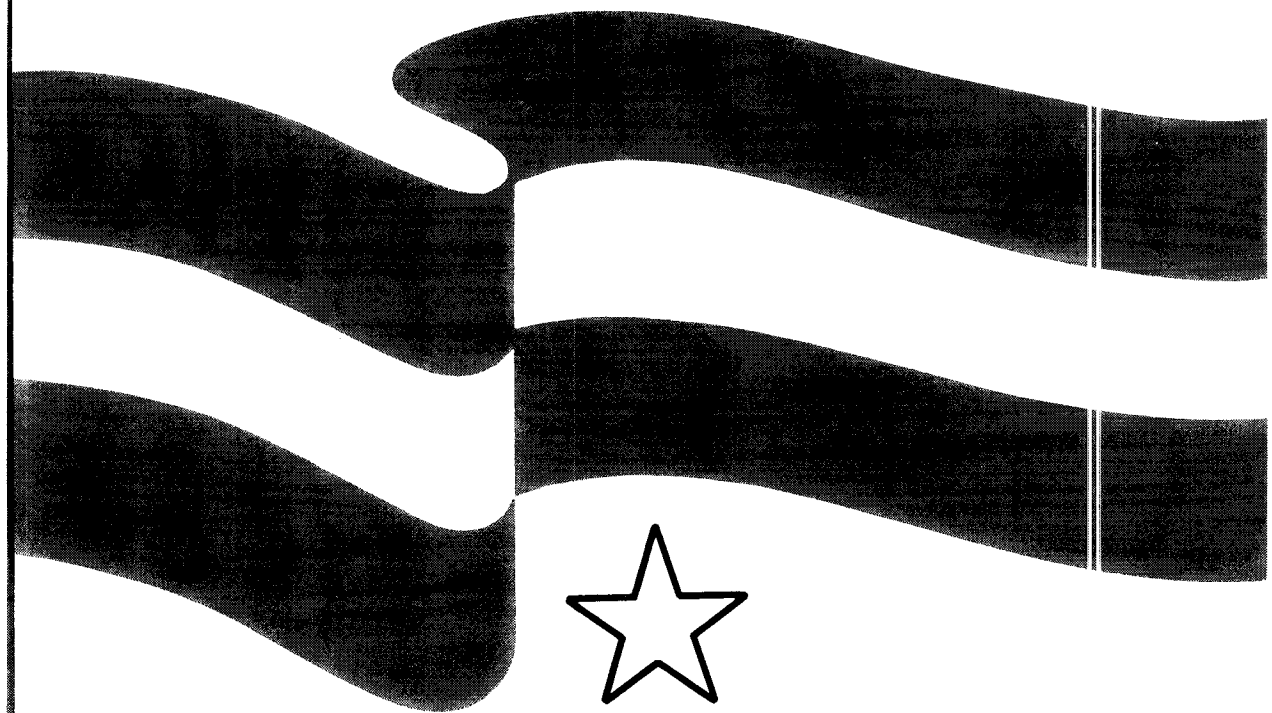

HEALTH STATUS OF VIETNAM VETERANS

VOLUME V
REPRODUCTIVE OUTCOMES AND CHILD HEALTH

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

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TABLE OF CONTENTS

SUMMARY

In this report, we describe the methods and results of the reproductive and child health component of the Vietnam Experience Study (VES) conducted by the Centers for Disease Control (CDC). In the VES, the health of a sample of male U.S. Army Vietnam veterans was compared with that of a similar group of Vietnam-era veterans who served elsewhere. The study included an analysis of postservice mortality, which has been published previously (Boyle *et al.*, 1987; Centers for Disease Control, 1987), a telephone interview, medical examination and psychological testing, which are presented in earlier volumes of this monograph, and an evaluation of reproductive outcomes and child health, presented here.

Two sources of data were used to examine reproductive outcomes and child health: reports by veterans during the telephone interview and hospital birth records of selected veterans' children. During the telephone interview, veterans were asked questions about their children covering the following areas: (1) pregnancies that ended early, including miscarriages, induced abortions, and tubal pregnancies; (2) date of birth, sex of child, and live-born or stillborn status for all births; (3) types of birth defects; (4) types of major health problems or impairments occurring in the first 5 years of life; (5) leukemia or other type of cancer; and (6) infant and child mortality.

Two substudies were added to the reproductive and child health component of the VES at the time of the interim analysis. The objective of the first substudy, the General Birth Defects (GBD) Study, was to compare the rates of total birth defects recorded on hospital birth records for children of Vietnam and non-Vietnam veterans in order to verify reported cohort differences found in the interview data. All veterans whose medical examinations were scheduled from January 1 to September 30, 1986, were asked to participate in this substudy.

In the second substudy, we sought hospital birth records for a small, select group of children with possible cerebrospinal malformations (CSMs). Eligible children for the CSM Study were obtained from the entire VES interview population. On the basis of the veterans' reports, we sought birth records for three types of children: (1) children with a reported CSM, (2) children with a reported condition that suggested a possible CSM, and (3) all children reported as stillborn. These children were selected in an attempt to identify all CSM cases among the children of interviewed veterans and to verify those cases by using hospital birth records.

Hospital birth records were obtained for over 91% of the births that were eligible for inclusion in the GBD Study of total birth defects. Among children of Vietnam veterans, 92.1% of the birth records were obtained, and among children of non-Vietnam veterans, 90.6% of the birth records were obtained.

In the CSM Study, the success rates for retrieving hospital records varied considerably by cohort status; records were obtained for 82.5% of the eligible children of Vietnam veterans and for 67.1% of the eligible children of non-Vietnam veterans. Non-Vietnam veterans were more difficult to locate and contact and much more likely to refuse to participate than were Vietnam veterans.

Crude rates of outcomes among veterans' children were computed. The denominator of the rates varied, depending on the outcome; total pregnancies, total births, and live births were the denominators most often used. The primary measure used to assess the association of Vietnam experience with reproductive outcomes was the OR. The precision of the OR estimate was evaluated by computing 95% confidence intervals (CI) . Odds ratios

were adjusted simultaneously for the following veteran characteristics by using multiple logistic regression methods: age of the veteran at the birth of the child (or at the time of the adverse pregnancy outcome), race, year of entry into Army, enlistment status, general technical (GT) aptitude test score, primary military occupational specialty (MOS), and number of years between enlistment and the birth of the child (or the time of the adverse pregnancy outcome). Two additional covariates were included in our analyses of records-based outcomes: maternal age; and gravidity. Other potential confounders, such as current marital status, education, cigarette smoking, alcohol use, and drug use were accounted for in many of the comparisons, when appropriate. Interactions between Vietnam service and each of the covariates were assessed. If an interaction was found, a standardized OR was computed. Stratified analyses were performed for selected outcomes to identify demographic subgroups at special risk. Also, selected military factors and self-reported experiences in Vietnam were examined to assess their influence on particular outcomes.

For most reproductive and child health outcomes studied, Vietnam veterans were more likely to report an adverse event than were non-Vietnam veterans. This pattern was observed for miscarriages, total and individual birth defects, cancer, and total and individual serious health problems. The tendency to report more adverse events for their children is consistent with the Vietnam veterans' reporting more adverse events with regard to their own health (Volume II). For most of the reproductive and child health outcomes examined in the interview, verification of reported events using objective data sources was not feasible. Consequently, the possibility of differential recall and/or reporting must be considered when interpreting the interview results.

For birth defects, a second source of information not subject to differential reporting was available for a subgroup of children included in the GBD Study. In the GBD Study, the rates of total birth defects recorded on hospital birth records were similar for the two cohorts. When defects were classified as major, minor, or suspected, the adjusted ORs were 1.1, 1.0, and 0.9, respectively. For all races combined, there were no differences between children of Vietnam and non-Vietnam veterans in the prevalence of total, major, minor, or suspected birth defects documented in hospital birth records. This finding supports the explanation of differential reporting in the interview and the conclusion that (at least for total birth defects evident at birth) children of Vietnam veterans were not at increased risk.

An analysis of total, major, minor, and suspected defects stratified by race shows that ORs vary considerably. The adjusted OR for total defects among children of black veterans is 3.3 compared with 0.9 for children of white veterans and 0.4 for children of Hispanic veterans and veterans of other races. This variability in the OR is also present for major and minor defects. The reasons for the apparent racial variation in the association between Vietnam service and total birth defects found in the GBD Study are unclear. The results are based on small numbers of children among black and Hispanic veterans and may be due to sampling variability. The findings for black children may be explained, in part, by the multiple occurrence of genetically determined defects in two families.

The analysis of potential CSM cases was done separately for stillbirths and live births in each cohort. Among reported stillbirths, birth records documented five CSMs among children of Vietnam veterans and six among children of non-Vietnam veterans. Among live-born children, birth records documented 21 CSMs among children of Vietnam veterans and six among children of non-Vietnam veterans. Because record retrieval rates varied

considerably by cohort status and negative responses were not verified, we did not calculate or compare rates of CSM cases in the two cohorts; the results are expressed as numbers of verified cases.

The number of verified CSMs in the Vietnam cohort is similar to the number that would be expected in the interview population on the basis of rates of these defects from two U.S. birth defect surveillance systems. In contrast, the number of records-based CSM cases among children of non-Vietnam veterans is much lower than would be expected. This suggests a deficit of ascertained CSMs among children of non-Vietnam veterans, rather than an excess among children of Vietnam veterans. These data may reflect true differences between the cohorts, or may reflect differences in the opportunity to identify and verify probable CSM cases.

In summary, Vietnam veterans reported more adverse reproductive and child health outcomes in the telephone interview than did non-Vietnam veterans. However, results of a substudy of birth defects documented on hospital birth records showed that Vietnam veterans were not at increased risk of fathering children with birth defects evident at birth. These results are consistent with the findings of three epidemiologic studies conducted since 1981 on the relationship of Vietnam service and birth defects in children of male veterans.

PART A

Telephone Interview Results

1. INTRODUCTION

The Centers for Disease Control (CDC) conducted a health interview survey of male Vietnam-era Army veterans to determine if those who served in Vietnam are at increased risk of incurring specific health problems compared with those who served elsewhere. The survey was part of the Vietnam Experience Study (VES), which was designed to assess health effects of the general Vietnam military experience. Results reported here are based on interviews of a random sample of veterans conducted during 1985 and 1986. Data were obtained about the past and present health of the veterans and their children. Results pertaining to reported pregnancy outcomes and the health of veterans' children are presented here; results pertaining to veterans' health are presented in Volume II (*Telephone Interview*) of this monograph (*Health Status of Vietnam Veterans*).

1.1 BACKGROUND

Since the late 1970s, questions have been raised about the possible long-term adverse health effects of military service in Vietnam. Vietnam veterans have voiced concerns about many conditions, including birth defects, adverse pregnancy outcomes, and other health problems in their children (Bogen, 1979; Dwyer and Smith, 1981; Stellman and Stellman, 1980). Many of these complaints have been attributed to exposure to Agent Orange, the dioxin-contaminated herbicide that was used extensively throughout South Vietnam between 1966 and 1970.

Our knowledge about the relationship between Vietnam service and adverse health outcomes in male veterans' children comes from the following sources: (1) case-control studies of congenital malformations in veterans' children, including one study of Australian veterans (Donovan *et al.*, 1983) and one of U.S. veterans (Erickson *et al.*, 1984a,c); (2) a morbidity survey of U.S. Air Force personnel who had engaged in aerial herbicide spraying in Vietnam (Operation Ranch Hand) that obtained information about reproductive outcomes, including fertility, miscarriage, infant death, birth defects, learning disabilities, and physical handicaps (Lathrop *et al.*, 1984); and (3) several Vietnamese studies, reviewed by Constable and Hatch (1985), including surveys of obstetric outcomes (birth defects and miscarriage rates) of wives of soldiers exposed and unexposed to herbicides and a case-control study of birth defects in relation to fathers' service in South Vietnam.

Questions about veterans' reproductive history and the health of their children were included in the VES health interview survey because of veterans' concerns and in the interest of conducting a comprehensive morbidity survey. This provides the opportunity to assess reproductive and child health outcomes in a systematic study of a broad cross section of Vietnam veterans and an appropriate comparison group.

1.2 STUDY DEVELOPMENT AND SUPPORT

A complete discussion of the VES development, support, and components can be found in Volume II, Section 1. The development, review, and approval of the VES telephone interview component are also presented there.

1.3 OVERVIEW OF PART A

Part A of this volume is a companion report to Volume II. Both are based on the same veteran study population, questionnaire, interview methods, and data collection procedures.

The procedures used to select, locate, and interview study veterans are explained in detail in Volume II and these details are not repeated here.

In Part A, we focus on the pregnancy and child health outcomes reported by veterans during the VES interview. More specifically, we describe the data, the methods of analyses, and the results, and we discuss these results. The description of the data and methods focuses primarily on items that are unique to the analysis of reproductive and child health outcomes or that were handled differently than in the analysis of veteran health outcomes. On several occasions we refer to the more complete descriptions of the data collection process in Volume II.

2. DATA AND METHODS

2.1 QUESTIONNAIRE CONTENT

The section of the VES health interview about the health status of veterans' children is reproduced in Appendix A. The questions cover the following major areas:

1. Basic data for all veterans' biologic children, including month and year of birth, sex of child, and live-born or stillborn status;
2. Birth defects or malformations diagnosed by a physician—up to two per child;
3. Physician-diagnosed major health problems or impairments occurring in the first 5 years of life, not including normal childhood diseases and injuries—up to three per child;
4. Leukemia and other types of cancer;
5. Infant and child mortality; and
6. Pregnancies fathered by the veteran that ended early, including miscarriages, induced abortions, and tubal pregnancies.

Within the section pertaining to child health, most of the questions are introductory questions about specific disease categories, such as birth defects or cancer. If the introductory question was answered positively, open-ended questions requesting the name of the specific condition followed. In other words, the veterans were not asked about the presence of specific birth defects or illnesses in their children; they were asked whether their children had any birth defects, and if so, to give the medical name of the birth defect. Questions about adverse pregnancy outcomes differed from this pattern. Veterans were asked if they had fathered any pregnancies that ended early. For each such pregnancy, they were asked if the outcome of the terminated pregnancy was a miscarriage, an induced abortion, or a tubal pregnancy.

2.2. DESCRIPTION OF OPEN-ENDED RESPONSES

The problems the veterans described in their responses to open-ended questions about their children's health problems ranged from vague symptoms to specific conditions expressed in precise medical terms. The quality of these responses varied with the type of problem being described. Responses describing childhood cancers were generally clear, reasonably specific, and accurately described a type of cancer. In contrast, responses describing specific birth defects were often problematic. These responses described conditions consistent with actual birth defects, miscellaneous problems and illnesses that were clearly not birth defects, and vague problems that, on the basis of the response alone, could not be assessed as to type and severity.

The quality of the birth defect responses may reflect two factors. First, the nature of the questions required the veterans to define the terms "birth defect" or "malformation" in order to give appropriate answers pertaining to their children. The responses to these questions clearly indicated that veterans defined these terms in various ways. Second, the veterans had to name or describe the reported birth defect. Veterans may be less familiar with birth defects than with childhood health problems such as pneumonia or ear infections, and, consequently they may be less able to name or fully describe them.

Table 1 illustrates the nature of the responses veterans gave to the birth defect questions. Responses such as "spina bifida" and "open spine" clearly refer to birth defects. Responses

Table 1. Examples of Responses Given by Veterans for Type of Birth Defect or Malformation Present in Their Children*

1. Hearing problem left ear	23. Feet turned out
2. Hyperactive	24. Club foot
3. Cross eyed	25. Hip malformed
4. Asthma	26. Unable to walk without assistance
5. Staph skin infection	27. Top of skull was oblong
6. Allergic to milk	28. Hole at base of tailbone
7. Chest deformity	29. Deformed calf muscle
8. Spina bifida	30. Skin tag - benign tumor on ear
9. Open spine	31. Born with no spleen
10. Water on the brain	32. Breech birth
11. Left eardrum sunken in	33. Premature
12. Aortic stenosis	34. Hyaline membrane disease
13. Oversize heart	35. Undeveloped lungs
14. Deformed heart	36. Jaundice
15. Pulmonary stenosis	37. High billy reuben count
16. Under developed trachia	38. Vitamin K deficiency
17. Perforated stomach – peritonitis	39. Anemia
18. Stomach problem	40. Trouble passing bowels
19. Stomach disorder	41. Seizures
20. Undescended testicle	
21. Oversize bladder	
22. Pigeon toed	

* These are the actual responses given by the veterans and entered by the interviewers; they have not been edited.

such as "asthma," "jaundice," and "anemia" clearly do not. Responses in a third group cannot be said with certainty to refer to a birth defect, an acquired illness, or a perinatal condition. Responses in this group are "hearing problem," "stomach problem," "unable to walk," "top of skull was oblong," "seizures," and "trouble passing bowels."

2.3 CODING OPEN-ENDED RESPONSES

All reported medical conditions were coded according to the International Classification of Diseases, Ninth revision (ICD-9) (World Health Organization, 1977). The data collection contractor, Research Triangle Institute (RTI), conducted a quality control procedure for all assigned codes, and both RTI and the Centers for Disease Control (CDC) did automated coding edits. In addition, RTI "blindly" recoded open-ended responses for a sample of 500 veterans. (See Volume II for more details on RTI's coding, coding edits, and quality control procedures.)

The specificity of the veterans' responses about birth defects in their children varied and were therefore especially difficult to code. This became evident during the interview and coding process, as members of CDC's professional staff reviewed the responses and the assigned codes received monthly from RTI. The problem was one of consistency; because many of the responses were vague, several different codes could be considered appropriate for a given response.

RTI's blind recoding of open-ended responses from a sample of 500 veterans also indicated that the birth defects responses were problematic. Agreement between the original coding and the recoding was 68%. When only the first three digits of the codes were considered, the agreement was 73%.

To improve the consistency of the coding for the questions on birth defects, a trained coder who had considerable experience with medical coding in pediatric hospitals reviewed all responses and original codes for the birth defects section of the questionnaire. The CDC's

professional staff supervised her work and reviewed it for consistency. With the CDC staff, she developed additional coding guidelines to be used in conjunction with the ICD-9. These guidelines are in Appendix B. Using the guidelines and the ICD-9, this coder achieved a 92% agreement in the entire four-digit code in a final blind recode of 200 responses. In addition to reviewing the responses to all birth defect questions, the coder reviewed all responses to questions pertaining to serious health problems and causes of infant mortality that RTI had originally coded as a birth defect.

2.4 ANALYTIC METHODS

In this section, we describe various issues related to the analysis of veterans' responses about the health of their children and adverse outcomes of pregnancy. Most comparisons are between the entire cohort of Vietnam veterans and the entire cohort of non-Vietnam veterans. Some comparisons use veterans who served in Germany or Korea, or a subgroup of Vietnam veterans as the comparison group; these variations are clearly stated. All health outcome results described in Part A of this volume are derived solely from reports from veterans and should be thought of as "reported" miscarriage, "reported" birth defects, etc., as opposed to conditions verified from medical records or through physical examinations.

2.4.1 Health Outcomes

The end points examined include adverse pregnancy outcomes, birth defects, cancer, serious health problems during the first 5 years of life, and infant and child mortality. In this section, we describe how veterans' reports of these outcomes have been categorized and organized for analysis and presentation.

Adverse Pregnancy Outcomes

Veterans were asked to enumerate all pregnancies they fathered that terminated in a miscarriage, induced abortion, tubal pregnancy (Appendix A, Question B-17), or stillbirth (Question B-03). In addition, for miscarriages, they were asked to estimate how advanced the pregnancies were (in weeks or months) when they ended. This information was used to examine the following: miscarriages for all trimesters combined and by specific trimester; induced abortions; tubal pregnancies; and stillbirths. In addition, we examined differences in the sex ratio of live-born and stillborn children fathered by Vietnam veterans compared with those fathered by non-Vietnam veterans.

Classification System for Birth Defects

For this analysis, a birth defect is defined as a response that was coded to any ICD-9 code within the range of 740.0-759.9. This range corresponds to the ICD-9 chapter on congenital anomalies. The response could have been given to a question about birth defects (Question B-07) or serious health problems (Question B-10). Some veterans reported birth defects in response to the questions about serious health problems; these reports were also classified as birth defects if they fell within the ICD-9 range of 740.0 - 759.9.

Tables 2 and 3 define the categories used in the analysis of reported birth defects among veterans' children and the ICD-9 codes corresponding to each category. The categories in Table 2 are mutually exclusive and exhaustive subdivisions of the entire congenital anomalies chapter and are based on the organ system affected. The specific birth defects listed in Table 3 include 11 sentinel defects, as defined by the World Health Organization, and additional selected defects. These specific defects are presented and analyzed

Table 2. ICD-9 Categories Used in the Analysis of Reported Birth Defects Among Veterans' Children

Category Title	ICD-9 Codes*
Total congenital anomalies	740-759
Nervous system anomalies	740-742
Eye anomalies	743
Ear, face, neck anomalies	744
Circulatory system and heart anomalies	745-747
Respiratory system anomalies	748
Digestive system anomalies	749-751
Genital anomalies	752
Urinary system anomalies	753
Musculoskeletal deformities	754-756
Anomalies of the integument	757
Chromosomal anomalies	758
Other and unspecified anomalies	759

* The range of codes includes all the four-digit codes contained within that range.

Table 3. Selected Birth Defects Examined in the Analysis of Reported Birth Defects Among Veterans' Children

Birth Defect	ICD-9 Codes
Anencephaly	740.0
Spina bifida	741.0-741.9
Hydrocephalus	742.3
Cleft palate	749.0
Total cleft lip	749.1-749.2
Esophageal atresia or stenosis, tracheo-esophageal fistula	750.3
Anorectal atresia or stenosis	751.2
Hypospadias	752.6
Congenital hip dislocation	754.3
Polydactyly	755.0
Limb reduction deformities	755.2-755.4
Down's syndrome	758.0

individually, because they are thought to be relatively common, easily diagnosed, and observable at birth (Flynt and Hay, 1979; International Clearinghouse for Birth Defects Monitoring Systems, 1986).

If a child was reported to have multiple defects, the child was counted in each category for which a birth defect was reported, but only once within a given category. For example, if a veteran reported a nervous system defect and a circulatory defect for a given child, that child was counted as an occurrence, or case, in both of those categories. However, if a veteran reported two nervous system defects for a given child, that child was counted as a case only once in the nervous system category.

Cancer

Veterans were asked if any of their children had ever had leukemia or some other form of cancer (Question B-11); if they responded affirmatively, they were asked to name the type of cancer (Question B-13). Cancers reported by veterans in response to the questions about serious health problems were also classified as cancers if they fell within the ICD-9 range of

140.0-208.9. Differences in total childhood cancer and cancer of specific sites were examined for children of Vietnam veterans compared with those of non-Vietnam veterans.

Classification System for Serious Health Problems

To evaluate the occurrence of serious health problems in veterans' children, we asked veterans to report physician-diagnosed major health problems or impairments that occurred in their children during the first 5 years of life. They could report up to three conditions per child. Veterans were instructed not to include normal childhood diseases and injuries or birth defects reported in a previous question (see Question B-08A).

All positive responses to the serious health problem questions (B-10) have been included in the present analysis. Responses have been grouped according to ICD-9 chapters and to more specific subdivisions within chapters. Table 4 defines categories used in the analysis of reported serious health problems. As with the analysis of birth defects, a child was counted in each category for which a serious health problem was reported, but only once within a given category.

Infant and Child Mortality

Two mortality rates were considered in this analysis: (1) infant mortality rate (the proportion of all live-born infants who die before reaching their first birthday) and (2) child mortality rate (the proportion of children surviving until 1 year of age who subsequently die). Because age-at-death information was not available, we could not analyze age-specific mortality patterns. We did, however, examine cause-specific infant mortality rates. Table 5 defines the categories used in the analysis of reported cause-specific infant mortality. (We did not obtain the information needed to examine cause-specific patterns in child mortality.)

Outcomes Occurring Before Military Service

About 11% of all children reported in the VES interview were conceived before the veterans' military experience and, consequently, were not influenced by any potential exposures associated with Army service. These children are not included in the main analyses presented in this monograph. In addition, pregnancies that occurred before the veterans' military experience (about 12% of all reported pregnancies) are generally not included. Occasionally, to define a baseline or a preexposure association, we examined the association of an outcome with Vietnam service among children conceived before the veterans' military experience. When we do this, we point it out.

Children are included in the main analyses pertaining to stillbirths or live-born children if they were conceived after the veteran was assigned to his primary duty location. Conception was estimated as the child's reported date of birth minus a term birth period of gestation. For veterans who left the United States to serve in a foreign country (Vietnam, Germany, or Korea), we obtained the starting date of the primary tour from military records. For veterans who served only in the continental United States, we estimated the starting date of the primary tour as the date of entry into the service plus 16 weeks. The 16 weeks represent the normal period of basic and advatraining and provide a realistic starting date for those assigned to duty in the U.S.A.

In the case of miscarriages, we estimated the time of conception as the reported date of the miscarriage minus the reported length of the gestation. For a small number of miscarriages (39 or 1.4%), the length of gestation was unknown, so we assumed a gestational period of 2 months. Veterans were not asked about the length of gestation for reported induced abortions or tubal pregnancies. Since most of these events were induced

Table 4. ICD-9 Categories Used in the Analysis of Reported Serious Health Problems Among Veterans' Children

Category Title	ICD-9 Codes*
Infectious and Parasitic Disease	001-139
Bacterial diseases	010-041
Viral diseases	045-079
Benign and Unspecified Neoplasms	210-239
Endocrine, Nutritional, Metabolic, and Immunity Disorders	240-279
Diabetes	250
Dehydration	276.5
Disease of the Blood and Blood-Forming Organs	280-289
Anemias	280-285
Mental Disorders	290-319
Hyperkinetic activity	314
Developmental disorders	315
Diseases of the Nervous System and Sense Organs	320-389
Meningitis	320-322
Epilepsy	345
Strabismus	378
Other disorders of the eye	360-377, 379
Diseases of the ear	380-389
Diseases of the Circulatory System	390-459
Diseases of the Respiratory System	460-519
Tonsillitis	463, 474
Allergic rhinitis	477
Pneumonia	480-486
Bronchitis	466, 490-491
Asthma	493
Diseases of the Digestive System	520-579
Hernias	550-553
Diseases of the Genitourinary System	580-629
Kidney, bladder, urinary tract infection	590, 595, 599.0
Diseases of the Skin and Subcutaneous Tissue	680-709
Dermatitis	691-693
Diseases of the Musculoskeletal System	710-739
Perinatal Conditions	760-779
Jaundice	774
Symptoms, Signs, and Ill-Defined Conditions	780-799
Convulsions	780.3
Fever of unknown origin	780.6
Rash	782.1
Speech disturbance	784.5
Cardiac murmur	785.2
Injury and Poisoning	800-999
Allergies, unspecified	995.3
Supplementary Classification	V01-V99
Problems with internal organs	V47

* When the fourth digit is not shown, the range of codes includes all the four-digit codes contained within that range.

abortions—most of which would have occurred early in pregnancy—we estimated the time of conception as the reported date of the event minus 2 months. (This 2-month estimate would err in the direction of including conceptions that actually occurred before the date of assignment to the primary tour. However, an estimate of more than 2 months would exclude some truly qualified pregnancies.) Events are included in the appropriate analyses if conception occurred after the veteran was assigned to his primary duty location.

Table 5. Classification of Causes of Death Used in the Analysis of Infant Mortality, by ICD-9 Codes

Condition	ICD-9 Codes*
Disorders related to short gestation and low birth weight	765
Respiratory distress syndrome and other respiratory conditions of fetus and newborn	769-770
Other perinatal conditions	760-764, 766-768, 771-779
Congenital malformations	740-759
Sudden infant death syndrome	798.0
Infectious diseases	001-139, 322, 323, 464, 480, 486
Injury and poisoning	800-999
Other	All other ICD codes

* When the fourth digit is not shown, the range of codes includes all the four-digit codes contained within that range.

2.4.2 COVARIATES CONSIDERED IN THE ANALYSIS

In investigating possible associations between place of service and various health outcomes in veterans' children, we evaluated the influence of other variables that are potential confounders or effect modifiers. Because specific information about each child and the child's mother was not available, the covariates used in the analyses pertain only to the veteran. We selected the covariates on the basis of the following considerations: (1) they may influence the veterans' perception and consequent reporting of reproductive and child health outcomes; (2) they may have been associated with different military experiences or reactions to the experience; (3) they may have been associated with different probabilities of assignment to Vietnam; and (4) they are consistent with the covariates selected for the analysis of veterans' health (see Volume II, Section 2.7.2).

In the analyses, several types of variables are considered as potential effect modifiers or confounders. Some of these variables come from military history records; others are from the VES telephone interview. All of the covariates are treated as categorical variables. Definitions of the categories used for each variable and the distributions of total births by cohort status and by covariate category are given in Tables 6 and 7. A discussion of each type of covariate follows.

Primary Covariates

Seven primary covariates were, for the most part, obtained from military history records. Two exceptions are the veteran's age at the time the event occurred and the number of years between entry into the Army and the event. For these two variables, the date of the child's birth or the reproductive outcome was obtained from the VES interview. The veteran's race was also obtained from the interview unless the veteran refused to give it; in that case, his race was taken from military history records. The covariates are:

1. Age of veteran at birth of child or at occurrence of adverse pregnancy outcome;
2. Veteran's race;
3. Army General Technical (GT) test score—a verbal/arithmetic placement examination taken at entry into the Army;
4. Enlistment status (draftee or volunteer);

Table 6. Definition and Categorization of *Primary Covariates* and Their Distribution Among Total Births, by Cohort Status

Characteristic (of Veteran)	Analysis Category	% of Total Births in Category	
		Vietnam	Non-Vietnam
Age at birth of child	≤25	33.0	32.3
	26-30	39.2	39.3
	31+	27.8	28.5
Race	White	81.0	79.9
	Black	12.0	12.0
	Hispanic and other	7.0	8.1
General Technical (GT) test score	040-089	26.5	23.1
	090-109	33.9	32.7
	110-129	30.1	32.1
	130-160	7.9	11.3
	missing	1.5	0.7
Enlistment status	Drafted	65.1	67.4
	Enlisted	35.0	32.6
Primary military occupational specialty	Tactical	35.5	27.4
	Other	64.5	72.6
Year of entry into Army	1965-66	35.5	39.0
	1967-69	56.0	39.5
	1970-71	8.5	21.5
Years between entry and birth	≤5	30.7	32.5
	6-10	40.4	39.7
	11+	29.0	27.7

Table 7. Definition and Categorization of *Secondary Covariates* and Their Distribution Among Total Births, by Cohort Status

Characteristic (of Veteran)	Analysis Category	% of Total Births in Category	
		Vietnam	Non-Vietnam
Smoking history (average number of cigarettes per day)	<10	31.7	35.5
	10-39	53.4	51.1
	40+	14.8	13.1
	missing	0.2	0.3
Alcohol use (average number of drinks per month)	≤30	55.2	56.8
	30-89	25.1	26.9
	90+	18.5	15.1
	missing	1.3	1.2
Educational attainment (in years)	<12	15.4	12.6
	12-15	68.8	67.9
	16+	15.8	19.5
Marital status (current)	Married	84.0	85.0
	Not married	16.0	15.0
	missing	<0.1	<0.1
Regular drug use in Army (at least once a week for at least 3 months)	None	73.7	80.7
	Marijuana only	17.8	11.9
	Hard drugs	7.9	7.0
	missing	0.6	0.4

5. Primary military occupational specialty (MOS) – the job for which the man was trained after he completed basic training;
6. Year of entry into the Army; and
7. Number of years between veteran's year of entry and child's year of birth (or year of adverse pregnancy outcome).

These seven covariates are evaluated for effect modification and confounding in all analyses of outcomes for which the number of cases is adequate (see Section 2.4.3).

Secondary Covariates

In addition to the covariates listed above, we considered the following five additional variables as potential confounders or effect modifiers when the number of cases was adequate:

1. Smoking history (average number of cigarettes per day) for current and ex-users);
2. Alcohol use (average number of drinks per month);
3. Educational attainment;
4. Marital status at the time of interview; and
5. Illicit drug use in the Army.

These variables were determined at the time of the interview and reflect cumulative behavior and experiences. Consequently, potential differences between the cohorts for values of these variables could represent differences (or a predisposition toward differences) existing before military service or differences resulting from military service. In this sense, they could be intervening variables in the causal chain for certain health outcomes. When risk estimates vary after being adjusted for these types of variables, we present both the adjusted and the unadjusted estimates. The adjusted estimates require careful interpretation.

2.4.3 Statistical Techniques

Univariate Analyses

For all outcomes considered, the first stage of the analysis addresses the hypotheses under study without consideration of, or adjustment for, any covariates. Numbers of cases and crude rates are presented for every outcome reported. The denominator for the rates varies, depending on the outcome; total pregnancies, total births, and live births are the denominators used for most of reported rates. Rates are generally presented per 100 pregnancies and per 1,000 births.

The primary measure used to assess the association of Vietnam experience with reproductive outcomes is the odds ratio (OR). The OR is defined as the ratio of the odds of reported disease among Vietnam veterans' children to the odds of reported disease among non-Vietnam veterans' children. The OR has statistical properties that make it amenable to multivariate statistical techniques, including logistic regression. Further, when the risk of disease is small, the value of the OR is nearly identical to the ratio of disease rates (Kelsey *et al.*, 1986). For all outcomes with a total number of cases (in both cohorts combined) of 10 or more, the crude OR and the 95% confidence interval (CI) were computed by using standard SAS software (SAS Institute, 1985).

Multivariate Analyses

In addition to the crude analyses, we used a multivariate modeling strategy to evaluate the primary and secondary covariates with respect to potential effect modification and confound