CHAPTER 15

CARDIOVASCULAR EVALUATION

INTRODUCTION

Background

Cardiac disease and peripheral vascular disease are not recognized sequelae of exposure to phenoxy herbicides, chlorophenols, or dioxin. Both bradycardia and tachycardia have been suggested following acute heavy exposure to the 2,4-D and 2,4,5-T components, but the cardiovascular effects after chronic low-dose exposure are essentially unknown.

Although a few recent studies have observed evidence of cardiac dysfunction, many investigators have concluded that the cardiovascular effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) have not been adequately assessed. A decrease in beta-adrenergic responsiveness and an increase in intracellular calcium in papillary muscle and the selective augmentation or decrease in various differential cardiac responses have been observed in guinea pigs, leading to the conclusion that TCDD causes a specific pattern of cardiac dysfunction.[1] Researchers have found a significant decrease in blood pressure and resting heart rates after the administration of TCDD to rats.[2] In guinea pigs, TCDD adversely affected the atrial muscle; in rats, it significantly decreased the positive inotropic effect of isoproterenol in papillary muscle.[2,3] In rabbits, TCDD has been shown to cause lipoprotein lipase activity reduction and other changes in the metabolic pathways and force of contraction in the aorta muscle, causing preatherosclerotic-type lesions typical of hyperlipidemia in aortic arches.[4-6] TCDD has also been shown to produce increased sensitivity of the heart to the arrhythmic effects of drugs affecting the cardiovascular system, including quinidine, reserpine, and strophanthin K in mice.[7]

Most earlier studies viewed the cardiac abnormalities as expected consequences of a moribund state, and not as indicators of primary cardiac toxicity. Following oral administration of 2,4-D and 2,4,5-T, sheep and cattle developed cardiac hemorrhages.[8] In another experiment,[9] a lethal oral dose of TCDD in young Rhesus monkeys produced increased heart weights. Horses and cats showed generalized vascular degeneration following exposure to soil contaminated with TCDD,[10] and mice and guinea pigs fed high amounts of TCDD manifested low heart weights.[11] A teratogenic experiment using 2,4,5-T in developing fish eggs showed graduated lethality and cardiovascular anomalies, which included enlarged veins and heart chambers.[12] Another study using ventricular muscle strips from chick embryos exposed to polychlorinated biphenyls (including TCDD) showed a marked decrease in contractibility.[13] This primary cardiotoxic response was presumably mediated by the Ah receptor and, as supported by another study with chick embryo hearts, was associated with increase prostaglandin synthesis.[14] Another study with rats found changes in measures of right and left atrial function, but of a stimulative nature rather than mechanical.[4]

Human case reports and epidemiologic studies have not detected significant cardiac abnormalities following exposure to herbicides or TCDD. In three case reports of acute 2,4-D poisoning, cardiac dilation and cardiac arrest were observed in the one fatal case,[15] while only transient nodal tachycardia was observed in one of the two nonfatal cases.[16,17] Three laboratory technicians with chloracne, neurological symptoms, and hypercholesterolemia following significant direct exposure to TCDD did not manifest any cardiac dysfunction;[18] however, of 10 industrial workers with chloracne, 4 complained of heart palpitations and shortness of breath.[19] In another two studies involving 128 industrial workers, no excess of cardiac complaints or findings was noted.[20-22] A case of intoxication with 2,4-D in a 51-year-old man was shown to prolong the Q-T interval in an electrocardiogram (coma was also induced).[23]

In two epidemiologic studies using similar cohorts from a Nitro, West Virginia, chemical plant, no significant cardiac impairments were detected in exposed workers.[24,25] However, one study found significantly lower levels of high density lipoprotein (HDL) cholesterol in individuals with chloracne, as contrasted to individuals without chloracne.[25] Two recent clinical-epidemiologic pilot studies of residential areas in Missouri contaminated by TCDD did not disclose any significant cardiac disease in exposed residents,[26,27] although a Times Beach study noted diminished peripheral pulses in the exposed group (as did the Baseline Air Force Health Study [AFHS]). The AFHS 1985 followup study found differences of borderline significance in verified heart disease that were not supported by other cardiac measurements.[28] Another study examined Vietnam veterans for cardiovascular lesions using chest radiographs.[29] This study found no difference in exposed and control study groups.

Because the herbicide literature has not identified consistent cardiovascular findings that merited a specific clinical focus, the AFHS has collected data by questionnaire, physical examination, laboratory testing, and medical record reviews that would identify group differences on a variety of cardiac endpoints.

The data collected can be classified into three major categories: central cardiac function, peripheral vascular function, and heart disease history. Central cardiac and peripheral vascular function were assessed by physical examination and laboratory procedures. Coronary heart disease (CHD) data have been gathered through questionnaire and medical records review. CHD has been of general concern in this study because both cohorts are largely within the high risk ages of 40 to 65.

Another component of the cardiovascular examination evaluates risk factors such as age, race, family history of heart disease, smoking, cholesterol, cholesterol-HDL ratio, personality type, changes in cortisol levels, body weight, and alcohol use.[30-35] Cholesterol can be viewed in two different ways. On the one hand, it is a potential confounding factor for cardiovascular disease that one would wish to adjust for in comparing groups of individuals exposed or not exposed to dioxin. However, hypercholesterolemia itself has been associated with acute exposure to chlorophenols and dioxin,[18,20,21,25,36,37] and the question arises as to whether this might have a future adverse impact on cardiovascular health. Therefore, analyses adjusting for this variable should be interpreted carefully. Chapter 13, Gastrointestinal Assessment, presents analyses of cholesterol and cholesterol-HDL ratio viewed as dependent variables. (No significant group difference was found for either variable.)

Baseline Summary Results

The 1982 Baseline examination found no statistically significant differences between the Ranch Hand and Comparison groups in systolic or diastolic blood pressure, the frequency of abnormal electrocardiographs (ECG), heart sound abnormalities, abnormal funduscopic findings, or carotid bruits. However, a statistically significant difference emerged in the frequency of abnormal peripheral pulses: 12.8 percent of the nonblack Ranch Hands exhibited absent or diminished peripheral pulses, compared to 9.4 percent of the nonblack Original Comparisons ($p=0.05$). This difference was consistent across various pulse combinations and remained statistically significant when all Ranch Hands were contrasted with all Comparisons, adjusting for age, lifetime smoking history, and cholesterol level.

No statistically significant differences were found between the two groups in the occurrence of reported or verified heart disease or heart attacks, although a significant group-by-lifetime smoking history interaction (for heart disease) was noted in the older (40 or more years of age) subgroup; i.e., older Ranch Hands smoking more than 10 pack-years developed more heart disease than their Comparisons, whereas older Ranch Hands smoking less than 10 pack-years exhibited less heart disease. No significant dose-response relationships of any of the cardiovascular response variables with the exposure index were noted.

Over 80 percent of the cardiac conditions reported on the study questionnaire were verified by a detailed review of medical records. There was also strong correlation between the past medical history of cardiac disease and the Baseline cardiovascular examination findings, although the differences in peripheral pulse abnormalities occurred primarily in older individuals without a history of cardiovascular disease.

Finally, the well-known risk factors of age, smoking, and cholesterol were found to be highly correlated with each other and with several of the cardiovascular response variables.

1985 Followup Study Summary Results

The cardiovascular health of both cohorts was assessed by collecting reported and record-verified heart disease events; measurements of central cardiac function by systolic blood pressure, abnormal heart sounds, and ECG findings; and evaluation of peripheral vascular function by diastolic blood pressure, funduscopic examination, presence of carotid bruits, and detailed manual and Doppler measurements of five peripheral pulses. Analyses were adjusted for age, race, occupation, percent body fat, cholesterol, HDL, cholesterol-HDL ratio, smoking history (lifetime and current smoking level), alcohol history (lifetime and current drinking level), personality score, and differential cortisol.

The analysis of cardiovascular disease history did not reveal significant group differences in reported or verified hypertension, reported heart disease, or reported or verified heart attacks. A significant difference did emerge in the proportion of individuals with verified heart disease: 24 percent in the Ranch Hands versus 20 percent in the Comparisons (p=0.054 unadjusted, p=0.036 adjusted). After further review of the medical records, this observation was found to be in error. There were no group differences in verified heart disease (relative risk = 1.1, 95% C.I.: [0.9-1.4]). There was good correlation between the verified cardiovascular history and the central and peripheral cardiovascular abnormalities detected at the physical examination, supporting accuracy and validity of the cardiovascular measurements.

The adjusted analyses of central cardiac function disclosed a significant group-by-age interaction involving systolic blood pressure in the Black cohort, with a mean systolic blood pressure greater in the Ranch Hands than in the Comparisons at younger age levels, but a lower mean pressure at the older ages; the group-by-age interaction was not significant in the nonblack cohort. Additionally, there was a significant group-by-lifetime smoking history interaction for the overall ECG findings and significant group-by-lifetime smoking history and group-by-percent body fat interactions for arrhythmia, but they all generally pointed to lower adjusted relative risks in the Ranch Hands.

In the analyses of peripheral vascular function, no significant overall group differences were observed for abnormalities involving radial, femoral, popliteal, posterior tibial, dorsalis pedis, or three anatomic aggregates of these pulses, either by manual palpation or Doppler techniques. This overall finding was in distinct contrast to the 1982 Baseline examination, which, by the manual palpation method, showed significant peripheral pulse deficits in the Ranch Hands. This reversal in pulse findings over the two examinations was primarily attributed to the rigid 4-hour tobacco abstinence applied prior to Doppler testing, although other factors may have been involved.

For manually determined pulse abnormalities, there was a significant group-by-race interaction for the popliteal pulses; a significant group-by-percent body fat interaction for the leg pulses; and significant group-by-occupation interactions for the posterior tibial, dorsalis pedis, and the three pulse aggregates (leg, peripheral, and all pulses). No interactions were encountered in the adjusted analyses of the Doppler results and none showed significant group differences. Of interest was the fact that the manual and Doppler techniques differed significantly in the detection of abnormalities for all pulse or pulse combinations except radial pulses.

For the exposure index analyses, the only statistically significant effects were those pointing to less bradycardia and less reported and verified heart disease in the medium exposure level category, as contrasted to the low exposure category, among the enlisted groundcrew. In many cases, there were too few abnormalities within the occupational categories to permit formal statistical tests. Overall, the exposure analyses were deemed unsupportive of any meaningful dose-response relationships.

The longitudinal analysis of the pulse index confirmed the significant group difference in the change in results from the Baseline examination to the

1985 followup examination, largely due to a relatively greater increase of pulse abnormalities in the Comparison group than in the Ranch Hand group. There was no significant difference between the two groups in the change in overall ECG findings between the Baseline and 1985 followup examinations.

The covariates were distributed similarly in the two groups, except for a slightly higher level (statistically significant) of current Ranch Hand smoking (also observed at Baseline) and a slightly lower mean percent body fat. The general covariate effects were strong and showed expected classical associations with the cardiovascular measurements. However, unexpected effects were consistently noted for personality score, with higher proportions of various cardiovascular abnormalities associated with scores in the Type B direction. (Although smoking was positively associated with many of the cardiovascular measurements, negative associations were seen between current smoking and reported and verified essential hypertension, and between lifetime smoking and verified hypertension.)

Parameters of the 1987 Cardiovascular Examination

Dependent Variables

The analysis of the 1987 cardiovascular examination was based on data from the questionnaire and physical examination and subsequent medical records verification. No laboratory examination data were analyzed as dependent variables, although data from the laboratory examination were used to construct selected covariates.

Questionnaire Data

During the Baseline, 1985 followup, and 1987 followup questionnaire health interview, each participant was asked if he ever had a heart condition since his tour of duty in Southeast Asia (SEA). Medical records were sought on all individuals to verify the reported conditions and to determine the time of occurrence of major cardiac events (including cardiovascular death). In addition, the review-of-systems portion of the physical examination recorded the overall history of heart trouble, as well as other serious illnesses.

Based on the self-reported information and the subsequent verification, three conditions, each classified as yes or no, were analyzed: essential hypertension, heart disease (excluding essential hypertension), and myocardial infarction. These endpoints were each analyzed twice, as reported and as verified by medical records.

The heart disease endpoint includes rheumatic fever with heart involvement, chronic rheumatic heart disease, hypertensive heart disease, ischemic heart disease, disease of pulmonary circulation, and other forms of heart disease (acute pericarditis and endocarditis, other diseases of the pericardium and endocardium, cardiomyopathy, conduction disorders and dysrhythmias, heart failure, and ill-defined descriptions of heart disease).

A series of morbidity-mortality analyses based on these conditions was also conducted. These analyses focused on the full Ranch Hand cohort and the first Comparison of the randomly ordered set matched to the Ranch Hands. Because of competing mortality and possible misclassification of the cause of death, the endpoints of (1) death (any cause) or verified nonfatal heart disease, and (2) death (any cause) or verified nonfatal myocardial infarction were examined to assess group differences in the most extreme case (i.e., all deaths being associated with cardiovascular disease). The other two endpoints examined were (3) fatal or nonfatal verified heart disease, and (4) fatal or nonfatal verified myocardial infarction or fatal heart disease. Each variable was classified as yes or no. These variables were based on the history of each individual from the end of his tour of duty in SEA to the present.

Participants with a verified history of diabetes or a 2-hour postprandial glucose level of 200 mg/dl or more, as well as individuals with a pre-SEA verified history of essential hypertension or heart disease, were excluded from the analyses of reported and verified essential hypertension, heart disease, and myocardial infarction. Only individuals with pre-SEA heart disease were excluded from the morbidity-mortality analysis.

Physical Examination Data

Cardiovascular data from the physical examination at the 1987 followup were divided into two main categories: central cardiac function and peripheral vascular function. In addition, associations between data from the physical examination and data on verified cardiovascular diseases were examined.

Central Cardiac Function

The assessment of central cardiac function at the cardiovascular examination was made by measurements of systolic blood pressure, heart sounds (by auscultation), and an ECG. Systolic blood pressure was determined in a sitting position by an automated electronic monitor on the nondominant arm placed at heart level; the systolic pressure corresponding to the lowest diastolic value of three readings was recorded. Detection of abnormal heart sounds was conducted by standard auscultation with the participant placed in sitting, supine, and left lateral supine positions. Fourth heart sounds were assessed; murmurs were graded in intensity and location and were judged to be functional (normal) or organic (abnormal) in nature. All examiners and diagnosticians were retrained on the detection of fourth heart sounds and the notation of innocent murmurs without recording them as abnormal heart sounds. ECGs were obtained after adherence to a 4-hour abstinence from tobacco. A standard 12-lead ECG was performed; an additional rhythm strip in lead II was produced if any deviation from normal was found. The following items were considered to be abnormal: right bundle branch block (RBBB), left bundle branch block (LBBB), nonspecific T-wave changes, bradycardia, tachycardia, arrhythmia, and other major diagnoses (e.g., atrial-ventricular block, evidence of a prior myocardial infarction).

Thus, the variables analyzed in the evaluation of the central cardiac function include systolic blood pressure, heart sounds, and eight conditions associated with the ECG. (An overall assessment of the ECG was analyzed, as well as the individual conditions of RBBB, LBBB, nonspecific T-wave changes, bradycardia, tachycardia, arrhythmia, and other diagnoses.) Systolic blood pressure was analyzed as a continuous variable and also as a discrete variable, classified as normal (≤140 mm Hg) or abnormal (>140 mm Hg). All other variables were dichotomized as normal/abnormal.

Participants with a verified history of diabetes or a 2-hour postprandial glucose level of 200 mg/dl or more and those with verified pre-SEA hypertension or heart disease were excluded from the analyses of the central cardiac function variables.

Peripheral Vascular Function

Peripheral vascular function was assessed during the cardiovascular examination by the diastolic blood pressure; funduscopic examination of small vessels; the presence or absence of carotid bruits; and manual palpation of the radial, femoral, popliteal, dorsalis pedis, and posterior tibial pulses. Diastolic blood pressure was measured by an automated electronic monitor. The recorded value represents the lowest diastolic value of three readings. Elevated diastolic blood pressure is an indicator of increased vascular resistance of the peripheral arterial system. The funduscopic examination was conducted with undilated pupils in a standard manner, with emphasis placed upon detection of arterio-venous nicking (a sign of chronic blood pressure elevation), hemorrhages, exudates, and papilledema. The presence or absence of carotid bruits was assessed by auscultation in both carotid arteries.

Diastolic blood pressure was analyzed as both a continuous and discrete variable, dichotomized as normal (≤90 mm Hg) or abnormal (>90 mm Hg). The funduscopic examination, carotid bruits, and the five aforementioned pulses were also dichotomized as abnormal/normal for analysis. Pulses were considered abnormal if diminished or absent on either side. In addition, three pulse indices were constructed from the radial, femoral, popliteal, dorsalis pedis, posterior tibial pulse, and carotid pulse measurements as follows:

- Leg pulses--femoral, popliteal, dorsalis pedis, and posterior tibial pulses
- Peripheral pulses--radial, femoral, popliteal, dorsalis pedis, and posterior tibial pulses
- All pulses--radial, femoral, popliteal, dorsalis pedis, posterior tibial, and carotid pulses.

Each of these indices was considered normal if all components were normal or abnormal if one or more pulses were abnormal.

Participants with a verified history of diabetes or a 2-hour postprandial glucose level of 200 mg/dl or more, or with a verified history of pre-SEA essential hypertension or heart disease were excluded from the analyses of the peripheral vascular function variables. Individuals with peripheral edema were excluded from the analysis of the individual peripheral pulses in addition to the analysis of the peripheral pulse indices affected by that excluded pulse.

Questionnaire-Physical Examination Associations

The central and peripheral cardiovascular examination findings were analyzed together with the verified cardiovascular disease endpoints to determine the degree of association of the 1987 followup examination and the medical history. In particular, pairwise associations of systolic and diastolic pressure, the overall ECG, heart sounds, the funduscopic examination, carotid bruits, and the peripheral pulses with verified essential hypertension, verified heart disease (excluding essential hypertension), and verified myocardial infarction were investigated.

The same medical exclusions as described previously for the individual variables were made for the questionnaire-physical examination associations.

Covariates

A number of covariates were examined in the cardiovascular examination, both in pairwise associations with the dependent variable and in adjusted statistical analyses. Many of these covariates are considered to be classical risk factors for CHD. Covariates examined included age, race, occupation, lifetime cigarette smoking history, current level of cigarette smoking, lifetime alcohol history, current alcohol use, cholesterol, HDL, cholesterol-HDL ratio, percent body fat, personality type, differential cortisol response, family history of heart disease, and family history of heart disease before the age of 50. Personality type was determined from the Jenkins Activity Survey administered during the 1985 followup examination, and differential cortisol response was determined from laboratory results from the 1985 laboratory examination. Family history of heart disease was defined as "yes" if the participant's brother(s) or father died of heart disease or a heart attack and "no" otherwise. Family history of heart disease before the age of 50 was defined as "yes" if the participant's brother(s) or father died of heart disease or a heart attack before his 50th birthday and "no" otherwise.

In the discussion of the covariate effects, 0 pack-year lifetime cigarette smokers will be referred to as "nonsmokers," at most 10 pack-year lifetime cigarette smokers will be referred to as "moderate lifetime smokers," and greater than 10 pack-year lifetime cigarette smokers will be referred to as "heavy lifetime smokers." The current cigarette smoking categories will be referred to as "nonsmokers," "former smokers," "moderate current smokers" (for those currently smoking >0-20 cigarettes per day), and "heavy current smokers" (for those currently smoking >20 cigarettes per day). Similarly, the lifetime alcohol use categories will be referred to as "nondrinkers" (0 drink-years), "moderate lifetime drinkers" (>0-40 drink-years), and "heavy lifetime drinkers" (>40 drink-years); and the current alcohol use categories will be referred to as "light current drinkers" (≤1 drink/day), "moderate current drinkers" (>1-4 drinks/day), and "heavy current drinkers" (>4 drinks/day). Finally, individuals with less than 10 percent body fat will be referred to as "lean," individuals with between 10 and 25 percent body fat will be referred to as "normal," and individuals with greater than 25 percent body fat will be referred to as "obese."

Participants at the 1987 followup examination who did not attend the 1985 followup examination had missing information for personality type and differential cortisol response. Individuals on corticosteroids in 1985 were excluded from analyses adjusting for differential cortisol. Individuals with fever ($\geq$100°F) or a positive hepatitis B surface antigen test were excluded from analyses adjusting for cholesterol, HDL, and cholesterol-HDL ratio.

Relation to Baseline and 1985 Followup Studies

The evaluation of the 1987 cardiovascular examination was similar to the Baseline examination and the 1985 followup. The Doppler evaluation of the peripheral pulses was not conducted for the 1987 followup. Also, the two history of heart disease covariates were added for the 1987 followup.

The cardiovascular longitudinal analysis focused on the overall ECG diagnosis, where group differences in the changes from Baseline to the 1987 followup were analyzed.

Statistical Methods

Most of the basic statistical analysis methods used in the cardiovascular examination are described in Chapter 7. Due to the large number of covariates, however, adjusted Ranch Hand versus Comparison contrasts were carried out as follows: (1) Models adjusting only for age, race, and occupation were examined first; followed by (2) models incorporating group-by-age, group-by-race, and group-by-occupation interactions. Analyses were then performed adjusting for (3) all covariates; and (4) all covariates, but with only one variable selected from among each of the following sets: (a) lifetime cigarette smoking history and current cigarette smoking level; (b) lifetime alcohol history and current alcohol use; (c) cholesterol, HDL, and the cholesterol-HDL ratio; and (d) family history of heart disease and family history of heart disease before the age of 50. The first three analyses were done for preliminary investigative purposes; only results from the last analysis are reported.

Table 15-1 summarizes the statistical analyses performed for the 1987 cardiovascular examination. The first part of this table describes the dependent variables analyzed. The second part of this table provides a further description of candidate covariates examined. Abbreviations are used extensively in the body of the table and are defined in footnotes.

Table 15-2 provides a list of the number of participants excluded and reasons for exclusion by group, as well as the number of participants with missing data for the dependent variables and covariates described in Table 15-1.

TABLE 15-1.

Statistical Analysis for the Cardiovascular Evaluation

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analyses
Reported Essential Hypertension	Q-SR, PE	D	No Yes	AGE,RACE,OCC, CSMOK,PACKYR, ALC,DRKYR, CHOL,HDL, CHOL/HDL, %BFAT,PERS, DIFCORT, HRTDIS, HRTDIS50	UC:CS,FT AC:LR CA:CS,FT UE:CS,FT AE:LR
Verified Essential Hypertension	Q-V, PE	D	No Yes	AGE,RACE,OCC, CSMOK,PACKYR, ALC,DRKYR, CHOL,HDL, CHOL/HDL, %BFAT,PERS, DIFCORT, HRTDIS, HRTDIS50	UC:CS,FT AC:LR CA:CS,FT UE:CS,FT AE:LR
Reported Heart Disease (Excluding Essential Hypertension)	Q-SR, PE	D	No Yes	AGE,RACE,OCC, CSMOK,PACKYR, ALC,DRKYR, CHOL,HDL, CHOL/HDL, %BFAT,PERS, DIFCORT, HRTDIS, HRTDIS50	UC:CS,FT AC:LR CA:CS,FT UE:CS,FT AE:LR
Verified Heart Disease (Excluding Essential Hypertension)	Q-V, PE	D	No Yes	AGE,RACE,OCC, CSMOK,PACKYR, ALC,DRKYR, CHOL,HDL, CHOL/HDL, %BFAT,PERS, DIFCORT, HRTDIS, HRTDIS50	UC:CS,FT AC:LR CA:CS,FT UE:CS,FT AE:LR

TABLE 15-1. (continued)

Statistical Analysis for the Cardiovascular Evaluation

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analyses
Reported Myocardial Infarction	Q-SR, PE	D	No Yes	AGE,RACE,OCC, CSMOK,PACKYR, ALC,DRKYR, CHOL,HDL, CHOL/HDL, %BFAT,PERS, DIFCORT, HRTDIS, HRTDIS50	UC:CS,FT AC:LR CA:CS,FT UE:CS,FT AE:LR
Verified Myocardial Infarction	Q-V, PE	D	No Yes	AGE,RACE,OCC, CSMOK,PACKYR, ALC,DRKYR, CHOL,HDL, CHOL/HDL, %BFAT,PERS, DIFCORT, HRTDIS, HRTDIS50	UC:CS,FT AC:LR CA:CS,FT UE:CS,FT AE:LR
Morbidity-Mortality Analysis	Q-V, PE	D	Living Deceased	--	Descriptive Only
Systolic Blood Pressure (mm Hg)	PE	D/C	Normal: <140 Abnormal: >140	AGE,RACE,OCC, CSMOK,PACKYR, ALC,DRKYR, CHOL,HDL, CHOL/HDL, %BFAT,PERS, DIFCORT, HRTDIS, HRTDIS50	UC:CS,FT,TT AC:LR,GLM CA:CC,TT,GLM, CS,FT UE:CS,FT, GLM,TT AE:LR,GLM

TABLE 15-1. (continued)

Statistical Analysis for the Cardiovascular Evaluation

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analyses
Heart Sounds	PE	D	Normal Abnormal	AGE,RACE,OCC, CSMOK,PACKYR, ALC,DRKYR, CHOL,HDL, CHOL/HDL, %BFAT,PERS, DIFCORT, HRTDIS, HRTDIS50	UC:CS,FT AC:LR CA:CS,FT UE:CS,FT AE:LR
ECG: Overall	PE	D	Normal Abnormal	AGE,RACE,OCC, CSMOK,PACKYR, ALC,DRKYR, CHOL,HDL, CHOL/HDL, %BFAT,PERS, DIFCORT, HRTDIS, HRTDIS50	UC:CS,FT AC:LR CA:CS,FT UE:CS,FT AE:LR L:OR
ECG: RBBB	PE	D	Normal Abnormal	AGE,RACE,OCC, CSMOK,PACKYR, ALC,DRKYR, CHOL,HDL, CHOL/HDL, %BFAT,PERS, DIFCORT, HRTDIS, HRTDIS50	UC:CS,FT AC:LR CA:CS,FT UE:CS,FT AE:LR
ECG: LBBB	PE	D	Normal Abnormal	AGE,RACE,OCC, CSMOK,PACKYR, ALC,DRKYR, CHOL,HDL, CHOL/HDL, %BFAT,PERS, DIFCORT, HRTDIS, HRTDIS50	UC:CS,FT AC:LR CA:CS,FT UE:CS,FT AE:LR

TABLE 15-1. (continued)

Statistical Analysis for the Cardiovascular Evaluation

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analyses
ECG: Nonspecific T-Waves	PE	D	Normal Abnormal	AGE,RACE,OCC, CSMOK,PACKYR, ALC,DRKYR, CHOL,HDL, CHOL/HDL, %BFAT,PERS, DIFCORT, HRTDIS, HRTDIS50	UC:CS,FT AC:LR CA:CS,FT UE:CS,FT AE:LR
ECG: Bradycardia	PE	D	Normal Abnormal	AGE,RACE,OCC, CSMOK,PACKYR, ALC,DRKYR, CHOL,HDL, CHOL/HDL, %BFAT,PERS, DIFCORT, HRTDIS, HRTDIS50	UC:CS,FT AC:LR CA:CS,FT UE:CS,FT AE:LR
ECG: Tachycardia	PE	D	Normal Abnormal	AGE,RACE,OCC, CSMOK,PACKYR, ALC,DRKYR, CHOL,HDL, CHOL/HDL, %BFAT,PERS, DIFCORT, HRTDIS, HRTDIS50	UC:CS,FT AC:LR CA:CS,FT UE:CS,FT AE:LR
ECG: Arrhythmia	PE	D	Normal Abnormal	AGE,RACE,OCC, CSMOK,PACKYR, ALC,DRKYR, CHOL,HDL, CHOL/HDL, %BFAT,PERS, DIFCORT, HRTDIS, HRTDIS50	UC:CS,FT AC:LR CA:CS,FT UE:CS,FT AE:LR

TABLE 15-1. (continued)

Statistical Analysis for the Cardiovascular Evaluation

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analyses
ECG: Other Diagnoses	PE	D	Normal Abnormal	AGE,RACE,OCC, CSMOK,PACKYR, ALC,DRKYR, CHOL,HDL, CHOL/HDL, %BFAT,PERS, DIFCORT, HRTDIS, HRTDIS50	UC:CS,FT AC:LR CA:CS,FT UE:CS,FT AE:LR
Diastolic Blood Pressure (mm Hg)	PE	D/C	Normal: <90 Abnormal: >90	AGE,RACE,OCC, CSMOK,PACKYR, ALC,DRKYR, CHOL,HDL, CHOL/HDL, %BFAT,PERS, DIFCORT, HRTDIS, HRTDIS50	UC:CS,FT,TT AC:LR,GLM CA:CC,TT,GLM, CS,FT UE:CS,FT, GLM,TT AE:LR,GLM
Funduscopic Examination	PE	D	Normal Abnormal	AGE,RACE,OCC, CSMOK,PACKYR, ALC,DRKYR, CHOL,HDL, CHOL/HDL, %BFAT,PERS, DIFCORT, HRTDIS, HRTDIS50	UC:CS,FT AC:LR CA:CS,FT UE:CS,FT AE:LR
Carotid Bruits	PE	D	Normal Abnormal	AGE,RACE,OCC, CSMOK,PACKYR, ALC,DRKYR, CHOL,HDL, CHOL/HDL, %BFAT,PERS, DIFCORT, HRTDIS, HRTDIS50	UC:CS,FT AC:LR CA:CS,FT UE:CS,FT AE:LR

TABLE 15-1. (continued)

Statistical Analysis for the Cardiovascular Evaluation

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analyses
Radial Pulses	PE	D	Normal Abnormal	AGE,RACE,OCC, CSMOK,PACKYR, ALC,DRKYR, CHOL,HDL, CHOL/HDL, %BFAT,PERS, DIFCORT, HRTDIS, HRTDIS50	UC:CS,FT AC:LR CA:CS,FT UE:CS,FT AE:LR
Femoral Pulses	PE	D	Normal Abnormal	AGE,RACE,OCC, CSMOK,PACKYR, ALC,DRKYR, CHOL,HDL, CHOL/HDL, %BFAT,PERS, DIFCORT, HRTDIS, HRTDIS50	UC:CS,FT AC:LR CA:CS,FT UE:CS,FT AE:LR
Popliteal Pulses	PE	D	Normal Abnormal	AGE,RACE,OCC, CSMOK,PACKYR, ALC,DRKYR, CHOL,HDL, CHOL/HDL, %BFAT,PERS, DIFCORT, HRTDIS, HRTDIS50	UC:CS,FT AC:LR CA:CS,FT UE:CS,FT AE:LR
Dorsalis Pedis Pulses	PE	D	Normal Abnormal	AGE,RACE,OCC, CSMOK,PACKYR, ALC,DRKYR, CHOL,HDL, CHOL/HDL, %BFAT,PERS, DIFCORT, HRTDIS, HRTDIS50	UC:CS,FT AC:LR CA:CS,FT UE:CS,FT AE:LR

TABLE 15-1. (continued)

Statistical Analysis for the Cardiovascular Evaluation

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analyses
Posterior Tibial Pulses	PE	D	Normal Abnormal	AGE,RACE,OCC, CSMOK,PACKYR, ALC,DRKYR, CHOL,HDL, CHOL/HDL, %BFAT,PERS, DIFCORT, HRTDIS, HRTDIS50	UC:CS,FT AC:LR CA:CS,FT UE:CS,FT AE:LR
Leg Pulses	PE	D	Normal Abnormal	AGE,RACE,OCC, CSMOK,PACKYR, ALC,DRKYR, CHOL,HDL, CHOL/HDL, %BFAT,PERS, DIFCORT, HRTDIS, HRTDIS50	UC:CS,FT AC:LR CA:CS,FT UE:CS,FT AE:LR
Peripheral Pulses	PE	D	Normal Abnormal	AGE,RACE,OCC, CSMOK,PACKYR, ALC,DRKYR, CHOL,HDL, CHOL/HDL, %BFAT,PERS, DIFCORT, HRTDIS, HRTDIS50	UC:CS,FT AC:LR CA:CS,FT UE:CS,FT AE:LR
All Pulses	PE	D	Normal Abnormal	AGE,RACE,OCC, CSMOK,PACKYR, ALC,DRKYR, CHOL,HDL, CHOL/HDL, %BFAT,PERS, DIFCORT, HRTDIS, HRTDIS50	UC:CS,FT AC:LR CA:CS,FT UE:CS,FT AE:LR
Questionnaire-Physical Exam	PE	D	Normal Abnormal	--	UC:CS,FT

TABLE 15-1. (continued)

Statistical Analysis for the Cardiovascular Evaluation

Covariates

Variable (Abbreviation)	Data Source	Data Form	Cutpoints
Age (AGE)	MIL	D/C	Born ≥1942 Born 1923-1941 Born ≤1922
Race (RACE)	MIL	D	Nonblack Black
Occupation (OCC)	MIL	D	Officer Enlisted Flyer Enlisted Groundcrew
Lifetime Cigarette Smoking History (PACKYR) (pack-years)	Q-SR	D/C	0 >0-10 >10
Current Cigarette Smoking (CSMOK) (cigarettes/day)	Q-SR	D/C	0-Never 0-Former >0-20 >20
Lifetime Alcohol History (DRKYR) (drink-years)	Q-SR	D/C	0 >0-40 >40
Current Alcohol Use (ALC) (drinks/day)	Q-SR	D/C	0-1 >1-4 >4
Cholesterol (CHOL) (mg/dl)	LAB	D/C	≤200 >200-230 >230
High Density Lipoprotein (HDL) (mg/dl)	LAB	D/C	≤40 >40-50 >50
Cholesterol-HDL Ratio (CHOL/HDL)	LAB	D/C	≤4.2 >4.2-5.5 >5.5
Percent Body Fat (%BFAT)	PE	D/C	Lean: <10% Normal: 10-25% Obese: >25%

TABLE 15-1. (continued)

Statistical Analysis for the Cardiovascular Evaluation

Covariates

Variable (Abbreviation)	Data Source	Data Form	Cutpoints
Personality Type (PERS)	PE (1985)	D/C	A Direction B Direction
Differential Cortisol Response (DIFCORT)	LAB (1985)	D/C	<0.6 ≥0.6-4.0 >4.0
Family History of Heart Disease (HRTDIS)	Q-SR	D	Yes No
Family History of Heart Disease Before Age 50 (HRTDIS50)	Q-SR	D	Yes No

Abbreviations:

Data Source:
- LAB--1987 SCRF laboratory results
- LAB (1985)--1985 SCRF laboratory results
- MIL--Air Force military records
- PE--1987 SCRF physical exam
- PE (1985)--1985 SCRF physical exam
- Q-V--1987 NORC questionnaire (verified)

Data Form:
- D--Discrete analysis only
- D/C--Discrete and continuous analyses for dependent variables; appropriate form for analysis (either discrete or continuous) for covariates.

Statistical Analyses:
- UC--Unadjusted core analyses
- AC--Adjusted core analyses
- CA--Dependent variable-covariate associations
- UE--Unadjusted exposure index analyses
- AE--Adjusted exposure index analyses
- L--Longitudinal analyses

Statistical Methods:
- CC--Pearson's product moment correlation coefficient
- CS--Pearson's chi-square test
- FT--Fisher's exact test
- GLM--General linear models analysis
- LR--Logistic regression analysis
- OR--Chi-square test on the odds ratio
- TT--Two-sample t-test

TABLE 15-2.

Number of Participants Excluded and With Missing Data for the Cardiovascular Evaluation by Group

Variable	Analysis Use	Group: Ranch Hand	Group: Comparison	Total
Verified History of Diabetes or 2-Hour Postprandial Glucose $\geq$200 mg/dl	EXC	98	121	219
Pre-SEA Verified Essential Hypertension or Heart Disease	EXC	20	34	54
Pitting and Nonpitting Edema	EXC[a]	22	30	52
Personality Type (1985)	COV	39	78	117
Differential Cortisol Response (1985)	COV	35	76	111
Corticosteroids (1985)	EXC[b]	5	9	14
Cholesterol	COV	1	2	3
HDL	COV	1	2	3
Cholesterol-HDL Ratio	COV	1	2	3
Temperature $\geq$100°F at Laboratory Examination	EXC[c]	1	3	4
Positive Hepatitis B Surface Antigen	EXC[c]	7	8	15
Femoral Pulses	DEP	1	1	2
Dorsalis Pulses	DEP	1	1	2
Posterior Pulses	DEP	1	2	3
Leg Pulses	DEP	2	1	3
Peripheral Pulses	DEP	2	1	3
All Pulses	DEP	4	3	7

Abbreviations: EXC--Exclusion
COV--Covariate (missing data)
DEP--Dependent variable (missing data)

[a]Exclusion from analyses of peripheral pulses only.
[b]Exclusion from analyses adjusted for differential cortisol response.
[c]Exclusion from analyses adjusted for cholesterol, HDL, or cholesterol-HDL ratio.

RESULTS

Ranch Hand and Comparison Group Contrasts

Questionnaire Variables

Table 15-3 contains the results of the unadjusted analyses for reported and verified essential hypertension, reported and verified heart disease, and reported and verified myocardial infarction. These tables give the percentage of individuals experiencing and not experiencing these events in each group, along with the estimated relative risks, 95 percent confidence intervals, and p-values. Table L-1, Appendix L, contains the results from examination of the pairwise associations between each of these variables and the covariates. Table 15-4 gives the results of the adjusted group comparisons.

Reported and Verified Essential Hypertension

All of the reported cases of essential hypertension were verified upon medical records review; thus, analyses based upon reported and verified events were identical. Approximately one-third of the individuals in each group had essential hypertension, with an unadjusted relative risk not significantly different from 1 (p=0.457).

Essential hypertension was significantly associated with age (p<0.001), lifetime cigarette smoking (p=0.024), current cigarette smoking (p=0.001), lifetime alcohol history (p<0.001), current alcohol use (p<0.001), cholesterol (p=0.001), cholesterol-HDL ratio (p=0.012), percent body fat (p<0.001), and family history of heart disease (p=0.001). The percentages of individuals with essential hypertension increased with age (25.5% for those born in or after 1942, 37.8% for those born between 1923 and 1941, and 55.2% for those born in or before 1922); cholesterol (27.8% for those with cholesterol levels ≤200 mg/dl, 34.3% for those with cholesterol levels 200-230 mg/dl, and 37.0% for those with cholesterol levels >230 mg/dl); cholesterol-HDL ratio (29.2%, 33.4%, and 36.9% for individuals with ratios ≤4.2, 4.2-5.5, and >5.5, respectively); and percent body fat (0.0% for lean individuals, 28.2% for normal individuals, and 55.3% for obese individuals). Moderate lifetime smokers had the lowest percentage of hypertension (28.4%), compared to nonsmokers and heavy lifetime smokers (34.2% and 35.0%, respectively). Nonsmokers and former smokers had a higher frequency of hypertension (34.1% and 36.9%, respectively) than moderate current smokers and heavy current smokers (26.0% and 28.7%, respectively). Heavy lifetime drinkers had a higher percentage with hypertension (42.6%) than moderate lifetime drinkers and nondrinkers (29.9% and 32.2%, respectively). The percentage with hypertension was greatest in moderate current drinkers (44.6%), intermediate in heavy current drinkers (40.3%), and lowest in light current drinkers (30.1%). Individuals with a family history of heart disease were also more likely to have hypertension than those without a family history of heart disease (39.4% vs. 31.1%).

Comparisons between the two groups adjusted for covariates detected significant effects of age (p<0.001), lifetime alcohol history (p=0.002),

TABLE 15-3.

Unadjusted Analysis for Cardiovascular Variables by Group (Questionnaire Data)

Variable	Statistic	Group: Ranch Hand		Group: Comparison		Est. Relative Risk (95% C.I.)	p-Value
Reported/Verified Essential Hypertension*	n	878		1,150			
	Number/%						
	Yes	297	33.8%	371	32.3%	1.07 (0.89,1.29)	0.457
	No	581	66.2%	779	67.7%		
Reported Heart Disease (Excluding Hypertension)	n	878		1,150			
	Number/%						
	Yes	340	38.7%	428	37.2%	1.07 (0.89,1.28)	0.488
	No	538	61.3%	722	62.8%		
Verified Heart Disease (Excluding Hypertension)	n	878		1,150			
	Number/%						
	Yes	337	38.4%	427	37.1%	1.06 (0.88,1.26)	0.564
	No	541	61.6%	723	62.9%		
Reported/Verified Myocardial Infarction*	n	878		1,150			
	Number/%						
	Yes	39	4.4%	53	4.6%	0.96 (0.63,1.47)	0.859
	No	839	95.6%	1,097	95.4%		

*No conditions reported that were not verified; therefore, reported and verified analyses are the same.

TABLE 15-4.

Adjusted Analysis for Cardiovascular Variables by Group (Questionnaire Data)

Variable	Statistic	Group: Ranch Hand	Group: Comparison	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Reported/Verified Essential Hypertension*	n	862	1,136	1.09 (0.90,1.33)	0.382	AGE (p<0.001) DRKYR (p=0.002) CHOL (p=0.004) %BFAT (p<0.001)
Reported Heart Disease (Excluding Hypertension)	n	878	1,150	1.08 (0.90,1.30)	0.402	AGE (p<0.001) RACE (p=0.008) CSMOK (p=0.004)
Verified Heart Disease (Excluding Hypertension)	n	878	1,150	1.07 (0.89,1.29)	0.464	AGE (p<0.001) RACE (p=0.007) CSMOK (p=0.002)
Reported/Verified Myocardial Infarction*	n	872	1,139	0.92 (0.59,1.43)**	0.702**	GRP*HRTDIS (p=0.042) AGE (p<0.001) PACKYR (p=0.001) CHOL/HDL (p<0.001)

*No conditions reported that were not verified; therefore, reported and verified analyses are the same.

**Group-by-covariate interaction (0.01<p≤0.05)—adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction.

GRP: Group (Ranch Hand, Comparison).

cholesterol (p=0.004), and percent body fat (p<0.001), but the adjusted relative risk was not significant (p=0.382).

Reported and Verified Heart Disease

All but four of the reported cases of heart disease were verified (three Ranch Hands and one Comparison). Consequently, analyses based upon reported and verified events gave very similar results. The percentage of individuals with reported and verified heart disease was similar in the Ranch Hand and Comparison groups in the unadjusted analyses (p=0.488 and p=0.564, respectively).

Both reported and verified heart disease were significantly associated with age (p<0.001 in each case); occupation (p=0.002 and p=0.001, respectively); current cigarette smoking (p=0.008 and p=0.003, respectively); and family history of heart disease (p=0.024 and p=0.033, respectively). In addition, the association between verified heart disease and race was also statistically significant (p=0.047). (The association between reported heart disease and race was borderline significant [p=0.053].) Reported heart disease increased with age (32.6% for those born in or after 1942, 41.0% for those born between 1923 and 1941, and 58.2% for those born in or before 1922). Blacks had a higher rate than nonblacks (46.9% vs. 37.3%); officers had a higher rate than enlisted flyers, who had a slightly higher rate than enlisted groundcrew (42.6%, 36.6%, and 34.4%, respectively). Former smokers had the highest rate of reported heart disease (40.9%), followed by nonsmokers (38.8%), moderate current smokers (36.6%), and heavy current smokers (30.2%). Individuals with a family history of heart disease had a higher rate than those without a family history of heart disease (42.5% vs. 36.5%). As noted above, these figures are nearly identical to those for verified heart disease.

Adjusted analyses of reported heart disease detected significant effects of age (p<0.001), race (p=0.008), and current cigarette smoking (p=0.004), but the relative risk for the two groups was near 1 (p=0.402). Results from the adjusted analysis of verified heart disease were essentially the same (p=0.464) as that of reported heart disease.

Reported and Verified Myocardial Infarction

All of the reported cases were verified upon medical records review. The percentage of individuals with myocardial infarction was slightly less in the Ranch Hand group than in the Comparison group, but not significant (unadjusted p=0.859).

Myocardial infarction was significantly associated with age (p<0.001), lifetime cigarette smoking (p<0.001), current cigarette smoking (p=0.015), cholesterol (p=0.007), HDL (p<0.001), cholesterol-HDL ratio (p<0.001), and family history of heart disease (p<0.001). The percentage of individuals with infarction increased with age (1.4% for those born in or after 1942, 6.1% for those born between 1923 and 1941, and 20.9% for those born in or before 1922) and lifetime cigarette smoking (2.3% for nonsmokers, 3.3% for moderate lifetime smokers, and 6.8% for heavy lifetime smokers). In terms of current cigarette smoking, the lowest frequency was among nonsmokers (2.3%) and the highest frequency was among former smokers (6.0%); moderate and heavy current smokers had intermediate values (4.7% and 4.9%, respectively). The percentage of individuals with myocardial infarction increased with increasing cholesterol levels (3.0% for those with cholesterol levels <200 mg/dl, 4.2% for those with levels 200-230 mg/dl, and 6.5% for those with levels 230 mg/dl); decreased with increasing HDL levels (8.2% for those with HDL levels <40 mg/dl, 3.5% for those with levels 40-50 mg/dl, and 2.6% for those with levels >50 mg/dl); and increased with increasing cholesterol-HDL ratios (2.9% for those with ratios ≤4.2, 3.5% for those with ratios 4.2-5.5, and 8.0% for those with ratios >5.5). Individuals with a family history of heart disease had more than double the rate of myocardial infarction than those without a history (7.8% vs. 3.6%).

In the adjusted analysis of myocardial infarction, a statistically significant group-by-family history of heart disease interaction was detected (p=0.042), as well as significant age (p<0.001), lifetime cigarette smoking (p=0.001), and cholesterol-HDL ratio (p<0.001) effects. This interaction is explored more fully in Appendix L, Table L-2, where the frequency distribution and adjusted relative risks stratified by family history of heart disease are provided. Of the Ranch Hands with a positive family history, 9.4 percent had disease, while only 6.6 percent of the Comparisons with a comparable history had disease. Of those men without a positive family history, 3.0 percent of the Ranch Hands and 4.1 percent of the Comparisons had disease. Neither of these within-stratum differences was statistically significant (p=0.278 and p=0.130, respectively). However, since the significance level was between 0.01 and 0.05, Table 15-4 also gives the results after deleting the interaction term from the model. For this model, the adjusted relative risk was not statistically significant (p=0.702).

Physical Examination Variables: Central Cardiac Function

Table 15-5 gives the results of the unadjusted analyses for the variables related to central cardiac function: systolic blood pressure, heart sounds, overall ECG abnormalities, RBBB, LBBB, nonspecific T-waves, bradycardia, tachycardia, arrhythmia, and other ECG diagnoses. The table gives the percentage of individuals with abnormal and normal findings, estimated relative risks, 95 percent confidence intervals, and p-values. For systolic blood pressure, results of a continuous analysis are also presented. Appendix L, Table L-1, gives the dependent variable-covariate associations, and Table 15-6 gives the results of the adjusted analyses.

<u>Systolic Blood Pressure</u>

The unadjusted mean systolic blood pressure was not significantly different in the two groups (p=0.809), nor was the percent with abnormal systolic blood pressure different (p=0.518).

Systolic blood pressure was significantly associated with age (p<0.001 for both continuous and discrete analyses); lifetime cigarette smoking (p=0.022, continuous); current cigarette smoking (p<0.001, continuous and p=0.002, discrete); lifetime alcohol history (p=0.016, continuous and p=0.006, discrete); current alcohol use (p=0.002, continuous and p=0.010, discrete);

TABLE 15-5.

Unadjusted Analysis for Cardiovascular Variables by Group (Central Cardiac Function)

Variable	Statistic	Group: Ranch Hand		Group: Comparison		Est. Relative Risk (95% C.I.)	p-Value
Systolic Blood Pressure	n	878		1,150			
	Mean	127.06		126.87		—	0.809
	95% C.I.	(125.90,128.22)		(125.85,127.89)			
	Number/%						
	Abnormal	170	19.4%	236	20.5%	0.93 (0.75,1.16)	0.518
	Normal	708	80.6%	914	79.5%		
Heart Sounds	n	878		1,150			
	Number/%						
	Abnormal	35	4.0%	53	4.6%	0.86 (0.56,1.33)	0.494
	Normal	843	96.0%	1,097	95.4%		
ECG-Overall	n	878		1,150			
	Number/%						
	Abnormal	138	15.7%	205	17.8%	0.86 (0.68,1.09)	0.208
	Normal	740	84.3%	945	82.2%		
RBBB	n	878		1,150			
	Number/%						
	Abnormal	4	0.5%	8	0.7%	0.65 (0.20,2.18)	0.479
	Normal	874	99.5%	1,142	99.3%		

TABLE 15-5. (continued)

Unadjusted Analysis for Cardiovascular Variables by Group (Central Cardiac Function)

Variable	Statistic	Group: Ranch Hand		Group: Comparison		Est. Relative Risk (95% C.I.)	p-Value
LBBB	n	878		1,150			
	Number/%						
	Abnormal	1	0.1%	4	0.4%	0.33 (0.04,2.93)	0.271
	Normal	877	99.9%	1,146	99.6%		
Nonspecific T-Waves	n	878		1,150			
	Number/%						
	Abnormal	93	10.6%	130	11.3%	0.93 (0.70,1.23)	0.611
	Normal	785	89.4%	1,020	88.7%		
Bradycardia	n	878		1,150			
	Number/%						
	Abnormal	37	4.2%	71	6.2%	0.67 (0.44,1.00)	0.049
	Normal	841	95.8%	1,079	93.8%		
Tachycardia	n	878		1,150			
	Number/%						
	Abnormal	0	0.0%	1	0.1%	—	0.999
	Normal	878	100.0%	1,149	99.9%		
Arrhythmia	n	878		1,150			
	Number/%						
	Abnormal	41	4.7%	39	3.4%	1.40 (0.89,2.18)	0.145
	Normal	837	95.3%	1,111	96.6%		

TABLE 15-5. (continued)

Unadjusted Analysis for Cardiovascular Variables by Group (Central Cardiac Function)

Variable	Statistic	Group: Ranch Hand		Group: Comparison		Est. Relative Risk (95% C.I.)	p-Value
ECG-Other Diagnosis	n	878		1,150			
	Number/%						
	Abnormal	158	18.0%	219	19.0%	0.93 (0.74,1.17)	0.548
	Normal	720	82.0%	931	81.0%		

—Estimated relative risk not applicable for continuous analysis of a variable; estimated relative risk/confidence interval not given due to cells with zero frequency.

TABLE 15-6.

Adjusted Analysis for Cardiovascular Variables by Group (Central Cardiac Function)

Variable	Statistic	Group: Ranch Hand	Group: Comparison	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Systolic Blood Pressure	n Adj. Mean 95% C.I.	873 128.60 (126.74,130.45)	1,149 128.18 (126.42,129.94)	—	0.579	AGE (p<0.001) RACE (p=0.039) OCC (p=0.015) ALC (p<0.001) %BFAT (p<0.001)
	n	834	1,064	0.94 (0.75,1.19)**	0.607**	GRP*CHOL/HDL (p=0.020) AGE (p<0.001) ALC (p=0.012) %BFAT (p<0.001) PERS (p=0.005)
Heart Sounds	n	878	1,150	0.86 (0.56,1.34)	0.503	AGE (p<0.001)
ECG-Overall	n	878	1,150	0.86 (0.67,1.09)	0.212	AGE (p<0.001) RACE (p=0.008) PACKYR (p=0.019) %BFAT (p=0.027)
RBBB	n	878	1,150	0.66 (0.20,2.21)	0.493[a]	AGE (p=0.008)
Nonspecific T-Waves	n	878	1,150	****	****	GRP*PACKYR (p=0.004) AGE (p<0.001) %BFAT (p<0.001)

TABLE 15-6. (continued)

Adjusted Analysis for Cardiovascular Variables by Group (Central Cardiac Function)

Variable	Statistic	Group: Ranch Hand	Group: Comparison	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Bradycardia	n	872	1,139	0.69 (0.46,1.04)	0.068	CSMOK (p<0.001) CHOL/HDL (p=0.006) %BFAT (p=0.004)
Arrhythmia	n	842	1,070	1.56 (0.98,2.49)	0.062	AGE (p<0.001) DIFCORT (p=0.010)
ECG-Other Diagnoses	n	878	1,150	0.93 (0.74,1.17)	0.539	AGE (p<0.001)

--Adjusted relative risk not applicable for continuous analysis of a variable.

[a]Adjusted for age only.

**Group-by-covariate interaction ($0.01<p\leq 0.05$)--adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction.

****Group-by-covariate interaction ($p\leq 0.01$)--adjusted relative risk, confidence interval, and p-value not presented.

cholesterol ($p<0.001$, continuous and $p=0.006$, discrete); cholesterol-HDL ratio ($p=0.007$, continuous); percent body fat ($p<0.001$, continuous and discrete); and personality type ($p=0.047$, continuous and $p=0.026$, discrete). Systolic blood pressure increased with age ($r=0.187$), with 14.2 percent abnormal among those born in or after 1942, 23.6 percent abnormal among those born between 1923 and 1941, and 41.8 percent abnormal among those born in or before 1922.

Systolic blood pressure was also positively associated with lifetime cigarette smoking, although the correlation was quite small ($r=0.051$). The association between systolic blood pressure and current cigarette smoking, however, was negative ($r=-0.102$). The greatest percent abnormal was among former smokers (24.2%), with nonsmokers, moderate current smokers, and heavy current smokers having 18.1 percent, 17.5 percent, and 15.9 percent abnormal, respectively.

Heavy lifetime drinkers had the highest percent abnormal (25.5%), compared to nondrinkers (19.2%) and moderate drinkers (18.5%). The correlation coefficient was 0.054. Systolic blood pressure was positively associated with current alcohol use ($r=0.070$), with 18.7 percent of light current drinkers exhibiting abnormalities, 24.6 percent of moderate current drinkers, and 28.4 percent of heavy current drinkers.

The associations with cholesterol and cholesterol-HDL ratio were both positive but slight ($r=0.097$ and $r=0.060$, respectively); 16.9 percent of individuals with cholesterol levels less than or equal to 200 mg/dl were abnormal, compared to 19.7 percent for individuals with levels between 200 and 230 mg/dl and 23.8 percent for individuals with levels greater than 230 mg/dl. Systolic blood pressure was positively associated with percent body fat ($r=0.234$); 12.5 percent of lean individuals were abnormal, 17.3 percent of normal individuals, and 32.6 percent of obese individuals. Finally, the association between systolic blood pressure and personality type was slightly negative ($r=-0.045$), with 18.2 percent of Type A personalities abnormal, as compared to 22.4 percent of Type Bs.

Adjusted continuous analyses detected significant effects of age ($p<0.001$), race ($p=0.039$), occupation ($p=0.015$), current alcohol use ($p<0.001$), and percent body fat ($p<0.001$), but the adjusted group means were not significantly different ($p=0.579$).

Adjusted discrete analyses detected significant effects of age ($p<0.001$), current alcohol use ($p=0.012$), percent body fat ($p<0.001$), and personality type ($p=0.005$), and a significant group-by-cholesterol-HDL ratio interaction ($p=0.020$). This interaction is explored in Appendix L, Table L-2. After stratification by levels of the cholesterol-HDL ratio, the adjusted relative risk was less than 1 for those with cholesterol-HDL ratios less than or equal to 4.2 or between 4.2 and 5.5, whereas the adjusted relative risk was greater than 1 for those with cholesterol-HDL ratios greater than 5.5. None of the within-stratum relative risks was statistically significant ($p=0.266$, $p=0.188$, and $p=0.111$, respectively). The adjusted relative risk was not significant when the interaction term was deleted from the model ($p=0.607$).

Heart Sounds

The percentage of individuals with abnormal heart sounds was not significantly different in the two groups (p=0.494) for the unadjusted contrast.

Significant associations were detected between abnormal heart sounds and age (p<0.001), current cigarette smoking (p=0.013), cholesterol-HDL ratio (p=0.020), and family history of heart disease (p=0.009). Abnormal heart sounds increased with age, with 2.7 percent abnormal among those born in or after 1942, 5.2 percent abnormal among those born between 1923 and 1941, and 13.4 percent abnormal among those born in or before 1922. Former smokers had the highest percent abnormal (5.8%), followed by moderate current smokers (4.4%), nonsmokers (3.9%), and heavy current smokers (1.5%). Individuals with cholesterol-HDL ratios less than or equal to 4.2 and those with ratios greater than 5.5 had a higher percent abnormal than those with ratios between 4.2 and 5.5 (4.6% and 5.9%, respectively, vs. 2.8%). The percent with abnormal heart sounds among individuals with a family history of heart disease was 6.7 percent, compared to 3.7 percent in those without a family history of heart disease.

Adjusted analyses detected a significant effect of age (p<0.001); the adjusted relative risk between the Ranch Hand and Comparison groups was not significant (p=0.503).

Overall ECG Findings

The Ranch Hands exhibited fewer overall abnormal ECG findings than the Comparisons--this unadjusted difference was not statistically significant (p=0.208).

Overall ECG findings were significantly associated with age (p<0.001), occupation (p=0.047), lifetime cigarette smoking (p=0.002), current cigarette smoking (p=0.003), cholesterol (p=0.045), and percent body fat (p=0.023). Abnormal findings increased with age (10.8%, 20.1%, and 47.8% abnormal in those born in or after 1942, between 1923 and 1941, and in or before 1922, respectively). Officers and enlisted flyers had a higher percent abnormal (18.5% and 19.3%, respectively) than enlisted groundcrew (14.7%). The percent with abnormal ECGs was greater in heavy lifetime smokers (20.3%) than nonsmokers or moderate lifetime smokers (14.2% and 14.4%, respectively). Former smokers had the greatest percent abnormal (20.5%), followed by heavy current smokers (16.8%), nonsmokers (14.2%), and moderate current smokers (13.2%). The percent abnormal increased with increasing cholesterol levels (15.2%, 16.0%, and 19.9% for those with cholesterol levels ≤200 mg/dl, 200-230 mg/dl, and 230 mg/dl, respectively). Both lean and obese individuals had a higher percent abnormal than normal individuals (25.0%, 21.6%, and 15.8%, respectively).

Adjusted analyses detected significant covariate effects of age (p<0.001), race (p=0.008), lifetime cigarette smoking (p=0.019), and percent body fat (p=0.027). The adjusted relative risk between the Ranch Hand and Comparison groups was not statistically significant (p=0.212).

RBBB

Only 12 individuals exhibited RBBB, 4 from the Ranch Hand group and 8 from the Comparison group; this unadjusted difference was not statistically significant (p=0.479).

RBBB was positively associated with age (p=0.011), with RBBB detected in 0.2 percent of those born in or after 1942, 0.8 percent of those born between 1923 and 1941, and 3.0 percent of those born in or before 1922.

Due to the small number of abnormalities, further analyses were conducted adjusting only for age. The age covariate from the analyses was statistically significant (p=0.008), but the adjusted relative risk was not significant (p=0.493).

LBBB

Five individuals exhibited LBBB: one from the Ranch Hand group and four from the Comparison group; this unadjusted difference was not statistically significant (p=0.271). No significant associations were detected with any of the covariates. The small number of abnormalities precluded adjusted analyses.

Nonspecific T-Waves

The percentage of individuals with nonspecific T-waves was not significantly different in the Ranch Hand and Comparison groups in the unadjusted analysis (p=0.611).

Significant covariate effects included age (p<0.001), lifetime cigarette smoking (p=0.002), current cigarette smoking (p=0.013), cholesterol (p=0.046), and percent body fat (p<0.001). T-wave findings increased with age (6.7%, 13.6%, and 26.9% in those born in or after 1942, between 1923 and 1941, and in or before 1922, respectively) and lifetime cigarette smoking (8.8%, 9.0%, and 13.7% in nonsmokers, moderate lifetime smokers, and heavy lifetime smokers, respectively). Moderate and heavy current smokers also had a higher percent abnormal (9.4% and 9.8%, respectively) than nonsmokers (8.8%); former smokers had the highest percent abnormal (13.8%). The percentages of abnormalities also increased with increasing cholesterol levels (9.0%, 11.1%, and 13.2% in those with cholesterol levels ≤200 mg/dl, 200-230 mg/dl, and >230 mg/dl, respectively). Lean and obese individuals had a higher percentage abnormal than normal weight subjects (25.0% and 17.0%, respectively, vs. 9.6%).

Adjusted analyses detected a significant group-by-lifetime cigarette smoking history interaction (p=0.004) in addition to age (p<0.001) and percent body fat effects (p<0.001). Appendix L, Table L-2, gives the results of this contrast stratified by lifetime cigarette smoking history. For nonsmokers and moderate lifetime cigarette smokers, the relative risk was less than 1, but for heavy lifetime cigarette smokers, the relative risk was greater than 1. None of these within-stratum relative risks reached statistical significance, although for nonsmokers the difference was borderline significant (p=0.052).

Bradycardia

In the unadjusted analysis, significantly fewer Ranch Hands than Comparisons had bradycardia: 4.2 percent versus 6.2 percent (Est. RR: 0.67, 95% C.I.: [0.44,1.00], p=0.049).

Bradycardia was significantly associated with lifetime cigarette smoking history (p=0.002), current cigarette smoking (p=0.002), HDL (p=0.002), cholesterol-HDL ratio (p<0.001), and family history of heart disease (p=0.038). Bradycardia decreased with lifetime smoking, from 7.2 percent in nonsmokers to 6.5 percent in moderate lifetime smokers and 3.4 percent in heavy lifetime smokers. An inverse relationship was also observed between bradycardia and current cigarette smoking: 7.2 percent in nonsmokers, 5.7 percent in former smokers, 5.3 percent in moderate current smokers, and 1.2 percent in heavy current smokers. The percent of individuals with bradycardia increased with increasing HDL levels (2.7% in those with HDL ≤40 mg/dl, 5.9% in those with HDL 40-50 mg/dl, and 7.1% in those with HDL >50 mg/dl) and decreased with increasing cholesterol-HDL ratio (8.5% in individuals with ratios ≤4.2, 4.3% in individuals with ratios 4.2-5.5, and 2.8% in individuals with ratios >5.5). Individuals with a family history of heart disease had a lower prevalence of bradycardia than those without a family history of heart disease (3.3% vs. 5.9%).

The adjusted model included significant effects of current cigarette smoking (p<0.001), cholesterol-HDL ratio (p=0.006), and percent body fat (p=0.004). The adjusted relative risk was of borderline statistical significance (Adj. RR: 0.69, 95% C.I.: [0.46,1.04], p=0.068).

Tachycardia

Only one individual, a member of the Comparison group, was found to have tachycardia; this unadjusted group difference was not statistically significant (p=0.999). Adjusted analyses were not performed on this variable.

Arrhythmia

A slightly higher percentage of Ranch Hands (4.7%) than Comparisons (3.4%) had arrhythmias, but the unadjusted difference was not statistically significant (p=0.145).

The occurrence of arrhythmia was significantly associated with age (p<0.001) and family history of heart disease (p=0.020). Arrhythmias were detected in only 2.0 percent of those born in or after 1942, compared to 4.5 percent of those born between 1923 and 1941 and 20.9 percent of those born in or before 1922. Six percent of the participants with a family history of heart disease had arrhythmias, compared to 3.4 percent in those without a family history of heart disease.

The adjusted analysis found a significant effect of age (p<0.001) and differential cortisol (p=0.010), and a borderline significant group effect (Adj. RR: 1.56, 95% C.I.: [0.98,2.49], p=0.062).

ECG-Other Diagnoses

Without adjustment for covariates, other ECG findings were not significantly different in the two groups (p=0.548).

Age, lifetime cigarette smoking, current alcohol use, and percent body fat were all significantly associated with other ECG abnormalities (p<0.001, p=0.008, p=0.044, and p=0.005, respectively). Occupation and current cigarette smoking had borderline significant associations (p=0.053 and p=0.051, respectively). The percent with abnormal findings increased with age (14.6%, 20.9%, and 34.3% in those born in or after 1942, between 1923 and 1941, and in or before 1922, respectively) and lifetime cigarette smoking history (15.3%, 17.4%, and 21.5% in nonsmokers, moderate lifetime smokers, and heavy lifetime smokers, respectively). Other ECG diagnoses were greater in moderate current drinkers than in light and heavy current drinkers (23.1% vs. 17.5% and 20.9%, respectively). Although the numbers were small, five of the eight lean individuals (62.5%) had abnormal findings, compared to 18.2 percent and 19.4 percent of normal and obese individuals, respectively. Officers and enlisted flyers had a higher percent abnormal than enlisted groundcrew (20.7%, 19.9%, and 16.3%, respectively). Former smokers and heavy current smokers had relatively more abnormalities than nonsmokers and moderate current smokers (20.5% and 21.0%, respectively, vs. 15.3% and 17.2%, respectively).

In the adjusted analysis, a significant age effect was detected (p<0.001), but the adjusted relative risk was essentially unchanged from the unadjusted value and not significantly different from 1 (p=0.539).

Physical Examination Variables: Peripheral Vascular Function

The results of the unadjusted analyses for the variables related to peripheral vascular function are presented in Table 15-7: diastolic blood pressure, funduscopic examination, carotid bruits, radial pulses, femoral pulses, popliteal pulses, dorsalis pedis pulses, posterior tibial pulses, and the three pulse aggregates (leg pulses, peripheral pulses, and all pulses). Appendix L, Table L-1 gives the dependent variable-covariate associations, and Table 15-8 gives the results of the adjusted analyses.

Diastolic Blood Pressure

The mean diastolic blood pressure was slightly greater in the Ranch Hand group than in the Comparison group; the unadjusted difference was marginally significant (75.18 mm Hg vs. 74.50 mm Hg, p=0.099). The percent with abnormal values was not significantly different in the two groups (p=0.496), based on the unadjusted analysis.

Diastolic blood pressure was significantly associated with age (p=0.001, continuous); lifetime cigarette smoking history (p=0.022, discrete); current cigarette smoking (p=0.005, continuous); lifetime alcohol history (p=0.010, continuous); current alcohol use (p=0.008, continuous and p<0.001, discrete); cholesterol and cholesterol-HDL ratio (p<0.001, continuous); percent body fat (p<0.001, continuous and p=0.028, discrete); and differential cortisol (p=0.012, continuous). Diastolic blood pressure was weakly correlated with

TABLE 15-7.

Unadjusted Analysis for Cardiovascular Variables by Group (Peripheral Vascular Function)

Variable	Statistic	Group: Ranch Hand		Group: Comparison		Est. Relative Risk (95% C.I.)	p-Value
Diastolic Blood Pressure	n	878		1,150			
	Mean	75.18		74.50		—	0.099
	95% C.I.	(74.80,75.80)		(73.98,75.02)			
	Number/%						
	Abnormal	43	4.9%	49	4.3%	1.16 (0.76,1.76)	0.496
	Normal	835	95.1%	1,101	95.7%		
Funduscopic Examination	n	878		1,150			
	Number/%						
	Abnormal	6	0.7%	9	0.8%	0.87 (0.31,2.46)	0.795
	Normal	872	99.3%	1,141	99.2%		
Carotid Bruits	n	878		1,150			
	Number/%						
	Abnormal	9	1.0%	4	0.4%	2.97 (0.91,9.67)	0.058
	Normal	869	99.0%	1,146	99.6%		
Radial Pulses	n	865		1,130			
	Number/%						
	Abnormal	2	0.2%	9	0.8%	0.29 (0.06,1.34)	0.076
	Normal	863	99.8%	1,121	99.2%		

TABLE 15-7. (continued)

Unadjusted Analysis for Cardiovascular Variables by Group (Peripheral Vascular Function)

Variable	Statistic	Group: Ranch Hand		Group: Comparison		Est. Relative Risk (95% C.I.)	p-Value
Femoral Pulses	n	865		1,130			
	Number/%						
	Abnormal	19	2.2%	10	0.9%	2.52 (1.16,5.44)	0.016
	Normal	846	97.8%	1,120	99.1%		
Popliteal Pulses	n	865		1,129			
	Number/%						
	Abnormal	29	3.4%	29	2.6%	1.32 (0.78,2.22)	0.304
	Normal	836	96.6%	1,100	97.4%		
Dorsalis Pedis Pulses	n	864		1,129			
	Number/%						
	Abnormal	107	12.4%	111	9.8%	1.30 (0.98,1.72)	0.071
	Normal	757	87.6%	1,018	90.2%		
Posterior Tibial Pulses	n	864		1,129			
	Number/%						
	Abnormal	30	3.5%	29	2.6%	1.18 (0.81,2.29)	0.240
	Normal	834	96.5%	1,100	97.4%		
Leg Pulses	n	864		1,129			
	Number/%						
	Abnormal	132	15.3%	138	12.2%	1.30 (1.00,1.67)	0.049
	Normal	732	84.7%	991	87.8%		

TABLE 15-7. (continued)

Unadjusted Analysis for Cardiovascular Variables by Group (Peripheral Vascular Function)

Variable	Statistic	Group: Ranch Hand		Group: Comparison		Est. Relative Risk (95% C.I.)	p-Value
Peripheral Pulses	n	864		1,129			
	Number/%						
	Abnormal	133	15.4%	143	12.7%	1.26 (0.97,1.62)	0.082
	Normal	731	84.6%	986	87.3%		
All Pulses	n	863		1,128			
	Number/%						
	Abnormal	133	15.4%	143	12.7%	1.26 (0.97,1.62)	0.081
	Normal	730	84.6%	985	87.3%		

--Estimated relative risk not applicable for continuous analysis of a variable.

TABLE 15-8.

Adjusted Analysis for Cardiovascular Variables by Group (Peripheral Vascular Function)

Variable	Statistic	Group: Ranch Hand	Group: Comparison	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Diastolic Blood Pressure	n Adj. Mean** 95% C.I.**	837 75.19 (74.58,75.80)	1,069 74.51 (73.97,75.05)	—	0.100**	GRP*AGE (p=0.028) ALC (p=0.006) %BFAT (p<0.001) DIFCORT (p=0.044)
	n	872	1,139	1.12 (0.74,1.72)**	0.586**	GRP*HRTDIS50 (p=0.043) HDL (p<0.001) %BFAT (p=0.002)
Femoral Pulses	n	831	1,055	2.52 (1.15,5.56)	0.018	AGE (p<0.001) %BFAT (p=0.006) PERS (p=0.003)
Popliteal Pulses	n	831	1,054	1.24 (0.73,2.11)	0.433	AGE (p=0.005) PACKYR (p=0.004) PERS (p=0.003)
Dorsalis Pedis Pulses	n	864	1,129	1.29 (0.97,1.72)	0.078	AGE (p<0.001) OCC (p<0.001)
Posterior Tibial Pulses	n	824	1,048	****	****	GRP*DIFCORT (p=0.004) AGE (p<0.001) RACE (p=0.037) CSMOK (p=0.021) %BFAT (p=0.002) PERS (p=0.028)

TABLE 15-8. (continued)

Adjusted Analysis for Cardiovascular Variables by Group (Peripheral Vascular Function)

Variable	Statistic	Group: Ranch Hand	Group: Comparison	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Leg Pulses	n	830	1,054	1.27 (0.97,1.66)	0.079	AGE (p<0.001) OCC (p<0.001) PERS (p=0.030)
Peripheral Pulses	n	830	1,054	1.23 (0.94,1.60)	0.129	AGE (p<0.001) OCC (p<0.001) PERS (p=0.035)
All Pulses	n	829	1,053	1.23 (0.94,1.60)	0.130	AGE (p<0.001) OCC (p<0.001) PERS (p=0.035)

—Adjusted relative risk not applicable for continuous analysis of a variable.

**Group-by-covariate interaction (0.01<p≤0.05)—adjusted relative risk/mean, confidence interval, and p-value derived from a model fitted after deletion of this interaction.

****Group-by-covariate interaction (p≤0.01)—adjusted relative risk, confidence interval, and p-value not presented.

age (r=0.071). Six percent of heavy lifetime cigarette smokers had abnormal values, compared to 3.7 percent of nonsmokers and 3.2 percent of moderate lifetime smokers. There was a small negative correlation with current cigarette smoking (r=-0.062). There were small positive correlations between diastolic blood pressure and lifetime and current alcohol use (r=0.057 and r=0.059, respectively). Moderate and heavy current drinkers had a higher percentage of abnormal blood pressure readings than light current drinkers (8.3% and 9.0%, respectively, vs. 3.6%). The correlation between diastolic blood pressure and cholesterol level was 0.111, and the correlation between diastolic blood pressure and cholesterol-HDL ratio was 0.077. Diastolic blood pressure increased with increasing percent body fat (r=0.196); with 0.0 percent, 4.0 percent, and 7.1 percent of lean, normal, and obese individuals exhibiting abnormal values, respectively. There was a small negative correlation with differential cortisol (r=-0.057).

In the adjusted continuous analysis, there were significant effects of current alcohol use (p=0.006), percent body fat (p<0.001), and differential cortisol (p=0.044), as well as a statistically significant group-by-age interaction (p=0.028). This interaction is explored in Appendix L, Table L-2, where adjusted group means (adjusted for current alcohol use, percent body fat, and differential cortisol) are compared in the two groups for each of the three age strata. In those born in or after 1942, the Ranch Hand adjusted mean was significantly greater than the Comparison adjusted mean (74.91 mm Hg vs. 73.56 mm Hg, p=0.026). In the middle and older age groups, the adjusted means were not significantly different (p=0.760 and p=0.996, respectively). Since the significance level of the group-by-age interaction did not reach the 1 percent level, Table 15-8 also gives the results of the group contrast comparison after deleting the interaction term from the model. The adjusted Ranch Hand (75.19 mm Hg) mean was marginally significantly greater (p=0.100) than the adjusted Comparison mean (74.51 mm Hg).

Adjusted discrete analyses detected significant effects of HDL (p<0.001) and percent body fat (p=0.002) and a significant interaction between group and family history of heart disease before age 50 (p=0.043). This interaction is also explored more fully in Appendix L, Table L-2, where, among individuals with a positive family history, a higher percentage of Ranch Hands than Comparisons exhibited abnormal values, with nearly equal percentage in the two groups in those without such a history. The former was of borderline significance (p=0.057), but based on very small numbers (5 of 26 Ranch Hands versus 1 of 30 Comparisons). After deletion of the interaction term from the model (Table 15-8), the adjusted relative risk between the two groups was not statistically significant (p=0.586).

Funduscopic Examination

Funduscopic abnormalities were detected in 0.7 percent of the Ranch Hands and 0.8 percent of the Comparisons; this unadjusted difference was not statistically significant (p=0.795).

Age, current cigarette smoking, and current alcohol use were significantly associated with funduscopic abnormalities (p=0.029, p=0.039, and p=0.006, respectively). In those born in or after 1942, 0.2 percent were abnormal, compared to 1.2 percent in those born between 1923 and 1941 and

0.0 percent in those born in or before 1922. Moderate and heavy current cigarette smokers had more abnormalities (1.8% and 1.2%, respectively) than nonsmokers and former smokers (0.4% in each case). Similarly, moderate and current drinkers had more abnormalities (2.0% and 1.5%, respectively) than light current drinkers (0.4%). Adjusted group comparisons were not performed due to the small number of abnormalities.

Carotid Bruits

Carotid bruits were also relatively rare, although here the group difference was of borderline significance, with 1.0 percent of the Ranch Hands exhibiting abnormalities, compared to 0.4 percent of the Comparisons (p=0.058). No significant covariate associations were found and adjusted analyses were not performed due to the small numbers.

Radial Pulses

Two (0.2%) Ranch Hands were found to have abnormal radial pulses, compared to nine (0.8%) Comparisons; this unadjusted difference was not statistically significant (p=0.076). Once again, no statistically significant associations were detected with any of the covariates, and adjusted analyses were not performed due to the small number of abnormalities.

Femoral Pulses

Based on the unadjusted analysis, a significantly greater percentage of Ranch Hands than Comparisons had femoral pulse abnormalities (Est. RR: 2.5[illegible]. 95% C.I.: [1.16, 5.44], p=0.016). Of the Ranch Hands, 2.2 percent had a femoral pulse abnormality, as compared to 0.9 percent of the Comparisons.

Abnormalities increased with age (p=0.001); 0.4 percent of those born in or after 1942 were abnormal, 2.1 percent of those born between 1923 and 1941, and 4.9 percent of those born in or before 1922. A significant association (p=0.007) was also detected between femoral pulse abnormalities and cholesterol-HDL ratio (0.6% of the individuals with ratios <4.2 were abnormal, compared to 2.5% of the individuals with ratios 4.2-5.5, and 1.2% of the individuals with ratios >5.5). Type B personalities also had significantly more abnormalities than Type A personalities (2.2% vs. 0.6%, p=0.008).

The relative risk remained statistically significant after adjustment for covariates (Adj. RR: 2.52, 95% C.I.: [1.15,5.56], p=0.018). Significant covariate effects in the adjusted model were age (p<0.001), percent body fat (p=0.006), and personality type (p=0.003).

Popliteal Pulses

There was no statistically significant difference between the two groups in the presence of popliteal pulses (p=0.304), based on the unadjusted analysis.

Significant covariate associations included age (p=0.003), lifetime cigarette smoking history (p<0.001), current cigarette smoking (p<0.001), lifetime alcohol history (p=0.011), percent body fat (p<0.001), and personality type (p=0.004). The percent with abnormal popliteal pulses increased with age (1.8%, 3.5%, and 8.2% in those born in or after 1942, between 1923 and 1941, and in or before 1922, respectively) and lifetime cigarette smoking history (0.4%, 2.5%, and 4.8% in nonsmokers, moderate lifetime smokers, and heavy lifetime smokers, respectively). Former smokers, moderate current smokers, and heavy current smokers all had a higher percent abnormal than nonsmokers (3.5%, 4.8%, and 4.0%, respectively, vs. 0.4%). The percent abnormal also increased with lifetime alcohol history (0.6%, 2.5%, and 4.7% in nondrinkers, moderate lifetime drinkers, and heavy lifetime drinkers, respectively). Two of seven (28.6%) lean individuals were abnormal, compared to 2.6 percent and 3.7 percent in normal and obese individuals, respectively. Type B individuals had a greater percent abnormal than Type A individuals (4.1% vs. 1.7%).

Adjusted analysis of the popliteal pulses detected significant age (p=0.005), lifetime cigarette smoking (p=0.004), and personality type (p=0.003) effects, but no significant group difference (p=0.433).

Dorsalis Pedis Pulses

There was a borderline significant difference between the Ranch Hand and Comparison groups in the percentage of participants with abnormal dorsalis pedis pulses, based on the unadjusted analysis (Ranch Hands: 12.4% vs. Comparisons: 9.8%, Est. RR: 1.30, 95% C.I.: [0.98,1.72], p=0.071).

Dorsalis pedis pulse abnormalities were significantly associated with age (p=0.001) and occupation (p=0.001). Abnormalities increased with age (8.6% in those born in or after 1942, 12.4% in those born between 1923 and 1941, and 21.3% in those born in or before 1922). Enlisted flyers had the highest percent abnormal (16.4%), followed by enlisted groundcrew (10.7%) and officers (8.8%).

Adjusted analysis revealed significant age (p<0.001) and occupation (p<0.001) effects; the adjusted relative risk was similar to the unadjusted value and remained borderline significant (Adj. RR: 1.29, 95% C.I.: [0.97,1.72], p=0.078).

Posterior Tibial Pulses

Without adjustment for covariates, the percentage of individuals with abnormal posterior tibial pulses was not significantly different in the two groups (p=0.240).

Significant covariate associations included age (p<0.001), lifetime cigarette smoking history (p=0.007), current cigarette smoking (p=0.005), lifetime alcohol history (p=0.011), percent body fat (p=0.009), and personality type (p=0.028). The prevalence of abnormalities increased with age (1.5% in those born in or after 1942, 3.6% in those born between 1923 and 1941, and 13.1% in those born in or before 1922) and lifetime cigarette smoking history (1.4% in nonsmokers, 2.5% in moderate lifetime cigarette smokers, and 4.2% in heavy lifetime cigarette smokers). Moderate current smokers had the highest percent abnormal (5.4%), followed by heavy current smokers (4.0%), former smokers (2.6%), and nonsmokers (1.4%). Abnormalities increased with lifetime alcohol history (1.2% in nondrinkers, 2.4% in moderate lifetime drinkers, and 4.9% in heavy lifetime drinkers). Abnormalities were detected in 14.3 percent of lean individuals and 3.4 percent of normal individuals, but in only 0.8 percent of obese individuals. Type B personalities had a higher percent abnormal than Type A personalities (3.9% vs. 2.0%).

The adjusted analyses detected a highly significant group-by-differential cortisol interaction (p=0.004), as well as significant age (p<0.001), race (p=0.037), current cigarette smoking (p=0.021), percent body fat (p=0.002), and personality type (p=0.028) effects. Upon stratification by differential cortisol (Appendix L, Table L-2), there was little difference between the Ranch Hand and Comparison groups in those with differential cortisol response of less than or equal to 0.6, but a significantly higher risk was found in those with differential cortisol of between 0.6 and 4.0 (Adj. RR: 3.04, 95% C.I.: [1.06,8.68], p=0.030). The relative risk was less than 1 (not statistically significant) in those with differential cortisol response of greater than 4.0.

Leg Pulses

Based on the unadjusted analysis, the Ranch Hands had significantly more aggregate leg pulse abnormalities (15.3%) than the Comparisons (12.2%) (Est. RR: 1.30, 95% C.I.: [1.00,1.67], p=0.049).

Leg pulse abnormalities were significantly associated with age (p<0.001), occupation (p=0.001), lifetime cigarette smoking history (p=0.012), current cigarette smoking (p=0.033), cholesterol-HDL ratio (p=0.045), and personality type (p=0.007). The percent abnormal increased with age (10.2%, 14.4%, and 29.5% in those born in or after 1942, born between 1923 and 1941, and born in or before 1922, respectively). Enlisted flyers had the highest percent abnormal (19.6%), followed by enlisted groundcrew (13.4%) and officers (11.1%). The percent abnormal increased with lifetime cigarette smoking history (10.5%, 12.9%, and 15.9% in nonsmokers, moderate lifetime smokers, and heavy lifetime smokers, respectively). Moderate current smokers had the highest percent abnormal (17.4%), heavy current smokers the second highest (14.5%), former smokers the third highest (13.7%), and nonsmokers the lowest (10.5%) percent abnormal. Abnormalities also increased with increasing cholesterol-HDL ratio (11.1%, 14.6%, and 15.6% in participants with ratios ≤4.2, 4.2-5.5, and >5.5, respectively). Type B personalities had a higher percent abnormal than Type A personalities (15.8% vs. 11.4%).

The adjusted analysis detected significant age (p<0.001), occupation (p<0.001), and personality type effects (p=0.030). The adjusted relative risk was of borderline significance (Adj. RR: 1.27, 95% C.I.: [0.97,1.66], p=0.079).

Peripheral Pulses

The Ranch Hands had a higher percentage of aggregate peripheral pulse abnormalities (15.4%) than the Comparisons (12.7%); the unadjusted relative risk was of borderline significance (Est. RR: 1.26, 95% C.I.: [0.97,1.62], p=0.082).

Significant covariate effects included age (p<0.001), occupation (p=0.001), lifetime cigarette smoking history (p=0.008), current cigarette smoking (p=0.023), cholesterol-HDL ratio (p=0.044), and personality type (p=0.009). Peripheral pulse abnormalities increased with age (10.4%, 15.9%, and 29.5% in those born in or after 1942, born between 1923 and 1941, and born in or before 1922, respectively). Enlisted flyers had the highest percent abnormal (19.9%), followed by enlisted groundcrew (13.7%) and officers (11.4%). Abnormalities increased with lifetime cigarette smoking history (10.7%, 13.0%, and 16.4% in nonsmokers, moderate lifetime smokers, and heavy lifetime smokers, respectively). Moderate current cigarette smokers had the highest percent abnormal (18.0%), followed by heavy current cigarette smokers (14.5%), former smokers (14.1%), and nonsmokers (10.7%). The percent abnormal increased with cholesterol-HDL ratio (11.4%, 14.8%, and 15.9% in individuals with ratios ≤4.2, 4.2-5.5, and >5.5, respectively). Type B personalities had a higher percent abnormal than Type A personalities (16.1% vs. 11.8%).

The adjusted analysis detected significant age (p<0.001), occupation (p<0.001), and personality type (p=0.035) effects, but the adjusted relative risk was not statistically significant (p=0.129).

All Pulses

The number of individuals with abnormal pulses of any kind was the same as that for peripheral pulses. The results of analyses of all pulses differed from that of peripheral pulse only as a result of missing values in two cases. Thus, the unadjusted relative risk was also of borderline significance here (p=0.081); the same covariate effects were detected as in the peripheral pulse analysis (in the same directions); and the adjusted relative risk was not statistically significant (p=0.130).

Association Between Cardiovascular Examination Findings and Verified Essential Hypertension, Verified Heart Disease, and Verified Myocardial Infarction

The major central and peripheral physical examination findings were cross-tabulated with the verified cardiovascular disease endpoints to assess the degree of correlation between the fifth-year followup physical examination and the past medical history. The results are shown in Table L-3 of Appendix L.

There were highly statistically significant associations between verified essential hypertension and systolic blood pressure (p<0.001), diastolic blood pressure (p<0.001), overall ECG findings (p<0.001), heart sounds (p<0.001), funduscopic abnormalities (p<0.001), and peripheral pulses (p=0.001); and a borderline significant association with carotid bruits (p=0.064). These were all in a positive direction, i.e., individuals with abnormal physical findings were more likely to have had a history of essential hypertension than those with normal physical findings.

Verified heart disease was significantly and positively associated with overall ECG findings ($p<0.001$), heart sounds ($p<0.001$), and carotid bruits ($p=0.010$). No significant association was detected between verified heart disease and systolic or diastolic blood pressure, funduscopic abnormalities, or peripheral pulses.

Finally, the verified occurrence of myocardial infarction was significantly associated with systolic blood pressure ($p=0.003$), ECG abnormalities ($p<0.001$), abnormal heart sounds ($p<0.001$), carotid bruits ($p=0.004$), and peripheral pulses ($p=0.002$). Again, these associations were all positive, i.e., the percent of individuals with a verified myocardial infarction was greater in those with abnormal physical examination findings than in those with normal physical parameters. The association between verified myocardial infarction and diastolic blood pressure was not statistically significant, nor was the association between verified myocardial infarction and funduscopic abnormalities.

The consistency between the physical examination findings and the past medical history exhibited by these associations supports the validity of the cardiovascular measurements, whether by medical records, physician assessments (e.g., heart sounds), or objective determinations (e.g., ECG).

Exposure Index Analyses

The frequency distributions for each cardiovascular variable at each level of the exposure index (low, medium, and high) within the Ranch Hand group are presented in Table 15-9. For systolic and diastolic blood pressure, means and 95 percent confidence intervals are also given for each exposure level. Separate analyses were performed within each occupational stratum (officers, enlisted flyers, and enlisted groundcrew). A p-value for testing the overall hypothesis of equal frequency distributions (or means) across the three exposure levels is included, as well as estimated relative risks and p-values for medium versus low ("M vs. L") and high versus low ("H vs. L") contrasts, respectively.

The results of adjusted exposure index analyses for all variables are presented in Table 15-10. Covariates examined included those from the core analyses; however, when data were sparse, fewer covariates were considered.

The final interpretation of the exposure index data must await the reanalysis of the clinical data using the results of the serum dioxin assay. This report is expected in 1991.

Questionnaire Variables

Reported and Verified Essential Hypertension

Although the percentage of individuals with essential hypertension (all reported events were verified) was greatest in the high exposure-level

TABLE 15-9.

Unadjusted Exposure Index for Cardiovascular Variables by Occupation

Variable	Occupation	Statistic	Exposure Index: Low		Exposure Index: Medium		Exposure Index: High		Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
Reported/ Verified Essential Hypertension*	Officer	n	113		111		106		Overall		0.446
		Number/%									
		Yes	33	29.2%	34	30.6%	39	36.8%	M vs. L	1.07 (0.60,1.90)	0.818
		No	80	70.8%	77	69.4%	67	63.2%	H vs. L	1.41 (0.80,2.49)	0.234
	Enlisted Flyer	n	52		53		51		Overall		0.247
		Number/%									
		Yes	19	36.5%	18	34.0%	25	49.0%	M vs. L	0.89 (0.40,1.99)	0.779
		No	33	63.5%	35	66.0%	26	51.0%	H vs. L	1.67 (0.76,3.68)	0.201
	Enlisted Groundcrew	n	133		140		119		Overall		0.977
		Number/%									
		Yes	43	32.3%	46	32.9%	40	33.6%	M vs. L	1.02 (0.62,1.70)	0.327
		No	90	67.7%	94	67.1%	79	66.4%	H vs. L	1.06 (0.63,1.70)	0.347
Reported Heart Disease (Excluding Hypertension)	Officer	n	113		111		106		Overall		0.145
		Number/%									
		Yes	57	50.4%	43	38.7%	42	39.6%	M vs. L	0.62 (0.36,1.06)	0.078
		No	56	49.6%	68	61.3%	64	60.4%	H vs. L	0.64 (0.38,1.10)	0.121
	Enlisted Flyer	n	52		53		51		Overall		0.941
		Number/%									
		Yes	22	42.3%	21	39.6%	20	39.2%	M vs. L	0.89 (0.41,1.95)	0.779
		No	30	57.7%	32	60.4%	31	60.8%	H vs. L	0.88 (0.40,1.93)	0.749
	Enlisted Groundcrew	n	133		140		119		Overall		0.371
		Number/%									
		Yes	48	36.1%	42	30.0%	45	37.8%	M vs. L	0.76 (0.46,1.26)	0.285
		No	85	63.9%	98	70.0%	74	62.2%	H vs. L	1.08 (0.64,1.80)	0.779

TABLE 15-9. (continued)

Unadjusted Exposure Index for Cardiovascular Variables by Occupation

Variable	Occupation	Statistic	Exposure Index: Low		Medium		High		Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
Verified Heart Disease (Excluding Hypertension)	Officer	n	113		111		106		Overall		0.145
		Number/%									
		Yes	57	50.4%	43	38.7%	42	39.6%	M vs. L	0.62 (0.36,1.06)	0.078
		No	56	49.6%	68	61.3%	64	60.4%	H vs. L	0.64 (0.38,1.10)	0.121
	Enlisted Flyer	n	52		53		51		Overall		0.941
		Number/%									
		Yes	22	42.3%	21	39.6%	20	39.2%	M vs. L	0.89 (0.41,1.95)	0.779
		No	30	57.7%	32	60.4%	31	60.8%	H vs. L	0.88 (0.40,1.93)	0.749
	Enlisted Groundcrew	n	133		140		119		Overall		0.278
		Number/%									
		Yes	48	36.1%	40	28.6%	44	37.0%	M vs. L	0.71 (0.43,1.18)	0.184
		No	85	63.9%	100	71.4%	75	63.0%	H vs. L	1.04 (0.62,1.74)	0.881
Reported/ Verified Myocardial Infarction*	Officer	n	113		111		106		Overall		0.568[a]
		Number/%									
		Yes	3	2.6%	6	5.4%	4	3.8%	M vs. L	2.10 (0.51,8.59)	0.303
		No	110	97.4%	105	94.6%	102	96.2%	H vs. L	1.44 (0.31,6.58)	0.638
	Enlisted Flyer	n	52		53		51		Overall		0.676[a]
		Number/%									
		Yes	4	7.7%	4	7.6%	2	3.9%	M vs. L	0.98 (0.23,4.14)	0.984
		No	48	92.3%	49	92.4%	49	96.1%	H vs. L	0.49 (0.09,2.80)	0.424
	Enlisted Groundcrew	n	133		140		119		Overall		0.644
		Number/%									
		Yes	6	4.5%	4	2.9%	6	5.0%	M vs. L	0.62 (0.17,2.26)	0.472
		No	127	95.5%	136	97.1%	113	95.0%	H vs. L	1.12 (0.35,3.58)	0.841

TABLE 15-9. (continued)

Unadjusted Exposure Index for Cardiovascular Variables by Occupation

Variable	Occupation	Statistic	Exposure Index: Low	Exposure Index: Medium	Exposure Index: High	Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
Systolic Blood Pressure	Officer	n	113	111	106	Overall		0.735
		Mean	125.46	127.25	126.02	M vs. L	—	0.443
		95% C.I.	(122.63, 128.29)	(123.92, 130.58)	(122.40, 129.64)	H vs. L	—	0.813
		Number/%				Overall		0.743
		Abnormal	18 15.9%	19 17.1%	21 19.8%	M vs. L	1.09 (0.54,2.21)	0.810
		Normal	95 84.1%	92 82.9%	85 80.2%	H vs. L	1.30 (0.65,2.61)	0.453
	Enlisted Flyer	n	52	53	51	Overall		0.037
		Mean	124.14	128.79	133.55	M vs. L	—	0.197
		95% C.I.	(119.13, 129.14)	(124.75, 132.84)	(127.69, 139.41)	H vs. L	—	0.010
		Number/%				Overall		0.132
		Abnormal	9 17.3%	11 20.8%	17 33.3%	M vs. L	1.25 (0.47,3.33)	0.653
		Normal	43 82.7%	42 79.2%	34 66.7%	H vs. L	2.39 (0.95,6.02)	0.064
	Enlisted Groundcrew	n	133	140	119	Overall		0.752
		Mean	126.23	127.79	127.14	M vs. L	—	0.453
		95% C.I.	(123.48, 128.97)	(124.74, 130.83)	(124.15, 130.14)	H vs. L	—	0.672
		Number/%				Overall		0.802
		Abnormal	23 17.3%	28 20.0%	24 20.2%	M vs. L	1.20 (0.65,2.20)	0.569
		Normal	110 82.7%	112 80.0%	95 79.8%	H vs. L	1.21 (0.64,2.28)	0.562

TABLE 1 (continued)

Unadjusted Exposure Index for Cardiovascular Variables by Occupation

Variable	Occupation	Statistic	Exposure Index: Low		Medium		High		Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
Heart Sounds	Officer	n	113		111		106		Overall		0.568[a]
		Number/%									
		Abnormal	5	4.4%	4	3.6%	2	1.9%	M vs. L	0.81 (0.21,3.09)	0.757
		Normal	108	95.6%	107	96.4%	104	98.1%	H vs. L	0.42 (0.08,2.19)	0.298
	Enlisted Flyer	n	52		53		51		Overall		0.114[a]
		Number/%									
		Abnormal	4	7.7%	0	0.0%	4	7.8%	M vs. L	—	0.114
		Normal	48	92.3%	53	100.0%	47	92.2%	H vs. L	1.02 (0.24,4.32)	0.976
	Enlisted Groundcrew	n	133		140		119		Overall		0.137[a]
		Number/%									
		Abnormal	7	5.3%	2	1.4%	7	5.9%	M vs. L	0.26 (0.05,1.28)	0.097
		Normal	126	94.7%	138	98.6%	112	94.1%	H vs. L	1.12 (0.38,3.31)	0.834
ECG-Overall	Officer	n	113		111		106		Overall		0.798
		Number/%									
		Abnormal	18	15.9%	21	18.9%	17	16.0%	M vs. L	1.23 (0.62,2.46)	0.555
		Normal	95	84.1%	90	81.1%	89	84.0%	H vs. L	1.01 (0.49,2.08)	0.984
	Enlisted Flyer	n	52		53		51		Overall		0.659
		Number/%									
		Abnormal	10	19.2%	13	24.5%	9	17.6%	M vs. L	1.36 (0.54,3.46)	0.516
		Normal	42	80.8%	40	75.5%	42	82.4%	H vs. L	0.90 (0.33,2.44)	0.834
	Enlisted Groundcrew	n	133		140		119		Overall		0.842
		Number/%									
		Abnormal	18	13.5%	16	11.4%	16	13.4%	M vs. L	0.82 (0.40,1.69)	0.596
		Normal	115	86.5%	124	88.6%	103	86.6%	h vs. L	0.99 (0.48,2.05)	0.984

TABLE 15-9. (continued)

Unadjusted Exposure Index for Cardiovascular Variables by Occupation

Variable	Occupation	Statistic	Exposure Index: Low		Medium		High		Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
RBBB	Officer	n	113		111		106		Overall		0.372[a]
		Number/%									
		Abnormal	0	0.0%	1	0.9%	0	0.0%	M vs. L	—	0.991
		Normal	113	100.0%	110	99.1%	106	100.0%	H vs. L	—	—
	Enlisted Flyer	n	52		53		51		Overall		0.594[a]
		Number/%									
		Abnormal	1	1.9%	0	0.0%	1	2.0%	M vs. L	—	0.990[a]
		Normal	51	98.1%	53	100.0%	50	98.0%	H vs. L	1.02 (0.06,16.76)	0.992
	Enlisted Groundcrew	n	133		140		119		Overall		0.317[a]
		Number/%									
		Abnormal	0	0.0%	0	0.0%	1	0.8%	M vs. L	—	—
		Normal	133	100.0%	140	100.0%	118	99.2%	H vs. L	—	0.944
LBBB	Officer	n	113		111		106		Overall		0.372[a]
		Number/%									
		Abnormal	0	0.0%	1	0.9%	0	0.0%	M vs. L	—	0.991
		Normal	113	100.0%	110	99.1%	106	100.0%	H vs. L	—	—
	Enlisted Flyer	n	52		53		51		Overall		—
		Number/%									
		Abnormal	0	0.0%	0	0.0%	0	0.0%	M vs. L	—	—
		Normal	52	100.0%	53	100.0%	51	100.0%	H vs. L	—	—
	Enlisted Groundcrew	n	133		140		119		Overall		—
		Number/%									
		Abnormal	0	0.0%	0	0.0%	0	0.0%	M vs. L	—	—
		Normal	133	100.0%	140	100.0%	119	100.0%	H vs. L	—	—

TABLE 15-9. (continued)

Unadjusted Exposure Index for Cardiovascular Variables by Occupation

Variable	Occupation	Statistic	Exposure Index: Low		Medium		High		Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
Nonspecific T-Waves	Officer	n	113		111		106		Overall		0.655
		Number/%									
		Abnormal	10	8.8%	14	12.6%	11	10.4%	M vs. L	1.49 (0.63,3.50)	0.363
		Normal	103	91.2%	97	87.4%	95	89.6%	H vs. L	1.19 (0.48,2.94)	0.704
	Enlisted Flyer	n	52		53		51		Overall		0.075
		Number/%									
		Abnormal	4	7.7%	12	22.6%	6	11.8%	M vs. L	3.51 (1.05,11.73)	0.041
		Normal	48	92.3%	41	77.4%	45	88.2%	H vs. L	1.60 (0.42,6.04)	0.490
	Enlisted Groundcrew	n	133		140		119		Overall		0.792
		Number/%									
		Abnormal	13	9.8%	11	7.9%	12	10.1%	M vs. L	0.79 (0.34,1.82)	0.575
		Normal	120	90.2%	129	92.1%	107	89.9%	H vs. L	1.04 (0.45,2.37)	0.936
Bradycardia	Officer	n	113		111		106		Overall		0.082
		Number/%									
		Abnormal	11	9.7%	4	3.6%	4	3.8%	M vs. L	0.35 (0.11,1.12)	0.077
		Normal	102	90.3%	107	96.4%	102	96.2%	H vs. L	0.36 (0.11,1.18)	0.093
	Enlisted Flyer	n	52		53		51		Overall		0.569[a]
		Number/%									
		Abnormal	3	5.8%	3	5.7%	1	2.0%	M vs. L	0.98 (0.19,5.09)	0.984
		Normal	49	94.2%	50	94.3%	50	98.0%	H vs. L	0.33 (0.03,3.25)	0.342
	Enlisted Groundcrew	n	133		140		119		Overall		0.333[a]
		Number/%									
		Abnormal	6	4.5%	3	2.1%	2	1.7%	M vs. L	0.46 (0.11,1.89)	0.285
		Normal	127	95.5%	137	97.9%	117	98.3%	H vs. L	0.36 (0.07,1.83)	0.219

TABLE 15-9. (continued)

Unadjusted Exposure Index for Cardiovascular Variables by Occupation

Variable	Occupation	Statistic	Exposure Index: Low		Exposure Index: Medium		Exposure Index: High		Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
Tachycardia	Officer	n	113		111		106		Overall		—
		Number/%									
		Abnormal	0	0.0%	0	0.0%	0	0.0%	M vs. L	—	—
		Normal	113	100.0%	111	100.0%	106	100.0%	H vs. L	—	—
	Enlisted Flyer	n	52		53		51		Overall		—
		Number/%									
		Abnormal	0	0.0%	0	0.0%	0	0.0%	M vs. L	—	—
		Normal	52	100.0%	53	100.0%	51	100.0%	H vs. L	—	—
	Enlisted Groundcrew	n	133		140		119		Overall		—
		Number/%									
		Abnormal	0	0.0%	0	0.0%	0	0.0%	M vs. L	—	—
		Normal	133	100.0%	140	100.0%	119	100.0%	H vs. L	—	—
Arrhythmia	Officer	n	113		111		106		Overall		0.427
		Number/%									
		Abnormal	7	6.2%	3	2.7%	6	5.7%	M vs. L	0.42 (0.11,1.67)	0.219
		Normal	106	93.8%	108	97.3%	100	94.3%	H vs. L	0.91 (0.30,2.80)	0.865
	Enlisted Flyer	n	52		53		51		Overall		0.002[a]
		Number/%									
		Abnormal	0	0.0%	0	0.0%	6	11.8%	M vs. L	—	—
		Normal	52	100.0%	53	100.0%	45	88.2%	H vs. L	—	0.025
	Enlisted Groundcrew	n	133		140		119		Overall		0.664
		Number/%									
		Abnormal	7	5.3%	5	3.6%	7	5.9%	M vs. L	0.67 (0.21,2.15)	0.497
		Normal	126	94.7%	135	96.4%	112	94.1%	H vs. L	1.12 (0.38,3.31)	0.834

TABLE 15-9. (continued)

Unadjusted Exposure Index for Cardiovascular Variables by Occupation

Variable	Occupation	Statistic	Exposure Index: Low		Medium		High		Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
ECG-Other Diagnoses	Officer	n	113		111		106		Overall		0.359
		Number/%									
		Abnormal	25	22.1%	26	23.4%	17	16.0%	M vs. L	1.08 (0.58,2.01)	0.818
		Normal	88	77.9%	85	76.6%	89	84.0%	H vs. L	0.67 (0.34,1.33)	0.254
	Enlisted Flyer	n	52		53		51		Overall		0.233
		Number/%									
		Abnormal	11	21.2%	13	24.5%	6	11.8%	M vs. L	1.21 (0.49,3.02)	0.682
		Normal	41	78.8%	40	75.5%	45	88.2%	H vs. L	0.50 (0.17,1.46)	0.204
	Enlisted Groundcrew	n	133		140		119		Overall		0.787
		Number/%									
		Abnormal	21	15.8%	23	16.4%	16	13.4%	M vs. L	1.05 (0.55,2.00)	0.889
		Normal	112	84.2%	117	83.6%	103	86.6%	H vs. L	0.83 (0.41,1.67)	0.603

TABLE 15-9. (continued)

Unadjusted Exposure Index for Cardiovascular Variables by Occupation

Variable	Occupation	Statistic	Exposure Index: Low	Medium	High	Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
Diastolic Blood Pressure	Officer	n	113	111	106	Overall		0.553
		Mean	74.82	74.20	75.58	M vs. L	—	0.619
		95% C.I.	(73.14,76.51)	(72.59,75.81)	(73.62,77.55)	H vs. L	—	0.549
		Number/%				Overall		0.014[a]
		Abnormal	2 1.8%	2 1.8%	9 8.5%	M vs. L	1.02 (0.14,7.36)	0.984
		Normal	111 98.2%	109 98.2%	97 91.5%	H vs. L	5.15 (1.09,24.42)	0.039
	Enlisted Flyer	n	52	53	51	Overall		0.498
		Mean	74.94	77.30	75.78	M vs. L	—	0.245
		95% C.I.	(72.49,77.39)	(74.32,80.28)	(72.81,78.76)	H vs. L	—	0.680
		Number/%				Overall		0.356[a]
		Abnormal	2 3.8%	6 11.3%	4 7.8%	M vs. L	3.19 (0.61,16.60)	0.168
		Normal	50 96.2%	47 88.7%	47 92.2%	H vs. L	2.13 (0.37,12.16)	0.395
	Enlisted Groundcrew	n	133	140	119	Overall		0.266
		Mean	74.86	76.05	74.29	M vs. L	—	0.273
		95% C.I.	(73.45,76.28)	(74.61,77.49)	(72.54,76.05)	H vs. L	—	0.612
		Number/%				Overall		0.285
		Abnormal	3 2.3%	8 5.7%	7 5.9%	M vs. L	2.63 (0.68,10.12)	0.162
		Normal	130 97.7%	132 94.3%	112 94.1%	H vs. L	2.71 (0.68,10.72)	0.156

TABLE 9. (continued)

Unadjusted Exposure Index for Cardiovascular Variables by Occupation

Variable	Occupation	Statistic	Exposure Index: Low		Exposure Index: Medium		Exposure Index: High		Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
Funduscopic Examination	Officer	n	113		111		106		Overall		0.364[a]
		Number/%									
		Abnormal	0	0.0%	2	1.8%	1	0.9%	M vs. L	—	0.489
		Normal	113	100.0%	109	98.2%	105	99.1%	H vs. L	—	0.968
	Enlisted Flyer	n	52		53		51		Overall		0.366[a]
		Number/%									
		Abnormal	1	1.9%	0	0.0%	0	0.0%	M vs. L	—	0.990
		Normal	51	98.1%	53	100.0%	51	100.0%	H vs. L	—	0.999
	Enlisted Groundcrew	n	133		140		119		Overall		0.164
		Number/%									
		Abnormal	0	0.0%	2	1.4%	0	0.0%	M vs. L	—	0.524
		Normal	133	100.0%	138	98.6%	119	100.0%	H vs. L	—	—
Carotid Bruits	Officer	n	113		111		106		Overall		0.382[a]
		Number/%									
		Abnormal	1	0.9%	0	0.0%	0	0.0%	M vs. L	—	0.999
		Normal	112	99.1%	111	100.0%	106	100.0%	H vs. L	—	0.999
	Enlisted Flyer	n	52		53		51		Overall		0.348[a]
		Number/%									
		Abnormal	2	3.8%	0	0.0%	2	3.9%	M vs. L	—	0.486
		Normal	50	96.2%	53	100.0%	49	96.1%	H vs. L	1.02 (0.14,7.53)	0.984
	Enlisted Groundcrew	n	133		140		119		Overall		0.123[a]
		Number/%									
		Abnormal	1	0.8%	0	0.0%	3	2.5%	M vs. L	—	0.974
		Normal	132	99.2%	140	100.0%	116	97.5%	H vs. L	3.41 (0.35,33.29)	0.289

TABLE 15-9. (continued)

Unadjusted Exposure Index for Cardiovascular Variables by Occupation

Variable	Occupation	Statistic	Exposure Index: Low		Medium		High		Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
Radial Pulses	Officer	n	113		110		102		Overall		0.390[a]
		Number/%									
		Abnormal	1	0.9%	0	0.0%	0	0.0%	M vs. L	—	0.999
		Normal	112	99.1%	110	100.0%	102	100.0%	H vs. L	—	0.999
	Enlisted Flyer	n	50		52		50		Overall		—
		Number/%									
		Abnormal	0	0.0%	0	0.0%	0	0.0%	M vs. L	—	—
		Normal	50	100.0%	52	100.0%	50	100.0%	H Vs. L	—	—
	Enlisted Groundcrew	n	131		140		117		Overall		0.374[a]
		Number/%									
		Abnormal	1	0.8%	0	0.0%	0	0.0%	M vs. L	—	0.967
		Normal	130	99.2%	140	100.0%	117	100.0%	H vs. L	—	0.999
Femoral Pulses	Officer	n	113		110		102		Overall		0.078[a]
		Number/%									
		Abnormal	1	0.9%	4	3.6%	0	0.0%	M vs. L	4.23 (0.46,38.42)	0.201
		Normal	112	99.1%	106	96.4%	102	100.0%	H vs. L	—	0.999
	Enlisted Flyer	n	50		52		50		Overall		0.171[a]
		Number/%									
		Abnormal	1	2.0%	2	3.8%	5	10.0%	M vs. L	1.96 (0.17,22.32)	0.589
		Normal	49	98.0%	50	96.2%	45	90.0%	H vs. L	5.44 (0.61,48.42)	0.129
	Enlisted Groundcrew	n	131		140		117		Overall		0.652[a]
		Number/%									
		Abnormal	3	2.3%	2	1.4%	1	0.8%	M vs. L	0.62 (0.10,3.76)	0.603
		Normal	128	97.7%	138	98.6%	116	99.2%	H vs. L	0.37 (0.04,3.59)	0.390

TABLE 9. (continued)

Unadjusted Exposure Index for Cardiovascular Variables by Occupation

Variable	Occupation	Statistic	Exposure Index: Low		Medium		High		Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
Popliteal Pulses	Officer	n	113		110		102		Overall		0.247[a]
		Number/%									
		Abnormal	3	2.6%	3	2.7%	0	0.0%	M vs. L	1.03 (0.20,5.22)	0.976
		Normal	110	97.4%	107	97.3%	102	100.0%	H vs. L	—	0.287
	Enlisted Flyer	n	50		52		50		Overall		0.328[a]
		Number/%									
		Abnormal	2	4.0%	2	3.8%	5	10.0%	M vs. L	0.96 (0.13,7.09)	0.968
		Normal	48	96.0%	50	96.2%	45	90.0%	H vs. L	2.67 (0.49,14.44)	0.254
	Enlisted Groundcrew	n	131		140		117		Overall		0.697[a]
		Number/%									
		Abnormal	6	4.6%	5	3.6%	3	2.6%	M vs. L	0.77 (0.23,2.59)	0.674
		Normal	125	95.4%	135	96.4%	114	97.4%	H vs. L	0.55 (0.13,2.24)	0.069
Dorsalis Pedis Pulses	Officer	n	113		110		102		Overall		0.557
		Number/%									
		Abnormal	13	11.5%	8	7.3%	10	9.8%	M vs. L	0.60 (0.24,1.52)	0.285
		Normal	100	88.5%	102	92.7%	92	90.2%	H vs. L	0.84 (0.35,2.00)	0.689
	Enlisted Flyer	n	50		52		50		Overall		0.811
		Number/%									
		Abnormal	9	18.0%	9	17.3%	11	22.0%	M vs. L	0.95 (0.34,2.64)	0.928
		Normal	41	82.0%	43	82.7%	39	78.0%	H vs. L	1.28 (0.48,3.44)	0.617
	Enlisted Groundcrew	n	130		140		117		Overall		0.689
		Number/%									
		Abnormal	18	13.8%	17	12.1%	12	10.3%	M vs. L	0.86 (0.42,1.75)	0.674
		Normal	112	86.2%	123	87.9%	105	89.7%	H vs. L	0.71 (0.33,1.55)	0.390

TABLE 15-9. (continued)

Unadjusted Exposure Index for Cardiovascular Variables by Occupation

Variable	Occupation	Statistic	Exposure Index: Low		Medium		High		Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
Posterior Tibial Pulses	Officer	n	113		110		102		Overall		0.153[a]
		Number/%									
		Abnormal	4	3.5%	4	3.6%	0	0.0%	M vs. L	1.03 (0.25,4.22)	0.976
		Normal	109	96.5%	106	96.4%	102	100.0%	H vs. L	—	0.149
	Enlisted Flyer	n	50		52		50		Overall		0.654[a]
		Number/%									
		Abnormal	3	6.0%	3	5.8%	5	10.0%	M vs. L	0.96 (0.18,4.99)	0.960
		Normal	47	94.0%	49	94.2%	45	90.0%	H vs. L	1.74 (0.39,7.71)	0.465
	Enlisted Groundcrew	n	130		140		117		Overall		0.443[a]
		Number/%									
		Abnormal	5	3.8%	2	1.4%	4	3.4%	M vs. L	0.36 (0.07,1.90)	0.230
		Normal	125	96.2%	138	98.6%	113	96.6%	H vs. L	0.88 (0.23,3.38)	0.857
Leg Pulses	Officer	n	113		110		102		Overall		0.616
		Number/%									
		Abnormal	16	14.2%	14	12.7%	10	9.8%	M vs. L	0.88 (0.41,1.91)	0.757
		Normal	97	85.8%	96	87.3%	92	90.2%	H vs. L	0.66 (0.28,1.53)	0.332
	Enlisted Flyer	n	50		52		50		Overall		0.239
		Number/%									
		Abnormal	10	20.0%	10	19.2%	16	32.0%	M vs. L	0.95 (0.36,2.53)	0.920
		Normal	40	80.0%	42	80.8%	34	68.0%	H vs. L	1.88 (0.76,4.69)	0.174
	Enlisted Groundcrew	n	130		140		117		Overall		0.756
		Number/%									
		Abnormal	21	16.2%	20	14.3%	15	12.8%	M vs. L	0.86 (0.44,1.68)	0.667
		Normal	109	83.8%	120	85.7%	102	87.2%	H vs. L	0.76 (0.37,1.56)	0.459

TABLE [illegible]. (continued)

Unadjusted Exposure Index for Cardiovascular Variables by Occupation

Variable	Occupation	Statistic	Exposure Index: Low		Medium		High		Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
Peripheral Pulses	Officer	n	113		110		102		Overall		0.616
		Number/%									
		Abnormal	16	14.2%	14	12.7%	10	9.8%	M vs. L	0.88 (0.41,1.91)	0.757
		Normal	97	85.8%	96	87.3%	92	90.2%	H vs. L	0.66 (0.28,1.53)	0.332
	Enlisted Flyer	n	50		52		50		Overall		0.239
		Number/%									
		Abnormal	10	20.0%	10	19.2%	16	32.0%	M vs. L	0.95 (0.36,2.53)	0.920
		Normal	40	80.0%	42	80.8%	34	68.0%	H vs. L	1.88 (0.76,4.69)	0.174
	Enlisted Groundcrew	n	130		140		117		Overall		0.651
		Number/%									
		Abnormal	22	16.9%	20	14.3%	15	12.8%	M vs. L	0.82 (0.42,1.58)	0.549
		Normal	108	83.1%	120	85.7%	102	87.2%	H vs. L	0.72 (0.36,1.47)	0.368
All Pulses	Officer	n	112		110		102		Overall		0.603
		Number/%									
		Abnormal	16	14.3%	14	12.7%	10	9.8%	M vs. L	0.88 (0.40,1.89)	0.734
		Normal	96	85.7%	96	87.3%	92	90.2%	H vs. L	0.65 (0.28,1.51)	0.317
	Enlisted Flyer	n	50		52		50		Overall		0.239
		Number/%									
		Abnormal	10	20.0%	10	19.2%	16	32.0%	M vs. L	0.95 (0.36,2.53)	0.920
		Normal	40	80.0%	42	80.8%	34	68.0%	H vs. L	1.88 (0.76,4.69)	0.174
	Enlisted Groundcrew	n	130		140		117		Overall		0.651
		Number/%									
		Abnormal	22	16.9%	20	14.3%	15	12.8%	M vs. L	0.82 (0.42,1.58)	0.549
		Normal	108	83.1%	120	85.7%	102	87.2%	H vs. L	0.72 (0.36,1.47)	0.368

*No conditions reported that were not verified; therefore, reported and verified analyses are the same.
[a]Small cell size may affect validity of p-value.
—Estimated relative risk not applicable for continuous analysis of a variable; estimated relative risk/confidence interval/p-value not given due to cells with zero frequency.

TABLE 15-10.

Adjusted Exposure Index for Cardiovascular Variables by Occupation

Variable	Occupation	Statistic	Exposure Index			Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value
			Low	Medium	High			
Reported/ Verified Essential Hypertension*	Officer	n	111	109	104	Overall		0.465
						M vs. L	0.88 (0.47,1.65)	0.682
						H vs. L	1.27 (0.69,2.33)	0.441
	Enlisted Flyer	n	51	52	51	Overall		0.457
						M vs. L	0.87 (0.37,2.07)	0.757
						H vs. L	1.48 (0.63,3.48)	0.373
	Enlisted Groundcrew	n	129	138	117	Overall		0.545
						M vs. L	1.34 (0.76,2.36)	0.156
						H vs. L	1.30 (0.72,2.33)	0.384
Reported Heart Disease (Excluding Hypertension)	Officer	n	113	111	106	Overall		0.040
						M vs. L	0.52 (0.30,0.90)	0.019
						H vs. L	0.57 (0.33,1.00)	0.082
	Enlisted Flyer	n	52	53	51	Overall		0.891
						M vs. L	0.90 (0.40,2.01)	0.795
						H vs. L	0.82 (0.37,1.83)	0.631
	Enlisted Groundcrew	n	133	140	119	Overall		0.575
						M vs. L	0.84 (0.50,1.42)	0.509
						H vs. L	1.11 (0.66,1.89)	0.689

TABLE 15-10. (continued)

Adjusted Exposure Index for Cardiovascular Variables by Occupation

Variable	Occupation	Statistic	Exposure Index Low	Exposure Index Medium	Exposure Index High	Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value
Verified Heart Disease (Excluding Hypertension)	Officer	n	113	111	106	Overall		0.040
						M vs. L	0.52 (0.30,0.90)	0.019
						H vs. L	0.57 (0.33,1.00)	0.082
	Enlisted Flyer	n	52	53	51	Overall		0.891
						M vs. L	0.90 (0.40,2.01)	0.795
						H vs. L	0.82 (0.37,1.83)	0.631
	Enlisted Groundcrew	n	133	140	119	Overall		0.442
						M vs. L	0.77 (0.45,1.30)	0.332
						H vs. L	1.08 (0.63,1.82)	0.787
Reported/ Verified Myocardial Infarction*	Officer	n	112	111	104	Overall		0.665
						M vs. L	2.02 (0.41,9.88)	0.384
						H vs. L	1.65 (0.32,8.51)	0.549
	Enlisted Flyer	n	52	53	51	Overall		0.713
						M vs. L	1.00 (0.23,4.35)	0.992
						H vs. L	0.52 (0.09,3.07)	0.472
	Enlisted Groundcrew	n	132	138	119	Overall		0.831
						M vs. L	0.90 (0.20,4.02)	0.897
						H vs. L	1.38 (0.36,5.35)	0.638

TABLE 15-10. (continued)

Adjusted Exposure Index for Cardiovascular Variables by Occupation

Variable	Occupation	Statistic	Exposure Index: Low	Exposure Index: Medium	Exposure Index: High	Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value
Systolic Blood Pressure	Officer	n	100	107	98	Overall		0.786
		Adj. Mean	129.39	131.03	130.00	M vs. L	—	0.495
		95% C.I.	(121.17, 137.61)	(123.16, 138.90)	(121.85, 138.15)	H vs. L	—	0.803
		n	103	107	99	Overall		0.700
						M vs. L	0.92 (0.43,1.96)	0.818
						H vs. L	1.25 (0.59,2.62)	0.562
	Enlisted Flyer	n	50	53	49	Overall		0.181
		Adj. Mean	126.79	130.16	133.35	M vs. L	—	0.357
		95% C.I.	(117.67, 135.92)	(122.03, 138.29)	(124.75, 141.96)	H vs. L	—	0.065
		n	50	53	49	Overall		0.430
						M vs. L	1.27 (0.44,3.67)	0.660
						H vs. L	1.91 (0.70,5.21)	0.208
	Enlisted Groundcrew	n	128	132	111	Overall		0.288
		Adj. Mean	129.52	132.79	130.66	M vs. L	—	0.120
		95% C.I.	(125.46, 133.59)	(128.57, 137.02)	(126.35, 134.97)	H vs. L	—	0.602
		n	128	134	111	Overall		0.573
						M vs. L	1.41 (0.73,2.72)	0.308
						H vs. L	1.28 (0.65,2.52)	0.478

TABLE 15-10. (continued)

Adjusted Exposure Index for Cardiovascular Variables by Occupation

Variable	Occupation	Statistic	Exposure Index: Low	Exposure Index: Medium	Exposure Index: High	Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value
Heart Sounds	Officer	n	113	111	106	Overall		0.491
						M vs. L	0.64 (0.16,2.51)	0.522
						H vs. L	0.38 (0.07,2.03)	0.258
	Enlisted Flyer	n	—	—	—	Overall		—
						M vs. L	—	—
						H vs. L	—	—
	Enlisted Groundcrew	n	133	140	119	Overall		0.258
						M vs. L	0.32 (0.06,1.60)	0.165
						H vs. L	0.99 (0.32,3.03)	0.984
ECG-Overall	Officer	n	113	111	106	Overall		0.920
						M vs. L	0.98 (0.47,2.03)	0.952
						H vs. L	0.87 (0.41,1.83)	0.704
	Enlisted Flyer	n	52	53	51	Overall		0.494
						M vs. L	1.39 (0.53,3.69)	0.503
						H vs. L	0.77 (0.27,2.15)	0.617
	Enlisted Groundcrew	n	131	135	112	Overall		0.975
						M vs. L	1.06 (0.48,2.36)	0.873
						H vs. L	1.09 (0.50,2.39)	0.826

TABLE 15-10. (continued)

Adjusted Exposure Index for Cardiovascular Variables by Occupation

Variable	Occupation	Statistic	Exposure Index: Low	Medium	High	Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value
Nonspecific T-Waves	Officer	n	113	111	106	Overall		0.883
						M vs. L	1.23 (0.50,3.02)	0.653
						H vs. L	1.03 (0.41,2.60)	0.952
	Enlisted Flyer	n	52	53	51	Overall		0.091
						M vs. L	3.22 (0.94,11.00)	0.063
						H vs. L	1.26 (0.32,4.97)	0.749
	Enlisted Groundcrew	n	133	140	119	Overall		0.975
						M vs. L	1.10 (0.45,2.70)	0.834
						H vs. L	1.01 (0.42,2.46)	0.976
Bradycardia	Officer	n	112	111	104	Overall		0.108**
						M vs. L	0.34 (0.10,1.14)**	0.082**
						H vs. L	0.37 (0.11,1.23)**	0.105**
	Enlisted Flyer	n	52	53	51	Overall		0.602
						M vs. L	0.85 (0.13,5.44)	0.865
						H vs. L	0.32 (0.03,3.75)	0.363
	Enlisted Groundcrew	n	132	138	119	Overall		0.369
						M vs. L	0.44 (0.10,1.82)	0.258
						H vs. L	0.39 (0.08,1.99)	0.254

TABLE 15-10. (continued)

Adjusted Exposure Index for Cardiovascular Variables by Occupation

Variable	Occupation	Statistic	Exposure Index: Low	Medium	High	Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value
Arrhythmia	Officer	n	102	108	101	Overall		0.325
						M vs. L	0.36 (0.09,1.48)	0.159
						H vs. L	0.75 (0.24,2.40)	0.631
	Enlisted Flyer	n	—	—	—	Overall		—
						M vs. L	—	—
						H vs. L	—	—
	Enlisted Groundcrew	n	131	134	114	Overall		0.967
						M vs. L	0.86 (0.26,2.90)	0.810
						H vs. L	0.99 (0.32,3.06)	0.992
ECG-Other Diagnoses	Officer	n	112	111	104	Overall		0.356**
						M vs. L	1.09 (0.56,2.14)**	0.803**
						H vs. L	0.67 (0.32,1.38)**	0.276**
	Enlisted Flyer	n	52	53	51	Overall		0.178
						M vs. L	1.27 (0.51,3.20)	0.610
						H vs. L	0.49 (0.16,1.44)	0.194
	Enlisted Groundcrew	n	133	140	119	Overall		0.566
						M vs. L	1.16 (0.60,2.25)	0.653
						H vs. L	0.79 (0.39,1.62)	0.529

TABLE 15-10. (continued)

Adjusted Exposure Index for Cardiovascular Variables by Occupation

Variable	Occupation	Statistic	Exposure Index: Low	Exposure Index: Medium	Exposure Index: High	Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value
Diastolic Blood Pressure	Officer	n	100	107	98	Overall		0.537
		Adj. Mean	75.49	75.30	76.64	M vs. L	--	0.886
		95% C.I.	(71.02,79.95)	(71.02,79.57)	(72.22,81.07)	H vs. L	--	0.383
		n	101	107	101	Overall		0.017
						M vs. L	1.03 (0.14,7.62)	0.976
						H vs. L	5.53 (1.12,27.36)	0.036
	Enlisted Flyer	n	50	53	49	Overall		0.464
		Adj. Mean	75.32	76.98	74.45	M vs. L	--	0.428
		95% C.I.	(70.10,80.55)	(72.33,81.64)	(69.52,79.37)	H vs. L	--	0.665
		n	50	53	49	Overall		0.434
						M vs. L	2.88 (0.53,15.76)	0.222
						H vs. L	1.97 (0.32,12.30)	0.465
	Enlisted Groundcrew	n	128	132	111	Overall		0.304**
		Adj. Mean**	77.60	78.93	77.31	M vs. L	--	0.227**
		95% C.I.**	(75.46,79.74)	(76.71,81.16)	(75.04,79.58)	H vs. L	--	0.801**
		n	129	134	113	Overall		0.222
						M vs. L	2.74 (0.69,10.88)	0.150
						H vs. L	2.89 (0.70,1.81)	0.142

TABLE 15-10. (continued)

Adjusted Exposure Index for Cardiovascular Variables by Occupation

Variable	Occupation	Statistic	Exposure Index: Low	Exposure Index: Medium	Exposure Index: High	Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value
Femoral Pulses	Officer	n	—	—	—	Overall		—
						M vs. L	—	—
						H vs. L	—	—
	Enlisted Flyer	n	50	52	50	Overall		0.208
						M vs. L	2.15 (0.19,24.79)	0.542
						H vs. L	5.32 (0.59,47.78)	0.136
	Enlisted Groundcrew	n	131	140	117	Overall		0.576
						M vs. L	0.80 (0.13,5.01)	0.810
						H vs. L	0.32 (0.03,3.25)	0.337
Popliteal Pulses	Officer	n	—	—	—	Overall		—
						M vs. L	—	—
						H vs. L	—	—
	Enlisted Flyer	n	50	52	50	Overall		0.419
						M vs. L	1.04 (0.14,7.93)	0.968
						H vs. L	2.59 (0.47,14.30)	0.276
	Enlisted Groundcrew	n	131	140	117	Overall		0.490
						M vs. L	1.04 (0.29,3.68)	0.960
						H vs. L	0.46 (0.11,2.02)	0.308

TABLE 15-10. (continued)

Adjusted Exposure Index for Cardiovascular Variables by Occupation

Variable	Occupation	Statistic	Exposure Index: Low	Exposure Index: Medium	Exposure Index: High	Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value
Dorsalis Pedis Pulses	Officer	n	113	110	102	Overall		0.535
						M vs. L	0.59 (0.23,1.51)	0.271
						H vs. L	0.82 (0.34,1.98)	0.667
	Enlisted Flyer	n	50	52	50	Overall		0.894
						M vs. L	1.04 (0.37,2.91)	0.944
						H vs. L	1.25 (0.46,3.38)	0.660
	Enlisted Groundcrew	n	130	140	117	Overall		0.613
						M vs. L	0.96 (0.46,1.97)	0.904
						H vs. L	0.69 (0.32,1.52)	0.358
Posterior Tibial Pulses	Officer	n	—	—	—	Overall		—
						M vs. L	—	—
						H vs. L	—	—
	Enlisted Flyer	n	50	52	50	Overall		0.746
						M vs. L	1.00 (0.17,6.00)	0.999
						H vs. L	1.68 (0.35,8.07)	0.516
	Enlisted Groundcrew	n	128	134	112	Overall		0.831
						M vs. L	0.60 (0.10,3.42)	0.562
						H vs. L	0.90 (0.20,4.00)	0.897

TABLE 15-10. (continued)

Adjusted Exposure Index for Cardiovascular Variables by Occupation

Variable	Occupation	Statistic	Exposure Index: Low	Exposure Index: Medium	Exposure Index: High	Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value
Leg Pulses	Officer	n	105	107	96	Overall		0.630
						M vs. L	0.89 (0.40,2.00)	0.779
						H vs. L	0.65 (0.27,1.60)	0.352
	Enlisted Flyer	n	49	52	48	Overall		0.475
						M vs. L	1.06 (0.38,2.95)	0.912
						H vs. L	1.70 (0.66,4.35)	0.271
	Enlisted Groundcrew	n	128	133	110	Overall		0.719
						M vs. L	1.08 (0.54,2.16)	0.826
						H vs. L	0.80 (0.38,1.68)	0.555
Peripheral Pulses	Officer	n	105	107	96	Overall		0.630
						M vs. L	0.89 (0.40,2.00)	0.779
						H vs. L	0.65 (0.27,1.60)	0.352
	Enlisted Flyer	n	49	52	48	Overall		0.475
						M vs. L	1.06 (0.38,2.95)	0.912
						H vs. L	1.70 (0.66,4.35)	0.271
	Enlisted Groundcrew	n	128	133	110	Overall		0.683
						M vs. L	1.01 (0.51,2.00)	0.976
						H vs. L	0.75 (0.36,1.57)	0.447

TABLE 15-10. (continued)

Adjusted Exposure Index for Cardiovascular Variables by Occupation

Variable	Occupation	Statistic	Exposure Index: Low	Exposure Index: Medium	Exposure Index: High	Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value
All Pulses	Officer	n	104	107	96	Overall		0.616
						M vs. L	0.88 (0.39,1.98)	0.764
						H vs. L	0.65 (0.26,1.58)	0.337
	Enlisted Flyer	n	49	52	48	Overall		0.475
						M vs. L	1.06 (0.38,2.95)	0.912
						H vs. L	1.70 (0.66,4.35)	0.271
	Enlisted Groundcrew	n	128	133	110	Overall		0.683
						M vs. L	1.01 (0.51,2.00)	0.976
						H vs. L	0.75 (0.36,1.57)	0.447

*No conditions reported that were not verified; therefore, reported and verified analyses are the same.

—Adjusted relative risk not applicable for continuous analysis of a variable; adjusted analysis not performed due to sparse cells.

**Exposure index-by-covariate interaction ($0.01<p\leq 0.05$)—adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction.

category, none of the differences, either unadjusted or adjusted, was statistically significant. The percent of individuals with hypertension in the medium exposure level category was similar to that in the low exposure category for each occupational stratum.

Reported and Verified Heart Disease

There were no statistically significant differences in the percentage of individuals with reported or verified heart disease for any occupational stratum in the unadjusted analyses. Differences were also nonsignificant in the adjusted analyses with the exception of the officer cohort, where the adjusted relative risk for the medium versus low contrast was significantly less than 1 (Adj. RR: 0.52, 95% C.I.: [0.30,0.90], p=0.019). The high versus low exposure level relative risk in the officers was also less than 1 and of borderline significance (p=0.082).

Reported and Verified Myocardial Infarction

There were no statistically significant differences, either unadjusted or adjusted, in any of the occupational strata.

Physical Examination Variables: Central Cardiac Function

Systolic Blood Pressure

In the officers and enlisted groundcrew, neither the mean values nor the percentage with abnormal blood pressure was significantly different across the three exposure levels (unadjusted or adjusted for covariates). In the enlisted flyers, however, there was a significant difference in the means that was consistent with a dose-response relationship: mean systolic blood pressures were 124.14, 128.79, and 133.55 in the low, medium, and high exposure level categories, respectively (p=0.037). The high versus low contrast was significant (p=0.010). After adjustment for covariates, however, the differences were still consistent with a dose-response relationship, but no longer statistically significant (p=0.181).

The percent with abnormal systolic blood pressure (>140 mm Hg) also increased with increasing exposure level, but did not reach statistical significance, either unadjusted or adjusted for covariates.

Heart Sounds

There were no statistically significant differences in abnormal heart sounds, either unadjusted or adjusted.

ECG-Overall

There were no statistically significant differences in overall ECG findings, either unadjusted or adjusted.

RBBB

There were only four individuals with RBBB--one officer, two enlisted flyers, and one enlisted groundcrew--and no significant exposure level effects. Adjusted analyses were not performed due to the small number of abnormalities.

LBBB

Only one Ranch Hand, an officer in the medium exposure level category, was found to have LBBB. Statistical analyses could therefore not be conducted.

Nonspecific T-Waves

There were no statistically significant differences, unadjusted or adjusted, for nonspecific T-wave findings in the officers or enlisted groundcrew. In the unadjusted analysis of the enlisted flyer cohort there was a borderline significant difference overall (p=0.075), with a significantly higher risk in the medium exposure level category as compared to the low exposure level category (Est. RR: 3.51, 95% C.I.: [1.05,11.73], p=0.041). This difference was of borderline significance after adjustment for covariates (p=0.063).

Bradycardia

There were no statistically significant differences in the occurrence of bradycardia in any of the three occupational strata in unadjusted analyses. The presence of bradycardia decreased with increasing exposure level in each occupational stratum.

Adjusted analyses did not detect significant exposure level effects in the enlisted flyers or enlisted groundcrew, but in the officers, there was a statistically significant exposure index-by-cholesterol-HDL ratio interaction (p=0.045). Appendix L, Table L-4, shows that there were fewer abnormalities in the medium and high exposure level categories as compared to the low exposure level category for individuals with ratios of at most 4.2 and for individuals with ratios between 4.2 and 5.5; whereas, in individuals with cholesterol-HDL ratios above 5.5, there were slightly more abnormalities in the medium and high exposure level categories as compared to the low exposure level category. The numbers were quite sparse, however. Table 15-10 also presents the results after deleting the interaction term from the model. The adjusted relative risks did not reach statistical significance.

Tachycardia

There were no cases of tachycardia among the Ranch Hands and stratified analyses were not performed.

Arrhythmia

There were no significant differences among the three exposure level categories, unadjusted or adjusted, in the presence of arrhythmia for either the officers or enlisted groundcrew. However, in the enlisted flyers, there was a statistically significant effect, with arrhythmia detected in six (11.8%) of the individuals in the high exposure level category, as compared to none in the low and none in the medium exposure level categories. The high versus low contrast is significant (p=0.025, Fisher's exact test). The number of abnormalities was too few for adjusted analyses.

ECG-Other Diagnoses

No significant differences emerged in the unadjusted analyses for any of the occupational strata, nor in the adjusted analyses for the enlisted flyers or enlisted groundcrew. There was, however, a statistically significant exposure index-by-age interaction in the officers (p=0.018). Upon stratification by age (Appendix L, Table L-4), there was an inverse dose-response relationship in those born in or after 1942, little difference among exposure level categories in those born between 1923 and 1941, and only four abnormalities in those born in or before 1922, all in the medium exposure level category. None of these within-stratum differences was statistically significant. After deleting the interaction term from the model (Table 15-10), the adjusted relative risks in the officers were not statistically significant.

Physical Examination Variables: Peripheral Vascular Function

Diastolic Blood Pressure

In the officers, there were no statistically significant differences in the mean diastolic blood pressure, either unadjusted or adjusted for covariates. The discrete analyses, however, detected a significantly greater percentage of abnormalities in the high exposure level category (p=0.039), which remained significant after covariate adjustment (Adj. RR: 5.53, 95% C.I.: [1.12,27.36], p=0.036). Those in the medium exposure level category did not exhibit an excess risk.

There were no significant differences, unadjusted or adjusted, in either the mean levels or the percent abnormal in the enlisted flyers.

In the enlisted groundcrew, there were no significant differences in the unadjusted continuous or discrete analyses, nor in the adjusted discrete analysis. The adjusted continuous analysis did reveal a significant exposure index-by-personality type interaction (p=0.012), which is examined more fully in Appendix L, Table L-4. This table shows that there was no significant difference in the exposure level means among those with Type A personalities; in Type B individuals, there was a significant difference (p=0.020), although not consistent with a dose-response relationship (adjusted means were 76.90, 80.52, and 76.80 in the low, medium, and high exposure level categories, respectively). Since the interaction did not reach the 1 percent significance level, Table 15-10 also presents the results after deletion of the interaction term from the model. The adjusted means could not be significantly different.

Funduscopic Examination

There were few funduscopic abnormalities and no evidence of exposure level effects. Adjusted analyses could not be performed on this variable.

Carotid Bruits

Again, there were few abnormalities and no significant differences among the exposure level groups. Adjusted analyses could not be performed on this variable.

Radial Pulses

Only two Ranch Hands had radial pulse abnormalities, both in the low exposure category. Adjusted analyses were not possible.

Femoral Pulses

There were no significant differences, unadjusted or adjusted, in femoral pulse abnormalities. There was a trend consistent with a dose-response relationship in the enlisted flyers, but it was not statistically significant. Analyses in the other occupational categories were unremarkable.

Popliteal Pulses

There were no statistically significant differences, unadjusted or adjusted, in the percentage of individuals with popliteal pulse abnormalities in the three exposure level categories for any of the occupational strata.

Dorsalis Pedis Pulses

No statistically significant differences were detected, unadjusted or adjusted, in any of the occupational strata.

Posterior Tibial Pulses

No significant differences were found.

Leg Pulses

For the aggregated variable combining all leg pulses, there were no significant differences, either unadjusted or adjusted for covariates.

Peripheral Pulses

The analysis of all peripheral pulses gave similar results to that for the leg pulses, i.e., no significant differences among the three exposure level categories within any occupational stratum, either unadjusted or adjusted for covariates.

All Pulses

Analysis of the aggregated index of all pulses did not reveal significant differences, either unadjusted or adjusted, for any of the occupational strata.

Exposure Index-by-Covariate Interactions

A summary of the significant exposure index-by-covariate interactions is presented in Table 15-11. Two occurred in the officers (one for bradycardia involving an interaction with cholesterol-HDL ratio, and one for ECG-other diagnoses involving an interaction with age) and one in the enlisted groundcrew (for diastolic blood pressure, involving an interaction with personality type).

Longitudinal Analysis

The overall ECG was investigated by longitudinal analysis. The change in status (normal or abnormal) between the 1982 Baseline and 1987 followup examination was determined for each subject participating at both examinations and the degree of change compared in the Ranch Hand and Comparison groups.

Table 15-12 gives summary statistics for the two examinations, as well as summary statistics of the 1985 followup examination for reference purposes. In both groups, the percent with abnormal findings declined from Baseline to the 1985 followup examination, and then increased somewhat at the 1987 followup, although not to the same level as that at Baseline. Table 15-13

TABLE 15-11.

Summary of Exposure Index-by-Covariate Interactions From Adjusted Analyses for Cardiovascular Variables

Variable	Occupation	Covariate	p-Value
Bradycardia	Officer	Cholesterol-HDL Ratio	0.045
ECG-Other Diagnoses	Officer	Age	0.018
Diastolic Blood Pressure	Enlisted Groundcrew	Personality Type	0.012

TABLE 15-12.

Summary Statistics for the Longitudinal Analysis of Overall ECG: 1982 Baseline, 1985 Followup, and 1987 Followup Examinations

Examination	Statistic	Group: Ranch Hand		Group: Comparison	
1982 Baseline	Abnormal	217	26.3%	275	28.2%
	Normal	609	73.7%	701	71.8%
1985 Followup	Abnormal	100	12.3%	127	13.2%
	Normal	712	87.7%	834	86.8%
1987 Followup	Abnormal	132	16.0%	179	18.3%
	Normal	694	84.0%	797	81.7%

Note: Summary statistics for the 1982 Baseline and the 1987 followup are based on 826 Ranch Hands and 976 Comparisons who participated in the 1982 Baseline and 1987 followup examinations. Summary statistics on 812 of these Ranch Hands and 961 of these Comparisons who also participated in the 1985 followup are included for reference purposes only.

TABLE 15-13.

Longitudinal Analyses of the Overall ECG: A Contrast of 1982 Baseline and 1987 Followup Examination Abnormalities

Group	1982 Baseline Exam	1987 Followup Exam: Abnormal	1987 Followup Exam: Normal	Odds Ratio (OR)*	p-Value (OR_{RH} vs. OR_C)
Ranch Hand	Abnormal	66	151	0.437	0.960
	Normal	66	543		
Comparison	Abnormal	103	172	0.442	
	Normal	76	625		

*Odds Ratio: $\frac{\text{Number Normal Baseline, Abnormal 1987 Followup}}{\text{Number Abnormal Baseline, Normal 1987 Followup}}$

presents tables for each of the Ranch Hand and Comparison groups, giving the number of individuals with abnormal ECGs at both the Baseline and 1987 followup examinations, the number abnormal at Baseline but normal at the 1987 followup, etc. Fewer individuals went from normal to abnormal than vice versa, with similar odds ratios in the two groups (p=0.960).

Morbidity-Mortality Analysis

For the cardiovascular evaluation, morbidity and mortality data on all Ranch Hands (diabetics included) and the first Comparison of the randomly ordered set matched to the Ranch Hands were compiled to estimate the frequency of four hierarchical endpoints combining both fatal and nonfatal events. Because of competing mortality and possible misclassification of the cause of death, the endpoints of (1) death (any cause) or verified nonfatal heart disease, and (2) death (any cause) or verified nonfatal myocardial infarction were examined first, followed by endpoints limited to (3) fatal or nonfatal verified heart disease, and (4) fatal or nonfatal verified myocardial infarction or fatal heart disease. The first two endpoints were used to ensure that any misclassification bias with regards to death would not affect the results.

The analysis was based on 1,254 Ranch Hands and 1,249 Comparisons. (Seven Ranch Hands and six Comparisons who had verified heart disease before service in SEA were excluded.) The history of each individual from the beginning of his tour of duty in SEA to the present was then reviewed. Histories of verified heart disease and myocardial infarction for living individuals who were noncompliant at Baseline and the two followup visits were missing. For the living noncompliant individuals, the observed rate in the compliant individuals was used to estimate the number of nonfatal events among the noncompliant individuals for each cohort. It was assumed that there were no nonfatal cardiovascular events in the noncompliant individuals who died due to a cause other than cardiovascular system failure. The results are shown in Table L-5 of Appendix L.

There were 85 deaths in the Ranch Hand group and 92 in the Comparisons. The estimated percentage of individuals who died from any cause or had a verified nonfatal history of heart disease (category 1) was 43.6 percent in the Ranch Hands and 43.9 percent in the Comparisons.

The estimated percentage of deaths from any cause or verified nonfatal myocardial infarction (category 2) was 10.0 percent in the Ranch Hands and 11.2 percent in the Comparisons.

Forty-two of the 85 deaths in the Ranch Hands and 41 of the 92 deaths in the Comparisons either were attributed to heart disease or were individuals who had verified heart disease histories. The estimated percentage of fatal and nonfatal verified heart disease (category 3) was 40.1 percent in the Ranch Hands and 39.8 percent in the Comparisons.

Among the 85 deaths in the Ranch Hands, 33 individuals died from cardiovascular disease or had a verified history of myocardial infarction, as compared to 29 of the 92 deaths in the Comparisons. The estimated percentage of fatal or nonfatal verified myocardial infarction or fatal heart disease (category 4) was 5.9 percent in the Ranch Hands and 6.1 percent in the Comparisons.

These contrasts must be interpreted guardedly since they involve several unverifiable assumptions. Nevertheless, they are consistent with the morbidity findings presented in the chapter and do not indicate excess cardiovascular risk in the Ranch Hands.

DISCUSSION

Of the diseases encountered by the primary care physician, circulatory disorders are among the most common. The sources of the noninvasive data analyzed in the current chapter occupy a time-honored place in cardiovascular practice. Specifically, the history, physical examination, chest x ray, and resting electrocardiogram remain highly reliable indices that can alert the clinician to the presence of underlying cardiovascular disease and point to the need for additional, more specific, noninvasive, or invasive studies. Though arbitrary, dividing data collection into central and peripheral cardiovascular functions is convenient and forms a reasonable basis for comparison of the cohorts under study.

The limitations of the history in cardiovascular diagnosis deserve emphasis. In peripheral vascular disease, for example, signs and symptoms will vary depending on the degree of development of collateral circulatory channels. While hemodynamically significant arterial disease of lower extremities is almost always associated with claudication, severe carotid occlusive disease can be present in the absence of symptoms of transient cerebral ischemia. Further, conclusive evidence shows that advanced coronary artery disease can occur in the absence of angina and present as "silent" myocardial ischemia.[38] Lastly, it is well recognized that the cardiovascular history, as related by patients, is often subject to error. The generic term "heart attack," for example, can be used to describe any type of cardiac event from an isolated episode of unstable angina or arrythmia, to an actual myocardial infarction. These imperfections highlight the importance of the type of medical record verification conducted in the current study.

In the cardiovascular assessment, particularly, the physical examination can provide valuable clues to the presence of asymptomatic but significant underlying disease. Because the examinations were conducted by internists rather than cardiologists, steps were taken to simplify data collection and to reduce interobserver differences among the examining physicians. All blood pressure readings, for example, were taken by automated sphygmomanometric instruments. Auscultory endpoints--murmurs and bruits--were recorded as present or absent by anatomic location, thus eliminating speculation as to specific valvular or vessel origin and hemodynamic significance. As markers of occult arterial occlusive disease, vascular bruits are relatively easy to detect and were carefully sought.

Pertinent to the longitudinal design of the AFHS, several of the physical findings recorded must be viewed in the context of the aging population under study. A gradual increase in systolic blood pressure will occur with advancing years. Related to the normal progression of arteriosclerosis and, more specifically, to arterial tortuosity, vascular bruits may occur in vessels free of occlusive disease, particularly in the carotid arteries. Again, all bruits were recorded by location without attempting to comment on the hemodynamic significance or specific vessel of origin (i.e., internal vs. external carotid). The occurrence of abnormal heart sounds, particularly S_4, would also be expected to increase with age.

The data collected in the current chapter were limited to the resting 12-lead electrocardiogram and the standard two-view chest x ray. This x ray is used to detect the presence of cardiac enlargement or abnormalities in pulmonary vasculature, as reported in Chapter 20, Pulmonary Disease. In current practice, these techniques are supplemented, but not replaced, by such noninvasive studies as the treadmill exercise test, nuclear isotope studies, and the echocardiogram. With few exceptions, these technically sophisticated and costly procedures do little more than confirm diagnoses that can be made based on data available in the current assessment. For example, when correlated with the history and physical examination, the chest x ray and electrocardiogram enable the clinician to draw highly accurate conclusions regarding the presence and hemodynamic significance of valvular heart disease of any etiology. As defined by the chest x ray, the pulmonary vascularity can provide reliable clues to the presence of global left ventricular dysfunction with pulmonary venous congestion and of pulmonary hypertension of any cause.

The dependent variable-covariate associations analyzed in the current chapter confirm findings that have been well documented in numerous long-term epidemiologic studies. The lack of clearly defined cardiovascular endpoints to dioxin exposure places a premium on the careful analysis of risk factors as potentially confounding variables. More than any other, the cardiovascular system is subject to the effects of lifestyle and heredity.

As a degenerative disease with multiple manifestations, arteriosclerosis develops in all organ systems over time. With few exceptions, an age-related increase in the incidence of abnormal physical findings was documented in both the Ranch Hand and Comparison groups. As expected, reported and verified heart disease and, particularly, previous myocardial infarction, were highly correlated with the classical risk factors of age, positive family history, and cigarette use. Although an apparent exception was the negative correlation between the systolic blood pressure and current cigarette use, this most likely reflects the contributions of former smokers, who have stopped smoking in response to a diagnosed disease. This is the group that had the highest percentage of abnormal systolic blood pressures (above 140 mm Hg). Lifetime cigarette use, on the other hand, was consistently positively associated with abnormalities in all variables analyzed.

The effects of current and lifetime alcohol consumption were less consistent. Clinically, it is clear that in cases of severe, chronic abuse, alcohol is directly cardiotoxic and can lead to an irreversible congestive cardiomyopathy. On the other hand, when consumed in moderation, alcohol may favorably influence the ratio of HDL to LDL cholesterol and may actually be protective with respect to the future development of cardiovascular disease.

Group comparisons generally revealed no significant differences between the Ranch Hand and Comparison cohorts. As in the Baseline examination (but not in the 1985 followup), Ranch Hands had a greater incidence of peripheral pulse abnormalities of the lower extremities than the Comparisons (15.3% vs.

12.2%). As noted above, the 1985 followup included Doppler ultrasound studies, which have proven to be more sensitive than traditional manual palpation. Further analysis of specific pulse sites suggests that the current group difference relates mainly to an increased incidence of femoral, rather than more peripheral, sites, a finding that should be relatively easy to confirm on subsequent examination cycles. Arterial occlusive disease is often unilateral rather than bilateral and can affect large vessels proximally or smaller vessels distally in segmental fashion. Distal circulation may be maintained by good collateral vessels even in the presence of proximal, partial pulse deficits. The Doppler should be more reliable than palpation in such cases, but neither method is perfect. This observed pulse difference does not appear to be related to exposure since abnormalities were not increased in the enlisted groundcrew, the group with the highest serum TCDD levels.

Recently, there has been renewed interest in the role of personality type as a risk factor for cardiovascular disease. In the current study, Type B personality was found to be associated with an increased incidence of elevated systolic blood pressure and with deficits in four of the five peripheral pulses assessed by palpation. Though at variance with classical teaching, these results are consistent with recent evidence that Type B personality may be at equal or greater risk than Type A for the development of coronary artery disease.[39]

In summary, the historical, physical examination, and laboratory data provide a reasonable basis for comparison of the cohorts under study and indicate that neither the Ranch Hand nor the Comparison group is at significant health detriment relative to the other. The slightly greater incidence of heart disease documented in the Ranch Hand cohort in the 1985 followup examination was not evident after continuing review of medical records. The incidence is now similar in the two groups. Finally, as in the Baseline examination (but not in the 1985 followup), a slightly greater incidence of pulse deficits has been found in the Ranch Hand group and will bear continued surveillance in future examination cycles as more accurate methods to measure the body burden of dioxin become available.

SUMMARY

The cardiovascular evaluation of the Ranch Hand and Comparison groups was based upon reported and verified heart disease events (essential hypertension, cardiac disease, and myocardial infarction); assessment of central cardiac function (systolic blood pressure, heart sounds, and ECG findings); and assessment of peripheral vascular function (diastolic blood pressure, funduscopic abnormalities, carotid bruits, and peripheral pulse abnormalities). Table 15-14 presents a summary of all of the unadjusted and adjusted group comparisons for these variables.

In the evaluation of heart disease from questionnaire data, there were no statistically significant differences, unadjusted or adjusted, in the frequency of reported/verified essential hypertension, reported heart disease, or verified heart disease. For reported/verified myocardial infarction, there was no statistically significant difference between the two groups in the unadjusted analysis, but in the adjusted analyses, there was a statistically

TABLE 15-14.

Overall Summary Results of Unadjusted and Adjusted Group Contrast Analyses of Cardiovascular Variables

Variable	Unadjusted	Adjusted	Direction of Results
<u>Questionnaire Variables</u>			
Reported/Verified Essential Hypertension*	NS	NS	
Reported Heart Disease (Excluding Hypertension)	NS	NS	
Verified Heart Disease (Excluding Hypertension)	NS	NS	
Reported/Verified Myocardial Infarction*	NS	** (NS)	
<u>Central Cardiac Function</u>			
Systolic Blood Pressure (continuous)	NS	NS	
Systolic Blood Pressure (discrete)	NS	** (NS)	
Heart Sounds	NS	NS	
ECG-Overall	NS	NS	
RBBB	NS	NS	
LBBB	NS	--	
Nonspecific T-Waves	NS	****	
Bradycardia	0.049	NS*	C>RH
Tachycardia	NS	--	
Arrhythmia	NS	NS*	RH>C
ECG-Other Diagnoses	NS	NS	

TABLE 15-14. (continued)

Overall Summary Results of Unadjusted and Adjusted Group Contrast Analyses of Cardiovascular Variables

Variable	Unadjusted	Adjusted	Direction of Results
<u>Peripheral Vascular Function</u>			
Diastolic Blood Pressure (continuous)	NS*	** (NS*)	RH>C
Diastolic Blood Pressure (discrete)	NS	** (NS)	
Funduscopic Examination	NS	--	
Carotid Bruits	NS*	--	RH>C
Radial Pulses	NS*	--	C>RH
Femoral Pulses	0.016	0.018	RH>C
Popliteal Pulses	NS	NS	
Dorsalis Pedis Pulses	NS*	NS*	RH>C
Posterior Tibial Pulses	NS	****	
Leg Pulses	0.049	NS*	RH>C
Peripheral Pulses	NS*	NS	RH>C
All Pulses	NS*	NS	RH>C

*No conditions reported that were not verified; therefore, reported and verified analyses are the same.

NS: Not significant ($p>0.10$).

** (NS): Group-by-covariate interaction ($0.01<p\leq0.05$); not significant when interaction is deleted; refer to Table L-2 for a detailed description of this interaction.

--Adjusted analyses not performed (sparse data).

****: Group-by-covariate interaction ($p\leq0.01$); refer to Table L-2 for a detailed description of this interaction.

NS*: Borderline significant ($0.05<p\leq0.10$).

C>RH: More abnormalities in Comparisons than in Ranch Hands.

RH>C: More abnormalities in Ranch Hands than in Comparisons.

** (NS*): Group-by-covariate interaction ($0.01<p\leq0.05$); borderline significant when interaction is deleted; refer to Table L-2 for a detailed description of this interaction.

significant group-by-family history of heart disease interaction (p=0.042). The relative risk was less than 1 in those with no family history of heart disease and greater than 1 in those with a family history of heart disease; neither within-stratum estimate of risk was statistically significant. An adjusted model fit after deletion of the interaction term was not statistically significant.

For the parameters of central cardiac function there were no statistically significant differences, unadjusted or adjusted, in the mean systolic blood pressure, nor in the percentage of individuals with abnormal heart sounds, overall ECG abnormalities, RBBB, LBBB, tachycardia, or other ECG diagnoses. In the discrete analysis of systolic blood pressure, there was no significant difference between the Ranch Hands and Comparisons in the unadjusted analysis, but a significant group-by-cholesterol-HDL ratio interaction was detected in the adjusted analysis (p=0.020). The adjusted relative risk was less than 1 in those with cholesterol-HDL ratios less than or equal to 4.2 and less than 1 in those with ratios between 4.2 and 5.5, but greater than 1 in those with cholesterol-HDL ratios greater than 5.5. However, none of these within-stratum relative risks was statistically significant, nor was the group comparison after deletion of the interaction term from the model. For nonspecific T-waves, the unadjusted difference was not statistically significant. However, there was a highly significant (p=0.004) group-by-lifetime cigarette smoking history interaction in the adjusted analysis. The relative risk was less than 1 in nonsmokers and moderate lifetime smokers and greater than 1 in heavy smokers. None of these within-stratum risks reached statistical significance. Significantly fewer Ranch Hands than Comparisons had bradycardia (Est. RR: 0.67, 95% C.I.: [0.44,1.00], p=0.049). The adjusted relative risk for bradycardia was borderline significant (Adj. RR: 0.69, 95% C.I.: [0.46,1.04], p=0.068). For arrhythmia there was no significant difference in the unadjusted analysis, but there was a borderline significant difference in the adjusted analysis (Adj. RR: 1.56, 95% C.I.: [0.98,2.49], p=0.062).

In the analysis of peripheral vascular function, no unadjusted or adjusted statistically significant differences were detected in funduscopic abnormalities or in popliteal pulses. The mean diastolic blood pressure was borderline significantly different in the two groups (unadjusted p=0.099); in the adjusted analysis, a significant group-by-age interaction was detected (p=0.028). In individuals born in or after 1942, the Ranch Hand adjusted mean was significantly greater than the Comparison adjusted mean (74.91 vs. 73.56 mm Hg, p=0.026). In those born between 1923 and 1941 and in those born in or before 1922, the adjusted group means were not significantly different. (The difference in the overall adjusted group means was borderline significant [p=0.100] after deleting the interaction term from the model.) The percent with abnormal diastolic blood pressure was not significantly different in the two groups in the unadjusted analysis, but in the adjusted discrete analysis there was a significant group-by-family history of heart disease before age 50 interaction (p=0.043). The relative risk was greater than 1 in those with a family history before age 50 and nearly equal to 1 in those without such a history. The former was of borderline significance (p=0.057) but was based on small numbers (5 of 26 Ranch Hands, 1 of 30 Comparisons). After deletion of the interaction term from the model, the adjusted relative risk was not statistically significant.

There was a borderline significant difference in the percentage of individuals with carotid bruits (Est. RR: 2.97, 95% C.I.: [0.91,9.67], p=0.058). For radial pulse abnormalities, there was also a borderline significant difference; in this case, the estimated relative risk was less than 1 (Est. RR: 0.29, 95% C.I.: [0.06,1.34], p=0.076). Adjusted analyses could not be performed because these abnormalities were so rare.

Both the unadjusted and the adjusted analyses of femoral pulses revealed a significantly greater percentage with abnormalities in the Ranch Hand group than in the Comparison group (p=0.016, unadjusted and p=0.018, adjusted). The estimated relative risk was 2.52 (95% C.I.: [1.16,5.44]) and the adjusted relative risk was 2.52 (95% C.I.: [1.15,5.56]). Both unadjusted and adjusted differences in dorsalis pedis pulses were borderline significant, with a higher percent abnormal in the Ranch Hands than in the Comparisons (Est. RR: 1.30, 95% C.I.: [0.98,1.72], p=0.071 and Adj. RR: 1.29, 95% C.I.: [0.97,1.72], p=0.078). In the case of posterior tibial pulses, there was no significant difference in the unadjusted analyses, but a highly significant group-by-differential cortisol interaction emerged in the adjusted analysis (p=0.004). There was little group difference in those with differential cortisol response less than or equal to 0.6, but the risk was significantly greater than 1 in those with differential cortisol levels between 0.6 and 4.0 (Adj. RR: 3.04, 95% C.I.: [1.06,8.68], p=0.030). The relative risk was less than 1 and not statistically significant in those with differential cortisol response greater than 4.0. In the variable combining all leg pulses, the Ranch Hands exhibited significantly more abnormalities than the Comparisons (Est. RR: 1.30, 95% C.I.: [1.00,1.67], p=0.049). The adjusted relative risk for leg pulses was of borderline significance (p=0.079). For peripheral pulses, the estimated relative risk was borderline significant (Est. RR: 1.26, 95% C.I.: [0.97,1.62], p=0.082). This was also the case for all pulses (Est. RR: 1.26, 95% C.I.: [0.97,1.62], p=0.081).

There was agreement between the physical examination findings and the past medical history, with a number of positive and statistically significant associations detected between various physical parameters and the heart disease history.

Exposure index analyses conducted within the Ranch Hand group did not detect any significant effects in any of the three occupational cohorts for reported/verified essential hypertension, reported/verified myocardial infarction, heart sounds, overall ECG findings, RBBB, LBBB, tachycardia, funduscopic examination findings, and carotid bruits, nor in any of the pulse variables or pulse aggregates. For reported and verified heart disease, there were no significant differences in the enlisted flyers or enlisted groundcrew. In the officers, the group with the lowest current serum TCDD levels, the adjusted medium versus low exposure level contrast was significantly less than 1 (p=0.019), and the high versus low contrast was also less than 1 and of borderline significance (p=0.082).

No significant differences were detected in the analysis of systolic blood pressure in the officers and enlisted groundcrew, but in the enlisted flyers there was a significant difference in the means that was consistent with a dose-response relationship (p=0.037)--mean values were 124.14, 128.79, and 133.55 in the low, medium, and high exposure level categories, respectively. After covariate adjustment, however, the differences were no longer statistically significant (p=0.181). There were no statistically significant differences in nonspecific T-wave findings in the officers or enlisted groundcrew. Although not entirely consistent with a dose-response relationship, there was a borderline significant difference in the enlisted flyers (p=0.075, unadjusted and p=0.091, adjusted).

No statistically significant exposure level effects were detected in the unadjusted analyses of bradycardia, nor in the adjusted analyses within the enlisted flyers or enlisted groundcrew. In the officers, however, a significant exposure index-by-cholesterol-HDL ratio interaction was detected (p=0.045). Upon stratification, there were fewer abnormalities in the medium and high exposure level categories than in the low exposure level category for those with cholesterol-HDL ratios less than or equal to 4.2 and for those with levels between 4.2 and 5.5, but slightly more abnormalities in the medium and high exposure level categories as compared to the low category for those with ratios greater than 5.5. These were all based upon small numbers.

For arrhythmia, there were no significant differences in the officers or enlisted groundcrew, but in the enlisted flyers, there were six abnormalities in the high exposure level category as compared to none in the low category and none in the medium category (p=0.025 for the high vs. low contrast). Adjusted analyses could not be performed due to the small numbers. For other ECG diagnoses, no significant differences were found except for a significant exposure index-by-age interaction in the officer cohort (p=0.018). The differences within each of the age strata were not consistent with a dose-response relationship, however. Finally, there were no significant exposure level effects on diastolic blood pressure in the enlisted flyers. In the officers, there was a significantly greater percentage of abnormalities in the higher exposure level category as compared to the low exposure level category (p=0.039), but there was no excess risk in the medium exposure level group. Also, in the enlisted groundcrew there was a significant exposure index-by-personality type interaction (p=0.012), but the within-stratum differences were not consistent with a dose-response relationship.

Longitudinal analysis of the overall ECG findings did not detect any significant differences between the Ranch Hand and Comparison groups in the change in the overall ECG status from Baseline to the 1987 followup examination. Mortality-morbidity analyses did not indicate excess cardiovascular risk in the Ranch Hands.

In summary, the cardiovascular evaluation showed that the health of the Ranch Hand and Comparison groups was similar for reported and verified heart disease and central cardiac function. For peripheral vascular function, the Ranch Hands had a marginally higher percentage of individuals with carotid bruits. There were also significant, or marginally significant, differences (more abnormalities in the Ranch Hands than in the Comparisons) in femoral pulses, dorsalis pedis pulses, and in the three pulse aggregates (leg, peripheral, and all pulses), as determined by manual palpation. These findings emphasize the importance of including further evaluations of peripheral pulses in subsequent examinations in this study.

CHAPTER 15

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