemic heart disease and diabetes mellitus. For continuous outcome variables, such as the results of most laboratory tests, a sample size of 2,000 per group should be sufficient to detect even modest differences between the two groups.

2.4 EXAMINATION BATTERY

The examination battery for the study was developed after we had consulted with national medical experts in a range of clinical specialties and with several review groups, including the Congressional Office of Technology Assessment, the Agent Orange Working Group Science Panel, and the Advisory Committee on Special Studies Relating to Possible Long-Term Health Effects of Phenoxy Herbicides and Contaminants ("Ranch Hand Panel").

Both the VES and the Agent Orange Study were designed to have a physical examination component. The VES was conducted first because the methods used to select the VES sample were not as difficult or as time consuming as the methods proposed for selecting the Agent Orange Study sample. While the VES was being conducted, a pilot study of Agent Orange exposure assessment indicated that the Agent Orange Study was not feasible and the study was not conducted (see Chapter 1). We had planned to use the same questionnaires and examination procedures for both studies. Thus, some of the tests in the VES were included because they were to be included in the Agent Orange Study, for which the hypothesis was far more specific.

The general approach was to limit the examinations and tests to those that measure current physical health in the simplest and most direct way possible. The selected

procedures were also limited to those that were not invasive or only minimally invasive, such as blood drawing. An initial battery of examinations and tests was evaluated in a pilot study of 147 veterans conducted in April 1985. After reviewing the results of the pilot study, we modified the examination battery in several ways.

The final set of examinations and tests is presented in Table 2.1. The list includes a category of tests that were added after the study began. The protocol outlined that the examination battery could be modified during the study (Centers for Disease Control, 1983). We anticipated that such modifications would be incorporated if results of preliminary data analyses suggested that a certain outcome deserved a more detailed evaluation, or, alternatively, if a more valid test became available for assessing a physiologic function or a specific health outcome. The only major modification of the battery, made near the end of the study, was to add several quantitative tests for an analysis of semen. Semen analysis was added after the early inspection of telephone interview responses indicated that a more

Table 2.1 Examinations and Tests Performed in the Medical Examination Component, Vietnam Experience Study

I. Clinical Examinations
- A. General physical examination
- B. Dermatologic examination
- C. Neurologic examination

II. Special Medical Tests
- A. Chest roentgenogram
- B. Electrocardiogram
- C. Pulmonary function
- D. Doppler evaluation of peripheral vasculature
- E. Hypersensitivity skin test
- F. Nerve conduction velocities
- G. Vibratory sensation
- H. Thermal sensation
- I. Audiometry
- J. Visual acuity

III. Laboratory Tests
- A. Hematologic assays
- B. Serum analytes
  - Blood urea nitrogen
  - Creatinine
  - Bilirubin (total, conjugated, unconjugated)
  - Alanine aminotransferase
  - Aspartate aminotransferase
  - γ-Glutamyl transferase
  - Lactic dehydrogenase
  - Alkaline phosphatase
  - Creatine kinase
  - Total cholesterol
  - HDL cholesterol
  - Triglycerides
  - Total protein
  - Albumin
  - Fasting glucose
  - δ-Aminolevulinic acid
- C. Hepatitis
  - Hepatitis B surface antigen
  - Hepatitis B surface antibody
  - Hepatitis B core antibody

Table 2.1 Examinations and Tests Performed in the Medical Examination Component, Vietnam Experience Study – Continued

D. Endocrine	
	Thyroxine (T4)
	T3 uptake
	Thyroid-stimulating hormone
	Dehydroepiandrosterone sulfate
	Luteinizing hormone
	Follicle-stimulating hormone
	Testosterone
E. Immunology	
	Ig A
	Ig G
	Ig M
	B lymphocytes
	T lymphocytes
	T4 lymphocytes
	T8 lymphocytes
F. Urinalysis	
G. 12-hour Urine	
	Creatinine
	Porphobilinogen
	D-Glucaric acid
	Uroporphyrin
	Heptacarboxyl porphyrin
	Hexacarboxyl porphyrin
	Pentacarboxyl porphyrin
	Coproporphyrin
H. Semen Analysis[a]	
I. Other	
	Erythrocyte sedimentation rate
	Prothrombin time
	Rapid plasma reagin test
	Stool occult blood
	Melioidosis antibody titer
	Breath alcohol level (days 1 and 2)

[a] Performed only during last 5 months of examinations.

detailed and objective assessment of reproductive function would be desirable. Adding these tests was feasible because of recent technological advances in automated semen analysis.

The specific methods used to perform each examination or test are described in the subsequent organ-specific chapters of this volume. In addition, a more detailed description of test procedures can be found in the several supplements to this monograph: the laboratory procedures are described in Supplement A (Laboratory Methods and Quality Control); the procedures for each of the other medical and psychological tests are described in Supplement C (Medical and Psychological Procedure Manuals and Forms).

2.5 CONDUCT OF EXAMINATIONS

The examinations were performed between June 3, 1985, and September 30, 1986, at Lovelace Medical Foundation (LMF) in Albuquerque, New Mexico; LMF performed the examinations under contract with CDC. In addition, LMF was responsible for scheduling the veterans for examinations, arranging their round-trip travel to Albuquerque, and providing their food and lodging during the testing period.

Recruitment and scheduling of participants required both mail and telephone contact with the veterans. An initial mailing was sent to all telephone interview participants preselected for

examination. This mailing explained the purpose of the study, described the tests that would be performed, and provided information about LMF and Albuquerque. The introductory letter stated that examination participants would be given a $300 stipend. The mailing also included a copy of the informed consent document that the veterans were required to sign.

Many veterans responded immediately to the initial mailing by calling LMF themselves to schedule examinations. Others, however, did not respond to the mailing, and LMF contacted them by telephone to request their participation and schedule their examinations. All reasonable efforts, including repeated telephone and mail contacts, were made to schedule as many veterans as possible.

Once a veteran had agreed to participate and had scheduled an examination he was put in contact with travel agents who assisted him in making the necessary travel arrangements. While in Albuquerque, all participants stayed at the same hotel.

The examination schedule required that the participants spend about 4 days in Albuquerque. Participants were examined in small groups of about 20 (range, 3 to 27). Four groups were examined per week, with medical examinations conducted on Monday through Thursday. Typically, participants arrived on the afternoon before their first examination day. Later that afternoon the group of new arrivals attended an orientation session in which testing procedures and schedules were described. At this meeting, participants were requested to sign the informed consent document. The next day, the participants underwent the medical examinations and tests at the Lovelace Medical Center Clinic. The third day, the veterans completed psychological and neuropsychological tests, conducted in a specially designed testing center at the hotel where they were staying. On the morning of the fourth day, the participants had individual meetings with an internist and a psychologist, who reviewed available examination results, discussed the findings with the participants, and suggested additional medical follow-up, as necessary.

To enhance the accuracy of some of the laboratory tests, we asked study participants to follow certain restrictions. Participants were instructed that for the 3 days before their scheduled arrival in Albuquerque they should not eat any red meat, pork, or sweets; drink any alcohol or use any mouthwash; take any multivitamins or vitamin C supplements; or take any nonprescription drugs, such as aspirin, acetaminophen, cold or hayfever medicines, or antacids, unless absolutely necessary. Participants were told to continue taking any drugs or medicines that were prescribed by a physician. Participants were also asked not to start a new exercise program, but they were told that if they were already in a regular program, they could continue it. The participants were also placed on an overnight fast, with only drinking water permitted, beginning at 7 p.m. on the evening before the medical examination day. The fast continued until after their blood was drawn the next morning. During the night before the medical examination day, the participants began collecting a 12-hour urine sample.

Because alcohol use could influence the results of several of the tests, all participants were given a breath alcohol test before the start of the medical examinations and again the following day, at the beginning of the psychological tests. A few study participants had a positive reading on the breath alcohol test, and their other tests were postponed until the breath alcohol test was negative.

2.6 QUALITY ASSURANCE

A great deal of emphasis was placed on obtaining the most accurate information possible and on collecting the information in the same fashion for both cohorts. Minimizing the

possibility of ascertaining health outcomes differentially in the two cohorts was of paramount concern. To ensure that the evaluation of the two groups was as similar as possible, LMF was never provided with information about where any of the participants had served while in the Army. Study participants were instructed not to volunteer information on their place of service to any of the physicians or technicians conducting the tests, and the examiners and technicians were instructed not to ask for such information.

Differential ascertainment of physical abnormalities could also arise if the veterans in one cohort were more likely to volunteer symptoms or health concerns during the examination—thereby causing the examiner to search more diligently for particular abnormalities. To minimize this possibility, we prohibited the examiners and technicians from taking any history from the participants during the examinations and tests; further, they were instructed not to allow the veterans to volunteer such information. Participants provided historical information only when they completed the medical history questionnaire, and the questionnaire information was not shared with any examiners or technicians.

Several methods were used to assure the quality of the data collected. High quality, standardized tests and procedures were employed, in particular those that are accurate and precise, objective, and easily administered on a large scale. To standardize the evaluation, we developed procedure manuals and data collection forms. The manuals outlined a uniform set and sequence of procedures for performing each specific test. Use of the data collection forms assured that information was collected and recorded the same way for each participant.

Only trained and qualified personnel performed the examinations and tests. The general physical, dermatologic, and neurologic examinations were performed by board-certified internists, dermatologists, and neurologists, respectively. Additionally, each physician was trained and certified to perform the examinations specifically designed or adapted for this study. Using standardized examinations ensured that all examination participants were evaluated in a comparable manner, by similar techniques.

Training and study-certification procedures for the three types of medical examiners were similar and involved the following steps. After the content and sequence of a standard examination had been developed, a physician-instructor demonstrated the examination on videotape. This videotape was used to train other examiners in the study. After viewing the videotape, the physician seeking certification was given the opportunity to practice the examination on a volunteer. This physician was then videotaped conducting an examination, and his or her performance was evaluated by three medical specialists who made up the "certification" committee. If his or her taped performance was acceptable, the physician was then observed performing a physical examination on a study participant. The physician was permitted to participate in the study only after he or she had conducted a satisfactory physical examination of a study participant.

All technicians who performed the various medical tests were certified by appropriate professional organizations, if such existed, or met the qualifications established by Lovelace Medical Foundation for technicians who perform the particular test. The training and standardization procedures for the technicians who performed some of the tests that are specific to particular organ systems are described in the methods sections of the appropriate organ-system chapters.

A standardized medical history questionnaire, developed for use in this study, was administered by physician's assistants. The performance of the physician's assistants in

administering the questionnaire was monitored daily by the clinic manager, who would either sit in on an interview or anonymously listen to the dialogue by means of an intercom installed in the interview rooms.

Performance of the examiners and technicians was monitored by both supervisors at LMF and by CDC staff. CDC staff made periodic site visits to the examination facilities to assure that the protocol was being followed and that contractual performance standards were being met.

Repeat testing was another means by which the quality and reproducibility of the tests and examinations were evaluated. About 5% of each of the following examinations or tests were repeated: general physical, dermatologic, and neurologic; audiometry; skin hypersensitivity; pulmonary function; peripheral vascular; visual acuity; and laboratory. The chest x-ray was not repeated but was read again "blindly" by a second radiologist. The results of these repeated tests are presented in the appropriate organ-system chapters and in greater detail in Supplement B (Medical and Psychological Data Quality).

The quality and variability of the data were also evaluated by extensive data quality checks. These included analyses of intertester variability and variation in test results over time. Some of these results are presented in the appropriate organ-system chapters; additional details can be found in Supplement B.

2.7 LABORATORY QUALITY CONTROL

Every effort was made to maintain the accurate identity and integrity of blood and urine specimens during their collection and processing, in order to provide the best quality laboratory data possible. Standardized protocols were developed for the collection and processing of all specimens, as well as for all laboratory test methods and procedures. All laboratory equipment was used strictly for this study and was operated by trained, certified laboratory technicians. To assure that standardized laboratory protocols were followed, two full-time, experienced quality control supervisors carefully monitored the technicians' work. A board-certified clinical pathologist provided overall supervision for the laboratory work.

Laboratory assays were controlled by using both bench and blind control specimens. Most bench control specimens, containing a precisely measured quantity of the substance being analyzed, were purchased from commercial vendors. When such control specimens were not commercially available, analytical standards were made by the Lovelace laboratory, using pooled quantities of urine or serum spiked with a known quantity of the analyte. For the T and B cell immunoassays, fresh blood samples were used; two specimens were drawn daily from a group of volunteer donors. Blind control specimens were obtained by splitting a participant's samples into two vials. One vial was labeled with the participant's identification number. The other vial was assigned a new number that could be referenced back to the participant's identification number. The laboratory technician could not distinguish these repeat samples from others.

In most instances, samples were analyzed on the day the specimen was collected. For all of the laboratory assays there were about 20 participant samples and 1 blind control specimen in each analytical run. Bench control samples were analyzed in duplicate or quadruplicate (depending on the assay) during each run. Bench control samples were interspersed with participant and blind control samples to impose control over the entire analytical run.

Quality assurance was monitored by using a statistical quality control program developed for daily evaluation of data obtained from analysis of the bench and blind control specimens. Quality control charts for run means, run ranges, and successive run ranges (the variation in run ranges on two successive days) were maintained at the bench by the laboratory technician. A run was declared "out of control" if any control value (*i.e.*, run mean, run range, or successive run range) for a given assay fell outside the 95% confidence limits on 2 successive days, or was outside the 99% confidence limits for that day. All "out of control" runs were evaluated for acceptance or rejection by the quality control supervisors or the laboratory director. If a run was rejected, all specimens in that run were reanalyzed.

All bench control data were reviewed weekly by the laboratory quality control supervisors using computer-generated monitoring reports. All bench control data were electronically transferred to CDC weekly and evaluated by CDC statisticians monthly. Data were reviewed for within- and among-day variation (as a measure of analytical precision) and for changes over time (as a measure of systematic error). Abnormal trends and other findings were reported back to the laboratory director, who evaluated the need for corrective action.

In addition to having its own strict internal laboratory quality control program, the Lovelace Clinical Laboratory enrolled in the proficiency testing programs of the College of American Pathologists, the CDC-National Heart, Lung, and Blood Institute Lipid Standardization Program, and the World Health Organization. For proficiency testing, these organizations sent materials of a known quantity to Lovelace. Those at Lovelace were unaware of the precise quantity of substance in the sample. Lovelace then made measurements and reported the values to the testing organizations. Proficiency testing results were then reported to CDC. These indicated that Lovelace's performance met the proficiency criteria of all three testing programs. The only laboratory assays not proficiency tested were those for δ-aminolevulinic acid, porphobilinogen, and D-glucaric acid; they were not tested because materials were not available (few clinical laboratories do these tests). Further details of quality-control procedures, laboratory methods, and the chronologic presentation of bench quality-control data are given in Supplement A (Laboratory Methods and Quality Control). Statistical evaluations of blind control data are given in Supplement B (Medical and Psychological Data Quality).

2.8 DATA COLLECTION AND PROCESSING

The medical examination and the clinical laboratory data were collected and processed separately at Lovelace Medical Foundation. Data from the medical examination (medical history interview and general physical, neurologic, and dermatologic examinations) and clinical tests (electrocardiograms, chest x-rays, nerve conduction studies, vibration and thermal thresholds, Doppler pulse examinations, skin hypersensitivity, auditory and visual acuity) were recorded onto forms specifically designed for data entry. Copies of these forms may be found in Supplement C (Medical and Psychological Procedure Manuals and Forms). During their training and orientation sessions, all medical examiners, interviewers, and clinical technicians were given instructions on how to complete the data entry forms. Forms were completed at the time of the examination. After the forms were completed, a trained data clerk visually reviewed them for completeness and consistency. Any problems identified by the clerk during this review, such as missing or inconsistent responses or responses that

required further clarification, were resolved before the veteran left Albuquerque. After this review, all data forms were placed in a systematic order in each participant's medical record folder.

Next, trained medical records clerks, working under the supervision of a Registered Records Administrator, coded several items that were collected as verbatim responses while the medical history questionnaire was being administered. These "items" included past and current employment, current medical problems, past hospitalizations and surgery, and current medications. For the occupational history, occupation and industry codes were assigned according to the 1980 U.S. Census Bureau system (U.S. Bureau of Census, 1982). Responses given for medical problems, hospitalizations, and surgery were coded according to the Ninth Revision of the International Classification of Diseases, Clinical Modification (U.S. Department of Health and Human Services, 1980). Medications were coded according to the June 1984 update of the Medication Code List (MCL) (Koch, 1982). Later, these MCL codes were converted into National Drug Code Directory class codes (U.S. Department of Health and Human Services, 1985).

For data entry, the records were organized into batches by date of examination and delivered to data entry personnel, who generated computer data tapes. All data were keyed by one data entry clerk and verified during reentry by a second clerk. As the data were entered, on-line data entry programs checked for valid codes and skip patterns. Invalid entries were automatically rejected, and the problem had to be corrected before additional entries could be made. After the data had been entered, the medical records were stored in a secure, fireproof file room, where they remained until data collection was completed.

The partially edited data tapes were sent monthly to CDC for further editing and preparation for statistical analysis. All medical examination data, upon receipt from Lovelace, were edited by using programs that checked each item for valid codes, out-of-range values, and errors in logic or consistency. Listings of edit failures were sent to Lovelace for verification or correction according to the medical record. Corrections were then returned to CDC, where appropriate changes were made in the master data files. After the editing was completed, the medical records were sent to the Federal Archive Record Center (FARC) in Atlanta, Georgia, for microfilming and storage. Later, these records were used to resolve minor discrepancies that were not identified during editing but that were observed during data analysis.

Laboratory data (from standard hematologic assays, T and B lymphocyte quantifications, serum chemistry assays, urinalyses, urine porphyrin measurements, and other selected assays) were processed separately through a mainframe computer used by Lovelace Clinical Laboratory. All laboratory values, after the laboratory director had reviewed and accepted them, were recorded on worksheets from instrument-generated (ticker-tape) printouts. The laboratory technician then entered the values from the worksheets into the mainframe computer via a terminal in an "unverified" mode. A second technician checked the values on the worksheets against the original instrument-generated values and verified the numbers entered into the mainframe. Data were sorted by participant to check for completeness, and then placed on a data tape, which was sent monthly to CDC. These laboratory data tapes were processed and edited like the medical examination data tapes, as previously described. All worksheets and quality control information were subsequently stored at the FARC in Atlanta.

2.9 APPROACH TO DATA ANALYSIS

The goal of the analyses was to obtain valid estimates of the association between service in Vietnam and particular adverse health conditions. These estimates were derived from analyses in which findings for the Vietnam veteran group as a whole were compared with findings for the non-Vietnam veteran group as a whole. Because the health measurements that were performed were so numerous and diverse and because the factors that could have comprised the "Vietnam Experience" were also numerous, an almost limitless number of associations could have been evaluated. To provide focus and coherence to the analyses, we specified, before the analyses, certain conditions as being of primary interest. The conditions were those that have been suggested as being related to dioxin or herbicide exposure or that may have been related to other aspects of military service in Vietnam, particularly combat and stress. Certain other conditions that were reported much more frequently than expected in the health interview were also evaluated in greater detail.

Although certain conditions were selected for more detailed analysis and presentation, basic comparisons of all test and examination results in the Vietnam and non-Vietnam groups are presented in Appendixes A-H to this volume.

2.10 COVARIATES, CONFOUNDING, AND INTERACTION

The selection criteria for the study were established in an effort to assure that the two cohorts would be as nearly similar as possible at the time of enlistment into the Army. Obtaining similar cohorts with regard to future predictors of health was an important objective, and the extent to which we met this goal needed to be thoroughly evaluated. We performed several analyses to make sure that the results were not influenced, or confounded, by differences between the two cohorts in health-influencing characteristics unrelated to military experience.

Analyses were also conducted to determine if certain subgroups of Vietnam veterans might be at different risk for particular conditions. In epidemiologic terms, the purpose of these analyses was to identify if there was any effect modification or interaction. Since we performed a large number of comparisons and tests, we took a conservative approach towards evaluating and presenting such results. Tests for interactions were performed only when the number of cases of a particular health outcome were sufficient to allow stable estimates of interaction. Stratum-specific results are presented only when differences in the measures of association among particular strata were substantive.

A set of six characteristics, or covariates, were specified before analysis as being of primary interest for consideration as potential confounders or effect modifiers. These six covariates are race, age at entry into the Army, year of entry into the Army, military occupational specialty (MOS), enlistment status (volunteer or draftee), and the entry general technical (GT) test score on the Army classification battery. Table 2.2 shows how these covariates were defined and categorized for analysis purposes. By including both age at entry and year of entry into the Army, all adjusted analyses would indirectly account for age at examination.

The six primary covariates were selected for the following reasons:

1. There is a sound basis for suspecting that they may influence health (age, race, GT score) or that they may have been associated with different military experiences or reactions to the experience (age at entry, race, MOS, year of entry, enlistment status).

Table 2.2 Primary Entry Covariates and Associated Categorizations Used in All Multivariate Analyses

Variable	Categories for Analysis
Race	White Black Other
Age at entry into Army, years	<20 ≥20
Year of entry into Army	1965-66 1967-69 1970-71
Primary military occupational specialty (MOS)[a]	Tactical Other
Enlistment status	Draftee Enlistee
General technical (GT) test score[b]	40-89 90-109 110-129 130-160

[a] The job for which the man was trained in the Army. "Tactical operations" includes jobs such as infantryman, armored vehicle crewman, artillery crewman, and combat engineer.
[b] A general aptitude test taken at entry into the service.

2. They may have been associated with different probabilities of assignment to Vietnam (MOS, year of entry, enlistment status).
3. None of them could have been influenced by the military service experience, since they were set before or shortly after enlistment; thus, they could not be considered intermediate variables in the causal chain of any of the health outcomes associated with military service.
4. None of them are subject to differential recall or reporting. The military service characteristics were abstracted from the military personnel files completed during active duty; the race designation, obtained from information supplied during the telephone interview, should not be subject to differential recall.

Although additional information on a veteran's service experience was available from military records, this information was not used to assess confounding or effect modification. This information includes military service characteristics that are intertwined with the service experience, and adjustment for these factors may not be appropriate (*e.g.*, discharge rank, type of discharge, length of service). Adjusting for these types of variables could result in indirectly adjusting for the "exposure" under study (*i.e.*, military service experience).

For the analysis of certain outcomes, we had to consider other covariates as potential confounders. Those under consideration varied, depending upon the outcome. The covariates most frequently included in the various analyses are listed in Table 2.3. Some of these variables could affect risk estimates in a way that makes the interpretation of cohort differences difficult. Acquisition of certain health-influencing behaviors may have been influenced by an individual's particular experiences while in the Army, and, as such, could be considered as an outcome related to military service (*e.g.*, smoking, alcohol use, drug use, postservice education, marital status, occupational status). Alternatively, in other analyses these same behaviors might be considered as intermediate events in the causal chain for subsequent health outcomes (*e.g.*, smoking and cardiovascular disease, alcohol

Table 2.3 Selected Secondary Covariates and Associated Categorizations Used in Multivariate Analyses

Variable	Categories for Analysis
Current alcohol consumption, drinks/month	0-29 30-89 ≥90
Cigarette smoking status	Never Former Current
Current illicit drug use	None Marijuana only Other (including marijuana)
Body mass index, kg/m^2	16-23 24-28 ≥29
Marital status	Never married Married Widowed, separated, or divorced
Current annual income, dollars[a]	<5,000-20,000 20,001-50,000 >50,000
Education, years completed[b]	0-11 12-15 ≥16
Occupational exposure to herbicides[c]	No Yes

[a] Combined family (gross) income for the year immediately preceding the year of telephone interview.
[b] Highest grade or year of regular schooling attained at time of telephone interview.
[c] Employment for at least 1 year in one or more of seven occupations (*e.g.*, farming) with potential exposure to herbicides.

use and liver dysfunction). In our analysis such variables cannot be completely ignored but when risk estimates vary after they have been adjusted for the variables, the adjusted results must be interpreted with caution.

A hypothetical example illustrates how these types of variables are handled in the analysis. Suppose Vietnam veterans are found to have an increased risk of liver dysfunction but also report increased use of alcohol and that after adjustment for alcohol use, the risk estimate for liver dysfunction is no longer elevated. We would not interpret the adjusted estimate as discounting the finding of elevated liver dysfunction among Vietnam veterans. Rather we would interpret the adjusted estimate as indicating that there is a difference in liver dysfunction in Vietnam and non-Vietnam veterans and that the difference seems to be explained by the increased use of alcohol by Vietnam veterans (which, in turn, may have been a consequence of the Vietnam experience). Such a finding would be important in distinguishing the mechanism of the liver disorder.

2.11 STATISTICAL METHODS

Because of the large number of health outcomes being evaluated, we developed a statistical analysis strategy that could be uniformly applied during the evaluation.

Statistical analysis consisted of basic comparisons of the prevalence (for dichotomous outcomes) or mean differences (for continuous outcomes) between the two cohorts. Multiple regression was used to test hypotheses and account for potential confounding and effect

modification associated with selected covariates. Two basic statistical models were used for regression analyses; they are referred to as "Model 1" and "Model 2." Model 1 consisted of variables defining the exposure groups (place of service), the six selected primary covariates described in Section 2.10, and all significant interaction terms between the exposure variable and each covariate. Model 2 included all variables in Model 1, other covariates selected as potential confounders or effect modifiers for particular health outcomes, and all significant interaction terms between the exposure variable and each covariate. The additional covariates included in the Model 2 analyses for a given outcome are described in each specific chapter and are footnoted in the tables in which the results are presented. Stepwise multiple regression (with a combination of forward stepping followed by backward elimination with $p=0.010$ to enter and $p=0.011$ to remove) was used to test for significant interactions (Dixon and Jennrich, 1983; Engelman, 1983). Significant interaction terms, along with all main effects of the covariates, were included in the final statistical model. This model was used to compute estimates and 95% confidence limits.

For dichotomous outcomes, we used multiple logistic regression for statistical modeling (Kleinbaum *et al.*, 1982). The extent of modeling for each outcome was based on the number of cases observed in the combined exposure groups. Guidelines, given in Table 2.4, were determined after we had examined the stability of the regression coefficient associated with the exposure variable at different levels of analysis. The results of logistic regression are presented as odds ratios (ORs) and 95% confidence limits (Kleinbaum *et al.*, 1982). For instance, an OR of 1.3 between the Vietnam and non-Vietnam cohorts can be interpreted as "the odds of having the health outcome is 30% higher for Vietnam veterans than for non-Vietnam veterans." Suppose that the 95% confidence limits about that estimate are 1.1 and 1.5. Intuitively, this interval implies that, with 95% certainty, the true value of the OR falls between 1.1 and 1.5.

When significant interaction terms were present in the final model, ORs and confidence limits were standardized across strata defined by the covariate involved in the interaction (Flanders and Rhodes, 1987; Wilcosky and Chambless, 1985). Standardized values were

Table 2.4 Levels of Analysis Performed To Compute Odds Ratios for Dichotomous Outcomes, by Number of Cases Observed

Number of Cases Observed[b]	Variables[a] Included in Analysis		
		Multivariate	
	Univariate	Model 1	Model 2
0-9	N	N	N
10-24	P	N	N
25-49	P	M	N
50-99	P	M	M
100-149	P	I	M
≥150	P	I	I

[a] N = analysis not done; P = place of service only; M = main effects only, no interaction terms; I = main effects with interaction terms.

[b] Total number of persons with particular health outcome in the combined cohorts.

estimated by using a single model with appropriate interaction terms. The following example illustrates how standardized OR's were calculated:

> Suppose there was a significant interaction between race and cohort status. With the model, an odds was estimated for each of three categories of race (white, black, and other) within the Vietnam and non-Vietnam cohorts. Each odds was then multiplied by a weight based on the proportion of veterans in each racial group for the combined cohorts. (In this case, the stratum weights would be 0.82 for whites, 0.11 for blacks, and 0.07 for other races.) These products were summed across strata for each cohort to yield weighted average odds for each cohort. The ratio of these odds for Vietnam versus non-Vietnam veterans gives the standardized OR.

For continuous outcomes, we used multiple linear regression for statistical modeling (Draper and Smith, 1981). For the most part, continuous variables were either normally distributed or log-normally distributed. Log normal data were transformed before analysis. The results of linear regression of the log-transformed outcomes are presented as the percent difference in the *ratio* of adjusted geometric means and 95% confidence limits. The results of linear regression of the untransformed outcomes are presented as the *difference* between adjusted arithmetic means. Different measures are presented for normal and log-normal distributions because adjusted estimates from multivariate regression analyses have different interpretations, depending on the types of transformation of the dependent variable. For measures with a log-normal distribution, interaction is assessed on a multiplicative scale, and for measures with a normal distribution, interaction is assessed on an additive scale. When the final model contained interaction terms, standardized estimates were computed by using the prediction equation obtained from the regression analysis.

For laboratory and clinical data that were continuously distributed, we compared the two cohorts on the basis of the proportion of laboratory (or test) values in the upper (or lower) tail of the distribution. In these comparisons, we do not imply that the cut point is necessarily of clinical significance; rather, we applied multiple logistic regression analysis to test the odds of having a value in the upper (or lower) tail of the distribution. Because of statistical considerations, we decided to define upper and lower reference values as the 95th and 5th percentiles, respectively, of the measure for the total study population of the two cohorts combined. For each measure, we defined a dichotomous outcome by dividing the participants into two groups (*i.e.*, those with values above and below the reference values), and logistic regression was used for modeling this outcome. Combining the results from logistic regression (*i.e.*, comparison of proportions) with those from multiple linear regression (*i.e.*, comparison of means) may indicate whether the entire distributions are shifted in one direction or the other between exposure groups or whether the difference between groups is only in the upper or lower tail of the distribution.

These approaches to statistical analysis were consistently used for evaluating health outcomes in the study. When alternate methods were used, they are described in the methods section of the appropriate chapters.

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CHAPTER 3

Description of Examination Participants

3. DESCRIPTION OF EXAMINATION PARTICIPANTS

In this chapter, we provide a detailed description of the rates of participation in the Vietnam Experience Study (VES) medical examinations and of factors that may have influenced participation in the two study cohorts. We then compare the characteristics of the examination participants in the two cohorts and note similarities and differences in selected demographic and socioeconomic characteristics.

3.1 PARTICIPATION RATES

Achieving high participation rates is an essential element of any epidemiologic study. High rates of participation are important in assuring that study participants accurately represent the entire study population and in minimizing the possibility that differential participation may have influenced the study findings. Much effort went into maximizing rates of participation in the VES medical examinations. However, as we planned the study, we realized that achieving very high rates of participation might be difficult for two main reasons. First, we anticipated that locating the men would be difficult because of the long time interval—up to 20 years in some cases—that had elapsed since they had been in the Army. Second, we realized that, of those men successfully located and interviewed, many would be unwilling to take the necessary time away from their families and their work and travel the long distances to the examination facility. Given these constraints, the study protocol set a goal of achieving an overall 60% rate of examination among all eligible veterans selected to participate in the examinations.

The study did achieve a 60% participation rate in the medical examinations. As previously indicated (Chapter 2), out of some 18,000 veterans eligible to participate in the telephone interview, a random sample was selected to participate in the examination component of the study. Overall, of the 7,448 veterans selected, 4,462 (60%) participated in the examinations (Table 3.1). The participation rates of the Vietnam and non-Vietnam cohorts, however, were different. Sixty-six percent (2,490/3,745) of the Vietnam veterans participated, whereas only 53% (1,972/3,703) of the non-Vietnam veterans participated in the examinations. In both groups, telephone interview participation rates were high—89% for the Vietnam cohort and 84% for the non-Vietnam cohort. Most of the loss in participation and the greatest differential between the two groups occurred between the telephone interview and medical examination step.

Given the overall participation rate and the differential participation rates between the two groups, factors that may have influenced participation in the two groups need to be carefully evaluated. Fortunately, much information is available from the military records and the telephone interviews that allows comparisons to be made of how examination participants may have differed from the entire eligible sample of potential participants.

Table 3.1 Examination Participation Among Vietnam and Non-Vietnam Veterans at Various Stages From Selection to Examination

	Vietnam		Non-Vietnam		Total	
Stage of Study	**No.**	**%**	**No.**	**%**	**No.**	**%**
Selected for examination	3745	100	3703	100	7448	100
Participated in telephone interview	3317	89	3126	84	6443	87
Participated in examinations	2490	66	1972	53	4462	60

One way to evaluate factors that influenced participation in the examinations is to examine the reasons for not participating. The reasons for not obtaining a telephone interview were similar in both study groups (Table 3.2). Half of those not interviewed simply could not be located. Of those who were located but not interviewed, the interview was not obtained mainly because the participant refused. Only a few participants in each group were incapable of participating in the interview because of a health-related reason. Ten veterans, four Vietnam and six non-Vietnam, had died after December 31, 1983, the date chosen for terminating vital status ascertainment in the mortality component of the VES. Twelve of the Vietnam veterans and fourteen of the non-Vietnam veterans were in jail during the time the VES interviews were being conducted and thus were not eligible to participate.

Among those interviewed by telephone but not undergoing the medical examination, reasons for not participating were similar in the two groups (Table 3.3). Those scheduling examinations at Lovelace Medical Center recorded the veterans' reasons for not participating. The most common reasons were work related. Here are some examples: the veteran could not get leave with pay from his job; the veteran was self-employed and could not afford to leave his job; the veteran was newly employed and could not jeopardize his job. The next most frequent reason for nonparticipation was having no interest in the study. Here are some of the responses: the veteran did not believe participation would benefit him; the veteran did not care about any benefits the study might have for veterans in general; the veteran could not be bothered, was too busy, or felt the study was a waste of time. Personal reasons were also a leading cause for nonparticipation—for example, the veteran did not like to travel; the veteran was suspicious of physicians, the Government, the Army, the Veterans Administration, and the like; the veteran was somewhat bitter about his Army service; the veteran was afraid of undergoing a physical examination. Only a few veterans in either group cited health-related reasons for not participating. Thirty-one veterans in each group gave illness as the first reason for not participating. Two participants in each group died after the telephone interview and before being able to participate in the examination.

In addition to examining reasons for not participating, we evaluated participation rates according to various military history characteristics and according to selected items from the telephone interview. These analyses were conducted to determine if specific characteristics were associated with substantial differences in rates of participation between the two groups and to determine what influence such differences may have had on the characteristics of the examination participants compared with those of all potential participants.

Table 3.2 Reasons for Not Participating in Telephone Interview Among Vietnam and Non-Vietnam Veterans Selected for Medical Examinations

Reason	Vietnam		Non-Vietnam	
	No.	%	No.	%
Unable to contact	250	58	337	58
Refused	157	37	215	37
Prison	12	3	14	2
Deceased after 12/31/83	4	1	6	1
Mental handicap	3	1	4	1
Physical handicap	1	<1	1	<1
Mental institution	1	<1	0	0
Total	428	100[a]	577	100[a]

[a] Sums of percentage values do not equal totals because of rounding.

Table 3.3 Primary Reasons for Not Participating in Medical Examinations Among Vietnam and Non-Vietnam Veterans Interviewed by Telephone

Reason	Vietnam		Non-Vietnam	
	No.	%	No.	%
Work-related	295	36	453	39
No interest	299	37	441	38
Personal reasons	185	22	200	17
Illness	31	4	31	3
Deceased	2	<1	2	<1
Active military duty	4	<1	2	<1
Unknown	11	1	25	2
Total	827	100[a]	1154	100[a]

[a] Sums of percentage values do not equal totals because of rounding.

Military history information, derived from military records completed during active duty in the Army, was available on all veterans who were selected to participate in the medical examination. Most of the military history characteristics did not have much influence on participation rates in either cohort (Table 3.4). For the different categories of year of entry, age at entry, type of enlistment, and race, differences in participation rates varied by less than five percentage points in both the Vietnam and the non-Vietnam cohorts. The military history variables that had the strongest influence on participation were general technical (GT) test score, type of discharge, and rank (pay grade) at discharge. In both cohorts, participation rates increased with increasing GT score and were higher for men with higher ranks at discharge and an honorable discharge status.

The net influence of differences in participation rate on the composition of the examination sample can be appreciated by comparing the distribution of the various characteristics in the sample of men who were examined with the distribution for the entire sample of men selected for examination. Since differences in participation rates according to the military history characteristics were, for the most part, not large, the distributions of military history characteristics for examination participants relative to all veterans selected for examination were similar (Table 3.5). Even for those variables that had the greatest influence on participation rates (type of discharge, discharge rank, general technical test score), the distributions for the examination participants differed little from those for the entire sample of veterans selected for examination.

A great deal of additional information is available from the telephone interviews for determining how the examination participants may have differed from the sample of veterans selected for examination. Although telephone interviews were not obtained from all veterans selected for examination, they were obtained on over 85%. Since the biggest loss in participation occurred between the telephone interview and medical examination step, much is known about the characteristics of most veterans who did not participate in the examinations.

Most of the demographic, socioeconomic, and lifestyle characteristics of the telephone interview participants had only a modest influence on examination participation rates (Table 3.6). In general, these characteristics had similar influences on both study groups. In both groups, the participation rate for blacks was greater than that for whites, and the participation rate for men in the youngest age group was greater than the rate in older age groups.

Table 3.4 Medical Examination Participation Rates Among Vietnam and Non-Vietnam Veterans, by Selected Demographic and Military Characteristics[a]

Characteristic	Vietnam		Non-Vietnam	
	Rate (%)[b]	No.[c]	Rate (%)[b]	No.[c]
Race				
White	67	2185	54	1721
Other	63	303	51	250
Age at Entry				
16-19	67	1300	51	836
20-33	66	1190	55	1076
Type of Enlistment				
Drafted	65	1537	52	1250
Volunteered	69	953	56	632
Primary MOS				
Tactical	67	847	50	439
Other	66	1643	54	1473
Enlistment General Technical (GT) Test Score				
0-89	61	579	50	420
90-109	65	806	48	535
110-129	71	807	57	675
130-160	74	257	65	301
Year of Entry				
1965-66	65	830	54	726
1967-69	67	1399	52	714
1970-71	70	261	55	502
Pay Grade at Discharge[d]				
E1-E3	57	235	45	323
E4-E5	68	2255	55	1619
Type of Discharge[e]				
Honorable	67	2442	54	1812
Other	46	46	41	129

[a] Information obtained from military records completed during active duty.
[b] Percent of eligible veterans selected for medical examination who underwent examination.
[c] Number of veterans with a particular characteristic who participated in the medical examinations.
[d] Grades E1-E3 correspond to the various ranks of private; E4-E5 correspond to ranks of corporal, sergeant, and specialist.
[e] Also called "character of service." Other includes underhonorable, other than honorable, undesirable, general-underhonorable, and dishonorable.

However, only in the Vietnam group was the participation rate lowest in the oldest age group. In both groups, education had a strong influence on participation, with an increase in participation rates with higher levels of education; the increase, however, appeared to be more pronounced in the non-Vietnam group. Income did not show a strong association with participation rates, except for the lowest income category, for which rates were increased in both cohorts. In both cohorts, men who were not currently married tended to be somewhat more likely to participate than men who were currently married. Employment status had little effect on participation rates. In both groups, men who lived in the northeast had the lowest participation rates.

Health-influencing behaviors were also evaluated for their effect on participation rates (Table 3.6). Cigarette smoking was found to have no relationship with participation rates. On the other hand, in both groups the rate of participation increased with the amount of alcohol use reported—although the trend was more marked in the non-Vietnam group. Regular use of illicit drugs also influenced participation rates in both groups. In the two groups,

Table 3.5 Comparison of Characteristics[a] of Vietnam and Non-Vietnam Veterans Selected for Medical Examination With Those of Veterans Undergoing Examination

Characteristic	Proportion (%) With Characteristic			
	Vietnam		Non-Vietnam	
	Selected (N=3745)	Examined (N=2490)	Selected (N=3703)	Examined (N=1972)
Race, White	87	82	87	81
Age at Entry, 16-19 Years	52	52	47	45
Enlistment Status, Drafted	63	62	67	65
Primary MOS, Tactical	34	34	27	25
Enlistment General Technical (GT) Test Score				
0-89	26	23	23	21
90-109	33	32	32	29
110-129	30	32	32	34
130-160	9	10	13	15
Year of Entry				
1965-66	34	33	37	37
1967-69	56	56	39	38
1970-71	10	10	25	25
Pay Grade at Discharge, E4-E5	89	91	81	84
Discharge, Honorable	97	98	91	93

[a] Information obtained from military records completed during active duty.

participation rates differed markedly for men who reported using drugs other than or in addition to marijuana. In the Vietnam group nearly all of these men (96%) participated in the examinations, whereas in the non-Vietnam group only 66% participated.

The modest influence of most of the demographic, socioeconomic, and lifestyle characteristics on participation rates in both cohorts is reflected in the similar distributions of these characteristics among those examined compared with the entire sample of telephone interview participants selected for examination (Table 3.7). The distribution of educational levels was not markedly different, even though educational level was a variable for which participation rates differed the most between the Vietnam and the non-Vietnam cohorts. The effect was largest in the most highly educated non-Vietnam veteran category (those who completed ≥16 years of education), but the increase was only 4%, from 21% in the interview participants to 25% in the examination participants. The prevalence of current cigarette smokers was essentially the same in the interview sample and the examination sample. The prevalence of alcohol consumption was also about the same in the two samples, with only a slightly greater prevalence of heavier drinkers among the examination participants. Current illicit drug use, which had the largest differential effect on participation rates, did not result in a large change in the drug-use distributions of the samples. This reflects the fact that few veterans reported use of drugs other than marijuana.

The health histories reported by telephone interview participants had a notable influence on examination participation (Table 3.8). In general, in both study cohorts some increase in participation rates was associated with most of the reported health conditions. In the Vietnam group, participation rates were higher among those whose self-perceived health status was "fair" or "poor". In the non-Vietnam group, the participation rate was higher for those whose self-perceived health status was "fair", but the few men who reported "poor" health had a lower rate. Within each cohort, the participation rates averaged 5 to 10 percentage points

Table 3.6 Medical Examination Participation Rates Among Vietnam and Non-Vietnam Veterans Who Had Telephone Interviews, by Selected Demographic, Socioeconomic, and Lifestyle Characteristics[a]

Characteristic	Vietnam		Non-Vietnam	
	Rate (%)[b]	No.[c]	Rate (%)[b]	No.[c]
Race				
White	74	2054	62	160
Black	80	286	69	23
Other	79	150	62	13
Age at Telephone Interview				
30-34	79	216	67	32
35-39	75	1853	62	118
≥40	73	421	63	46
Marital Status				
Currently married	74	1821	62	145
Other	80	667	67	51
Education (Years)				
0-11	70	341	54	19
12-15	75	1679	61	127
16-18	81	470	74	49
Employment Status				
Employed	75	2251	63	179
Unemployed	78	238	66	18
Income ($1,000)				
<10	80	244	70	19
10-30	75	1150	63	87
30-50	75	804	63	62
>50	75	244	61	24
Current Residence				
Midwest	78	727	63	57
Northeast	68	408	56	30
South	74	832	64	65
West	79	492	66	40
Foreign	84	31	85	3
Cigarette Smoker				
No	75	1377	64	114
Yes	75	1110	62	82
Alcohol Use (Avg. Drinks/Mo.)				
0-29	73	1308	61	112
30-89	77	687	64	52
≥90	78	460	69	30
Illicit Drug Use (Past Year)				
None	74	2151	62	175
Marijuana only	80	252	75	17
Other	96	75	66	2

[a] Information obtained from telephone interview.
[b] Percent of eligible veterans interviewed by telephone who underwent medical examination.
[c] Number of veterans with a particular characteristic who participated in the medical examinations.

higher for those reporting various medical conditions. The data suggest that, in the non-Vietnam cohort, the following conditions had a slightly greater influence on participation rates: any hospitalizations after discharge from the Army, any physical impairment, benign tumors, history of hepatitis or jaundice, history of liver cirrhosis, and any urinary conditions.

The largest differential effects on participation rates for the health history variables were associated with conditions that were reported infrequently. For example, a history of chloracne resulted in an increased participation rate in the Vietnam group, but a decreased

Table 3.7 Comparison of Demographic, Socioeconomic, and Lifestyle Characteristics[a] of Vietnam and Non-Vietnam Veterans Selected for Medical Examination and Interviewed by Telephone With Those of Veterans Undergoing Examination

	Proportion (%) With Characteristic			
	Vietnam		Non-Vietnam	
Characteristic	Interviewed (N=3317)	Examined (N=2490)	Interviewed (N=3126)	Examined (N=1972)
Race				
White	83	82	82	81
Black	11	11	11	12
Other	6	6	7	7
Age at Telephone Interview				
30-34	8	9	15	16
35-39	74	74	61	60
≥40	17	17	23	23
Married	75	73	75	74
Education (Years)				
0-11	15	14	12	10
12-15	68	67	67	65
16-18	17	19	21	25
Unemployed	9	10	9	9
Income ($1,000)				
<10	9	10	9	10
10-30	46	46	44	44
30-50	32	32	32	32
>50	10	10	13	12
Current Residence				
Midwest	28	29	29	29
Northeast	18	16	17	16
South	34	33	33	33
West	19	20	19	20
Foreign	1	1	1	2
Cigarette Smoker	45	45	43	42
Alcohol Use (Avg. Drinks/Mo.)				
0-29	54	53	58	57
30-89	27	28	26	27
≥90	18	18	14	15
Illicit Drug Use (Past Year)				
None	88	86	91	89
Marijuana only	10	10	7	9
Other	2	3	1	1

[a] Information obtained from telephone interview.

participation rate in the non-Vietnam group. However, so few men had a history of chloracne that they would not be expected to have much of an influence on the other medical examination findings. A history of a malignant cancer was also associated with an increased participation rate in the Vietnam group, but not in the non-Vietnam group. Again, very few men had a history of malignant cancer.

Several of the important medical conditions reported during the telephone interview had essentially no effect on the participation rate in either group. These conditions included: gastric or peptic ulcer, hypertension, fertility difficulties, and current use of medications.

The higher participation rates among those reporting certain medical conditions did not markedly alter in either cohort the prevalence of these conditions among those examined compared with those selected for examination and interviewed by telephone (Table 3.9). In

general, the prevalence of most of the conditions tended to increase on the order of one or two percentage points at the most. More importantly, prevalence ratios for the Vietnam group relative to the non-Vietnam group were not appreciably changed in the examination sample compared with the interview sample. For nearly all the conditions, the prevalence ratios remained the same or changed only by 0.1. For example, the prevalence ratio of fair-to-poor perceived health was 1.7 in the interview participants and 1.8 in the examination participants. Similarly, the ratio for any hospitalization since discharge remained at 1.1 for those interviewed and those examined, and the ratio for any physical impairment only changed from 1.2 to 1.1.

The conditions that showed the largest change in prevalence ratios were relatively rare conditions. For any malignancy, the prevalence ratio increased from 1.1 in the interview sample to 1.4 in the participant sample, the ratio for history of liver cirrhosis decreased from 1.4 to 1.2, and for history of chloracne the ratio increased from 4.3 to 4.8. Even for these conditions, the changes were not great, and since the conditions are rare, the effect on other examination findings is likely to be small.

Table 3.8 Medical Examination Participation Rates Among Vietnam and Non-Vietnam Veterans Who Had Telephone Interviews, by Selected Medical History Characteristics[a]

	Vietnam		Non-Vietnam	
Medical History Characteristic	**Rate (%)[b]**	**No.[c]**	**Rate (%)[b]**	**No.[c]**
Perceived Health Status				
Excellent	73	764	63	335
Good	74	1219	62	911
Fair	80	428	69	193
Poor	80	77	61	33
Hospitalized in Army				
No	73	1362	61	1302
Yes	77	1113	67	535
Hospitalized Since Discharge				
No	73	1200	59	996
Yes	77	1286	68	874
Counseling for Drug, Alcohol, Emotional Problem (Past Year)				
No	74	2155	62	1777
Yes	83	333	74	193
Admitted to Treatment Program for Drug, Alcohol, EmotionalProblem (Past Year)				
No	75	2395	63	1816
Yes	85	94	71	56
Any Physical Impairment				
No	74	1817	61	1494
Yes	79	670	69	476
Current Medication Use				
No	75	2004	62	1518
Yes	77	486	66	354
Hypertension				
No	75	1837	63	1547
Yes	77	651	63	424
Malignant Cancer (Since Discharge)				
No	75	2440	63	1944
Yes	89	47	62	28

Table 3.8 Medical Examination Participation Rates Among Vietnam and Non-Vietnam Veterans Who Had Telephone Interviews, by Selected Medical History Characteristics[a]

Medical History Characteristic	Vietnam		Non-Vietnam	
	Rate (%)[b]	No.[c]	Rate (%)[b]	No.[c]
Benign Growth (Since Discharge)				
No	74	1951	62	1578
Yes	80	534	70	393
Diabetes				
No	75	2444	63	1941
Yes	81	46	70	30
Any Skin Conditions (Since Discharge)				
No	72	1642	62	1520
Yes	81	847	69	452
Chloracne				
No	75	2425	63	1963
Yes	84	48	54	7
Gastric or Peptic Ulcer				
No	75	2192	63	1773
Yes	77	290	64	193
Hepatitis or Jaundice				
No	75	2330	63	1864
Yes	78	158	72	106
Liver Cirrhosis				
No	75	2469	63	1961
Yes	82	18	73	11
Urinary Condition (Since Discharge)				
No	74	2068	62	1664
Yes	79	420	70	307
Fertility Difficulty				
No	74	1940	63	1657
Yes	78	544	61	309

[a] Information obtained from telephone interview.
[b] Percent of eligible veterans interviewed by telephone who underwent medical examination.
[c] Number of veterans with a particular characteristic who participated in the medical examinations.

As part of the telephone interview, participants were asked a series of questions on neurological or muscular symptoms that they may have had during the 4 week period before the interview. For the most part, the influence of these symptoms on participation rates was similar to that generally seen for the medical history characteristics (Table 3.10). In both groups, there tended to be increased participation by veterans who had experienced the symptoms, and in both groups this influence was similar for most specific symptoms. The prevalences of all the neurological or muscular symptoms were similar in the examination sample compared with the entire sample of telephone interview participants selected for examination, with only a slight increase in prevalence among those examined (Table 3.11). All the prevalence ratios remained essentially the same.

In both cohorts there was an observed association between having certain psychological symptoms during the 6 months before the telephone interview and participating in the medical examinations (Table 3.12). The symptoms were related primarily to stress, anxiety, depression, memory, and concentration. For all symptoms, there was increased participation by veterans who experienced these symptoms frequently compared with those who experienced such symptoms infrequently. In general, the increase in participation rates

Table 3.9 Comparison of Medical History Characteristics[a] Among Vietnam and Non-Vietnam Veterans Selected for Medical Examination and Interviewed by Telephone With Those Among Veterans Undergoing Examination

	Proportion (%) With Characteristic				Prevalence Ratio	
	Vietnam		Non-Vietnam		Vietnam/Non-Vietnam	
Medical History Characteristic	Interviewed (N=3317)	Examined (N=2490)	Interviewed (N=3126)	Examined (N=1972)	Interviewed	Examined
Perceived health status fair or poor	19	20	11	11	1.7	1.8
Hospitalized in Army	44	45	32	34	1.4	1.3
Hospitalized since discarge	50	52	46	49	1.1	1.1
Counseling for drug, alcohol, emotional problem (past year)	12	13	8.4	9.8	1.4	1.3
Treatment for drug, alcohol, emotional problem (past year)	3.3	3.8	2.5	2.8	1.3	1.4
Any physical impairment	26	27	22	24	1.2	1.1
Current medication use	19	20	17	18	1.1	1.1
Hypertension	26	26	22	22	1.2	1.2
Malignant cancer (since discharge)	1.6	1.9	1.4	1.4	1.1	1.4
Benign growth (since discharge)	20	21	18	20	1.1	1.0
Diabetes	1.7	1.9	1.4	1.5	1.2	1.3
Any skin conditions (since discharge)	32	34	21	23	1.5	1.5
Chloracne	1.7	1.9	0.4	0.4	4.3	1.8
Gastric or peptic ulcer	11	12	10	10	1.1	1.2
Hepatitis or jaundice	6.1	6.4	4.7	5.4	1.3	1.2
Liver cirrhosis	0.7	0.7	0.5	0.6	1.4	1.2
Urinary condition (since discharge)	16	17	14	16	1.1	1.1
Fertility difficulty	21	22	16	16	1.3	1.4

[a] Information obtained from telephone interview.

among symptomatic veterans was similar in the two cohorts. However, the data suggest that the feeling that "life is meaningless" may have had a relatively stronger influence on participation rates in the non-Vietnam cohort.

Although in both cohorts there was increased participation among those who reported frequently experiencing psychological symptoms, the prevalences of men who experienced the symptoms more frequently were not greatly different between those examined and those interviewed by telephone (Table 3.13). For almost all psychological symptoms and in both cohorts, the prevalence of participants in whom symptoms occurred frequently was higher in the examination sample than in the interview sample, but the increase was modest—on the order of one to three percentage points at the most. The prevalence ratios for most of the symptoms were virtually unchanged. The largest change was for the feeling that life is meaningless, for which the prevalence ratio decreased from 2.0 to 1.7.

Attitudes, feelings, and memories regarding the Army also affected participation rates in both groups (Table 3.14). In both groups, negative or unpleasant feelings or memories about the Army tended to result in increased participation rates. Even though those with the least favorable attitude toward or memories of the Army were more likely to participate, the