CHAPTER 15

CARDIOVASCULAR ASSESSMENT

INTRODUCTION

Background

Animal research into the cardiotoxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD, or dioxin) has focused on acute biochemical and functional abnormalities associated with high-level exposure. In one study (1), rats were found to have significant reductions in pulse and blood pressure 6 days after administration of 40 μg/kg of TCDD by gavage and were less responsive to the chronotropic effect of isoproterenol, a beta-agonist. The authors of the study, noting a 66 percent reduction in serum thyroxin, postulated a down regulation of beta-receptors associated with the hypothyroid state rather than a direct cardiotoxic effect. Their findings were consistent with other studies that documented changes in myocardial beta-receptors with reduced serum indices of thyroid function and decreased beta-adrenergic responsiveness to isoproterenol in the ventricular papillary muscle of guinea pigs (2,3). Experiments into the effects of TCDD on myocardial contractility in rat (4) and guinea pig (5) atrial muscle have yielded mixed results; the primary cardiotoxic effects remain unclear.

The biochemical effects of TCDD on cardiac muscle have been the subject of several reports. An increase in lipid peroxidation and a decrease in superoxide dismutase activity were noted in the hearts of female rats subsequent to TCDD administration (1). Dose-dependent decreases in adipose tissue lipoprotein lipase activity and hepatic low-density lipoprotein binding occurred in rabbits (6) and other laboratory animals (7) in association with elevated serum triglycerides. Though electron microscopic studies have documented pre-atherosclerotic lesions in the aortic arch in association with these biochemical abnormalities, the relevance of these findings to the development of cardiovascular disease in humans is uncertain.

Human case reports and epidemiologic studies generally have not detected significant cardiovascular abnormalities following exposure to herbicides or TCDD. In three case reports of acute 2,4-dichlorophenoxyacetic (2,4-D) poisoning, cardiac dilation and arrest were observed in the one fatal case (8), while transient nodal tachycardia was observed in one of the two non-fatal cases (9,10). Three laboratory technicians with chloracne, neurological symptoms, and hypercholesterolemia following significant direct exposure to TCDD did not develop any signs or symptoms of cardiac dysfunction (11). In one report of 10 industrial workers with chloracne, 4 complained of cardiac palpitations and shortness of breath (12). In other studies involving 128 industrial workers, there was no subjective or objective evidence for associated heart disease (13-15).

At present, there is no evidence that humans experience chronic cardiovascular sequelae consequent to low dose exposure to phenoxy herbicides. In a case report of coma induced by 2,4-D intoxication in a 51-year-old man, the Q-T interval became prolonged in serial electrocardiograms, but it was not clear whether this was a primary cardiotoxic effect or secondary to electrolyte imbalance (16). In contrast, no electrocardiographic abnormalities were noted in a more recent report of coma similarly induced in a 61-year-old woman (17).

In reports of the 1976 Seveso, Italy industrial accident, a slight but statistically non-significant increase in mortality from ischemic heart disease was noted in men but may have been related to other risk factors, particularly the situational stress associated with the accident (18,19). In two epidemiologic studies using similar cohorts from a Nitro, West Virginia chemical plant, no manifestations of cardiovascular disease were noted in exposed workers (20,21). However, one of these reports documented significantly lower levels of high-density lipoprotein (HDL) cholesterol in those individuals with chloracne versus those without (21). Other alterations in lipid metabolism and the potential associated risk of cardiovascular disease have been discussed in a recent review article (22).

Previous reports of the Air Force Health Study (AFHS) have yielded variable results in the assessment of peripheral pulses. In the Baseline and the 1987 followup examinations, when pulses were examined manually, an increased prevalence of pulse deficits was noted in the Ranch Hand cohort relative to Comparisons (23,24), findings noted as well as in the clinical-epidemiologic studies of residents exposed to TCDD in Times Beach, Missouri (25,26). In the 1985 AFHS followup examination, which incorporated Doppler peripheral vascular studies into the protocol, no significant group differences were found (27). When the 1987 examination data were analyzed in light of serum dioxin levels, Ranch Hand participants had marginally or significantly higher percentages of manually examined peripheral pulse abnormalities than Comparisons (28). Also, results based on the 1994 AFHS mortality update indicated a significant increase in the number of deaths caused by diseases of the circulatory system among Ranch Hand nonflying enlisted personnel (29) ($p=0.03$, standardized mortality ratio$=1.60$, 95% C.I.$=[1.05,2.35]$).

Summary of Previous Analyses of the Air Force Health Study

1982 Baseline Study 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 non-Black Ranch Hands exhibited absent or diminished peripheral pulses, compared to 9.4 percent of the non-Black Original Comparison ($p=0.05$). No statistically significant differences were found between the two groups in the occurrence of reported or verified heart disease or heart attacks.

Greater than 80 percent of the cardiac conditions reported on the study questionnaire were verified by a detailed review of medical records. There was also a 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 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. There were no group differences in verified heart disease (RR=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.

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 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.

1987 Followup Study Summary Results

The assessment of the central cardiac function also found the groups to be similar, although significantly fewer Ranch Hands than Comparisons had bradycardia and more Ranch Hands than Comparisons had arrhythmias (marginally significant).

For the peripheral vascular function, significant or marginally significant differences were detected for five of the eight measurements. Ranch Hands had a higher or marginally higher mean or percent abnormal for diastolic blood pressure (continuous), carotid bruits, femoral pulses, and dorsalis pedis pulses than did Comparisons. (No difference between the two groups was detected in the discrete analysis of diastolic blood pressure.) The percentage of radial pulse abnormalities was marginally higher in Comparisons than in Ranch Hands. On the three pulse indices (leg, peripheral, and all pulses), Ranch Hands had marginally or significantly higher percentages of abnormalities than Comparisons.

Serum Dioxin Analysis of 1987 Followup Study Summary Results

The cardiovascular evaluation found a marginally significant association between initial dioxin and a decrease in the reported history of heart disease and a significant negative association with verified history of heart disease in some analyses. In addition, the analyses of categorized current dioxin also indicated a decrease in verified history of heart disease for Ranch Hands with the highest current dioxin levels relative to Comparisons with background levels. These Ranch Hands also had more essential hypertension by history (after removing percent body fat and cholesterol from the model).

The analyses of the peripheral vascular function variables displayed significantly higher mean levels of diastolic blood pressure for Ranch Hands in the low and high categories than Comparisons (without adjustment for percent body fat). Similar to the analysis of systolic blood pressure, the discretized analysis of diastolic blood pressure did not display a significant association with dioxin within the low and high current dioxin categories. Ranch Hands generally exhibited a significant or marginally significant higher risk of absent femoral, dorsalis pedis, and posterior tibial pulses relative to Comparisons. These observations could represent a subclinical effect and emphasize the importance of continued followup and evaluation in subsequent examination phases of the study.

Parameters for the Cardiovascular Assessment

Dependent Variables

The analysis of the cardiovascular assessment was based on data collected from the 1992 questionnaire and physical examination and subsequent medical records verification. No laboratory examination data were analyzed as cardiovascular dependent variables, although data from the laboratory examination were used in covariate analyses.

Medical Records Data

During the Baseline, 1985, and 1987 health interviews, each participant was asked whether he had a heart condition. Medical records were sought to verify all reported conditions and to determine the time of occurrence of major cardiac events. In addition, the self-reported review-of-systems recorded the overall history of heart trouble and other serious illnesses. Data collected in a similar fashion at the 1992 followup was verified and combined with data from the three previous examinations to create a lifetime history for three conditions: essential hypertension, heart disease (excluding essential hypertension), and myocardial infarction. Each of these conditions was classified as "yes" or "no" and analyzed.

Participants with a verified pre-SEA heart condition were excluded from all analyses. A pre-SEA heart condition includes pre-SEA myocardial infarction, but does not include pre-SEA essential hypertension. Therefore, participants with a verified pre-SEA history of essential hypertension were also excluded from the analysis of verified history of essential hypertension.

Physical Examination Data

Cardiovascular data analyzed from the 1992 physical examination were divided into two main categories: central cardiac function and peripheral vascular function.

Central Cardiac Function—The assessment of the 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 by an Critikon Dinamap 1846SXP® automated electronic monitor with 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 by the internist examiners to be functional (normal) or organic (abnormal) in nature.

ECGs were obtained after adherence to at least a 4-hour abstinence from tobacco. The standard 12-lead ECG was performed, and an additional 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 ST- and T-wave changes, bradycardia (a resting pulse rate less than 50 beats per minute), tachycardia (a resting pulse rate greater than 100 beats per minute), arrhythmia (any irregularity of heart rhythm including premature beats but excluding normal sinus rhythm), evidence of a prior myocardial infarction, and other diagnoses (e.g., ventricular aneurysm, Wolff-Parkinson-White syndrome). It is recognized that some arrhythmias (e.g., atrial flutter, atrial fibrillation, and junctional rhythm) may require more evaluation and surveillance than others, but all were grouped together for evaluation in this study.

Variables analyzed in the evaluation of the central cardiac function included systolic blood pressure, heart sounds, an overall ECG assessment, and eight conditions associated with the ECG. These eight conditions are RBBB, LBBB, nonspecific ST- and T-wave changes, bradycardia, tachycardia, arrhythmia, evidence of a prior myocardial infarction, and other diagnoses. Systolic blood pressure was analyzed as both a continuous variable and also as a discrete variable, classified as "normal" (≤140 mm Hg) and "abnormal" (>140 mm Hg). All other variables were dichotomized as "normal" or "abnormal".

Participants with a verified pre-SEA heart condition were excluded from all analyses of the central cardiac function variables.

Peripheral Vascular Function—The peripheral vascular function was assessed during the cardiovascular examination by the diastolic blood pressure; funduscopic examination of small vessels; presence or absence of carotid bruits; determination of the radial, femoral, popliteal, dorsalis pedis, and posterior tibial pulses by Doppler techniques; a kidney, urethra, and bladder (KUB) x ray focusing on vascular calcifications; and a measure of intermittent claudication and vascular insufficiency. Diastolic blood pressure was measured by the Critikon Dinamap 1846SXP® monitor. The recorded value represents the lowest diastolic value of three readings. Elevated diastolic blood pressure is an indicator of increased peripheral vascular resistance. Diastolic blood pressure was analyzed as both a continuous and a discrete variable, dichotomized as "normal" (≤90 mm Hg) and "abnormal" (>90 mm Hg).

The funduscopic examination was conducted with undilated pupils in a standard manner, with emphasis placed upon the detection of arteriovenous nicking (a sign of chronic blood pressure elevation), hemorrhages, exudates, papilledema, diabetic retinopathy, disk pallor, and arteriolar spasm. The presence or absence of carotid bruits was assessed by auscultation over both carotid arteries.

The Doppler procedure for examining pulses is a progressive array of measurements designed to determine whether a pulse abnormality exists, where the obstruction is most likely located, and whether it has functional implications. The determination of a pulse abnormality was based upon an analysis of recorded Doppler waveform morphology. Pulsatility, systolic forward flow, diastolic reverse flow, and diastolic oscillations were examined.

The funduscopic examination, carotid bruits, and the five pulses also were dichotomized as "abnormal" or "normal" (or "presence" or "absence") and analyzed. Pulses were considered abnormal if diminished or absent on either side. In addition, two pulse indices were constructed from the radial, femoral, popliteal, dorsalis pedis, and posterior tibial 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

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

The KUB x ray is used to detect hardening of the arteries and to screen for vascular disease. If no abnormalities were present or the only abnormality for a KUB result was the presence of kidney stones, then the KUB x ray was defined as normal. Kidney stones, as diagnosed from the KUB x ray, were examined separately in the Renal Assessment. Participants with a verified pre-SEA heart condition were excluded from the analysis of all peripheral vascular function endpoints.

Self-Reported Questionnaire Data

In the 1992 questionnaire, each participant was asked a series of questions regarding pain in his calf muscles while walking. The self-reported answers were used to detect intermittent claudication and vascular insufficiency (yes, no), which indicate an insufficient oxygen supply to the leg muscles.

Participants with a verified pre-SEA heart condition were excluded from the analysis of this variable.

Associations of Coronary Heart Disease from Medical Records and Physical Examination Results

The central cardiac and peripheral vascular functions were analyzed together with essential hypertension, heart disease excluding essential hypertension, and myocardial infarction to determine the degree of association between medical history and the 1992 followup examination results.

Covariates

A number of covariates were examined for inclusion in the adjusted analyses of the cardiovascular assessment. Many of these covariates are considered to be classical risk factors for chronic heart disease (CHD). Covariates examined included age, race, military occupation, lifetime cigarette smoking history, current level of cigarette smoking, lifetime alcohol history, current alcohol use, cholesterol, HDL, cholesterol-HDL ratio, body fat, personality type, diabetic status, family history of heart disease, family history of heart disease before the age of 45, and use of blood pressure medication.

The lifetime alcohol history covariate was based on self-reported information from the 1992 questionnaire and combined with similar information gathered at the 1987 followup. The respondent's average daily alcohol consumption was determined for various drinking stages throughout his lifetime, and an estimate of the corresponding total number of drink-years (1 drink-year is the equivalent of drinking 1.5 ounces of 80-proof alcoholic beverage per day for 1 year) was derived. The current alcohol covariate was based on the average drinks per day for the month prior to completing the questionnaire.

Current cigarette smoking and lifetime cigarette smoking history were based on self-reported questionnaire data. For lifetime cigarette smoking history, the respondent's average smoking was estimated over his lifetime, assuming 365 packs of cigarettes equal 1 pack-year.

Cholesterol, HDL, and the cholesterol-HDL ratio were all based on 1992 laboratory measurements. Cutpoints were chosen based on medical opinion.

Body fat was calculated from a metric body mass index (30); the formula is

$$\textit{Body Fat (in percent)} = \frac{\textit{Weight (kg)}}{[\textit{Height (m)}]^2} \times 1.264 - 13.305.$$

This variable was analyzed in both the discrete and continuous forms. For purposes of discrete analyses, body fat was dichotomized as "lean" or "normal" ($\leq$25 percent) and "obese" ($>$25 percent).

Personality type was determined from the Jenkins Activity Survey administered during the 1992 examination. Family history of heart disease was defined as "yes" if the participant's mother, father, sister(s), or brother(s) had heart trouble or heart disease and "no" otherwise. Family history of heart disease before the age of 45 was defined as "yes" if the participant's mother, father, sister(s), or brother(s) had heart trouble or heart disease before the age of 45 and "no" otherwise. Blood pressure medication (yes, no) was used as a covariate for the analysis of the systolic and diastolic blood pressure variables only.

Whereas diabetics were excluded from analyses in previous cycles of the AFHS, diabetic class was used as a covariate in the analysis of the 1992 followup. Diabetes is a known risk factor for cardiovascular disease; however, diabetes exhibited a significant positive association with dioxin in the serum dioxin analysis of the 1987 followup. Incorporating diabetic class as a covariate and investigating it as a main effect and also in interactions with dioxin allowed the study of diabetes and dioxin simultaneously in relation to cardiovascular disease.

Because of the large number of candidate covariates and some covariates being highly correlated, selected variables from each of the following sets were used as candidate covariates: (1) lifetime cigarette smoking history and current level of cigarette smoking, (2) lifetime alcohol history and current alcohol use, (3) cholesterol, HDL, and the cholesterol-HDL ratio, and (4) family history of heart disease and family history of heart disease before the age of 45.

The variables selected were chosen by preliminary analyses of the possible confounding effects of the covariates, and associations with the dependent variables, in conjunction with medical opinion. Based on the preliminary analyses, the subset of these covariates used in the adjusted analyses were lifetime cigarette smoking history, current level of cigarette smoking, lifetime alcohol history, total cholesterol, HDL, and family history of heart disease.

For essential hypertension, heart disease excluding essential hypertension, and myocardial infarction, current level of cigarette smoking, and current alcohol consumption were not examined as candidate covariates. The current levels of these covariates are not appropriate as a risk factor for an endpoint based on post-SEA history. For example, smoking five packs of cigarettes today has no bearing on a heart attack 10 years ago. More appropriately, lifetime alcohol history and lifetime cigarette smoking history were used to investigate the cumulative effects of alcohol and cigarette smoking on these endpoints.

Statistical Methods

Chapter 7, Statistical Methods, describes basic statistical methods used throughout this report. The modeling strategy was modified for the adjusted analyses of the cardiovascular endpoints. For these variables, only the covariate main effects and exposure-by-covariate interactions were examined; the pairwise covariate interactions were not investigated because of the large number of covariates. Table 15-1 summarizes the statistical analyses performed for the cardiovascular assessment. The first part of this table describes the dependent variables and identifies the candidate covariates and the statistical methods. The second part of this table further describes the candidate covariates. Abbreviations used in the body of the table are defined at the end of the table. Dependent variable data were missing for some participants. The number of participants with missing data and those excluded due to pre-SEA conditions are provided in Table 15-2.

Analyses of data collected at the 1987 followup study indicated that dioxin was associated with military occupation. In general, enlisted personnel had higher levels of dioxin than officers, with enlisted groundcrew having higher levels than enlisted flyers. Consequently, adjustment for military occupation in statistical models using dioxin as a measure of exposure may improperly mask an actual dioxin effect. However, occupation also can be a surrogate for socioeconomic effects. Failure to adjust for occupation could overlook important risk factors related to lifestyle. If occupation was found to be significantly associated with a dependent variable in the 1992 followup analyses and was retained in the final statistical models using dioxin as a measure of exposure, the dioxin effect was evaluated in the context of two models. Analyses were performed with and

Table 15-1.
Statistical Analyses for the Cardiovascular Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analysis
Essential Hypertension	MR-V	D	Yes No	AGE,RACE,OCC, PACKYR,DRKYR, CHOL,HDL, CHOL/HDL,BFAT, PERS,DIAB,HRTDIS, HRTDIS45	U:LR,CS A:LR
Heart Disease (Excluding Essential Hypertension)	MR-V	D	Yes No	AGE,RACE,OCC, PACKYR,DRKYR, CHOL,HDL, CHOL/HDL,BFAT, PERS,DIAB,HRTDIS, HRTDIS45	U:LR,CS A:LR
Myocardial Infarction	MR-V	D	Yes No	AGE,RACE,OCC, PACKYR,DRKYR, CHOL,HDL, CHOL/HDL,BFAT, PERS,DIAB,HRTDIS, HRTDIS45	U:LR,CS A:LR
Systolic Blood Pressure (mm Hg)	PE	D/C	Abnormal: >140 Normal: ≤ 140	AGE,RACE,OCC, PACKYR,CSMOK, DRKYR,ALC,CHOL, HDL,CHOL/HDL, BFAT,PERS,DIAB, HRTDIS,HRTDIS45, BPMED	U:LR,CS, GLM,TT A:LR,GLM L:LR,GLM
Heart Sounds	PE	D	Abnormal Normal	AGE,RACE,OCC, PACKYR,CSMOK, DRKYR,ALC,CHOL, HDL,CHOL/HDL, BFAT,PERS,DIAB, HRTDIS,HRTDIS45	U:LR,CS A:LR
Overall Electrocardiograph (ECG)	PE	D	Abnormal Normal	AGE,RACE,OCC, PACKYR,CSMOK, DRKYR,ALC,CHOL, HDL,CHOL/HDL, BFAT,PERS,DIAB, HRTDIS,HRTDIS45	U:LR,CS A:LR

Table 15-1. (Continued)
Statistical Analyses for the Cardiovascular Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analysis
ECG: Right Bundle Branch Block (RBBB)	PE	D	Abnormal Normal	AGE,RACE,OCC, PACKYR,CSMOK, DRKYR,ALC,CHOL,HDL, CHOL/HDL,BFAT,PERS, DIAB,HRTDIS,HRTDIS45	U:LR,CS A:LR
ECG: Left Bundle Branch Block (LBBB)	PE	D	Abnormal Normal	AGE,RACE,OCC, PACKYR,CSMOK, DRKYR,ALC,CHOL,HDL, CHOL/HDL,BFAT,PERS, DIAB,HRTDIS,HRTDIS45	U:LR,CS A:LR
ECG: Non-specific ST-and T-Wave Changes	PE	D	Abnormal Normal	AGE,RACE,OCC, PACKYR,CSMOK, DRKYR,ALC,CHOL,HDL, CHOL/HDL,BFAT,PERS, DIAB,HRTDIS,HRTDIS45	U:LR,CS A:LR
ECG: Bradycardia	PE	D	Abnormal Normal	AGE,RACE,OCC, PACKYR,CSMOK, DRKYR,ALC,CHOL,HDL, CHOL/HDL,BFAT,PERS, DIAB,HRTDIS,HRTDIS45	U:LR,CS A:LR
ECG: Tachycardia	PE	D	Abnormal Normal	AGE,RACE,OCC, PACKYR,CSMOK, DRKYR,ALC,CHOL,HDL, CHOL/HDL,BFAT,PERS, DIAB,HRTDIS,HRTDIS45	U:LR,CS A:LR
ECG: Arrhythmia	PE	D	Abnormal Normal	AGE,RACE,OCC, PACKYR,CSMOK, DRKYR,ALC,CHOL,HDL, CHOL/HDL,BFAT,PERS, DIAB,HRTDIS,HRTDIS45	U:LR,CS A:LR
ECG: Evidence of Prior Myocardial Infarction	PE	D	Abnormal Normal	AGE,RACE,OCC, PACKYR,CSMOK, DRKYR,ALC,CHOL,HDL, CHOL/HDL,BFAT,PERS, DIAB,HRTDIS,HRTDIS45	U:LR,CS A:LR
ECG: Other Diagnoses	PE	D	Abnormal Normal	AGE,RACE,OCC, PACKYR,CSMOK, DRKYR,ALC,CHOL,HDL, CHOL/HDL,BFAT,PERS, DIAB,HRTDIS,HRTDIS45	U:LR,CS A:LR

Table 15-1. (Continued)
Statistical Analyses for the Cardiovascular Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analysis
Diastolic Blood Pressure (mm Hg)	PE	D/C	Abnormal: >90 Normal: ≤90	AGE,RACE,OCC, PACKYR,CSMOK, DRKYR,ALC,CHOL,HDL, CHOL/HDL,BFAT,PERS, DIAB,HRTDIS,HRTDIS45, BPMED	U:LR,CS, GLM,TT A:LR,GLM
Funduscopic Examination	PE	D	Abnormal Normal	AGE,RACE,OCC, PACKYR,CSMOK, DRKYR,ALC,CHOL,HDL, CHOL/HDL,BFAT,PERS, DIAB,HRTDIS,HRTDIS45	U:LR,CS A:LR
Carotid Bruits	PE	D	Abnormal Normal	AGE,RACE,OCC, PACKYR,CSMOK, DRKYR,ALC,CHOL,HDL, CHOL/HDL,BFAT,PERS, DIAB,HRTDIS,HRTDIS45	U:LR,CS A:LR
Radial Pulses	PE	D	Abnormal Normal	AGE,RACE,OCC, PACKYR,CSMOK, DRKYR,ALC,CHOL,HDL, CHOL/HDL,BFAT,PERS, DIAB,HRTDIS,HRTDIS45	U:LR,CS A:LR
Femoral Pulses	PE	D	Abnormal Normal	AGE,RACE,OCC, PACKYR,CSMOK, DRKYR,ALC,CHOL,HDL, CHOL/HDL,BFAT,PERS, DIAB,HRTDIS,HRTDIS45	U:LR,CS A:LR L:LR
Popliteal Pulses	PE	D	Abnormal Normal	AGE,RACE,OCC, PACKYR,CSMOK, DRKYR,ALC,CHOL,HDL, CHOL/HDL,BFAT,PERS, DIAB,HRTDIS,HRTDIS45	U:LR,CS A:LR L:LR
Dorsalis Pedis Pulses	PE	D	Abnormal Normal	AGE,RACE,OCC, PACKYR,CSMOK, DRKYR,ALC,CHOL,HDL, CHOL/HDL,BFAT,PERS, DIAB,HRTDIS,HRTDIS45	U:LR,CS A:LR L:LR
Posterior Tibial Pulses	PE	D	Abnormal Normal	AGE,RACE,OCC, PACKYR,CSMOK, DRKYR,ALC,CHOL,HDL, CHOL/HDL,BFAT,PERS, DIAB,HRTDIS,HRTDIS45	U:LR,CS A:LR L:LR

Table 15-1. (Continued)
Statistical Analyses for the Cardiovascular Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analysis
Leg Pulses	PE	D	Abnormal Normal	AGE,RACE,OCC, PACKYR,CSMOK, DRKYR,ALC,CHOL, HDL,CHOL/HDL,BFAT, PERS,DIAB,HRTDIS, HRTDIS45	U:LR,CS A:LR L:LR
Peripheral Pulses	PE	D	Abnormal Normal	AGE,RACE,OCC, PACKYR,CSMOK, DRKYR,ALC,CHOL, HDL,CHOL/HDL,BFAT, PERS,DIAB,HRTDIS, HRTDIS45	U:LR,CS A:LR L:LR
Kidney, Urethra, and Bladder (KUB) X Ray Excluding Kidney Stones	PE	D	Abnormal Normal	AGE,RACE,OCC, PACKYR,CSMOK, DRKYR,ALC,CHOL, HDL,CHOL/HDL,BFAT, PERS,DIAB,HRTDIS, HRTDIS45	U:LR,CS A:LR
Intermittent Claudication and Vascular Insufficiency (ICVI) Index	Q-SR	D	Abnormal Normal	AGE,RACE,OCC, PACKYR,CSMOK, DRKYR,ALC,CHOL, HDL,CHOL/HDL,BFAT, PERS,DIAB,HRTDIS, HRTDIS45	U:LR,CS A:LR

Table 15-1. (Continued)
Statistical Analyses for the Cardiovascular Assessment

Covariates

Variable (Abbreviation)	Data Source	Data Form	Cutpoints
Age (AGE)	MIL	D/C	Born ≥ 1942 Born < 1942
Race (RACE)	MIL	D	Black Non-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 >200-239 >239
High Density Lipoprotein (HDL) (mg/dl)	LAB	D/C	0-35 >35
Cholesterol-HDL Ratio (CHOL/HDL)	LAB	D/C	0-5 >5
Diabetic Class (DIAB)	LAB/MR-V	D	Diabetic: past history or ≥200 mg/dl 2-hr. postprandial glucose Impaired: ≥140-<200 mg/dl 2-hr. postprandial glucose Normal: <140 mg/dl 2-hr. postprandial glucose
Body Fat (BFAT) (percent)	PE	D/C	Obese: >25% Lean or Normal: ≤25%
Personality Type (PERS)	PE	D	A direction B direction
Family History of Heart Disease (HRTDIS)	Q-SR	D	Yes No
Family History of Heart Disease Before Age 45 (HRTDIS45)	Q-SR	D	Yes No
Taking Blood Pressure Medication (BPMED)	Q-SR/MR-V	D	Yes No

Abbreviations

Data Source:	LAB	=	1992 laboratory results
	MIL	=	Air Force military records
	MR-V	=	Medical records (verified)
	PE	=	1992 physical and psychological exams
	Q-SR	=	1992 health questionnaires (self-reported)
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:	U	=	Unadjusted analyses
	A	=	Adjusted analyses
	L	=	Longitudinal analyses
Statistical Methods:	CS	=	Chi-square contingency table analysis (continuity-adjusted for 2×2 tables)
	GLM	=	General linear models analysis
	LR	=	Logistic regression analysis
	TT	=	Two-sample t-test

Table 15-2.
Number of Participants with Missing Data for, or Excluded from, the Cardiovascular Assessment

Variable	Variable Use	Group: Ranch Hand	Group: Comparison	Dioxin (Ranch Hands Only): Initial	Dioxin (Ranch Hands Only): Current	Categorized Dioxin: Ranch Hand	Categorized Dioxin: Comparison
Systolic Blood Pressure	DEP	1	0	0	1	1	0
Heart Sounds	DEP	4	3	1	3	3	2
Overall ECG	DEP	1	2	1	1	1	2
ECG: RBBB	DEP	0	2	0	0	0	1
ECG: LBBB	DEP	0	2	0	0	0	1
ECG: Non-specific ST- and T-Wave Changes	DEP	0	2	0	0	0	1
ECG: Arrhythmia	DEP	0	1	0	0	0	1
ECG: Evidence of Prior Myocardial Infarction	DEP	2	4	1	2	2	4
Diastolic Blood Pressure	DEP	1	0	0	1	1	0
Funduscopic Examination	DEP	8	5	5	7	7	3
Carotid Bruits	DEP	0	1	0	0	0	1
Popliteal Pulses	DEP	0	2	0	0	0	1
Dorsalis Pedis Pulses	DEP	2	2	1	2	2	1
Posterior Tibial Pulses	DEP	0	2	0	0	0	1
Leg Pulses	DEP	2	1	1	2	2	1
Peripheral Pulses	DEP	2	1	1	2	2	1
KUB X Ray Excluding Kidney Stones	DEP	2	1	1	2	2	1

Table 15-2. (Continued)
Number of Participants with Missing Data for, or Excluded from, the Cardiovascular Assessment

		Group		Dioxin (Ranch Hands Only)		Categorized Dioxin	
Variable	Variable Use	Ranch Hand	Comparison	Initial	Current	Ranch Hand	Comparison
ICVI Index	DEP	0	3	0	0	0	3
Lifetime Cigarette Smoking History	COV	1	2	0	1	1	2
Current Cigarette Smoking	COV	0	2	0	0	0	2
Lifetime Alcohol History	COV	22	21	13	20	20	18
Current Alcohol Use	COV	10	18	7	9	9	16
Cholesterol	COV	0	1	0	0	0	0
HDL	COV	14	13	9	13	13	10
Cholesterol-HDL Ratio	COV	14	13	9	13	13	10
Diabetic Class	COV	1	2	0	1	1	1
Personality Type	COV	1	1	1	1	1	1
Family History of Heart Disease	COV	13	14	8	13	13	12
Family History of Heart Disease Before Age 45	COV	35	31	22	35	35	28
Pre-SEA Essential Hypertension	EXC	11	16	7	10	10	15
Pre-SEA Heart Disease	EXC	12	19	7	10	10	17

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

Note: 952 Ranch Hands and 1,281 Comparisons;
520 Ranch Hands for initial dioxin; 894 Ranch Hands for current dioxin;
894 Ranch Hands and 1,063 Comparisons for categorized dioxin.
One Ranch Hand missing total lipids for current dioxin.

without occupation in the final models to investigate whether conclusions regarding the association between the health endpoint and dioxin differed.

Similarly, dioxin exhibited a significant positive association with body fat, cholesterol, HDL, and diabetes in the serum dioxin analysis of the 1987 followup data, and these associations also are seen in the 1992 followup analyses (see Chapter 8). These covariates, which must be introduced to the adjusted model, are all known risk factors for heart diseases; however, it is recognized that adjusting for them has the potential to over-adjust the model for the effects of dioxin exposure. To investigate the effects of adjustment for these covariates, when body fat, cholesterol, HDL, or diabetic class was found to be significantly associated with a dependent variable and retained in the final model, the dioxin effect was evaluated in the context of two models. Analyses again were performed with and without these covariates in the model to investigate whether conclusions regarding the associations between the health endpoint and dioxin differed.

The results of the analyses without occupation, body fat, cholesterol, HDL, and diabetic class in the final adjusted model are presented in Appendix K-3 and are only discussed in the text if the level of significance differs from the original final adjusted model (significant versus nonsignificant).

Longitudinal Analysis

The cardiovascular longitudinal analyses were based on the relationship of exposure to changes in systolic blood pressure between the 1982 and 1992 SCRF examinations and six pulse measurements between the 1985 and 1992 SCRF examinations. The longitudinal analyses for systolic blood pressure were based on this variable in both the continuous and discrete forms. The six pulse measurements included femoral pulses, popliteal pulses, dorsalis pedis pulses, posterior tibial pulses, leg pulses, and peripheral pulses. The 1985 and 1992 measurements are used because the Doppler assessment of pulses was conducted at these two examinations.

RESULTS

Dependent Variable-Covariate Associations

Results of the tests of association between the cardiovascular dependent variables and covariates are presented in Appendix Table K-1-1. These associations are based on combined group data; participants with pre-SEA heart conditions were excluded from the association analyses of all cardiovascular endpoints, and participants with pre-SEA essential hypertension were excluded from the association analyses for verified essential hypertension.

The percentage of participants with a history of post-SEA essential hypertension increased with age ($p<0.001$), increased as the total cholesterol levels increased ($p=0.006$), decreased as the HDL cholesterol levels increased ($p=0.006$), and increased with obesity ($p<0.001$). Moderate lifetime smokers had the lowest history of essential hypertension (35.2%), as compared to nonsmokers and heavy lifetime smokers (38.5% and 40.9% respectively). Heavy lifetime drinkers had a higher history of essential hypertension (48.5%)

than moderate lifetime drinkers and nondrinkers (34.5% and 38.8% respectively) ($p<0.001$). A higher percentage of the diabetics had a history of post-SEA essential hypertension (58.8%) than the glucose-impaired participants and non-diabetics (54.1% and 32.2% respectively) ($p<0.001$). Participants with a family history of essential heart disease were more likely to have had hypertension than those without a family history of heart disease ($p<0.001$).

The number of participants with a history of post-SEA heart disease increased with age ($p<0.001$). Officers had more heart disease (54.2%) than enlisted flyers and enlisted groundcrew (49.7% and 44.0% respectively) ($p<0.001$). Participants with a family history of heart disease were more likely to have had post-SEA heart disease (52.6%) than those without a family history of heart disease (44.1%) ($p<0.001$).

The number of participants with a history of post-SEA myocardial infarction increased with age ($p<0.001$) and lifetime cigarette smoking history ($p<0.001$). The percentage of participants with a history of myocardial infarction decreased as the HDL cholesterol levels increased ($p<0.001$). A higher percentage of diabetics and glucose-impaired participants had a history of myocardial infarction (11.9% and 10.5%) than non-diabetics (5.3%) ($p<0.001$). Participants with a family history of heart disease were nearly twice as likely to have had myocardial infarction than those without a family history of heart disease (8.6% vs. 4.4%) ($p<0.001$).

Systolic blood pressure in its continuous form increased with age ($p<0.001$), lifetime alcohol history ($p=0.027$), cholesterol ($p<0.001$), and body fat ($p<0.001$). Diabetic participants had the highest mean systolic blood pressures followed by glucose-impaired participants and non-diabetics ($p<0.001$). Officers had the highest mean systolic blood pressure (123.46 mm Hg) followed by enlisted flyers (122.00 mm Hg) and enlisted groundcrew (120.65 mm Hg) ($p=0.005$). Current cigarette smoking was negatively associated with systolic blood pressure ($p<0.001$). Participants with a family history of heart disease had higher mean systolic blood pressure (122.61 mm Hg) than those without (120.94 mm Hg) ($p=0.037$). Also, participants taking blood pressure medication at the time of the 1992 examination had a higher mean systolic blood pressure (131.68 mm Hg) than those not taking medication (119.57 mm Hg) ($p<0.001$).

The prevalence of elevated systolic blood pressure increased with age ($p<0.001$) and decreased with current cigarette smoking ($p=0.004$). Participants who never smoked and participants who previously smoked but currently do not smoke had a higher prevalence of elevated systolic blood pressure (16.9% and 17.2% respectively) than those who currently smoke up to 20 cigarettes per day (11.4%) and those who currently smoke more than 20 cigarettes per day (9.5%). The prevalence of elevated systolic blood pressure increased with obesity ($p<0.001$). Diabetics had the highest systolic blood pressures, followed by glucose-impaired participants and non-diabetics ($p<0.001$). A higher percentage of participants with Type B personalities had elevated systolic blood pressure (16.9%) than participants with Type A personalities (13.5%) ($p=0.032$). Also, participants taking blood pressure medication at the time of the 1992 examination had a higher prevalence of abnormally elevated systolic blood pressure (28.8%) than those not taking medication (12.2%) ($p<0.001$).

As lifetime ($p=0.001$) and current cigarette smoking increased ($p<0.001$), the prevalence of abnormal heart sounds decreased. Abnormal heart sounds were more prevalent in obese participants than in lean participants ($p=0.004$).

Abnormal overall ECG findings increased with age ($p<0.001$). Enlisted flyers had a higher prevalence of abnormal overall ECG findings (25.7%) than did officers (24.9%) and enlisted groundcrew (18.8%) ($p=0.002$). Moderate lifetime smokers had the lowest prevalence of abnormal overall ECG findings (18.0%) compared to nonsmokers and heavy lifetime smokers (21.2% and 26.0% respectively) ($p=0.001$). Prevalence of abnormal overall ECG findings was greatest in diabetic participants, followed by glucose-impaired participants and non-diabetics ($p<0.001$).

The percentage of participants with RBBB increased with age ($p=0.032$), and RBBB was highest in diabetics (3.1%) compared to participants classified as normal or glucose-impaired (1.1% and 1.2%) ($p=0.018$).

No candidate covariates were statistically associated with LBBB.

The prevalence of non-specific ST- and T- wave changes increased with age ($p<0.001$). A higher percentage of Blacks had non-specific ST- and T- wave changes (23.8%) than non-Blacks (13.8%) ($p=0.003$). The prevalence of non-specific ST- and T- wave changes was higher for enlisted flyers (19.1%) than for officers and enlisted groundcrew (14.8% and 12.3%) ($p=0.006$). Moderate lifetime smokers had a lower percentage of non-specific ST- and T- wave changes (10.6%) than the nonsmokers (13.3%) and heavy smokers (17.9%) ($p<0.001$). Non-specific ST- and T- wave changes increased with obesity ($p=0.002$). Diabetics had the highest non-specific ST- and T-wave changes, followed by glucose-impaired participants and non-diabetics ($p<0.001$).

Obese participants had a lower prevalence of bradycardia (0.7%) than participants with normal body fat percentage (3.4%) ($p=0.001$). Diabetics had the lowest incidence of bradycardia (0.9%) compared to glucose-impaired participants and non-diabetics (1.2% and 3.2% respectively) ($p=0.021$).

No candidate covariates were statistically associated with tachycardia.

The prevalence of arrhythmia, defined as any irregularity of heart rhythm including premature beats but excluding normal sinus rhythm, increased with age ($p<0.001$). Diabetic participants were most likely to have arrhythmia, followed by glucose-impaired participants and non-diabetics ($p=0.005$).

The prevalence of ECG evidence of a prior myocardial infarction increased with age ($p<0.001$) and lifetime cigarette smoking history ($p=0.001$) and decreased with HDL cholesterol levels ($p<0.001$). Those participants who currently smoke up to 20 cigarettes per day were more likely to show ECG evidence of a prior myocardial infarction (5.3%) than those who never smoked (1.7%), those who previously smoked but currently do not smoke (3.7%), and those who currently smoke more than 20 cigarettes per day (4.3%) ($p=0.021$). A higher percentage of participants with Type B personalities had ECG evidence of a prior myocardial infarction (4.1%) than participants with Type A personalities (2.5%) ($p=0.042$). Diabetics had the highest percentage of evidence of a prior myocardial infarction (6.6%) compared to glucose-impaired participants and non-diabetics (4.5% and 2.6% respectively) ($p=0.001$).

Heavy smokers (1.1%) had a higher prevalence of other abnormal diagnoses than the non-smokers (0.8%) and moderate smokers (0.0%) ($p=0.030$).

Diastolic blood pressure in its continuous form increased with cholesterol ($p<0.001$) and body fat ($p<0.001$). Diabetic participants had the highest diastolic blood pressures, followed by glucose-impaired participants and non-diabetics ($p<0.001$). Diastolic blood pressure decreased for increasing levels of lifetime ($p<0.001$) and current cigarette smoking ($p<0.001$). Also, individuals taking blood pressure medication at the time of the 1992 examination had a higher mean diastolic blood pressure (75.81 mm Hg) than those not taking medication (71.44 mm Hg) ($p<0.001$).

Moderate lifetime smokers had the highest prevalence of elevated diastolic blood pressure (4.0%), followed by non-smokers (3.8%) and heavy smokers (1.8%) ($p=0.019$). The prevalence of elevated diastolic blood pressure was greater for obese individuals than for participants with normal body fat levels ($p=0.001$). Also, participants taking blood pressure medication at the time of the 1992 examination had a higher prevalence of abnormally elevated diastolic blood pressure (4.8%) than those not taking medication (2.6%) ($p=0.024$).

The prevalence of abnormal funduscopic examinations increased with age ($p<0.001$) and lifetime cigarette smoking history ($p=0.005$). Those participants who currently smoke more than 20 cigarettes per day had a higher prevalence of abnormal funduscopic examinations (11.5%) than those who never smoked (3.8%), those who previously smoked but currently do not (6.6%), and those who currently smoke up to 20 cigarettes per day (6.1%) ($p=0.001$). Non-drinkers had a higher prevalence of abnormal funduscopic examinations (9.8%) than moderate lifetime drinkers and heavy drinkers (5.2% and 8.4% respectively) ($p=0.007$). A higher percentage of diabetics and glucose-impaired participants had abnormal funduscopic examinations (9.1% and 9.8%) than non-diabetics (5.2%) ($p=0.001$), and participants with a family history of heart disease were more likely to have an abnormal funduscopic examination result than those with no family history of heart disease ($p=0.004$).

The prevalence of carotid bruits increased with age ($p=0.001$). A smaller percentage of diabetics had carotid bruits (1.9%) than glucose-impaired participants (3.2%); non-diabetics had the smallest percentage of carotid bruits (1.2%) ($p=0.037$).

No candidate covariates were significantly associated with radial pulses.

The prevalence of abnormal (diminished or absent) femoral pulses increased with age ($p=0.012$), lifetime cigarette smoking history ($p=0.031$), current cigarette smoking ($p<0.001$), and lifetime alcohol consumption ($p=0.027$). A higher percentage of diabetics had diminished or absent femoral pulses (2.8%) than glucose-impaired participants and non-diabetics (1.2% and 0.4% respectively) ($p<0.001$).

The percentage of participants with abnormal (diminished or absent) popliteal pulses increased with age ($p<0.001$), lifetime cigarette smoking history ($p=0.001$), and current cigarette smoking ($p<0.001$). The prevalence of diminished or absent popliteal pulses increased as HDL cholesterol levels decreased ($p=0.032$), and was greatest in those participants classified as diabetic, followed by those classified as glucose-impaired and normal ($p<0.001$).

The prevalence of abnormal (diminished or absent) dorsalis pedis pulses increased with age ($p<0.001$), lifetime ($p<0.001$) and current cigarette smoking ($p<0.001$). Diabetics had the highest prevalence of diminished dorsalis pedis pulses (13.8%) followed by glucose-impaired participants (6.0%) and non-diabetics (11.4%) ($p<0.001$).

The prevalence of abnormal (diminished or absent) posterior tibial pulses increased with age ($p<0.001$) and lifetime ($p<0.001$) and current cigarette smoking ($p<0.001$). Heavy lifetime drinkers (>40 drink-years) had a higher prevalence of diminished or absent posterior tibial pulses (4.9%) than non-drinkers and moderate lifetime drinkers (each with 2.2% abnormal) ($p=0.006$). A higher percentage of diabetics had diminished posterior tibial pulses (7.5%) than glucose-impaired participants or non-diabetics (5.3% and 1.7%) ($p<0.001$).

The overall prevalence of abnormal (diminished or absent) leg pulses increased with age ($p<0.001$), lifetime ($p<0.001$) and current cigarette smoking ($p<0.001$), and lifetime alcohol history ($p=0.027$). A higher percentage of diabetic participants had diminished or absent leg pulses (15.3%) than those glucose-impaired participants and non-diabetics (13.0% and 6.5%) ($p<0.001$).

The prevalence of abnormal (diminished or absent) peripheral pulses increased with age ($p<0.001$) and lifetime ($p<0.001$) and current smoking history ($p<0.001$). Diabetics had a higher percentage of diminished or absent peripheral pulses (15.9%) than those glucose-impaired participants and non-diabetics (13.4% and 6.7%) ($p<0.001$).

The prevalence of abnormal KUB x rays increased with age ($p<0.001$). Heavy lifetime smokers (>10 pack-years) had the highest prevalence of abnormal KUB x rays (34.3%) compared to non-smokers and moderate lifetime smokers (28.4% and 28.2% respectively) ($p=0.010$). Participants with more than 40 drink-years had a higher percentage of abnormal KUB x rays (36.3%) than participants who never drank (31.3%) and drinkers with less than 40 drink-years (28.9%) ($p=0.006$). A higher percentage of diabetics had abnormal KUB x rays (42.5%) than those glucose-impaired participants and non-diabetics (30.8% and 28.5% respectively) ($p<0.001$). Participants with Type B personalities had a higher prevalence of abnormal KUB x rays than those with Type A personalities ($p=0.017$).

The prevalence of intermittent claudication and vascular insufficiency (ICVI) indices increased with age ($p<0.001$), lifetime ($p<0.001$) and current cigarette smoking history ($p=0.001$), and total cholesterol level ($p=0.002$). Heavy lifetime drinkers (>40 drink-years) had the highest prevalence of abnormal ICVI indices (4.3%) followed by non-drinkers (3.0%) and moderate drinkers (2.2%) ($p=0.040$). The prevalence of abnormal ICVI indices was greatest in diabetics, followed by glucose-impaired participants and non-diabetics

($p<0.001$). Participants with a family history of heart disease had a higher prevalence of abnormal ICVI indices (3.4%) than those with no family history of heart disease (1.9%) ($p=0.050$).

In summary, the covariate tests of association found that older participants were more likely than younger participants to have a verified history of essential hypertension, heart disease, and myocardial infarction and were also at higher risk for nearly all of the central cardiac and peripheral vascular function endpoints. Racial differences showed that Blacks were more likely than non-Blacks to have higher diastolic blood pressure and abnormal nonspecific and T- and ST-wave changes. Of the occupational categories, officers had the highest prevalence of post-SEA heart disease and the highest systolic blood pressure values while enlisted flyers had highest prevalence of nonspecific T- and ST-wave changes and overall ECG abnormalities.

Associations with the cigarette smoking covariates found that, as expected, heavy smokers were more likely than non-smokers to have a history of myocardial infarction and pulse deficits. A history of heavy alcohol consumption (>40 drink-years) was highly associated with ICVI index abnormalities. Participants with high total cholesterol and HDL cholesterol had higher systolic or diastolic blood pressure. Obesity was highly associated with increased blood pressure and essential hypertension.

The covariate tests of associations found that, as expected, diabetics were more likely than nondiabetics to have a history of essential hypertension and myocardial infarction, increased blood pressure levels, and diminished pulses. Also, as expected family history of heart disease was associated with an increase in the participant's history of post-SEA essential hypertension, heart disease, and myocardial infarction. Finally, participants taking blood pressure medication at the time of the 1992 examination had significantly higher mean systolic and diastolic blood pressure levels than the participants not taking any medication.

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

The central and peripheral physical examination findings were cross-tabulated with the verified cardiovascular disease endpoints to assess the degree of correlation between the 10th-year followup physical examination and the past medical history. The results are shown in Appendix Table K-1-2.

There were statistically significant associations between verified history of post-SEA essential hypertension and all of the central cardiac function variables except LBBB ($p=0.652$) and tachycardia ($p=0.594$). For the peripheral vascular function endpoints, four of the pulse indices (radial, femoral, leg, and peripheral pulses) were not significantly associated with the history of essential hypertension ($p>0.13$). However, for all peripheral vascular function variables participants who were abnormal were more likely to have a history of hypertension than those who were normal.

The verified history of post-SEA heart disease (excluding essential hypertension) was significantly or marginally significantly associated with all of the central cardiac function endpoints. These associations were all positive associations indicating that participants with an abnormal central cardiac function measure were more likely to have a history of hypertension than those who where normal. The verified history of heart disease also was significantly or marginally significantly associated with all of the peripheral vascular function endpoints except diastolic blood pressure and three pulse indices (radial, femoral, and popliteal). Similar to the central cardiac function endpoints, participants with abnormal peripheral vascular function indicators, except for diastolic blood pressure, were more likely to have a verified history of heart disease than those who were normal.

In contrast to essential hypertension and heart disease, the verified history of myocardial infarction was only significantly associated with approximately half of the central cardiac function endpoints: overall ECG ($p<0.001$), RBBB ($p=0.002$), non-specific T- and ST-wave changes ($p<0.001$), arrhythmia ($p<0.001$), ECG evidence of prior myocardial infarction ($p<0.001$), and ECG other diagnoses ($p<0.001$). However, for all but one of the central cardiac function variables, tachycardia, participants who were abnormal were more likely to have a history of post-SEA myocardial infarction than those who were normal. Similar to the verified history of heart disease, the verified history of myocardial infarction was significantly or marginally significantly associated with all of the peripheral vascular function variables except diastolic blood pressure and three pulse indices (radial, femoral, and popliteal). Similar to the central cardiac function endpoints, participants with abnormal peripheral vascular function indicators except for diastolic blood pressure, were more likely to have a verified history of myocardial infarction than those who were normal.

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 Analysis

The following section presents the results of the statistical analyses of the dependent variables shown in Table 15-1. Dependent variables are grouped into three sections: those derived and verified from a review of medical records, data obtained during the 1992 physical examination, and one variable based on self-reported information from the questionnaire.

Unadjusted and adjusted analyses of six models are presented for each variable. Model 1 examines the relationship between the dependent variable and group (Ranch Hand or Comparison). Model 2 explores the relationship between the dependent variable and an extrapolated initial dioxin measure for Ranch Hands who had a 1987 dioxin measurement greater than 10 ppt. If a participant did not have a 1987 dioxin level, a 1992 level was used. A statistical adjustment for the percent of body fat at the participant's time of duty in SEA and the change in the percent of body fat from the time of duty in SEA to the date of the blood draw for dioxin is included in this model to account for body-fat-related differences in elimination rate (31). Model 3 dichotomizes the Ranch Hands in Model 2 based on their initial dioxin measures; these two categories of Ranch Hands are referred to as the "low Ranch Hand" category and the "high Ranch Hand" category. These participants are added to Ranch Hands and Comparisons with current serum dioxin levels (1987, if available; 1992, if the 1987 level was not available) at or below 10 ppt to create a total of four categories. Ranch Hands with current serum dioxin levels at or below 10 ppt are referred to as the "background Ranch Hand" category. The relationship between the dependent variable in each of the three Ranch Hand categories and the dependent variable in the "Comparison" category is examined. A fourth contrast, exploring the relationship of the dependent variable in the low Ranch Hand category and the high Ranch Hand category combined, also is conducted. This combination is referred to in the text and tables as the "low plus high Ranch Hand" category. As in Model 2, a statistical adjustment is made for the percent of body fat at the participant's time of duty in SEA and the change in the percent of body fat from the time of duty in SEA to the date of the blood draw for dioxin.

Models 4, 5, and 6 examine the relationship between the dependent variable and 1987 dioxin levels in all Ranch Hands with a dioxin measurement. If a participant did not have a 1987 dioxin measurement, a 1992 measurement was utilized in determining the current dioxin level. The measure of dioxin in Model 4 is lipid-adjusted, whereas whole-weight dioxin is used in Models 5 and 6. Model 6 differs from Model 5 in that a statistical adjustment for total lipids is included in Model 6. Further details on dioxin and the modeling strategy are found in Chapters 2 and 7 respectively.

Results of investigation for group-by-covariate and dioxin-by-covariate interactions are referenced in the text, and tabular results are presented in Appendix K-2. As described previously, additional analyses were performed when occupation, total cholesterol, HDL cholesterol, percent body fat, or diabetic class were retained in the final models for Models 2 through 6. Results excluding these covariates from these models are tabled in Appendix K-3, and dioxin-by-covariate interactions with occupation excluded from these models are presented in Appendix K-4. Results from analyses excluding these covariates are discussed in the text only if a meaningful change occurred (that is, changes between significant results, marginally significant results, and nonsignificant results).

Verified Medical Records Variables

Essential Hypertension

The unadjusted and adjusted Model 1 analyses of essential hypertension did not find a significant difference between Ranch Hands and Comparisons (Table 15-3(a,b): $p>0.20$ for unadjusted and adjusted results). The significant covariates in the adjusted analysis were age, race, diabetic class, lifetime alcohol history, family history of heart disease, total cholesterol, and body fat.

Similarly, Models 2 and 3 did not display a significant association between initial dioxin and essential hypertension for the unadjusted and adjusted analyses (Table 15-3(c-f): $p>0.14$ for all analyses). The final adjusted model for Model 2 contained age, race, lifetime alcohol history, family history of heart disease, and diabetic class. After excluding diabetic class from Model 2, the analysis showed a marginally significant direct association between essential hypertension and initial dioxin (Appendix Table K-3-1(a): $p=0.079$, Adj.

Table 15-3.
Analysis of Verified Essential Hypertension

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Yes**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***930***	***38.6***	***1.01 (0.85,1.21)***	***0.922***
	Comparison	***1,248***	***38.3***		
Officer	Ranch Hand	355	37.5	0.91 (0.69,1.20)	0.547
	Comparison	488	39.8		
Enlisted Flyer	Ranch Hand	160	44.4	1.25 (0.82,1.91)	0.347
	Comparison	198	38.9		
Enlisted Groundcrew	Ranch Hand	415	37.3	1.02 (0.79,1.33)	0.922
	Comparison	562	36.8		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***0.99 (0.82,1.20)***	***0.952***	AGE (p<0.001) RACE (p=0.028)
Officer	0.83 (0.61,1.13)	0.245	DIAB (p<0.001) DRKYR (p<0.001)
Enlisted Flyer	1.35 (0.85,2.12)	0.202	HRTDIS (p<0.001) CHOL (p=0.060)
Enlisted Groundcrew	1.03 (0.77,1.38)	0.837	BFAT (p<0.001)

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 15-3. (Continued)
Analysis of Verified Essential Hypertension

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	166	38.0	1.08 (0.94,1.24)	0.304
Medium	170	40.0		
High	171	47.4		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
486	1.13 (0.96,1.32)	0.143	AGE (p=0.062) RACE (p=0.062) DIAB (p=0.001) DRKYR (p=0.001) HRTDIS (p=0.001)

[a] Adjusted for percent body fat at the time of duty in SEA, and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 15-3. (Continued)
Analysis of Verified Essential Hypertension

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,033	38.9		
Background RH	368	34.2	1.00 (0.77,1.30)	0.993
Low RH	249	38.6	0.90 (0.67,1.21)	0.479
High RH	258	45.0	1.09 (0.82,1.46)	0.549
Low plus High RH	507	41.8	0.99 (0.79,1.25)	0.953

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,006			AGE ($p<0.001$) RACE ($p=0.029$) DRKYR ($p<0.001$) CHOL ($p=0.010$) HRTDIS ($p<0.001$) DIAB ($p<0.001$)
Background RH	355	0.95 (0.72,1.25)	0.709	
Low RH	238	0.83 (0.61,1.14)	0.254	
High RH	248	1.20 (0.88,1.63)	0.254	
Low plus High RH	486	1.00 (0.79,1.27)	0.998	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 15-3. (Continued)
Analysis of Verified Essential Hypertension

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Yes/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	33.6 (292)	37.0 (289)	45.2 (294)	1.18 (1.08,1.30)	<0.001
5	33.0 (297)	36.2 (287)	46.7 (291)	1.19 (1.10,1.29)	<0.001
6[c]	33.1 (296)	36.2 (287)	46.7 (291)	1.14 (1.04,1.24)	0.005

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin+1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	841	1.14 (1.02,1.28)	0.021	AGE (p<0.001) RACE (p=0.108) DRKYR (p<0.001) BFAT (p<0.001) HRTDIS (p<0.001) DIAB (p=0.001)
5	841	1.15 (1.04,1.27)	0.005	AGE (p<0.001) RACE (p=0.098) DRKYR (p<0.001) BFAT (p<0.001) HRTDIS (p<0.001) DIAB (p=0.002)
6[d]	840	1.11 (1.00,1.23)	0.049	AGE (p<0.001) RACE (p=0.072) DRKYR (p<0.001) BFAT (p<0.001) HRTDIS (p<0.001) DIAB (p=0.004)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.
[b] Relative risk for a twofold increase in current dioxin.
[c] Adjusted for log_2 total lipids.
[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

RR=1.15). The final adjusted model for Model 3 accounted for age, race, lifetime alcohol history, total cholesterol, family history of heart disease, and diabetic class.

The unadjusted analyses for Models 4 through 6 showed a significant positive association between essential hypertension and current dioxin (Table 15-3(g): $p \leq 0.005$, Est. RR≥1.14). The percentages of Ranch Hands with a history of essential hypertension increased with increasing levels of current dioxin for all three models. For Model 4, the percentages of Ranch Hands with a history of essential hypertension were 33.6, 37.0, and 45.2 for the low, medium, and high current dioxin categories respectively; for Model 5, the percentages were 33.0, 36.2, and 46.7; and for Model 6 the percentages were 33.1, 36.2, and 46.7. Similarly, the adjusted analyses of Models 4 through 6 also showed a significant direct association between current dioxin and essential hypertension (Table 15-3(h); $p < 0.05$, Est. RR≥1.11). Models 4, 5, and 6 were adjusted for age, race, family history of heart disease, body fat, diabetic class, and lifetime alcohol history.

Heart Disease (Excluding Hypertension)

The unadjusted Model 1 analysis of a history of heart disease excluding essential hypertension did not find a significant difference between Ranch Hands and Comparisons (Table 15-4(a): p=0.481). However, after stratifying the analysis by occupation, a marginally significant association between group and heart disease was detected for enlisted flyers (Table 15-4(a): p=0.093, Est. RR=1.46). For the enlisted flyer stratum, 55.0 percent of Ranch Hands had a history of heart disease as compared to 45.5 percent of Comparisons. The adjusted analysis displayed a significant interaction between group and lifetime alcohol history (Table 15-4(b): p=0.019). Stratified results of the group-by-lifetime alcohol history interaction are presented in Appendix Table K-2-1. The adjusted analyses excluding this interaction revealed no significant overall difference in the history of heart disease for the two groups. However, as in the unadjusted analysis, stratification by occupation revealed a marginally significant group difference for enlisted flyers (Table 15-4(b): p=0.059, Adj. RR=1.51). The covariates of age, family history of heart disease, and total cholesterol also were significant in the final model.

The unadjusted analysis for Model 2 showed a significant inverse association between heart disease and initial dioxin (Table 15-4(c): p=0.019, Est. RR=0.85). The percentages of Ranch Hands with a history of heart disease decreased as levels of initial dioxin increased (low, 52.7%; medium, 51.2%; high, 38.4%). The adjusted Model 2 analysis revealed a significant interaction between initial dioxin and personality type (Table 15-4(d): p=0.040). Stratified results of this interaction are presented in Appendix Table K-2-1. After removal of the initial dioxin-by-personality type interaction, the adjusted Model 2 analysis did not disclose a significant association between heart disease and initial dioxin (Table 15-4(d): p=0.274). The adjusted model for Model 2 also contained age, lifetime alcohol history, family history of heart disease, and total cholesterol. When total cholesterol was excluded from the model, the initial dioxin-by-personality type interaction was no longer significant, and the results remained nonsignificant (Appendix Table K-3-2(a): p=0.205).

In the Model 3 unadjusted analysis, Ranch Hands in the high dioxin category exhibited significantly less heart disease (41.3%) than Comparisons (49.7%) (Table 15-4(e): p=0.016,

Table 15-4.
Analysis of Verified Heart Disease (Excluding Essential Hypertension)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Yes**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***940***	***49.8***	***1.07 (0.90,1.26)***	***0.481***
	Comparison	***1,262***	***48.2***		
Officer	Ranch Hand	361	54.0	0.99 (0.75,1.30)	0.997
	Comparison	492	54.3		
Enlisted Flyer	Ranch Hand	160	55.0	1.46 (0.96,2.22)	0.093
	Comparison	202	45.5		
Enlisted Groundcrew	Ranch Hand	419	44.2	1.01 (0.79,1.31)	0.973
	Comparison	568	43.8		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.07 (0.90,1.28)****	***0.423****	GROUP*DRKYR (p=0.019) AGE (p<0.001) HRTDIS (p=0.001) CHOL (p=0.009)
Officer	1.00 (0.76,1.34)**	0.962**	
Enlisted Flyer	1.51 (0.98,2.33)**	0.059**	
Enlisted Groundcrew	1.00 (0.77,1.30)**	0.996**	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

** 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; refer to Appendix Table K-2-1 for further analysis of this interaction.

Table 15-4. (Continued)
Analysis of Verified Heart Disease (Excluding Essential Hypertension)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	169	52.7	0.85 (0.74,0.98)	0.019
Medium	172	51.2		
High	172	38.4		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
491	0.92 (0.80,1.07)**	0.274**	INIT*PERS (p=0.040) AGE (p=0.003) DRKYR (p=0.049) HRTDIS (p=0.011) CHOL (p=0.115)

[a] Adjusted for percent body fat at the time of duty in SEA, and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-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; refer to Appendix Table K-2-1 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.
INIT = Initial Dioxin.

Table 15-4. (Continued)
Analysis of Verified Heart Disease (Excluding Essential Hypertension)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,046	49.7		
Background RH	371	53.4	1.18 (0.93,1.50)	0.174
Low RH	254	53.5	1.11 (0.84,1.47)	0.448
High RH	259	41.3	0.71 (0.53,0.94)	0.016
Low plus High RH	513	47.4	0.89 (0.72,1.10)	0.280

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,034			AGE (p<0.001) CHOL (p=0.024) PERS (p=0.082) HRTDIS (p=0.004)
Background RH	366	1.09 (0.85,1.39)	0.515	
Low RH	248	1.10 (0.82,1.46)	0.533	
High RH	256	0.80 (0.60,1.06)	0.126	
Low plus High RH	504	0.94 (0.75,1.17)	0.556	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 15-4. (Continued)
Analysis of Verified Heart Disease (Excluding Essential Hypertension)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Yes/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	54.6 (293)	51.7 (294)	43.4 (297)	0.87 (0.80,0.96)	0.004
5	53.0 (298)	54.6 (291)	42.0 (295)	0.89 (0.82,0.97)	0.004
6[c]	52.9 (297)	54.6 (291)	42.0 (295)	0.89 (0.81,0.97)	0.005

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin+1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	871	0.92 (0.84,1.01)	0.079	AGE ($p<0.001$) HRTDIS ($p=0.044$)
5	871	0.93 (0.85,1.00)	0.062	AGE ($p<0.001$) HRTDIS ($p=0.044$)
6[d]	870	0.93 (0.85,1.01)	0.100	AGE ($p<0.001$) HRTDIS ($p=0.046$)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Est. RR=0.71); all other contrasts for the unadjusted Model 3 analysis were statistically nonsignificant ($p>0.17$). After adjusting for age, total cholesterol, personality type, and family history of heart disease, the Model 3 adjusted analysis did not detect a significant association between heart disease and categorized dioxin (Table 15-4(f): $p>0.12$).

The unadjusted analyses of Models 4 through 6 revealed significant inverse associations between heart disease and current dioxin (Table 15-4(g): $p \leq 0.005$, Est. RR$\leq$0.89). For Model 4, the percentages of Ranch Hands with heart disease were 54.6, 51.7, and 43.4 for low, medium, and high current dioxin categories respectively; for Model 5, the percentages were 53.0, 54.6, and 42.0; and for Model 6, the percentages were 52.9, 54.6, and 42.0. The adjusted analyses for Models 4 and 5 revealed marginally significant inverse associations between current dioxin and heart disease (Table 15-4(h): $p=0.079$, Adj. RR=0.92 and $p=0.062$, Adj. RR=0.93 respectively). The adjusted analysis for Model 6 did not reveal a statistically significant association with heart disease ($p=0.100$). Models 4, 5, and 6 were adjusted for age and family history of heart disease.

Myocardial Infarction

The unadjusted analysis performed for Model 1 found no significant difference between myocardial infarction and group (Table 15-5(a): $p \geq 0.70$ for all unadjusted analyses). The adjusted analysis revealed a significant interaction between group and body fat (Table 15-5(b): $p=0.035$). Stratified results of the group-by-body fat interaction are presented in Appendix Table K-2-2. After removing the group-by-body fat interaction from the adjusted model, no significant difference between groups was detected (Table 15-5(b): $p>0.26$). Occupation, age, lifetime cigarette smoking history, heart disease, and HDL cholesterol were significant covariates in Model 1.

Models 2 and 3 did not show a significant association between dioxin and a history of myocardial infarction for the unadjusted analyses (Table 15-5(c,e): $p>0.48$ for all unadjusted analyses). The adjusted Model 2 analyses did not reveal a significant association between initial dioxin and myocardial infarction (Table 15-5(d): $p>0.29$). The covariates age, race, family history of heart disease, and HDL cholesterol were significant in the adjusted Model 2 analysis. The adjusted analysis for Model 3 revealed a significant interaction between categorized dioxin and body fat (Table 15-5(f): $p=0.030$). Stratified results of this interaction are displayed in Appendix Table K-2-2. The adjusted Model 3 analysis after deletion of this interaction did not reveal any significant associations between categorized dioxin and myocardial infarction (Table 15-5(f): $p>0.35$). The covariates age, occupation, HDL cholesterol, lifetime cigarette smoking history, and family history of heart disease also were significant in the final adjusted model. After excluding occupation, HDL cholesterol, and body fat from the final model, the Model 3 adjusted analysis exhibited a marginally significant difference between Ranch Hands in the high dioxin category and Comparisons (Appendix Table K-3-3(b): $p=0.093$, Adj. RR=1.58). In this analysis, a higher percentage of Ranch Hands exhibited a history of myocardial infarction than Comparisons.

The unadjusted analyses for Models 4 through 6 did not disclose any significant associations between a history of myocardial infarction and current dioxin (Table 15-5(g): $p>0.56$ for all analyses). Each of the adjusted analyses for Models 4 through 6 detected a

Table 15-5.
Analysis of Verified Myocardial Infarction

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Percent Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***940***	***6.9***	***1.03 (0.74,1.44)***	***0.936***
	Comparison	***1,262***	***6.7***		
Officer	Ranch Hand	361	5.8	0.86 (0.49,1.51)	0.700
	Comparison	492	6.7		
Enlisted Flyer	Ranch Hand	160	10.0	1.21 (0.59,2.48)	0.737
	Comparison	202	8.4		
Enlisted Groundcrew	Ranch Hand	419	6.7	1.09 (0.65,1.82)	0.842
	Comparison	568	6.2		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	***0.96 (0.67,1.36)*****	***0.810*****	GROUP*BFAT (p=0.035) OCC (p=0.020) AGE (p<0.001) PACKYR (p=0.010) HRTDIS (p<0.001) HDL (p<0.001)
Officer	0.71 (0.39,1.30)**	0.269**	
Enlisted Flyer	1.23 (0.58,2.61)**	0.580**	
Enlisted Groundcrew	1.08 (0.62,1.85)**	0.793**	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

** 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; refer to Appendix Table K-2-2 for further analysis of this interaction.

Table 15-5. (Continued)
Analysis of Verified Myocardial Infarction

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	169	5.3	1.04 (0.81,1.33)	0.772
Medium	172	10.5		
High	172	5.8		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
496	1.15 (0.88,1.51)	0.296	AGE (p=0.002) RACE (p=0.069) HRTDIS (p=0.043) HDL (p=0.068)

[a] Adjusted for percent body fat at the time of duty in SEA, and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 15-5. (Continued)
Analysis of Verified Myocardial Infarction

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	**n**	**Percent Yes**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,046	6.4		
Background RH	371	6.2	1.04 (0.64,1.71)	0.868
Low RH	254	6.3	0.90 (0.51,1.58)	0.701
High RH	259	8.1	1.20 (0.72,2.02)	0.489
Low plus High RH	513	7.2	1.05 (0.69,1.59)	0.838

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	**n**	**Adj. Relative Risk (95% C.I.)[ac]**	**p-Value**	**Covariate Remarks**
Comparison	1,026			DXCAT*BFAT (p=0.030) AGE (p<0.001) OCC (p=0.066) PACKYR (p=0.021) HDL (p=0.005) HRTDIS (p<0.001)
Background RH	361	1.00 (0.59,1.71)**	0.995**	
Low RH	245	0.79 (0.43,1.44)**	0.439**	
High RH	251	1.30 (0.74,2.27)**	0.355**	
Low plus High RH	496	1.02 (0.65,1.59)**	0.941**	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-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; refer to Appendix Table K-2-2 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.
DXCAT = Categorized Dioxin.

Table 15-5. (Continued)
Analysis of Verified Myocardial Infarction

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Yes/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	5.8 (293)	6.1 (294)	8.4 (297)	1.03 (0.86,1.23)	0.773
5	5.4 (298)	5.5 (291)	9.5 (295)	1.05 (0.90,1.22)	0.567
6[c]	5.1 (297)	5.5 (291)	9.5 (295)	1.00 (0.85,1.19)	0.978

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	857	1.02 (0.82,1.27)**	0.826**	CURR*RACE (p=0.045) AGE (p<0.001) OCC (p=0.093) PACKYR (p=0.083) HDL (p=0.027) HRTDIS (p=0.008)
5	857	1.03 (0.86,1.24)**	0.762**	CURR*RACE (p=0.042) AGE (p<0.001) OCC (p=0.096) PACKYR (p=0.082) HDL (p=0.029) HRTDIS (p=0.007)
6[d]	856	1.12 (0.93,1.35)**	0.228**	CURR*RACE (p=0.032) AGE (p<0.001) PACKYR (p=0.042) HDL (p=0.048) HRTDIS (p=0.010)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.
[b] Relative risk for a twofold increase in current dioxin.
[c] Adjusted for log_2 total lipids.
[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-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; refer to Appendix Table K-2-2 for further analysis of this interaction.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.
CURR = Current Dioxin.

significant interaction between current dioxin and race (Table 15-5(h): $p \leq 0.05$). In each of these analyses, only one Black Ranch Hand had a history of myocardial infarction, and he was in the low current dioxin category for each model, while nearly one half of the non-Black Ranch Hands with a history of myocardial infarction were in the high current dioxin category for each model. Stratified analyses of these interactions are presented in Appendix Table K-2-2. After deletion of these interactions from the adjusted models, the adjusted analyses did not find any significant associations between current dioxin and myocardial infarction (Table 15-5(h): $p \geq 0.22$). Each of the adjusted analyses for Models 4 through 6 also accounted for age, lifetime cigarette smoking history, family history of heart disease, and HDL cholesterol; Models 4 and 5 also were adjusted for occupation. After excluding occupation and HDL cholesterol from the final adjusted models, the current dioxin-by-race interaction remained significant for Models 4 through 6. Stratified analyses of these interactions can be found in Appendix Table K-4-1. After deletion of the interaction from the models excluding occupation and HDL, the results were nonsignificant (Table K-3-3(c): $p > 0.10$).

Physical Examination Data

Systolic Blood Pressure (Continuous)

The unadjusted and adjusted Model 1 analyses of systolic blood pressure in its continuous form did not reveal a significant difference in means between Ranch Hands and Comparisons (Table 15-6(a,b): $p \geq 0.18$ for all analyses). The adjusted model included the covariates age, current cigarette smoking, body fat, diabetic class, total cholesterol, HDL cholesterol, and use of blood pressure medication.

The unadjusted analyses for Models 2 and 3 did not exhibit a significant association between initial dioxin and systolic blood pressure in its continuous form (Table 15-6(c,e): $p > 0.19$ for all analyses). The adjusted analysis for Model 2 revealed a highly significant interaction between initial dioxin and diabetic class (Table 15-6(d): $p = 0.008$). Stratified results of this interaction are displayed in Appendix Table K-2-3. These results were nonsignificant (Appendix Table K-2-3(a): $p > 0.18$); however, the results show that mean systolic blood pressure changes very little as initial dioxin increases for non-diabetic Ranch Hands, increases as initial dioxin increases for Ranch Hands classified as impaired, and decreases as initial dioxin increases for diabetic Ranch Hands. The covariates age, HDL cholesterol, body fat, use of blood pressure medication, and diabetic class also were significant in the final adjusted model. The Model 3 adjusted analyses were not statistically significant (Table 15-6(f): $p > 0.36$). Model 3 was adjusted for age, current cigarette smoking, total cholesterol, HDL cholesterol, body fat, use of blood pressure medication, and diabetic class.

The unadjusted analyses for Models 4 and 5 showed marginally significant and significant positive associations between mean systolic blood pressure and current dioxin (Table 15-6(g): $p = 0.067$, slope=0.777 and $p = 0.016$, slope=0.884 respectively). For both models, the mean systolic blood pressure increased as the current dioxin levels increased. For Model 4 the unadjusted systolic blood pressure means were 120.75 mm Hg, 121.72 mm Hg, and 122.73 mm Hg for the low, medium, and high current categories respectively. For

Table 15-6.
Analysis of Systolic Blood Pressure (mm Hg)
(Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Mean**	**Difference of Means (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***939***	***121.56***	***-0.69 (-2.25,0.87)***	***0.386***
	Comparison	***1,262***	***122.25***		
Officer	Ranch Hand	361	123.57	0.19 (-2.42,2.79)	0.889
	Comparison	492	123.38		
Enlisted Flyer	Ranch Hand	159	121.81	-0.34 (-3.93,3.24)	0.852
	Comparison	202	122.15		
Enlisted Groundcrew	Ranch Hand	419	119.74	-1.57 (-3.85,0.72)	0.180
	Comparison	568	121.31		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED						
Occupational Category	**Group**	**n**	**Adjusted Mean**	**Difference of Adjusted Means (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***Ranch Hand***	***924***	***125.55***	***-0.92 (-2.35,0.51)***	***0.206***	AGE (p<0.001)
	Comparison	***1,247***	***126.47***			CSMOK (p=0.001)
Officer	Ranch Hand	353	125.80	-0.87 (-3.17,1.43)	0.461	BFAT (p<0.001) DIAB (p<0.001)
	Comparison	489	126.66			CHOL (p=0.010)
Enlisted Flyer	Ranch Hand	155	125.36	-0.45 (-3.98,3.08)	0.802	HDL (p=0.004)
	Comparison	198	125.81			BPMED (p<0.001)
Enlisted Groundcrew	Ranch Hand	416	125.44	-1.13 (-3.27,1.00)	0.297	
	Comparison	560	126.57			

[a] Covariates and associated p-values correspond to final model on all participants with available data.

Table 15-6. (Continued)
Analysis of Systolic Blood Pressure (mm Hg)
(Continuous)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[a]		
Initial Dioxin	n	Mean	Adj. Mean[a]	R^2	Slope (Std. Error)[b]	p-Value
Low	169	122.17	122.85	0.080	-0.721 (0.597)	0.227
Medium	172	123.33	123.63			
High	172	122.43	121.46			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[b]			
Initial Dioxin	n	Adj. Mean[b]	R^2	Adj. Slope (Std. Error)	p-Value	Covariate Remarks
Low	168	****	0.172	****	****	INIT*DIAB (p=0.008) AGE (p=0.004) BFAT (p=0.009) HDL (p=0.030) BPMED (p=0.001)
Medium	168	****				
High	168	****				

[a] Adjusted for percent body fat at the time of duty in SEA, and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

**** Log_2 (initial dioxin)-by-covariate interaction ($p \leq 0.01$); adjusted mean, slope, standard error, and p-value not presented; refer to Appendix Table K-2-3 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 15-6. (Continued)
Analysis of Systolic Blood Pressure (mm Hg)
(Continuous)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[a]	Difference of Mean vs. Comparisons (95% C.I.)	p-Value
Comparison	1,046	122.37	122.32		
Background RH	370	120.48	122.18	-0.15 (-2.27,1.98)	0.893
Low RH	254	123.02	122.36	0.04 (-2.41,2.48)	0.977
High RH	259	122.29	120.70	-1.62 (-4.05,0.81)	0.191
Low plus High RH	513	122.65	121.52	-0.80 (-2.68,1.09)	0.407

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED					
Dioxin Category	n	Adj. Mean[b]	Difference of Adj. Mean vs. Comparisons (95% C.I.)	p-Value	Covariate Remarks
Comparison	1,034	126.43			AGE (p<0.001) CSMOK (p<0.001) CHOL (p=0.009) HDL (p=0.005) BFAT (p=0.001) BPMED (p<0.001) DIAB (p<0.001)
Background RH	365	125.49	-0.94 (-2.97,1.09)	0.365	
Low RH	250	125.45	-0.98 (-3.31,1.35)	0.410	
High RH	254	126.04	-0.39 (-2.74,1.96)	0.745	
Low plus High RH	504	125.75	-0.69 (-2.49,1.12)	0.455	

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 15-6. (Continued)
Analysis of Systolic Blood Pressure (mm Hg)
(Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED						
	Current Dioxin Category Mean/(n)			Analysis Results for Log_2 (Current Dioxin + 1)		
Model[a]	Low	Medium	High	R^2	Slope (Std. Error)	p-Value
4	120.75 (292)	121.72 (294)	122.73 (297)	0.004	0.777 (0.424)	0.067
5	120.10 (297)	121.99 (291)	123.14 (295)	0.007	0.884 (0.365)	0.016
6[b]	120.17 (296)	121.99 (291)	123.14 (295)	0.009	0.616 (0.394)	0.119

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED							
	Current Dioxin Category Adjusted Mean/(n)			Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	Low	Medium	High	R^2	Adj. Slope (Std. Error)	p-Value	Covariate Remarks
4	126.62** (289)	124.71** (289)	126.16** (291)	0.183	0.027 (0.420)**	0.948**	CURR*DIAB (p=0.038) AGE (p=0.002) CSMOK (p=0.007) HDL (p=0.139) BFAT (p<0.001) BPMED (p<0.001)
5	126.15 (296)	125.19 (288)	126.19 (285)	0.177	0.100 (0.362)	0.783	AGE (p=0.002) CSMOK (p=0.005) HDL (p=0.142) BFAT (p<0.001) DIAB (p=0.001) BPMED (p<0.001)
6[c]	126.21 (295)	125.19 (288)	126.14 (285)	0.176	0.056 (0.387)	0.885	AGE (p=0.002) CSMOK (p=0.006) HDL (p=0.142) BFAT (p<0.001) DIAB (p=0.001) BPMED (p<0.001)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.
[b] Adjusted for log_2 total lipids.
[c] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table K-2-3 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Model 5, the unadjusted systolic blood pressure means were 120.10 mm Hg, 121.99 mm Hg, and 123.14 mm Hg. The unadjusted analysis for Model 6 was not statistically significant (Table 15-6(g): p=0.119). The adjusted analysis for Model 4 revealed a significant current dioxin-by-diabetic class interaction (Table 15-6(h): p=0.038). Stratified analyses of this interaction are displayed in Appendix Table K-2-3. After deletion of the interaction, the adjusted analysis did not reveal a significant association between current dioxin and systolic blood pressure (Table 15-6(h): p=0.948). The results of the adjusted analyses of Models 5 and 6 also were nonsignificant (Table 15-6(h): p>0.78). The adjusted Models 4 through 6 contained the covariates age, current cigarette smoking, HDL cholesterol, body fat, and use of blood pressure medication. The adjusted models for both Models 5 and 6 also contained the covariate diabetic class. After excluding the covariates HDL cholesterol, body fat, and diabetic class from the adjusted models, all three models revealed a significant positive association between current dioxin and systolic blood pressure in continuous form (Appendix Table K-3-4(c): p= 0.011, slope=1.055; p=0.004, slope=1.020; and p=0.019, slope=0.901 for Models 4, 5, and 6 respectively).

Systolic Blood Pressure (Discrete)

The unadjusted Model 1 analysis of discretized systolic blood pressure did not display a significant difference between Ranch Hands and Comparisons (Table 15-7(a): p>0.64 for all unadjusted analyses). After adjusting for significant covariates, the Model 1 analysis uncovered a group-by-total cholesterol interaction (Table 15-7(b): p=0.028). For further investigation of this group-by-total cholesterol interaction, stratified results are presented in Appendix Table K-2-4. After excluding this interaction from the model, the adjusted analysis did not detect any significant differences in discretized systolic blood pressure between Ranch Hands and Comparisons (Table 15-7(b): p>0.22 for all adjusted analyses). The adjusted model also included the covariates age, diabetic class, body fat, HDL cholesterol, and use of blood pressure medication.

Models 2 and 3 did not reveal a significant association between initial dioxin and discretized systolic blood pressure for the unadjusted or the adjusted analyses (Table 15-7 (c-f): p>0.42 for all unadjusted and adjusted analyses). The adjusted model for Model 2 accounted for age and body fat. The Model 3 analysis was adjusted for age, current cigarette smoking, HDL cholesterol, body fat, diabetic class, and use of blood pressure medication.

The unadjusted analyses for Models 4 and 6 did not reveal significant associations between discretized systolic blood pressure and current dioxin (Table 15-7(g): p=0.103 and p=0.124 respectively). The Model 5 unadjusted analysis showed a marginally significant direct association between current dioxin and systolic blood pressure (Table 15-7(g): p=0.061, Est. RR=1.11). In Model 5, the percentage of Ranch Hands with an abnormal systolic blood pressure value (i.e., >140 mm Hg) increased with increasing levels of current dioxin (low, 12.5%; medium, 16.5%; high, 18.0%). The adjusted analyses for Models 4 through 6 did not show significant results (Table 15-7(h): p>0.42 for all adjusted analyses). Models 4 through 6 were adjusted for age, diabetic class, body fat, and use of blood pressure medication. After excluding body fat and diabetic class from each of the final models for Models 4 through 6, all three models showed significant positive associations between

Table 15-7.
Analysis of Systolic Blood Pressure
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***939***	***15.2***	***0.97 (0.77,1.23)***	***0.853***
	Comparison	***1,262***	***15.6***		
Officer	Ranch Hand	361	16.6	0.90 (0.63,1.29)	0.641
	Comparison	492	18.1		
Enlisted Flyer	Ranch Hand	159	17.0	1.17 (0.67,2.07)	0.685
	Comparison	202	14.9		
Enlisted Groundcrew	Ranch Hand	419	13.4	0.97 (0.67,1.40)	0.942
	Comparison	568	13.7		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***0.93 (0.72,1.19)*****	***0.540*****	GROUP*CHOL (p=0.028) AGE (p<0.001)
Officer	0.79 (0.53,1.16)**	0.224**	DIAB (p=0.002)
Enlisted Flyer	1.15 (0.63,2.08)**	0.649**	BFAT (p<0.001) HDL (p=0.055)
Enlisted Groundcrew	1.00 (0.67,1.48)**	0.990**	BPMED (p<0.001)

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

** 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; refer to Appendix Table K-2-4 for further analysis of this interaction.

Table 15-7. (Continued)
Analysis of Systolic Blood Pressure
(Discrete)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	169	17.2	0.97 (0.81,1.15)	0.691
Medium	172	16.9		
High	172	17.4		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
513	1.04 (0.86,1.25)	0.691	AGE (p=0.022) BFAT (p=0.079)

[a] Adjusted for percent body fat at the time of duty in SEA, and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 15-7. (Continued)
Analysis of Systolic Blood Pressure
(Discrete)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,046	16.1		
Background RH	370	13.5	0.97 (0.69,1.38)	0.871
Low RH	254	16.9	0.99 (0.68,1.44)	0.966
High RH	259	17.4	0.95 (0.65,1.37)	0.776
Low plus High RH	513	17.2	0.97 (0.73,1.30)	0.832

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	**n**	**Adj. Relative Risk (95% C.I.)[ac]**	**p-Value**	**Covariate Remarks**
Comparison	1,034			AGE (p<0.001) CSMOK (p=0.084) HDL (p=0.065) BFAT (p=0.040) DIAB (p=0.005) BPMED (p<0.001)
Background RH	365	0.86 (0.60,1.24)	0.428	
Low RH	250	0.87 (0.59,1.29)	0.489	
High RH	254	1.12 (0.76,1.66)	0.572	
Low plus High RH	504	0.98 (0.73,1.33)	0.916	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 15-7. (Continued)
Analysis of Systolic Blood Pressure
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	14.0 (292)	15.0 (294)	17.8 (297)	1.11 (0.98,1.25)	0.103
5	12.5 (297)	16.5 (291)	18.0 (295)	1.11 (1.00,1.23)	0.061
6[c]	12.5 (296)	16.5 (291)	18.0 (295)	1.10 (0.98,1.23)	0.124

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	882	1.05 (0.91,1.21)	0.540	AGE (p=0.013) DIAB (p=0.058) BFAT (p<0.001) BPMED (p<0.001)
5	882	1.04 (0.91,1.17)	0.584	AGE (p=0.014) DIAB (p=0.059) BFAT (p<0.001) BPMED (p=0.001)
6[d]	881	1.06 (0.92,1.21)	0.426	AGE (p=0.013) DIAB (p=0.048) BFAT (p<0.001) BPMED (p<0.001)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

current dioxin and discretized systolic blood pressure (Appendix Table K-3-5(c): p=0.027, Adj. RR=1.16 for Model 4; p=0.025, Adj. RR=1.14 for Model 5; and p=0.025, Adj. RR=1.16 for Model 6).

Heart Sounds

The unadjusted Model 1 analysis did not show a significant difference in the presence of heart sounds between Ranch Hands and Comparisons (Table 15-8(a): p>0.41 for all unadjusted analyses). The adjusted Model 1 analysis uncovered a significant group-by-age interaction (Table 15-8(b): p=0.025). Race and current cigarette smoking also were significant covariates in the final model. The results after removing the interaction from the adjusted analyses were nonsignificant (Table 15-8(b): p>0.29 for all adjusted analyses). Stratified analyses for the group-by-age interaction are presented in Appendix Table K-2-5.

The unadjusted analyses of Models 2 and 3 did not display a significant association between initial dioxin and heart sounds (Table 15-8(c,e): p>0.59 for all unadjusted analyses). However, the adjusted analyses for Models 2 and 3 revealed significant initial dioxin-by-age and categorized dioxin-by-age interactions (Table 15-8(d,f): p=0.027 and p=0.036 respectively). Stratified results of these interaction are presented in Appendix Table K-2-5. In addition to the initial dioxin-by-age interaction, Model 2 also was adjusted for diabetic class and family history of heart disease. Model 3 was adjusted for lifetime cigarette smoking history, current cigarette smoking, and diabetic class in addition to the categorized dioxin-by-age interaction. After removal of the interactions, the adjusted results for Models 2 and 3 were nonsignificant (Table 15-8(d,f): p>0.41).

Models 4 through 6 did not reveal any significant relationships between current dioxin and heart sounds (Table 15-8(g,h): p>0.13 for all unadjusted and adjusted analyses). Models 4 and 5 accounted for age, current cigarette smoking, family history of heart disease, and diabetic class. The final model for Model 6 contained the covariates age, lifetime cigarette smoking history, family history of heart disease, and diabetic class.

Overall Electrocardiograph (ECG)

The unadjusted analysis for Model 1 did not reveal a significant association between the overall ECG findings and group (Table 15-9(a): p>0.15 for all unadjusted analyses). The adjusted analysis, however, revealed a marginally significant overall difference between Ranch Hands and Comparisons (Table 15-9(b): p=0.074, Adj. RR=0.82). After stratifying the adjusted Model 1 analysis by occupation, the analyses exhibited a marginally significant association between group and overall ECG for officers (Table 15-9(b): p=0.099, Adj. RR=0.76). Model 1 accounted for age, race, lifetime cigarette smoking history, body fat, and diabetic class.

The unadjusted analysis of Model 2 did not show a significant association between initial dioxin and the prevalence of an abnormal overall ECG (Table 15-9(c): p=0.127). The adjusted analysis displayed a significant interaction between initial dioxin and total cholesterol (Table 15-9(d): p=0.027). The final adjusted model also accounted for age, race, and diabetic class. Stratified results of the interaction are presented in Appendix Table

Table 15-8.
Analysis of Heart Sounds

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	*Ranch Hand*	*936*	*20.5*	*1.02 (0.83,1.26)*	*0.888*
	Comparison	*1,259*	*20.2*		
Officer	Ranch Hand	360	23.6	1.10 (0.80,1.52)	0.625
	Comparison	492	22.0		
Enlisted Flyer	Ranch Hand	158	20.3	1.30 (0.76,2.23)	0.412
	Comparison	202	16.3		
Enlisted Groundcrew	Ranch Hand	418	17.9	0.88 (0.63,1.21)	0.466
	Comparison	565	20.0		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	*1.04 (0.84,1.28)***	*0.732***	GROUP*AGE (p=0.025) RACE (p=0.058) CSMOK (p<0.001)
Officer	1.10 (0.79,1.52)**	0.567**	
Enlisted Flyer	1.34 (0.78,2.30)**	0.290**	
Enlisted Groundcrew	0.89 (0.64,1.24)**	0.504**	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

** 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; refer to Appendix Table K-2-5 for further analysis of this interaction.

Table 15-8. (Continued)
Analysis of Heart Sounds

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	169	21.3	0.96 (0.82,1.13)	0.648
Medium	171	24.0		
High	172	18.6		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
504	0.99 (0.83,1.17)**	0.895**	INIT*AGE (p=0.027) DIAB (p=0.040) HRTDIS (p=0.091)

[a] Adjusted for percent body fat at the time of duty in SEA, and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-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; refer to Appendix Table K-2-5 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 15-8. (Continued)
Analysis of Heart Sounds

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,044	19.8		
Background RH	369	19.5	1.01 (0.75,1.37)	0.936
Low RH	253	21.7	1.10 (0.78,1.53)	0.596
High RH	259	20.8	1.04 (0.74,1.46)	0.820
Low plus High RH	512	21.3	1.07 (0.82,1.39)	0.626

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,041			DXCAT*AGE (p=0.036) PACKYR (p=0.100) CSMOK (p=0.004) DIAB (p=0.033)
Background RH	367	1.00 (0.73,1.35)**	0.984**	
Low RH	253	1.10 (0.79,1.55)**	0.572**	
High RH	259	1.13 (0.80,1.60)**	0.483**	
Low plus High RH	512	1.12 (0.86,1.46)**	0.415**	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-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; refer to Appendix Table K-2-5 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 15-8. (Continued)
Analysis of Heart Sounds

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	18.6 (291)	23.1 (294)	19.9 (296)	1.03 (0.92,1.15)	0.631
5	18.2 (296)	23.0 (291)	20.4 (294)	1.03 (0.94,1.13)	0.549
6[c]	18.3 (295)	23.0 (291)	20.4 (294)	1.04 (0.93,1.15)	0.496

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	867	1.09 (0.96,1.23)	0.178	AGE (p=0.007) CSMOK (P=0.015) HRTDIS (p=0.064) DIAB (p=0.107)
5	867	1.08 (0.97,1.20)	0.155	AGE (p=0.007) CSMOK (p=0.014) HRTDIS (p=0.064) DIAB (p=0.104)
6[d]	865	1.09 (0.97,1.22)	0.139	AGE (p=0.001) DIAB (p=0.118) PACKYR (p=0.033) HRTDIS (p=0.072)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 15-9.
Analysis of Overall Electrocardiograph (ECG)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***940***	***20.7***	***0.86 (0.70,1.05)***	***0.151***
	Comparison	***1,260***	***23.4***		
Officer	Ranch Hand	361	22.7	0.82 (0.59,1.12)	0.240
	Comparison	491	26.5		
Enlisted Flyer	Ranch Hand	160	26.3	1.05 (0.66,1.69)	0.924
	Comparison	202	25.2		
Enlisted Groundcrew	Ranch Hand	419	16.9	0.81 (0.58,1.13)	0.240
	Comparison	567	20.1		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks**[a]
All	***0.82 (0.67,1.02)***	***0.074***	AGE ($p<0.001$) RACE ($p=0.006$) PACKYR ($p=0.054$) BFAT ($p=0.044$) DIAB ($p=0.010$)
Officer	0.76 (0.55,1.05)	0.099	
Enlisted Flyer	1.07 (0.65,1.73)	0.801	
Enlisted Groundcrew	0.79 (0.56,1.12)	0.185	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 15-9. (Continued)
Analysis of Overall Electrocardiograph (ECG)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	169	24.9	0.88 (0.75,1.04)	0.127
Medium	172	22.7		
High	172	17.4		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
513	0.99 (0.83,1.19)**	0.951**	INIT*CHOL (p=0.027) AGE (p<0.001) RACE (p=0.046) DIAB (p=0.011)

[a] Adjusted for percent body fat at the time of duty in SEA, and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-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; refer to Appendix Table K-2-6 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 15-9. (Continued)
Analysis of Overall Electrocardiograph (ECG)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,044	23.9		
Background RH	371	17.0	0.70 (0.52,0.96)	0.027
Low RH	254	25.2	1.00 (0.73,1.38)	0.992
High RH	259	18.1	0.66 (0.46,0.94)	0.021
Low plus High RH	513	21.6	0.82 (0.64,1.07)	0.139

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	**n**	**Adj. Relative Risk (95% C.I.)[ac]**	**p-Value**	**Covariate Remarks**
Comparison	1,043			AGE (p<0.001) RACE (p=0.005) DIAB (p=0.042)
Background RH	370	0.62 (0.45,0.85)	0.003	
Low RH	254	0.88 (0.63,1.23)	0.454	
High RH	259	0.79 (0.54,1.14)	0.201	
Low plus High RH	513	0.84 (0.64,1.10)	0.194	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 15-9. (Continued)
Analysis of Overall Electrocardiograph (ECG)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	16.4 (293)	22.4 (294)	20.2 (297)	1.03 (0.92,1.16)	0.561
5	16.4 (298)	21.3 (291)	21.4 (295)	1.04 (0.95,1.15)	0.388
6[c]	16.5 (297)	21.3 (291)	21.4 (295)	1.02 (0.91,1.13)	0.764

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	883	1.11 (0.98,1.26)	0.112	AGE ($p<0.001$) RACE ($p=0.080$) CSMOK ($p=0.111$) DIAB ($p=0.002$)
5	883	1.09 (0.97,1.22)**	0.130**	CURR*CHOL ($p=0.026$) AGE ($p<0.001$) RACE ($p=0.084$) CSMOK ($p=0.103$) DIAB ($p=0.001$)
6[d]	882	1.09 (0.97,1.23)**	0.154**	CURR*CHOL ($p=0.026$) AGE ($p<0.001$) RACE ($p=0.090$) CSMOK ($p=0.097$) DIAB ($p=0.001$)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($0.01<p\leq0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table K-2-6 for further analysis of this interaction.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

K-2-6. After the interaction was removed from the model, the adjusted Model 2 analysis did not reveal any significant results. The Model 3 unadjusted analysis exhibited a significantly lower percentage of abnormal overall ECG findings for the background Ranch Hand (17.0%) and high Ranch Hand (18.1%) categories than for the Comparison category (23.9%) (Table 15-9(e): background RH:p=0.027, Est. RR=0.70; high RH:p=0.021, Est. RR=0.66). After adjusting for covariates, Model 3 revealed a significant difference only between background Ranch Hands and Comparisons (Table 15-9(f): p=0.003, Adj. RR=0.62). Model 3 was adjusted for the covariates age, race, and diabetic class.

The unadjusted analyses for Models 4 through 6 did not reveal significant associations between current dioxin and the overall ECG findings (Table 15-9(g): p>0.38 for all unadjusted analyses). The adjusted analysis for Model 4 showed no significant relationship between current dioxin and overall ECG. The covariates age, race, current cigarette smoking, and diabetic class were significant in the final adjusted model. The adjusted analyses for Models 5 and 6 revealed significant current dioxin-by-total cholesterol interactions (Table 15-9(h): p=0.026 for both models). Stratified results of these interactions are presented in Appendix Table K-2-6. Age, race, current cigarette smoking, and diabetic class also were significant in the final adjusted models. After removing the interactions from the final models, the adjusted analyses of Models 5 and 6 did not show any significant results (Table 15-9(h): p≥0.13). However, after excluding diabetic class from Model 4, and diabetic class and total cholesterol from Models 5 and 6, the adjusted analyses exhibited significant and marginally significant direct associations between current dioxin and overall ECG (Appendix Table K-3-7(c): p=0.024, Adj. RR=1.15; p=0.018, Adj. RR=1.14; p=0.054, Adj. RR=1.12 respectively).

Right Bundle Branch Block (RBBB)

The Model 1 unadjusted analysis did not show a significant difference in RBBB between Ranch Hands and Comparisons (Table 15-10(a): p>0.28 for all unadjusted results). The adjusted analysis of Model 1 uncovered significant interactions between group and diabetic class and between group and current cigarette smoking (Table 15-8(b): p=0.036 and p=0.016 respectively). Age and race also were significant covariates in the final model. After removing the interactions from the adjusted analyses, all results were nonsignificant (Table 15-8(b): p>0.14 for all adjusted analyses). Stratified results of the interactions with group are presented in Appendix Table K-2-7.

Neither Model 2 nor Model 3 revealed a significant relationship between dioxin and RBBB for the unadjusted analyses (Table 15-10(c,e): p>0.36 for all unadjusted analyses). The adjusted analyses for Models 2 and 3 revealed significant interactions between initial dioxin and lifetime cigarette smoking history and between categorized dioxin and diabetic class respectively (Table 15-10(d,f): p=0.020 and p=0.023). Stratified results of these interactions are presented in Appendix Table K-2-7. In addition to the interaction, current cigarette smoking, age, and diabetic class were significant in the adjusted analysis of Model 2. Model 3 also was adjusted for age, race, and lifetime cigarette smoking history. After removing the dioxin-by-covariate interactions, the adjusted analyses of Models 2 and 3 did not find a significant relationship between dioxin and RBBB (Table 15-10(d,f): p>0.32 for all adjusted analyses).

Table 15-10.
Analysis of ECG: Right Bundle Branch Block (RBBB)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***940***	***1.3***	***0.85 (0.41,1.75)***	***0.785***
	Comparison	***1,260***	***1.5***		
Officer	Ranch Hand	361	0.6	0.39 (0.08,1.87)	0.373
	Comparison	491	1.4		
Enlisted Flyer	Ranch Hand	160	3.1	3.21 (0.61,16.77)	0.283
	Comparison	201	1.0		
Enlisted Groundcrew	Ranch Hand	419	1.2	0.67 (0.23,1.99)	0.648
	Comparison	568	1.8		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***0.82 (0.39,1.71)*****	***0.594*****	GROUP*DIAB (p=0.036) GROUP*CSMOK (p=0.016) AGE (p=0.001) RACE (p=0.047)
Officer	0.36 (0.07,1.76)**	0.207**	
Enlisted Flyer	3.45 (0.65,18.14)**	0.144**	
Enlisted Groundcrew	0.65 (0.22,1.94)**	0.438**	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

** Group-by-covariate interactions ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table K-2-7 for further analysis of these interactions.

Table 15-10. (Continued)
Analysis of ECG: Right Bundle Branch Block (RBBB)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	169	1.8	1.09 (0.68,1.75)	0.720
Medium	172	2.3		
High	172	1.2		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
513	1.32 (0.77,2.28)**	0.323**	INIT*PACKYR (p=0.020) AGE (p=0.030) CSMOK (p=0.140) DIAB (p=0.033)

[a] Adjusted for percent body fat at the time of duty in SEA, and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-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; refer to Appendix Table K-2-7 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 15-10. (Continued)
Analysis of ECG: Right Bundle Branch Block (RBBB)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,045	1.4		
Background RH	371	0.8	0.56 (0.16,1.97)	0.367
Low RH	254	1.6	1.04 (0.34,3.17)	0.948
High RH	259	1.9	1.33 (0.48,3.74)	0.584
Low plus High RH	513	1.8	1.18 (0.51,2.75)	0.695

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,042			DXCAT*DIAB (p=0.023) AGE (p=0.055) RACE (p=0.092) PACKYR (p=0.081)
Background RH	369	0.54 (0.15,1.89)**	0.332**	
Low RH	254	0.90 (0.29,2.80)**	0.855**	
High RH	259	1.56 (0.55,4.42)**	0.407**	
Low plus High RH	513	1.18 (0.50,2.76)**	0.706**	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-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; refer to Appendix Table K-2-7 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 15-10. (Continued)
Analysis of ECG: Right Bundle Branch Block (RBBB)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	0.7 (293)	1.4 (294)	2.0 (297)	1.25 (0.87,1.81)	0.233
5	0.7 (298)	1.4 (291)	2.0 (295)	1.20 (0.86,1.67)	0.283
6[c]	0.7 (297)	1.4 (291)	2.0 (295)	1.26 (0.89,1.80)	0.200

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	883	1.49 (1.00,2.21)	0.054	AGE (p=0.013) PACKYR (p=0.024)
5	883	1.37 (0.96,1.97)	0.082	AGE (p=0.015) PACKYR (p=0.025)
6[d]	882	1.51 (1.02,2.25)	0.038	AGE (p=0.013) PACKYR (p=0.021)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Models 4 through 6 did not show significant relationships between current dioxin and RBBB for the unadjusted analyses (Table 15-10(g): $p \geq 0.20$ for all unadjusted analyses). The adjusted analyses detected marginally significant positive associations between current dioxin and RBBB for Models 4 and 5 (Table 15-10(h): $p=0.054$, Adj. RR=1.49; $p=0.082$, Adj. RR=1.37) and a significant positive association for Model 6 (Table 15-10(h): $p=0.038$, Adj. RR=1.51). The prevalence of RBBB increased with increasing levels of current dioxin for all three models. Age and lifetime cigarette smoking history were significant covariates in the final adjusted models for Models 4 through 6.

Left Bundle Branch Block (LBBB)

For Model 1, only 1 Ranch Hand and 10 Comparisons experienced LBBB. The Ranch Hand was an officer, and the Comparisons were mixed among occupational strata (7 officers, 1 enlisted flyer, 2 enlisted groundcrew). The single Ranch Hand diagnosed with LBBB was in the low initial dioxin category for Models 2 and 3 and in the medium current dioxin category for Models 4, 5, and 6. There also were three Comparisons with LBBB in the Model 3 analysis. Relative risks, confidence intervals, and p-values are not presented due to the sparse number of abnormalities (Table 15-11(a-d)).

Non-Specific ST- and T-Wave Changes

The Model 1 analyses of non-specific ST- and T-wave changes did not detect any statistically significant results (Table 15-12(a,b): $p>0.24$ for all analyses). The adjusted model accounted for age, race, lifetime cigarette smoking history, total cholesterol, and body fat.

The unadjusted analyses for Models 2 and 3 did not reveal any significant associations between initial dioxin and non-specific ST- and T-wave changes (Table 15-12(c,e): $p>0.14$ for all unadjusted analyses). After adjustment for the significant covariates age, race, personality type, diabetic class, and body fat, the Model 2 analysis did not display a significant relationship between initial dioxin and non-specific ST- and T-wave changes (Table 15-12(d): $p=0.613$). The Model 3 adjusted analysis resulted in a categorized dioxin-by-lifetime cigarette smoking history interaction (Table 15-12(f): $p=0.031$). Age, race, total cholesterol, body fat, and diabetic class were also significant in the final adjusted model. Stratified results of the dioxin-by-lifetime cigarette smoking history interaction are displayed in Appendix Table K-2-8. After the interaction was removed from the model, the adjusted analysis exhibited a marginally significant difference between background Ranch Hands and Comparisons (Table 15-12(f): $p=0.057$, Adj. RR=0.68). Fewer Ranch Hands experienced abnormal non-specific ST- and T-wave changes than Comparisons.

The unadjusted analyses for Models 4 through 6 did not show any statistically significant associations between current dioxin and non-specific ST- and T-wave changes (Table 15-12(g): $p>0.12$ for all unadjusted analyses). The adjusted analyses for Models 4, 5, and 6 displayed significant positive relationships between current dioxin and non-specific ST- and T-wave changes (Table 15-12(h): $p=0.017$, Adj. RR=1.20; $p=0.015$, Adj. RR=1.18; $p=0.028$, Adj. RR=1.17). Models 4, 5, and 6 accounted for age, race, lifetime cigarette smoking, and diabetic class in the adjusted final model.

Table 15-11.
Analysis of ECG: Left Bundle Branch Block (LBBB)

a) MODEL 1: RANCH HANDS VS. COMPARISONS			
Occupational Category	**Group**	**n**	**Percent Abnormal**
All	***Ranch Hand***	***940***	***0.1***
	Comparison	***1,260***	***0.8***
Officer	Ranch Hand	361	0.3
	Comparison	491	1.4
Enlisted Flyer	Ranch Hand	160	0.0
	Comparison	201	0.5
Enlisted Groundcrew	Ranch Hand	419	0.0
	Comparison	568	0.4

b) MODEL 2: RANCH HANDS — INITIAL DIOXIN		
	Initial Dioxin Category Summary Statistics	
Initial Dioxin	**n**	**Percent Abnormal**
Low	169	0.6
Medium	172	0.0
High	172	0.0

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 15-11. (Continued)
Analysis of ECG: Left Bundle Branch Block (LBBB)

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY		
Dioxin Category	**n**	**Percent Abnormal**
Comparison	1,045	0.7
Background RH	371	0.0
Low RH	254	0.4
High RH	259	0.0
Low plus High RH	513	0.2

d) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN			
	Current Dioxin Category Percent Abnormal/(n)		
Model[a]	**Low**	**Medium**	**High**
4	0.0 (293)	0.3 (294)	0.0 (297)
5	0.0 (298)	0.3 (291)	0.0 (295)
6	0.0 (297)	0.3 (291)	0.0 (295)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

Note: Model 3: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.
Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 15-12.
Analysis of ECG: Non-Specific ST- and T-Wave Changes

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***940***	***14.0***	***0.96 (0.75,1.22)***	***0.757***
	Comparison	***1,260***	***14.6***		
Officer	Ranch Hand	361	15.0	1.02 (0.70,1.50)	0.982
	Comparison	491	14.7		
Enlisted Flyer	Ranch Hand	160	20.6	1.19 (0.70,2.02)	0.605
	Comparison	201	17.9		
Enlisted Groundcrew	Ranch Hand	419	10.7	0.78 (0.53,1.15)	0.249
	Comparison	568	13.4		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***0.95 (0.74,1.22)***	***0.670***	AGE (p<0.001) RACE (p<0.001) PACKYR (p=0.001) CHOL (p=0.120) BFAT (p<0.001)
Officer	0.98 (0.67,1.46)	0.939	
Enlisted Flyer	1.22 (0.71,2.09)	0.478	
Enlisted Groundcrew	0.79 (0.52,1.18)	0.245	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 15-12. (Continued)
Analysis of ECG: Non-Specific ST- and T-Wave Changes

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	169	16.0	0.91 (0.76,1.10)	0.336
Medium	172	17.4		
High	172	12.8		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
512	1.05 (0.86,1.29)	0.613	AGE (p<0.001) RACE (p=0.011) PERS (p=0.077) DIAB (p=0.030) BFAT (p=0.023)

[a] Adjusted for percent body fat at the time of duty in SEA, and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 15-12. (Continued)
Analysis of ECG: Non-Specific ST- and T-Wave Changes

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,045	14.7		
Background RH	371	10.5	0.75 (0.52,1.10)	0.144
Low RH	254	16.9	1.10 (0.75,1.59)	0.631
High RH	259	13.9	0.86 (0.58,1.27)	0.442
Low plus High RH	513	15.4	0.97 (0.72,1.31)	0.856

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	**n**	**Adj. Relative Risk (95% C.I.)[ac]**	**p-Value**	**Covariate Remarks**
Comparison	1,042			DXCAT*PACKYR (p=0.031)
Background RH	369	0.68 (0.46,1.01)**	0.057**	AGE (p<0.001) RACE (p<0.001)
Low RH	254	0.95 (0.64,1.40)**	0.778**	CHOL (p=0.146)
High RH	259	1.04 (0.69,1.57)**	0.860**	BFAT (p=0.011) DIAB (p=0.043)
Low plus High RH	513	0.99 (0.72,1.35)**	0.932**	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-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; refer to Appendix Table K-2-8 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 15-12. (Continued)
Analysis of ECG: Non-Specific ST- and T-Wave Changes

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	9.2 (293)	15.6 (294)	15.2 (297)	1.09 (0.96,1.24)	0.200
5	9.4 (298)	14.8 (291)	15.9 (295)	1.09 (0.98,1.23)	0.128
6[c]	9.4 (297)	14.8 (291)	15.9 (295)	1.06 (0.94,1.20)	0.331

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	882	1.20 (1.03,1.40)	0.017	AGE (p<0.001) RACE (p=0.018) DIAB (p=0.007) PACKYR (p=0.011)
5	882	1.18 (1.03,1.34)	0.015	AGE (p<0.001) RACE (p=0.016) DIAB (p=0.009) PACKYR (p=0.011)
6[d]	881	1.17 (1.02,1.35)	0.028	AGE (p<0.001) RACE (p=0.016) DIAB (p=0.010) PACKYR (p=0.011)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

ECG: Bradycardia

Analysis of bradycardia found no significant overall difference between Ranch Hands and Comparisons in the unadjusted or adjusted analyses for Model 1 (Table 15-13(a,b): $p>0.20$ for unadjusted and adjusted analyses). However, stratifying the Model 1 analyses by occupation displayed a significant association between group and bradycardia for enlisted flyers for both the unadjusted and adjusted analyses (Table 15-13(a,b): p=0.033, Est. RR=9.20 and p=0.047, Adj. RR=8.46). The percentage of enlisted flyer Ranch Hands with bradycardia (4.4%) was significantly greater than the percentage of enlisted flyer Comparisons with bradycardia (0.5%). The final model in the adjusted analysis contained the covariates diabetic class, body fat, total cholesterol, and HDL cholesterol.

Model 2 did not show any significant results for the unadjusted analyses (Table 15-13(c): p=0.108). However, the adjusted analysis revealed a significant inverse relationship between initial dioxin and bradycardia (Table 15-13(d): p=0.030, Adj. RR=0.52). The percentage of Ranch Hands with bradycardia decreased as initial dioxin increased (low, 3.0%; medium, 2.9%; high, 0.6%). The final adjusted model accounted for age, personality type, lifetime alcohol history, total cholesterol, and HDL cholesterol. In Model 3, the unadjusted analysis exhibited a significantly higher percentage of individuals with bradycardia in the background Ranch Hand category (4.9%) than in the Comparison category (2.2%) (Table 15-13(e): p=0.023, Est. RR=2.09). The adjusted analysis revealed a significant categorized dioxin-by-personality type interaction (Table 15-13(f): p=0.015). The covariates age, total cholesterol, HDL cholesterol, and body fat also were in the final adjusted model. Further examination of the interaction between dioxin and personality type is displayed in Appendix Table K-2-9. After removal of the interaction from the model, the difference in the prevalence of bradycardia between background Ranch Hands and Comparisons remained significant (Table 15-13(f): p=0.021, Adj. RR=2.15).

The unadjusted analyses for Models 4, 5, and 6 all displayed significant or marginally significant inverse relationships between bradycardia and current dioxin (Table 15-13(g): p=0.012, Est. RR=0.70; p=0.011, Est. RR=0.76; p=0.053, Est. RR=0.79). The percentages of Ranch Hands with bradycardia in the low, medium, and high current dioxin categories for Model 4 were 5.5, 3.1, and 1.3 percent respectively. The percentages for Models 5 and 6 similarly decreased as current dioxin increased (low, 4.7%; medium, 3.8%; high, 1.4%). The adjusted analysis for Model 4 revealed significant current dioxin-by-personality type and current dioxin-by-diabetic class interactions (Table 15-13(h): p=0.007 and p=0.013 respectively). Stratified results of these interactions are displayed in Appendix Table K-2-9. Lifetime alcohol history and HDL cholesterol also were accounted for in the final adjusted model. After removing the interactions in Model 4, the adjusted model revealed a significant inverse relationship between current dioxin and bradycardia (Table 15-13(h): p=0.074, Adj. RR=0.77). Adjusting for covariates in Models 5 and 6 resulted in a current dioxin-by-personality type interaction (Table 15-13(h): p=0.013 and p=0.015 respectively). Further examination of these interactions is displayed in Appendix Table K-2-9. The covariates age, lifetime alcohol history, and HDL cholesterol also were significant in the final models. A significant inverse association between current dioxin and bradycardia was revealed after removing the interaction from the final adjusted models for Models 5 and 6 (Table 15-13(h): p=0.020, Adj. RR=0.76 and p=0.049, Adj. RR=0.078).

Table 15-13.
Analysis of ECG: Bradycardia

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***940***	***3.2***	***1.40 (0.84,2.35)***	***0.250***
	Comparison	***1,262***	***2.3***		
Officer	Ranch Hand	361	3.6	0.98 (0.48,2.04)	0.999
	Comparison	492	3.7		
Enlisted Flyer	Ranch Hand	160	4.4	9.20 (1.12,75.54)	0.033
	Comparison	202	0.5		
Enlisted Groundcrew	Ranch Hand	419	2.4	1.36 (0.56,3.31)	0.644
	Comparison	568	1.8		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.41 (0.83,2.37)***	***0.203***	DIAB (p=0.116) BFAT (p=0.043) CHOL (p=0.010) HDL (p=0.004)
Officer	1.01 (0.48,2.10)	0.990	
Enlisted Flyer	8.46 (1.03,69.75)	0.047	
Enlisted Groundcrew	1.38 (0.57,3.37)	0.478	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 15-13. (Continued)
Analysis of ECG: Bradycardia

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	169	3.0	0.66 (0.37,1.15)	0.108
Medium	172	2.9		
High	172	0.6		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
490	0.52 (0.28,0.99)	0.030	AGE (p=0.017) PERS (p=0.008) DRKYR (p=0.034) CHOL (p=0.023) HDL (p=0.049)

[a] Adjusted for percent body fat at the time of duty in SEA, and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 15-13. (Continued)
Analysis of ECG: Bradycardia

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,046	2.2		
Background RH	371	4.9	2.09 (1.10,3.94)	0.023
Low RH	254	3.1	1.42 (0.62,3.23)	0.404
High RH	259	1.2	0.55 (0.16,1.87)	0.341
Low plus High RH	513	2.1	1.00 (0.48,2.08)	0.992

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	**n**	**Adj. Relative Risk (95% C.I.)[ac]**	**p-Value**	**Covariate Remarks**
Comparison	1,036			DXCAT*PERS (p=0.015) AGE (p=0.011) CHOL (p=0.033) HDL (p=0.005) BFAT (p=0.022)
Background RH	367	2.15 (1.12,4.14)**	0.021**	
Low RH	249	1.43 (0.61,3.31)**	0.408**	
High RH	254	0.45 (0.13,1.60)**	0.219**	
Low plus High RH	503	0.92 (0.43,1.95)**	0.829**	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-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; refer to Appendix Table K-2-9 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 15-13. (Continued)
Analysis of ECG: Bradycardia

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	5.5 (293)	3.1 (294)	1.3 (297)	0.70 (0.53,0.94)	0.012
5	4.7 (298)	3.8 (291)	1.4 (295)	0.76 (0.62,0.94)	0.011
6[c]	4.7 (297)	3.8 (291)	1.4 (295)	0.79 (0.63,1.00)	0.053

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	849	0.77 (0.57,1.04)**	0.074**	CURR*PERS (p=0.007) CURR*DIAB (p=0.013) DRKYR (p=0.028) HDL (p=0.029)
5	850	0.76 (0.61,0.96)**	0.020**	CURR*PERS (p=0.013) AGE (p=0.086) DRKYR (p=0.036) HDL (p=0.015)
6[d]	849	0.78 (0.61,1.00)**	0.049**	CURR*PERS (p=0.015) AGE (p=0.103) DRKYR (p=0.044) HDL (p=0.019)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table K-2-9 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

ECG: Tachycardia

For Model 1, only three Ranch Hands and two Comparisons experienced tachycardia. Summary statistics for Model 1 are presented in Table 15-14(a). Two of the Ranch Hands with tachycardia were officers, and the third was enlisted groundcrew. The two Comparisons with tachycardia were enlisted groundcrew. Due to the sparse number of abnormalities, the unadjusted analysis by occupational strata and the adjusted analyses were not performed. Also, since only one of the Ranch Hands with tachycardia had a dioxin measurement (low initial dioxin category and medium current dioxin category), the Models 2, 3, 4, 5, and 6 analyses could not be performed; therefore relative risks, confidence intervals, and p-values are not presented (Table 15-14(b-d)).

ECG: Arrhythmia

The Model 1 analysis of arrhythmia did not uncover any statistically significant results (Table 15-15(a,b): $p>0.42$ for all analyses). Covariate adjustment for Model 1 accounted for age.

The unadjusted analyses for Models 2 and 3 showed no significant relationships between arrhythmia and initial dioxin (Table 15-15(c,e): $p>0.37$ for all unadjusted analyses). The adjusted analysis for Model 2 revealed significant initial dioxin-by-HDL cholesterol and initial dioxin-by-current cigarette smoking interactions (Table 15-15(d): $p=0.007$ and $p=0.015$ respectively). Stratified results of these interactions are shown in Appendix Table K-2-10. Age and diabetic class also were significant in the final adjusted model. After removal of the interactions, the final model did not reveal any significant results (Table 15-15(d): $p=0.826$). Adjusting for covariates in Model 3 revealed a significant categorized dioxin-by-HDL cholesterol interaction (Table 15-15(f): $p=0.045$). Age also was significant in the final adjusted model. Further examination of the categorized dioxin-by-HDL cholesterol interaction is presented in Appendix Table K-2-10. After removal of the interaction, the final model was statistically nonsignificant (Table 15-15(f): $p>0.18$ for all adjusted analyses).

Models 4 through 6 did not display any significant associations between arrhythmia and current dioxin for the unadjusted analyses (Table 15-15(g): $p>0.22$ for all unadjusted analyses). The adjusted analysis for Model 4 showed a marginally significant positive association between current dioxin and arrhythmia (Table 15-15(h); $p=0.052$, Adj. RR=1.25). Age was the only significant covariate in the final model. The Model 5 and 6 adjusted analyses revealed significant current dioxin-by-current cigarette smoking interactions (Table 15-15(h): $p=0.019$ for both models). Further examination of these interactions is presented in Appendix Table K-2-10. Age also was accounted for in the final adjusted models for Models 5 and 6. After removing the interactions from the final models, marginally significant positive associations between current dioxin and arrhythmia were revealed (Table 15-15(h): $p=0.067$, Adj. RR=1.20 and $p=0.087$, Adj. RR=1.21).

Table 15-14.
Analysis of ECG: Tachycardia

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED			
Occupational Category	**Group**	**n**	**Percent Abnormal**
All	***Ranch Hand***	***940***	***0.3***
	Comparison	***1,262***	***0.2***
Officer	Ranch Hand	361	0.6
	Comparison	492	0.0
Enlisted Flyer	Ranch Hand	160	0.0
	Comparison	202	0.0
Enlisted Groundcrew	Ranch Hand	419	0.2
	Comparison	568	0.4

b) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED		
Initial Dioxin Category Summary Statistics		
Initial Dioxin	**n**	**Percent Abnormal**
Low	169	0.6
Medium	172	0.0
High	172	0.0

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 15-14. (Continued)
Analysis of ECG: Tachycardia

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED		
Dioxin Category	**n**	**Percent Abnormal**
Comparison	1,046	0.2
Background RH	371	0.0
Low RH	254	0.4
High RH	259	0.0
Low plus High RH	513	0.2

d) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED			
	Current Dioxin Category Percent Abnormal/(n)		
Model[a]	**Low**	**Medium**	**High**
4	0.0 (293)	0.3 (294)	0.0 (297)
5	0.0 (298)	0.3 (291)	0.0 (295)
6	0.0 (297)	0.3 (291)	0.0 (295)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

Note: Model 3: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.
Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 15-15.
Analysis of ECG: Arrhythmia

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	Group	n	Percent Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***940***	***4.7***	***1.04 (0.69,1.55)***	***0.940***
	Comparison	***1,261***	***4.5***		
Officer	Ranch Hand	361	5.0	0.94 (0.51,1.74)	0.964
	Comparison	491	5.3		
Enlisted Flyer	Ranch Hand	160	4.4	0.79 (0.30,2.10)	0.824
	Comparison	202	5.4		
Enlisted Groundcrew	Ranch Hand	419	4.5	1.30 (0.69,2.47)	0.521
	Comparison	568	3.5		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	***1.02 (0.68,1.54)***	***0.912***	AGE ($p<0.001$)
Officer	0.92 (0.49,1.72)	0.799	
Enlisted Flyer	0.78 (0.29,2.07)	0.614	
Enlisted Groundcrew	1.30 (0.68,2.50)	0.423	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 15-15. (Continued)
Analysis of ECG: Arrhythmia

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	169	6.5	0.96 (0.72,1.27)	0.759
Medium	172	5.8		
High	172	4.7		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
504	1.03 (0.76,1.40)**	0.826**	INIT*HDL (p=0.007) INIT*CSMOK (p=0.015) AGE (p=0.024) DIAB (p=0.051)

[a] Adjusted for percent body fat at the time of duty in SEA, and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interactions ($p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table K-2-10 for further analysis of these interactions.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 15-15. (Continued)
Analysis of ECG: Arrhythmia

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,045	4.4		
Background RH	371	3.2	0.76 (0.40,1.45)	0.403
Low RH	254	5.9	1.29 (0.70,2.35)	0.414
High RH	259	5.4	1.20 (0.64,2.23)	0.569
Low plus High RH	513	5.7	1.24 (0.77,2.01)	0.378

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,036			DXCAT*HDL (p=0.045) AGE (p<0.001)
Background RH	367	0.65 (0.33,1.28)**	0.208**	
Low RH	250	1.24 (0.67,2.28)**	0.496**	
High RH	254	1.54 (0.81,2.90)**	0.187**	
Low plus High RH	504	1.36 (0.84,2.23)**	0.215**	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interaction ($0.01<p\leq0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table K-2-10 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 15-15. (Continued)
Analysis of ECG: Arrhythmia

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	2.7 (293)	6.1 (294)	5.1 (297)	1.14 (0.93,1.40)	0.225
5	2.0 (298)	6.9 (291)	5.1 (295)	1.12 (0.93,1.34)	0.239
6[c]	2.0 (297)	6.9 (291)	5.1 (295)	1.10 (0.90,1.35)	0.336

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	884	1.25 (1.00,1.56)	0.052	AGE (p<0.001)
5	884	1.20 (0.99,1.47)**	0.067**	CURR*CSMOK (p=0.019) AGE (p<0.001)
6[d]	883	1.21 (0.97,1.50)**	0.087**	CURR*CSMOK (p=0.019) AGE (p<0.001)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table K-2-10 for further analysis of this interaction.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

ECG: Evidence of Prior Myocardial Infarction

Analysis of ECG evidence of prior myocardial infarction did not show a significant difference between Ranch Hands and Comparisons in the unadjusted analysis for Model 1 (Table 15-16(a): $p>0.74$ for all unadjusted analyses). The adjustment for covariates revealed a significant group-by-body fat interaction (Table 15-16(b): $p=0.020$). Age, personality type, current cigarette smoking, family history of heart disease, and HDL cholesterol also were significant in the final adjusted model. The final model after exclusion of the group-by-body fat interaction did not detect a significant association between group and evidence of prior myocardial infarction (Table 15-16(b): $p\geq0.44$ for all adjusted analyses). Further analysis of the group-by-body fat interaction is presented in Appendix Table K-2-11.

Models 2 and 3 did not display any significant relationships between initial dioxin and ECG evidence of prior myocardial infarction for the unadjusted analyses (Table 15-16(c,e): $p>0.32$). The adjusted analysis of Model 2 revealed a significant initial dioxin-by-diabetic class interaction (Table 15-16(d): $p=0.020$). Examination of the initial dioxin-by-diabetic class interaction is provided in Appendix Table K-2-11. The final model was also adjusted for race, current cigarette smoking, and personality type. After removing the interaction from the final model, no significant association between initial dioxin and evidence of prior myocardial infarction was found (Table 15-16(d): $p=0.668$). The adjusted Model 3 analysis also did not detect any significant associations between categorized dioxin and evidence of prior myocardial infarction (Table 15-16(f): $p>0.29$ for all analyses). Age, current cigarette smoking, HDL cholesterol, personality type, and family history of heart disease were significant covariates in the final adjusted model.

The unadjusted analyses for Models 4 through 6 did not result in any significant associations between current dioxin and ECG evidence of prior myocardial infarction (Table 15-16(g): $p>0.17$ for all unadjusted analyses). For Models 4 and 5, the adjusted analyses revealed a marginally significant and a significant positive relationship between current dioxin and evidence of prior myocardial infarction (Table 15-16(h): $p=0.095$, Adj. RR=1.25 and $p=0.020$, Adj. RR=1.31 respectively). Age, race, and current cigarette smoking also were accounted for in the final adjusted Model 4 and Model 5 analyses, and Model 5 also adjusted for body fat. The adjusted analysis for Model 6 did not find a significant association between current dioxin and evidence of prior myocardial infarction (Table 15-16(h): $p=0.225$). The final adjusted model contained age, race, current cigarette smoking, body fat, and personality type.

ECG: Other Diagnoses

The unadjusted analysis of other ECG diagnoses did not reveal a significant difference between Ranch Hands and Comparisons for Model 1 (Table 15-17(a): $p>0.10$ for all unadjusted analyses). However, after adjusting the model for age and current cigarette smoking, a marginally significant overall difference between Ranch Hands and Comparisons was found (Table 15-17(b): $p=0.064$, Adj. RR=2.68). A higher percentage of Ranch Hands (1.1%) had other abnormal ECG diagnoses than Comparisons (0.4%). The adjusted analyses stratified by occupational category were not statistically significant ($p>0.14$).

Table 15-16.
Analysis of ECG: Evidence of Prior Myocardial Infarction

a) MODEL 1: RANCH HANDS VS. COMPARISONS —UNADJUSTED

Occupational Category	Group	n	Percent Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*938*	*3.4*	*1.00 (0.63,1.59)*	*0.999*
	Comparison	*1,258*	*3.4*		
Officer	Ranch Hand	360	3.6	0.84 (0.41,1.69)	0.745
	Comparison	489	4.3		
Enlisted Flyer	Ranch Hand	160	4.4	1.11 (0.39,3.13)	0.999
	Comparison	202	4.0		
Enlisted Groundcrew	Ranch Hand	418	2.9	1.17 (0.53,2.55)	0.851
	Comparison	567	2.5		

b) MODEL 1: RANCH HANDS VS. COMPARISONS—ADJUSTED

Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
All	*0.92 (0.57,1.49)***	*0.738***	GROUP*BFAT (p=0.020) AGE (p<0.001) PERS (p=0.090) CSMOK (p=0.050) HRTDIS (p=0.076) HDL (p=0.003)
Officer	0.75 (0.36,1.56)**	0.440**	
Enlisted Flyer	1.13 (0.38,3.36)**	0.822**	
Enlisted Groundcrew	1.06 (0.47,2.35)**	0.896**	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

** 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; refer to Appendix Table K-2-11 for further analysis of this interaction.

Table 15-16. (Continued)
Analysis of ECG: Evidence of Prior Myocardial Infarction

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	169	1.8	1.18 (0.85,1.65)	0.326
Medium	171	5.3		
High	172	3.5		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
511	1.08 (0.76,1.53)**	0.668**	INIT*DIAB (p=0.020) RACE (p=0.139) CSMOK (p=0.066) PERS (p=0.028)

[a] Adjusted for percent body fat at the time of duty in SEA, and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-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; refer to Appendix Table K-2-11 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 15-16. (Continued)
Analysis of ECG: Evidence of Prior Myocardial Infarction

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,042	3.2		
Background RH	370	3.0	1.00 (0.49,2.01)	0.990
Low RH	254	2.8	0.78 (0.34,1.80)	0.563
High RH	258	4.3	1.26 (0.62,2.57)	0.518
Low plus High RH	512	3.5	1.02 (0.56,1.84)	0.955

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,021			AGE ($p<0.001$) CSMOK ($p=0.076$) HDL ($p=0.035$) PERS ($p=0.149$) HRTDIS ($p=0.018$)
Background RH	361	0.82 (0.39,1.72)	0.593	
Low RH	244	0.76 (0.32,1.78)	0.527	
High RH	250	1.47 (0.71,3.05)	0.298	
Low plus High RH	494	1.08 (0.59,1.98)	0.803	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hands.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 15-16. (Continued)
Analysis of ECG: Evidence of Prior Myocardial Infarction

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	2.7 (292)	2.7 (294)	4.4 (296)	1.12 (0.88,1.43)	0.361
5	2.7 (297)	1.7 (291)	5.4 (294)	1.16 (0.94,1.44)	0.176
6[c]	2.7 (296)	1.7 (291)	5.4 (294)	1.06 (0.84,1.34)	0.623

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	882	1.25 (0.97,1.63)	0.095	AGE (p=0.001) RACE (p=0.123) CSMOK (p=0.008)
5	882	1.31 (1.04,1.65)	0.020	AGE (p=0.001) RACE (p=0.130) CSMOK (p=0.018) BFAT (p=0.118)
6[d]	880	1.17 (0.91,1.51)	0.225	AGE (p=0.002) RACE (p=0.140) CSMOK (p=0.031) BFAT (p=0.094) PERS (p=0.138)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 15-17.
Analysis of ECG: Other Diagnoses

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***940***	***1.1***	***2.70 (0.92,7.94)***	***0.105***
	Comparison	***1,262***	***0.4***		
Officer	Ranch Hand	361	0.8	2.05 (0.34,12.35)	0.727
	Comparison	492	0.4		
Enlisted Flyer	Ranch Hand	160	1.3	2.54 (0.23,28.31)	0.839
	Comparison	202	0.5		
Enlisted Groundcrew	Ranch Hand	419	1.2	3.42 (0.66,17.70)	0.241
	Comparison	568	0.4		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***2.68 (0.91,7.93)***	***0.064***	AGE (p=0.022) CSMOK (p=0.049)
Officer	2.10 (0.34,12.85)	0.422	
Enlisted Flyer	2.37 (0.21,26.38)	0.484	
Enlisted Groundcrew	3.38 (0.65,17.63)	0.149	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 15-17. (Continued)
Analysis of ECG: Other Diagnoses

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	169	0.6	1.36 (0.78,2.38)	0.288
Medium	172	0.6		
High	172	2.3		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
513	1.36 (0.78,2.38)	0.288	

[a] Adjusted for percent body fat at the time of duty in SEA, and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 15-17. (Continued)
Analysis of ECG: Other Diagnoses

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,046	0.1		
Background RH	371	1.1	10.0 (1.11,90.7)	0.040
Low RH	254	0.4	4.4 (0.27,70.0)	0.298
High RH	259	1.9	23.2 (2.68,202.0)	0.004
Low plus High RH	513	1.2	13.4 (1.60,112.0)	0.016

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	**n**	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks**
Comparison	--			
Background RH	--	--	--	
Low RH	--	--	--	
High RH	--	--	--	
Low plus High RH	--	--	--	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

--: Adjusted analyses not presented due to the sparse number of Comparisons with abnormalities.

Note: RH = Ranch Hands.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 15-17. (Continued)
Analysis of ECG: Other Diagnoses

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	1.0 (293)	0.7 (294)	1.7 (297)	1.12 (0.74,1.70)	0.585
5	1.0 (298)	0.7 (291)	1.7 (295)	1.12 (0.78,1.61)	0.554
6[c]	1.0 (297)	0.7 (291)	1.7 (295)	1.11 (0.75,1.64)	0.615

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	882	1.18 (0.72,1.94)**	0.501**	CURR*OCC (p=0.048) CSMOK (p=0.037) PERS (p=0.114) DIAB (p=0.110)
5	882	1.25 (0.81,1.93)**	0.304**	CURR*RACE (p=0.037) CURR*OCC (p=0.037) CSMOK (p=0.048) PERS (p=0.086) BFAT (p=0.125) DIAB (p=0.118)
6[d]	881	1.22 (0.76,1.96)**	0.392**	CURR*RACE (p=0.036) CURR*OCC (p=0.035) CSMOK (p=0.045) PERS (p=0.087) BFAT (p=0.122) DIAB (p=0.121)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.
[b] Relative risk for a twofold increase in current dioxin.
[c] Adjusted for log_2 total lipids.
[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-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; refer to Appendix Table K-2-12 for further analysis of this interaction.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

The Model 2 unadjusted analysis did not detect a significant association between initial dioxin and other ECG diagnoses (Table 15-17(c): p=0.288). No significant covariates were retained in the final adjusted model, therefore, the adjusted results are identical to the unadjusted results. The unadjusted analysis of Model 3 revealed significantly higher percentages of abnormal other ECG diagnoses for Ranch Hands in the background (1.1%), high (1.9%), and low plus high (1.2%) dioxin categories than for Comparisons (0.1%) (Table 15-17(e): p=0.040, Est. RR=10.0 for background RH; p=0.004, Est. RR=23.2 for high RH; and p=0.016, Est. RR=13.4 for low plus high RH). Due to a sparse number of individuals with abnormal other diagnoses, the adjusted analysis for Model 3 was not performed.

The unadjusted analyses of other ECG diagnoses for Models 4, 5, and 6 did not find a significant association with current dioxin (Table 15-17(g): p>0.55 for all unadjusted analyses). Adjusting for covariates in Models 4, 5, and 6 resulted in a significant current dioxin-by-occupation interaction (Table 15-17(h): p=0.048, p=0.037, p=0.035 respectively). Models 5 and 6 also displayed significant current dioxin-by-race interactions (Table 15-17(h): p=0.037 and p=0.036 respectively). Further examination of these interactions is displayed in Appendix Table K-2-12. The covariates current cigarette smoking, personality type, and diabetic class also were significant in the adjusted analysis of Models 4, 5, and 6. Body fat also was significant in the adjusted analyses for Models 5 and 6. After deletion of the interactions with current dioxin from the final models, the adjusted results were nonsignificant (Table 15-17(h): p>0.30).

Physical Examination: Peripheral Vascular Function Variables

Diastolic Blood Pressure (Continuous)

There was no significant difference in mean diastolic blood pressure in its continuous form between Ranch Hands and Comparisons in the unadjusted analyses for Model 1 (Table 15-18(a): p≥0.17 for all unadjusted analyses). The adjusted analyses for Model 1 revealed a significant group-by-age interaction (Table 15-18(b): p=0.022). Further analysis of this interaction is presented in Appendix Table K-2-13. After removal of the group-by-age interaction, the adjusted analysis did not reveal any significant differences between Ranch Hands and Comparisons for continuous diastolic blood pressure (Table 15-18(b): p>0.25 for all adjusted analyses). The covariates race, current cigarette smoking, lifetime cigarette smoking history, body fat, diabetic class, total cholesterol, and use of blood pressure medication were significant in the final model.

The unadjusted analyses for Models 2 and 3 did not reveal any significant relationships between initial dioxin and diastolic blood pressure in its continuous form (Table 15-18(c,e): p>0.44 for all unadjusted analyses). After adjusting for significant covariates, Model 2 displayed a highly significant interaction between initial dioxin and occupation (Table 15-18(d): p=0.001). Further investigation of this interaction is presented in Appendix Table K-2-13. Analysis of this interaction showed officers had a significant positive slope (p=0.001), indicating increased diastolic blood pressure as initial dioxin increased. Race, body fat, and use of blood pressure medication also were significant in the final adjusted

Table 15-18.
Analysis of Diastolic Blood Pressure (mm Hg)
(Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Mean**	**Difference of Means (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***939***	***72.04***	***-0.47 (-1.29,0.35)***	***0.263***
	Comparison	***1,262***	***72.50***		
Officer	Ranch Hand	360	72.27	-0.06 (-1.42,1.30)	0.932
	Comparison	492	72.34		
Enlisted Flyer	Ranch Hand	160	72.41	-0.49 (-2.61,1.62)	0.647
	Comparison	202	72.90		
Enlisted Groundcrew	Ranch Hand	419	71.68	-0.82 (-2.00,0.35)	0.170
	Comparison	568	72.51		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED						
Occupational Category	**Group**	**n**	**Adj. Mean**	**Difference of Adj. Means (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***Ranch Hand***	***937***	***74.01*****	***-0.46 (-1.24,0.33)*****	***0.257*****	GROUP*AGE (p=0.022)
	Comparison	***1,258***	***74.46*****			RACE (p=0.132)
Officer	Ranch Hand	359	74.24**	-0.31 (-1.57,0.96)**	0.635**	CSMOK (p=0.007)
	Comparison	492	74.54**			PACKYR (p=0.013)
Enlisted Flyer	Ranch Hand	160	74.72**	-0.29 (-2.22,1.65)**	0.772**	BFAT (p<0.001)
	Comparison	201	75.01**			DIAB (p=0.004)
Enlisted Groundcrew	Ranch Hand	418	73.65**	-0.66 (-1.84,0.52)**	0.273**	CHOL (p<0.001)
	Comparison	565	74.31**			BPMED (p<0.001)

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

** Group-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted mean, difference of adjusted means, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table K-2-13 for further analysis of this interaction.

Table 15-18. (Continued)
Analysis of Diastolic Blood Pressure (mm Hg)
(Continuous)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[a]		
Initial Dioxin	n	Mean	Adj. Mean[a]	R^2	Slope (Std. Error)	p-Value
Low	169	71.14	71.39	0.037	0.288 (0.322)	0.671
Medium	172	73.33	73.41			
High	172	73.23	72.89			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[b]			
Initial Dioxin	n	Adj. Mean[b]	R^2	Adj. Slope (Std. Error)	p-Value	Covariate Remarks
Low	169	****	0.106	****	****	INIT*OCC (p=0.001)
Medium	172	****				RACE (p=0.009) BFAT (p=0.012)
High	172	****				BPMED (p=0.010)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

**** Log_2 (initial dioxin)-by-covariate interaction ($p \leq 0.01$); adjusted mean, adjusted slope, standard error, and p-value not presented; refer to Appendix Table K-2-13 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 15-18. (Continued)
Analysis of Diastolic Blood Pressure (mm Hg)
(Continuous)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED					
Dioxin Category	n	Mean	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)	p-Value
Comparison	1,046	72.46	72.43		
Background RH	370	71.42	72.02	-0.41 (-1.56,0.74)	0.484
Low RH	254	72.07	71.92	-0.52 (-1.83,0.80)	0.444
High RH	259	73.07	72.46	0.03 (-1.28,1.34)	0.964
Low plus High RH	513	72.57	72.19	-0.24 (-1.26,0.78)	0.643

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED					
Dioxin Category	n	Adj. Mean[b]	Difference of Adj. Mean vs. Comparisons (95% C.I.)	p-Value	Covariate Remarks
Comparison	1,034	73.91**			DXCAT*HRTDIS (p=0.040) PACKYR (p=0.017) CSMOK (p=0.001) CHOL (p<0.001) BFAT (p=0.005) BPMED (p<0.001) DIAB (p=0.006)
Background RH	363	73.27**	-0.64 (-1.76,0.48)**	0.265**	
Low RH	249	73.19**	-0.71 (-2.01,0.58)**	0.279**	
High RH	256	74.00**	0.09 (-1.19,1.38)**	0.887**	
Low plus High RH	505	73.60**	-0.31 (-1.30,0.69)**	0.546**	

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted mean, difference of adjusted means, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table K-2-13 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 15-18. (Continued)
Analysis of Diastolic Blood Pressure (mm Hg)
(Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED						
	Current Dioxin Category Mean/(n)			Analysis Results for Log_2 (Current Dioxin + 1)		
Model[a]	Low	Medium	High	R^2	Slope (Std. Error)	p-Value
4	71.67 (292)	71.29 (294)	73.30 (297)	0.009	0.643 (0.228)	0.005
5	71.29 (297)	71.40 (291)	73.58 (295)	0.013	0.656 (0.196)	0.001
6[b]	71.63 (296)	71.43 (291)	73.24 (295)	0.016	0.492 (0.212)	0.020

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED							
	Current Dioxin Category Adjusted Mean/(n)			Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	Low	Medium	High	R^2	Adj. Slope (Std. Error)	p-Value	Covariate Remarks
4	75.41 (291)	74.24 (294)	76.11 (297)	0.117	0.310 (0.265)	0.241	AGE (p=0.006) RACE (p=0.052) OCC (p=0.096) CSMOK (p=0.001) CHOL (p=0.005) BFAT (p<0.001) BPMED (p<0.001) DIAB (p=0.026)
5	75.18 (296)	74.30 (291)	76.31 (295)	0.117	0.291 (0.228)	0.202	AGE (p=0.006) RACE (p=0.051) OCC (p=0.091) CSMOK (p=0.001) CHOL (p=0.008) BFAT (p<0.001) BPMED (p<0.001) DIAB (p=0.028)
6[c]	75.22 (295)	74.31 (291)	76.29 (295)	0.117	0.267 (0.243)	0.243	AGE (p=0.006) RACE (p=0.050) OCC (p=0.094) CSMOK (p=0.001) CHOL (p=0.028) BFAT (p<0.001) BPMED (p<0.001) DIAB (p=0.033)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.
[b] Adjusted for log_2 total lipids.
[c] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

model.' The adjusted analysis of Model 3 revealed a significant interaction between categorized dioxin and family history of heart disease (Table 15-18(f): p=0.040). Stratified results of this interaction are shown in Appendix Table K-2-13. After deletion of this interaction from the model, the adjusted analyses did not show a significant relationship between dioxin and continuous diastolic blood pressure (Table 15-18(f): p>0.26 for all adjusted analyses). Lifetime cigarette smoking history, current cigarette smoking, total cholesterol, body fat, use of blood pressure medication, and diabetic class also were accounted for in the final adjusted model.

The unadjusted analyses of Models 4, 5, and 6 revealed highly significant direct associations between diastolic blood pressure in its continuous form and current dioxin (Table 15-18(g): p=0.005, p=0.001, and p=0.020 respectively). In Model 4, the unadjusted mean diastolic blood pressures in the low, medium, and high current dioxin categories increased with increasing levels of current dioxin (low, 71.67 mm Hg; medium, 71.29 mm Hg; high, 73.30 mm Hg). Similarly for Model 5, the unadjusted mean diastolic blood pressure levels were 71.29, 71.40, and 73.58 mm Hg for the low, medium, and high current dioxin categories, and for Model 6 they were 71.63, 71.43, and 73.24 mm Hg for the low, medium, and high current dioxin categories. The adjusted analyses for Models 4, 5, and 6 did not show any significant relationships between mean diastolic blood pressure in its continuous form and current dioxin (Table 15-18(h): p>0.20). The final adjusted models for Models 4, 5, and 6 each contained the covariates age, race, occupation, current cigarette smoking, total cholesterol, body fat, diabetic class, and use of blood pressure medication. After excluding the covariates occupation, total cholesterol, body fat, and diabetic class, the adjusted analyses for Models 4, 5, and 6 displayed significant and marginally significant direct associations between current dioxin and diastolic blood pressure in its continuous form (Appendix Table K-3-14(c): p=0.020, p=0.005, and p=0.070 respectively).

Diastolic Blood Pressure (Discrete)

Diastolic blood pressure, when categorized as normal (≤90 mm Hg) or abnormal (>90 mm Hg), did not reveal a significant group difference in the unadjusted or adjusted Model 1 analyses (Table 15-19(a,b): p>0.17 for unadjusted and adjusted analyses). The adjusted analysis accounted for personality type, lifetime cigarette smoking history, body fat, total cholesterol, and use of blood pressure medication.

Model 2 did not show a significant association between initial dioxin and discretized diastolic blood pressure in the unadjusted or adjusted analyses (Table 15-19(c,d): p>0.34). Model 3 also showed no relationship between dioxin and diastolic blood pressure for the unadjusted analyses (Table 15-19(e): p>0.32 for all unadjusted contrasts). A highly significant interaction between categorized dioxin and family history of heart disease was revealed in the adjusted Model 3 analysis (Table 15-19(f): p=0.009). For further investigation of this interaction, the analysis stratified by family history of heart disease is presented in Appendix Table K-2-14. The stratified analyses did not find any significant associations between current dioxin and diastolic blood pressure in its discrete form. Lifetime cigarette smoking history, body fat, personality type, and use of blood pressure medication also were significant in the final model.

Table 15-19.
Analysis of Diastolic Blood Pressure
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***939***	***2.8***	***0.85 (0.52,1.40)***	***0.601***
	Comparison	***1,262***	***3.2***		
Officer	Ranch Hand	360	3.1	1.00 (0.46,2.21)	0.999
	Comparison	492	3.0		
Enlisted Flyer	Ranch Hand	160	3.8	1.54 (0.46,5.12)	0.694
	Comparison	202	2.5		
Enlisted Groundcrew	Ranch Hand	419	2.1	0.57 (0.26,1.26)	0.225
	Comparison	568	3.7		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***0.85 (0.51,1.40)***	***0.516***	PERS (p=0.112) PACKYR (p=0.001) BFAT (p=0.004) CHOL (p=0.022) BPMED (p=0.064)
Officer	1.02 (0.46,2.26)	0.963	
Enlisted Flyer	1.41 (0.42,4.78)	0.581	
Enlisted Groundcrew	0.58 (0.26,1.28)	0.177	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 15-19. (Continued)
Analysis of Diastolic Blood Pressure
(Discrete)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	169	1.2	1.19 (0.83,1.70)	0.343
Medium	172	3.5		
High	172	4.7		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
513	1.17 (0.82,1.67)	0.406	PACKYR (p=0.110)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 15-19. (Continued)
Analysis of Diastolic Blood Pressure
(Discrete)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,046	3.1		
Background RH	370	2.4	0.87 (0.41,1.86)	0.721
Low RH	254	2.0	0.62 (0.24,1.61)	0.328
High RH	259	4.2	1.28 (0.63,2.60)	0.490
Low plus High RH	513	3.1	0.96 (0.52,1.77)	0.896

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	**n**	**Adj. Relative Risk (95% C.I.)[ac]**	**p-Value**	**Covariate Remarks**
Comparison	1,034			DXCAT*HRTDIS (p=0.009) PACKYR (p=0.009) BFAT (p=0.016) PERS (p=0.047) BPMED (p=0.037)
Background RH	364	****	****	
Low RH	248	****	****	
High RH	256	****	****	
Low plus High RH	504	****	****	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

**** Categorized dioxin-by-covariate interaction ($p \leq 0.01$); adjusted relative risk, confidence interval, and p-value not presented; refer to Appendix Table K-2-14 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 15-19. (Continued)
Analysis of Diastolic Blood Pressure
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	2.4 (292)	1.7 (294)	4.4 (297)	1.21 (0.94,1.57)	0.154
5	2.0 (297)	1.7 (291)	4.7 (295)	1.18 (0.94,1.49)	0.167
6[c]	2.0 (296)	1.7 (291)	4.7 (295)	1.22 (0.95,1.56)	0.125

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	869	1.25 (0.87,1.79)	0.219	AGE (p=0.069) OCC (p=0.126) PACKYR (p=0.036) HDL (p=0.141) BPMED (p=0.019)
5	869	1.20 (0.87,1.65)	0.255	AGE (p=0.067) OCC (p=0.135) PACKYR (p=0.032) HDL (p=0.146) BPMED (p=0.020)
6[d]	868	1.26 (0.89,1.78)	0.176	AGE (p=0.076) OCC (p=0.133) PACKYR (p=0.048) HDL (p=0.126) BPMED (p=0.016)

[a] Model 4: Log_2 (lipid-adjusted (current dioxin + 1).
Model 5: Log_2 (whole-weight (current dioxin + 1).
Model 6: Log_2 (whole-weight (current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

The unadjusted and adjusted analyses for Models 4 through 6 did not reveal any significant relationships between the prevalence of abnormally high diastolic blood pressure and current dioxin in Ranch Hands (Table 15-19(g,h): $p>0.12$ for unadjusted and adjusted analyses). The final adjusted models for Models 4, 5, and 6 each contained age, occupation, lifetime cigarette smoking history, HDL cholesterol, and use of blood pressure medication.

Funduscopic Examination

The unadjusted and adjusted analyses of funduscopic examination for Model 1 did not show any significant overall difference between Ranch Hands and Comparisons (Table 15-20(a,b): $p=0.103$ and $p=0.116$ respectively). However, stratifying the analyses by occupation revealed marginally significant positive associations between group and the funduscopic examination results for enlisted flyers (Table 15-20(a,b): $p=0.069$, Est. RR=2.19 and $p=0.072$, Adj. RR=2.06). In the enlisted flyer stratum, 11.3 percent of Ranch Hands had an abnormal funduscopic examination result as compared to 5.5 percent of Comparisons. The final model was adjusted for age, occupation, lifetime cigarette smoking history, current cigarette smoking, and family history of heart disease.

The Model 2 unadjusted analysis did not detect a significant relationship between initial dioxin and funduscopic exam results (Table 15-20(c): $p=0.193$). A significant initial dioxin-by-race interaction was revealed in the adjusted analysis (Table 15-20(d): $p=0.014$). Stratified results of the initial dioxin-by-race interaction are shown in Appendix Table K-2-15. After removal of the interaction, the adjusted analysis of Model 2 did not show a significant association between the funduscopic examination results and initial dioxin (Table 15-20(d): $p=0.624$). In addition to the initial dioxin-by-race interaction, the final model for Model 2 contained the covariates occupation, current cigarette smoking, body fat, and diabetic class. In Model 3, the unadjusted analysis revealed a marginally significant difference in the prevalence of abnormal funduscopic examination results between Ranch Hands in the high initial dioxin category and Comparisons (Table 15-20(e): $p=0.061$, Est. RR=1.64). The percentage of Ranch Hands with abnormal funduscopic examinations in the high initial dioxin category was 8.9 percent as compared to 5.3 percent in the Comparison category. After adjusting the model for covariates, the Model 3 analysis did not show any significant associations (Table 15-20(f): $p>0.12$ for all adjusted analyses). However, after excluding occupation from the final model, a significant difference between Ranch Hands in the high initial dioxin category and Comparisons was revealed (Appendix Table K-3-16(b): $p=0.021$, Adj. RR=1.87). In addition to occupation, age, race, lifetime cigarette smoking history, and family history of heart disease were all significant in the final adjusted model.

The unadjusted analyses of the funduscopic examination results detected a marginally significant positive association with current dioxin in Model 4 and a significant positive association with current dioxin in Model 5 (Table 15-20(g): $p=0.076$, Est. RR=1.17 and $p=0.045$, Est. RR=1.17 respectively). For Model 4, the percentages of Ranch Hands with abnormal funduscopic examinations were 5.5, 6.2, and 9.2 percent for the low, medium, and high lipid-adjusted current dioxin categories respectively. Similarly, the percentages for Models 5 and 6 were 6.1, 5.5, and 9.2 percent for the low, medium, and high whole-weight current dioxin categories. After adjustment for covariates, Model 4 continued to display a marginally significant positive relationship, and Models 5 and 6 displayed significant positive

Table 15-20.
Analysis of Funduscopic Examination

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	Group	n	Percent Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*933*	*7.3*	*1.35 (0.96,1.91)*	*0.103*
	Comparison	*1,257*	*5.5*		
Officer	Ranch Hand	358	6.1	1.46 (0.79,2.70)	0.289
	Comparison	490	4.3		
Enlisted Flyer	Ranch Hand	159	11.3	2.19 (1.00,4.79)	0.069
	Comparison	200	5.5		
Enlisted Groundcrew	Ranch Hand	416	6.7	1.03 (0.62,1.72)	0.999
	Comparison	567	6.5		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	*1.33 (0.93,1.89)*	*0.116*	AGE ($p<0.001$) OCC ($p=0.007$) PACKYR ($p=0.065$) CSMOK ($p=0.133$) HRTDIS ($p=0.007$)
Officer	1.45 (0.78,2.70)	0.237	
Enlisted Flyer	2.06 (0.94,4.53)	0.072	
Enlisted Groundcrew	1.01 (0.60,1.71)	0.961	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 15-20. (Continued)
Analysis of Funduscopic Examination

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	167	5.4	1.17 (0.93,1.48)	0.193
Medium	171	7.6		
High	171	9.4		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
509	1.07 (0.81,1.43)**	0.624**	INIT*RACE (p=0.014) OCC (p=0.103) CSMOK (p=0.113) BFAT (p=0.056) DIAB (p=0.029)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-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; refer to Appendix Table K-2-15 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 15-20. (Continued)
Analysis of Funduscopic Examination

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,043	5.3		
Background RH	369	6.2	1.31 (0.79,2.18)	0.298
Low RH	251	6.0	1.05 (0.58,1.89)	0.883
High RH	258	8.9	1.64 (0.98,2.74)	0.061
Low plus High RH	509	7.5	1.34 (0.87,2.06)	0.190

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,032			AGE ($p<0.001$) RACE ($p=0.062$) OCC ($p=0.024$) PACKYR ($p=0.048$) HRTDIS ($p=0.001$)
Background RH	363	1.45 (0.85,2.46)	0.171	
Low RH	246	1.00 (0.54,1.83)	0.987	
High RH	255	1.54 (0.89,2.67)	0.121	
Low plus High RH	501	1.25 (0.80,1.96)	0.321	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 15-20. (Continued)
Analysis of Funduscopic Examination

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	5.5 (291)	6.2 (292)	9.2 (295)	1.17 (0.99,1.39)	0.076
5	6.1 (296)	5.5 (289)	9.2 (293)	1.17 (1.00,1.37)	0.045
6[c]	6.1 (295)	5.5 (289)	9.2 (293)	1.14 (0.96,1.34)	0.132

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	863	1.21 (1.00,1.46)	0.054	AGE (p=0.044) PACKYR (p=0.036) HRTDIS (p=0.018) DIAB (p=0.117)
5	863	1.19 (1.01,1.42)	0.042	AGE (p=0.042) PACKYR (p=0.038) HRTDIS (p=0.019) DIAB (p=0.139)
6[d]	863	1.21 (1.01,1.45)	0.037	AGE (p=0.012) PACKYR (p=0.049) HRTDIS (p=0.032)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

relationships between current dioxin and funduscopic examination (Table 15-20(h): p=0.054, Adj. RR=1.21; p=0.042, Adj. RR=1.19; and p=0.037, Adj. RR=1.21). Models 4 and 5 accounted for age, lifetime cigarette smoking history, family history of heart disease, and diabetic class in the adjusted final model. Model 6 accounted for age, lifetime cigarette smoking history, and family history of heart disease.

Carotid Bruits

The unadjusted and adjusted Model 1 analyses of carotid bruits did not reveal any significant differences in the prevalence of carotid bruits between Ranch Hands and Comparisons (Table 15-21(a,b): p>0.17 for unadjusted and adjusted analyses). The final adjusted model contained the covariates age, race, and lifetime alcohol history.

Models 2 and 3 did not show any significant results for the unadjusted analyses (Table 15-21(c,e): p>0.36). The adjusted Model 2 analysis revealed significant interactions between initial dioxin and lifetime cigarette smoking history and between initial dioxin and family history of heart disease (Table 15-21(d): p=0.001 and p=0.039 respectively). Stratified results of these interactions are displayed in Appendix Table K-2-16. The adjusted Model 2 analysis also accounted for the covariates age, occupation, and lifetime alcohol history. The results of the analysis of the adjusted model without the interactions were nonsignificant (Table 15-21(d): p=0.146). The adjusted Model 3 analysis revealed a significant categorized dioxin-by-lifetime alcohol history interaction (Table 15-21(f): p=0.023). The covariates age and race also were significant in the final adjusted model. Examination of the categorized dioxin-by-lifetime alcohol history interaction is provided in Appendix Table K-2-16. Removal of the interaction from the model did not reveal any significant results (Table 15-21(f): p>0.32).

The unadjusted analyses for Models 4 and 5 did not show any significant relationship between current dioxin and carotid bruits (Table 15-21(g): p>0.18). However, the unadjusted analysis of Model 6 did show a marginally significant negative association between current dioxin and the prevalence of carotid bruits (Table 15-21(g): p=0.087, Est. RR=0.76). The percentage of Ranch Hands with carotid bruits decreased with increasing levels of dioxin for Model 6 (low, 2.0%; medium, 2.1%; high, 1.4%). The adjusted analysis for Model 4 revealed a highly significant interaction between current dioxin and total cholesterol (Table 15-21(h): p=0.006), and the adjusted analyses for Models 5 and 6 revealed significant interactions between current dioxin and family history of heart disease (p=0.005 and p=0.004 respectively). Stratified results of these interactions are presented in Appendix Table K-2-16. Analyses using Models 5 and 6 indicated a significant relative risk less than one for participants with no family history of heart disease (p≤0.002). In addition to the interactions with current dioxin, Model 4 was adjusted for age; Model 5 was adjusted for age and lifetime alcohol history; and Model 6 was adjusted for age, lifetime cigarette smoking history, lifetime alcohol history, and total cholesterol.

Radial Pulses

The unadjusted analyses performed in Models 1 through 6 did not detect any significant associations between radial pulses and group or dioxin (Table 15-22(a-h): p>0.12). Due to

Table 15-21.
Analysis of Carotid Bruits

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***940***	***1.8***	***1.43 (0.72,2.85)***	***0.394***
	Comparison	***1,261***	***1.3***		
Officer	Ranch Hand	361	1.4	0.75 (0.25,2.27)	0.817
	Comparison	492	1.8		
Enlisted Flyer	Ranch Hand	160	2.5	2.56 (0.46,14.18)	0.482
	Comparison	202	1.0		
Enlisted Groundcrew	Ranch Hand	419	1.9	2.19 (0.71,6.74)	0.264
	Comparison	567	0.9		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.52 (0.75,3.09)***	***0.245***	AGE (p<0.001) RACE (p=0.108) DRKYR (p=0.119)
Officer	0.84 (0.27,2.60)	0.759	
Enlisted Flyer	2.57 (0.46,14.31)	0.282	
Enlisted Groundcrew	2.22 (0.71,6.98)	0.172	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 15-21. (Continued)
Analysis of Carotid Bruits

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	169	3.0	0.79 (0.45,1.37)	0.382
Medium	172	1.2		
High	172	1.2		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
492	0.64 (0.34,1.21)**	0.146**	INIT*PACKYR (p=0.001) INIT*HRTDIS (p=0.039) AGE (p=0.003) OCC (p=0.029) DRKYR (p=0.027)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interactions ($p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table K-2-16 for further analysis of these interactions.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 15-21. (Continued)
Analysis of Carotid Bruits

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,045	1.4		
Background RH	371	1.9	1.30 (0.52,3.26)	0.569
Low RH	254	2.4	1.56 (0.60,4.10)	0.363
High RH	259	1.2	0.79 (0.23,2.79)	0.719
Low plus High RH	513	1.8	1.18 (0.51,2.75)	0.694

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	**n**	**Adj. Relative Risk (95% C.I.)[ac]**	**p-Value**	**Covariate Remarks**
Comparison	1,028			DXCAT*DRKYR (p=0.023) AGE (p<0.001) RACE (p=0.114)
Background RH	364	1.23 (0.48,3.14)**	0.667**	
Low RH	248	1.65 (0.61,4.43)**	0.321**	
High RH	252	1.13 (0.32,4.05)**	0.852**	
Low plus High RH	500	1.43 (0.60,3.39)**	0.417**	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-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; refer to Appendix Table K-2-16 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 15-21. (Continued)
Analysis of Carotid Bruits

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	2.0 (293)	2.0 (294)	1.3 (297)	0.78 (0.54,1.13)	0.183
5	2.0 (298)	2.1 (291)	1.4 (295)	0.84 (0.63,1.11)	0.223
6[c]	2.0 (297)	2.1 (291)	1.4 (295)	0.76 (0.56,1.03)	0.087

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	884	****	****	CURR*CHOL (p=0.006) AGE (p=0.004)
5	851	****	****	CURR*HRTDIS (p=0.005) AGE (p=0.007) DRKYR (p=0.056)
6[d]	850	****	****	CURR*HRTDIS (p=0.004) AGE (p=0.004) PACKYR (p=0.134) DRKYR (p=0.081) CHOL (p=0.076)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

**** Log_2 (current dioxin + 1)-by-covariate interaction ($p \leq 0.01$); adjusted relative risk, confidence interval, and p-value not presented; refer to Appendix Table K-2-16 for further analysis of this interaction.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 15-22.
Analysis of Radial Pulses

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***940***	***0.4***	***1.07 (0.29,4.01)***	***0.999***
	Comparison	***1,262***	***0.4***		
Officer	Ranch Hand	361	0.6	2.74 (0.25,30.28)	0.787
	Comparison	492	0.2		
Enlisted Flyer	Ranch Hand	160	0.0	--	--
	Comparison	202	0.0		
Enlisted Groundcrew	Ranch Hand	419	0.5	0.68 (0.12,3.71)	0.969
	Comparison	568	0.7		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks**
All	--	--	
Officer	--	--	
Enlisted Flyer	--	--	
Enlisted Groundcrew	--	--	

--: Estimated relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities; adjusted analyses not performed due to the sparse number of abnormalities.

Table 15-22. (Continued)
Analysis of Radial Pulses

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	169	1.2	0.34 (0.06,1.98)	0.124
Medium	172	0.0		
High	172	0.0		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
--	--	--	

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

--: Adjusted analyses not performed due to the sparse number of abnormalities.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 15-22. (Continued)
Analysis of Radial Pulses

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,046	0.5		
Background RH	371	0.5	1.00 (0.19,5.28)	0.995
Low RH	254	0.8	1.73 (0.33,9.06)	0.515
High RH	259	0.0	--	--
Low plus High RH	513	0.4	0.88 (0.17,4.60)	0.881

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	**n**	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks**
Comparison	--			
Background RH	--	--	--	
Low RH	--	--	--	
High RH	--	--	--	
Low plus High RH	--	--	--	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

--: Estimated relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities; adjusted analyses not performed due to the sparse number of abnormalities.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 15-22. (Continued)
Analysis of Radial Pulses

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	0.7 (293)	0.7 (294)	0.0 (297)	0.55 (0.25,1.20)	0.122
5	0.7 (298)	0.7 (291)	0.0 (295)	0.70 (0.42,1.16)	0.192
6[c]	0.7 (297)	0.7 (291)	0.0 (295)	0.65 (0.38,1.12)	0.150

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	884	0.55 (0.25,1.20)	0.122	
5	884	0.70 (0.42,1.16)	0.192	
6[c]	883	0.65 (0.38,1.12)	0.150	

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

the sparse number of individuals with abnormal radial pulses for Models 1 through 3 (Models 1 and 3: 4 Ranch Hands and 5 Comparisons, Model 2: 2 Ranch Hands), the adjusted analyses for these models are not presented. The adjusted analyses of Models 4 through 6 did not retain any significant covariates; therefore, the adjusted results are the same as the unadjusted results for Models 4 through 6.

Femoral Pulses

The unadjusted and adjusted Model 1 analyses of femoral pulses did not reveal any significant group differences (Table 15-23(a,b): $p>0.17$ for unadjusted and adjusted analyses). The adjusted analysis accounted for current cigarette smoking, total cholesterol, HDL cholesterol, body fat, and diabetic class.

Model 2 showed a marginally significant negative association between initial dioxin and the prevalence of abnormal femoral pulses in the unadjusted analysis (Table 15-23(c): $p=0.076$, Est. RR=0.59). The percentages of individuals with abnormal femoral pulses were 3.6, 1.2, and 0.6 percent in the low, medium, and high initial dioxin categories. The adjusted analysis for Model 2 also revealed a significant inverse relationship between initial dioxin and femoral pulses (Table 15-23(d): $p=0.020$, Adj. RR=0.46). The covariates current cigarette smoking, body fat, and personality type were significant in the final adjusted model. The unadjusted and adjusted analyses of femoral pulses for Model 3 revealed significant differences in the prevalence of abnormal femoral pulses between Ranch Hands in the low initial dioxin category and Comparisons and between Ranch Hands in the low plus high dioxin category and Comparisons (Table 15-23(e,f): $p\leq0.035$, RR>3.4). Ranch Hands showed higher percentages of abnormal femoral pulses than the Comparisons. The percentage of Comparisons with abnormal femoral pulses was 0.5 percent while the corresponding percentage was 2.8 percent for Ranch Hands in the low dioxin category and 1.8 percent for Ranch Hands in the low plus high dioxin category. Current cigarette smoking and diabetic class were significant in the final adjusted Model 3 analysis.

Femoral pulses were not found to be significantly associated with current dioxin in the unadjusted or adjusted analyses of Models 4, 5, and 6 (Table 15-23(g,h): $p>0.68$ for unadjusted and adjusted analyses). The final adjusted models for Models 4 and 5 accounted for current cigarette smoking, personality type, and diabetic class. Model 6 accounted for current cigarette smoking and diabetic class in the final adjusted model.

Popliteal Pulses

Analysis of popliteal pulses revealed a significant overall difference between Ranch Hands and Comparisons in the unadjusted analyses for Model 1 (Table 15-24(a): $p=0.035$, Est. RR=2.34). In the unadjusted analysis, 2.0 percent of the Ranch Hands had abnormal popliteal pulses as compared to 0.9 percent of the Comparisons. Similarly, the adjusted analysis for Model 1 found a significant group difference in the prevalence of abnormal popliteal pulses (Table 15-24(b): $p=0.022$, Adj. RR=2.47). Stratifying the adjusted analysis by occupation displayed a marginally significant difference between Ranch Hands and Comparisons for the enlisted groundcrew (Table 15-24(b): $p=0.070$, Adj. RR=3.24). Age,

Table 15-23.
Analysis of Femoral Pulses

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***940***	***1.2***	***2.12 (0.82,5.50)***	***0.178***
	Comparison	***1,262***	***0.6***		
Officer	Ranch Hand	361	1.1	2.75 (0.50,15.07)	0.426
	Comparison	492	0.4		
Enlisted Flyer	Ranch Hand	160	1.3	0.84 (0.14,5.09)	0.999
	Comparison	202	1.5		
Enlisted Groundcrew	Ranch Hand	419	1.2	3.42 (0.66,17.70)	0.241
	Comparison	568	0.4		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.90 (0.71,5.08)***	***0.196***	CSMOK (p=0.013) CHOL (p=0.088) HDL (p=0.075) BFAT (p=0.015) DIAB (p<0.001)
Officer	2.40 (0.41,14.06)	0.333	
Enlisted Flyer	0.79 (0.12,5.01)	0.803	
Enlisted Groundcrew	3.16 (0.58,17.23)	0.183	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 15-23. (Continued)
Analysis of Femoral Pulses

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	169	3.6	0.59 (0.31,1.13)	0.076
Medium	172	1.2		
High	172	0.6		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
512	0.46 (0.22,0.98)	0.020	CSMOK (p=0.006) BFAT (p=0.042) PERS (p=0.022)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 15-23. (Continued)
Analysis of Femoral Pulses

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,046	0.5		
Background RH	371	0.3	0.57 (0.07,4.93)	0.609
Low RH	254	2.8	5.44 (1.70,17.40)	0.004
High RH	259	0.8	1.54 (0.29,8.12)	0.613
Low plus High RH	513	1.8	3.52 (1.16,10.70)	0.026

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,043			CSMOK (p=0.001) DIAB (p=0.022)
Background RH	370	0.61 (0.07,5.45)	0.660	
Low RH	254	5.89 (1.73,20.00)	0.005	
High RH	259	1.37 (0.25,7.62)	0.716	
Low plus High RH	513	3.46 (1.09,11.00)	0.035	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin $\leq$ 10 ppt.
Background (Ranch Hand): Current Dioxin $\leq$ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin $\leq$ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 15-23. (Continued)
Analysis of Femoral Pulses

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	0.3 (293)	2.4 (294)	0.7 (297)	1.04 (0.68,1.58)	0.869
5	0.3 (298)	2.4 (291)	0.7 (295)	1.08 (0.75,1.56)	0.688
6[c]	0.3 (297)	2.4 (291)	0.7 (295)	1.02 (0.69,1.52)	0.915

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	882	1.00 (0.67,1.49)	0.996	CSMOK (p=0.013) PERS (p=0.039) DIAB (p=0.019)
5	882	1.03 (0.74,1.42)	0.877	CSMOK (p=0.013) PERS (p=0.038) DIAB (p=0.021)
6[d]	882	1.00 (0.69,1.44)	0.988	CSMOK (p=0.018) DIAB (p=0.037)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 15-24.
Analysis of Popliteal Pulses

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***940***	***2.0***	***2.34 (1.11,4.95)***	***0.035***
	Comparison	***1,260***	***0.9***		
Officer	Ranch Hand	361	1.9	2.41 (0.70,8.29)	0.259
	Comparison	491	0.8		
Enlisted Flyer	Ranch Hand	160	2.5	1.69 (0.37,7.67)	0.760
	Comparison	201	1.5		
Enlisted Groundcrew	Ranch Hand	419	1.9	2.75 (0.82,9.18)	0.157
	Comparison	568	0.7		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks**[a]
All	***2.47 (1.12,5.47)***	***0.022***	AGE (p=0.001)
Officer	2.48 (0.64,9.66)	0.191	CSMOK (p<0.001)
Enlisted Flyer	1.63 (0.34,7.79)	0.542	CHOL (p=0.135)
Enlisted Groundcrew	3.24 (0.91,11.50)	0.070	DIAB (p<0.001)

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 15-24. (Continued)
Analysis of Popliteal Pulses

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	169	3.6	0.85 (0.56,1.29)	0.430
Medium	172	3.5		
High	172	1.7		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
513	0.83 (0.48,1.44)	0.502	AGE (p=0.002) CSMOK (p<0.001) BFAT (p=0.023) DIAB (p=0.065)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 15-24. (Continued)
Analysis of Popliteal Pulses

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,045	1.1		
Background RH	371	0.5	0.51 (0.11,2.31)	0.378
Low RH	254	2.8	2.48 (0.95,6.52)	0.064
High RH	259	3.1	2.94 (1.15,7.50)	0.024
Low plus High RH	513	2.9	2.71 (1.22,6.00)	0.014

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	**n**	**Adj. Relative Risk (95% C.I.)[ac]**	**p-Value**	**Covariate Remarks**
Comparison	1,042			AGE (p=0.002) CSMOK (p<0.001) BFAT (p=0.084) DIAB (p=0.001)
Background RH	370	0.46 (0.09,2.30)	0.345	
Low RH	254	2.63 (0.93,7.46)	0.069	
High RH	259	3.54 (1.27,9.87)	0.016	
Low plus High RH	513	3.04 (1.27,7.26)	0.012	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 15-24. (Continued)
Analysis of Popliteal Pulses

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	0.7 (293)	2.4 (294)	2.7 (297)	1.17 (0.86,1.60)	0.330
5	0.3 (298)	2.7 (291)	2.7 (295)	1.24 (0.94,1.64)	0.128
6[c]	0.3 (297)	2.7 (291)	2.7 (295)	1.11 (0.81,1.50)	0.521

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	883	1.30 (0.92,1.85)	0.145	AGE (p=0.001) CSMOK (p<0.001) DIAB (p=0.013)
5	883	****	****	CURR*OCC (p=0.007) AGE (p=0.001) CSMOK (p=0.001) BFAT (p=0.144) DIAB (p=0.061)
6[d]	882	1.22 (0.85,1.77)**	0.277**	CURR*OCC (p=0.014) AGE (p<0.001) CSMOK (p=0.001) BFAT (p=0.150) DIAB (p=0.075)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-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; refer to Appendix Table K-2-17 for further analysis of this interaction.

**** Log_2 (current dioxin + 1)-by-covariate interaction ($p \leq 0.01$); adjusted relative risk, confidence interval, and p-value not presented; refer to Appendix Table K-2-17 for further analysis of this interaction.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

current cigarette smoking, total cholesterol, and diabetic class were significant in the final adjusted model.

The unadjusted and adjusted analyses for Model 2 did not show a significant association between initial dioxin and popliteal pulses (Table 15-24(c,d): $p \geq 0.43$). Age, current cigarette smoking, body fat, and diabetic class were significant in the final adjusted model. Both the unadjusted and adjusted Model 3 analyses revealed marginally significant and significant associations between the prevalence of abnormal popliteal pulses and categorized dioxin (Table 15-24(e,f)): low Ranch Hands versus Comparisons (p=0.064, Est. RR=2.48; p=0.069, Adj. RR=2.63), high Ranch Hands versus Comparisons (p=0.024, Est. RR=2.94; p=0.016, Adj. RR=3.54), and low plus high Ranch Hands versus Comparisons (p=0.014, Est. RR=2.71; p=0.012, Adj. RR=3.04). The percentage of individuals with abnormal popliteal pulses in the Comparison, background Ranch Hand, low Ranch Hand, high Ranch Hand, and low plus high Ranch Hands categories were 1.1, 0.5, 2.8, 3.1, and 2.9 percent respectively. Age, current cigarette smoking, body fat, and diabetic class were accounted for in the adjusted analysis.

Models 4 through 6 did not reveal any significant associations between popliteal pulses and current dioxin in the unadjusted analyses (Table 15-24(g): $p > 0.12$). The results of the adjusted Model 4 analysis also were nonsignificant (Table 15-24(h): p=0.145). Age, current cigarette smoking, and diabetic class were significant in the adjusted Model 4 analysis. However, after removing diabetic class from the model, a significant association between current dioxin and popliteal pulses was revealed in Model 4 (Appendix Table K-3-19(c): p=0.049, Adj. RR=1.42). Adjusting for covariates in Models 5 and 6 revealed significant interactions between current dioxin and occupation (Table 15-24(h): p=0.007 and p=0.014 respectively). Stratified results of these interactions are presented in Appendix Table K-2-17. In the Model 5 and 6 analyses, the officers exhibited a significant relative risk greater than one (p=0.003, Adj. RR=5.53 and p=0.010, Adj. RR=4.86 respectively). After removing the interaction from the Model 6 adjusted analysis, the results were nonsignificant (Table 15-24(h): p=0.277). Models 5 and 6 were adjusted for age, current cigarette smoking, body fat, and diabetic class in addition to the current dioxin-by-occupation interaction.

Dorsalis Pedis Pulses

The analysis of dorsalis pedis pulses did not reveal a significant overall difference between Ranch Hands and Comparisons for Model 1 in the unadjusted or adjusted analyses (Table 15-25(a,b): $p > 0.17$). However, stratifying the Model 1 adjusted analysis by occupation displayed a marginally significant association between group and dorsalis pedis pulses for the enlisted groundcrew (Table 15-25(b): p=0.091, Adj. RR=1.53). In the enlisted groundcrew stratum, 9.3 percent of Ranch Hands had abnormal dorsalis pedis pulses as compared to 6.3 percent of Comparisons.

The unadjusted analyses for Models 2 and 3 did not show a significant relationship between dorsalis pedis pulses and initial dioxin (Table 15-25(c,e): $p > 0.23$ for all unadjusted analyses). In Model 2, a significant interaction between initial dioxin and lifetime cigarette smoking history was revealed after adjusting for covariates (Table 15-25(d): p=0.047). Age, occupation, and diabetic class also were significant in the final adjusted model. After

Table 15-25.
Analysis of Dorsalis Pedis Pulses

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***938***	***8.6***	***1.26 (0.92,1.72)***	***0.175***
	Comparison	***1,260***	***7.0***		
Officer	Ranch Hand	360	8.1	1.22 (0.72,2.04)	0.544
	Comparison	491	6.7		
Enlisted Flyer	Ranch Hand	160	8.1	0.85 (0.41,1.77)	0.799
	Comparison	201	9.5		
Enlisted Groundcrew	Ranch Hand	418	9.3	1.52 (0.95,2.44)	0.103
	Comparison	568	6.3		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.20 (0.87,1.66)***	***0.279***	AGE (p<0.001)
Officer	1.12 (0.66,1.91)	0.664	PACKYR (p<0.001) HDL (p=0.040)
Enlisted Flyer	0.76 (0.35,1.65)	0.492	BFAT (p=0.002)
Enlisted Groundcrew	1.53 (0.93,2.50)	0.091	DIAB (p=0.001)

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 15-25. (Continued)
Analysis of Dorsalis Pedis Pulses

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	169	7.7	1.02 (0.81,1.28)	0.892
Medium	172	11.0		
High	171	7.6		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
	Analysis Results for Log_2 (Initial Dioxin)[c]		
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
512	0.91 (0.69,1.20)**	0.488**	INIT*PACKYR (p=0.047) AGE (p=0.074) OCC (p=0.011) DIAB (p=0.001)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-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; refer to Appendix Table K-2-18 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 15-25. (Continued)
Analysis of Dorsalis Pedis Pulses

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,045	7.7		
Background RH	370	8.9	1.14 (0.74,1.76)	0.540
Low RH	254	7.9	0.99 (0.59,1.66)	0.968
High RH	258	9.7	1.33 (0.83,2.15)	0.238
Low plus High RH	512	8.8	1.15 (0.78,1.70)	0.467

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	**n**	**Adj. Relative Risk (95% C.I.)[ac]**	**p-Value**	**Covariate Remarks**
Comparison	1,042			DXCAT*AGE (p=0.038) PACKYR (p=0.012) CSMOK (p=0.039) DIAB (p=0.001)
Background RH	368	1.12 (0.72,1.74)**	0.613**	
Low RH	254	0.91 (0.54,1.54)**	0.728**	
High RH	258	1.39 (0.85,2.27)**	0.194**	
Low plus High RH	512	1.13 (0.76,1.67)**	0.559**	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-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; refer to Appendix Table K-2-18 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 15-25. (Continued)
Analysis of Dorsalis Pedis Pulses

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	8.5 (293)	7.8 (293)	10.1 (296)	1.01 (0.86,1.18)	0.905
5	9.1 (297)	7.6 (291)	9.9 (294)	1.01 (0.88,1.16)	0.895
6[c]	9.1 (296)	7.6 (291)	9.9 (294)	1.00 (0.87,1.16)	0.964

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	880	1.11 (0.93,1.33)	0.245	AGE (p=0.003) PACKYR (p=0.001) CHOL (p=0.112) BFAT (p=0.027) DIAB (p=0.003)
5	880	1.10 (0.94,1.28)	0.237	AGE (p=0.003) PACKYR (p=0.001) CHOL (p=0.093) BFAT (p=0.026) DIAB (p=0.003)
6[d]	866	1.10 (0.93,1.29)	0.264	AGE (p=0.002) PACKYR (p=0.003) HDL (p=0.138) BFAT (p=0.018) DIAB (p=0.004)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

removing the initial dioxin-by-lifetime cigarette smoking history interaction from the adjusted model, no significant relationship between dorsalis pedis pulses and initial dioxin was detected (Table 15-25(d): p=0.488). Stratified results of the interaction are presented in Appendix Table K-2-18. The Model 3 adjusted analysis displayed a significant categorized dioxin-by-age interaction (Table 15-25(f): p=0.038) as well as the covariates lifetime cigarette smoking history, current cigarette smoking, and diabetic class. After deleting the interaction from the final model, the adjusted Model 3 analysis did not reveal a significant relationship between categorized dioxin and dorsalis pedis pulses (Table 15-25(f): p>0.19). Further investigation of the categorized dioxin-by-age interaction is presented in Appendix Table K-2-18.

Models 4 through 6 did not display any significant associations between dorsalis pedis pulses and current dioxin in the unadjusted or adjusted analyses (Table 15-25(g,h): p>0.23 for all analyses). The adjusted analyses for Models 4 and 5 accounted for the covariates age, lifetime cigarette smoking history, total cholesterol, body fat, and diabetic class. Model 6 accounted for age, lifetime cigarette smoking history, HDL cholesterol, body fat, and diabetic class in the final adjusted model.

Posterior Tibial Pulses

The unadjusted Model 1 analysis of posterior tibial pulses revealed a significant difference between Ranch Hands and Comparisons (Table 15-26(a): p=0.049, Est. RR=1.69). Abnormal posterior tibial pulses were noted in 3.8 percent of the Ranch Hands as compared to 2.3 percent of the Comparisons. After stratifying the unadjusted analysis by occupation, the Model 1 results displayed a marginally significant association between group and posterior tibial pulses for the enlisted groundcrew (Table 15-26(a): p=0.074, Est. RR=2.14). In the enlisted groundcrew stratum, Ranch Hands had 4.1 percent abnormal posterior tibial pulses as compared to 1.9 percent of Comparisons. Similarly, the adjusted analyses also revealed a marginally significant difference between Ranch Hands and Comparisons overall and for the enlisted groundcrew stratum (Table 15-26(b): p=0.070, Adj. RR=1.63 and p=0.073, Adj. RR=2.14 respectively). Model 1 accounted for age, race, current cigarette smoking, body fat, and diabetic class.

The unadjusted Model 2 analysis of posterior tibial pulses did not find a significant association with initial dioxin (Table 15-26(c): p=0.260). Adjustment for covariates in Model 2 revealed significant initial dioxin-by-occupation, initial dioxin-by-lifetime cigarette smoking history, and initial dioxin-by-family history of heart disease interactions (Table 15-26(d): p=0.011, p=0.001, and p=0.028 respectively). Age, current cigarette smoking, body fat, and diabetic class also were significant in the final adjusted model. The adjusted Model 2 analysis after removal of the interactions did not show a significant association between posterior tibial pulses and initial dioxin (Table 15-26(d): p=0.298). Stratification of each interaction is presented in Appendix Table K-2-19 for further examination. The unadjusted analysis of posterior tibial pulses for Model 3 revealed a significant difference in the prevalence of diminished posterior tibial pulses between Ranch Hands in the high dioxin category and Comparisons (Table 15-26(e): p=0.017, Est. RR=2.35) as well as low plus high Ranch Hands and Comparisons (Table 15-26(e): p=0.022, Est. RR=2.00). The percentage of individuals with abnormal posterior tibial pulses in the Comparison, high

Table 15-26.
Analysis of Posterior Tibial Pulses

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	Group	n	Percent Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***940***	***3.8***	***1.69 (1.03,2.78)***	***0.049***
	Comparison	***1,260***	***2.3***		
Officer	Ranch Hand	361	3.0	1.26 (0.55,2.88)	0.747
	Comparison	491	2.4		
Enlisted Flyer	Ranch Hand	160	5.0	1.71 (0.58,5.04)	0.477
	Comparison	201	3.0		
Enlisted Groundcrew	Ranch Hand	419	4.1	2.14 (0.99,4.62)	0.074
	Comparison	568	1.9		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	***1.63 (0.96,2.76)***	***0.070***	AGE (p<0.001) RACE (p=0.098) CSMOK (p<0.001) BFAT (p<0.001) DIAB (p<0.001)
Officer	1.18 (0.49,2.84)	0.718	
Enlisted Flyer	1.65 (0.53,5.13)	0.391	
Enlisted Groundcrew	2.14 (0.93,4.88)	0.073	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 15-26. (Continued)
Analysis of Posterior Tibial Pulses

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	169	5.3	0.82 (0.58,1.17)	0.260
Medium	172	5.8		
High	172	2.3		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
505	0.77 (0.46,1.28)**	0.298**	INIT*OCC (p=0.011) INIT*PACKYR (p=0.001) INIT*HRTDIS (p=0.028) AGE (p=0.007) CSMOK (p<0.001) BFAT (p=0.003) DIAB (p<0.001)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interactions ($p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table K-2-19 for further analysis of these interactions.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 15-26. (Continued)
Analysis of Posterior Tibial Pulses

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,045	2.3		
Background RH	371	2.7	1.10 (0.52,2.33)	0.812
Low RH	254	3.9	1.67 (0.78,3.57)	0.184
High RH	259	5.0	2.35 (1.16,4.76)	0.017
Low plus High RH	513	4.5	2.00 (1.10,3.61)	0.022

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,033			DXCAT*CSMOK (p=0.031) AGE (p<0.001) RACE (p=0.020) HDL (p=0.097) BFAT (p=0.003) DIAB (p=0.005)
Background RH	366	1.03 (0.47,2.29)**	0.937**	
Low RH	250	1.55 (0.69,3.48)**	0.285**	
High RH	254	2.36 (1.08,5.15)**	0.031**	
Low plus High RH	504	1.90 (1.00,3.62)**	0.050**	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-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; refer to Appendix Table K-2-19 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 15-26. (Continued)
Analysis of Posterior Tibial Pulses

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	2.4 (293)	4.4 (294)	4.4 (297)	1.01 (0.79,1.28)	0.949
5	2.3 (298)	4.8 (291)	4.1 (295)	1.05 (0.86,1.30)	0.610
6[c]	2.4 (297)	4.8 (291)	4.1 (295)	0.98 (0.79,1.23)	0.880

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	883	1.20 (0.93,1.57)	0.171	AGE (p<0.001) RACE (p=0.122) CSMOK (p=0.001) BFAT (p=0.005) DIAB (p=0.023)
5	883	1.23 (0.98,1.54)	0.072	AGE (p<0.001) RACE (p=0.112) CSMOK (p=0.001) BFAT (p=0.004) DIAB (p=0.029)
6[d]	882	1.17 (0.92,1.50)	0.207	AGE (p<0.001) RACE (p=0.098) CSMOK (p=0.001) BFAT (p=0.004) DIAB (p=0.041)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Ranch Hand, and low plus high Ranch Hand categories were 2.3, 5.0, and 4.5 percent. Adjusting the model for covariates revealed a significant interaction between categorized dioxin and current cigarette smoking (Table 15-26(f): p=0.031). The final model also accounted for age, race, HDL cholesterol, body fat, and diabetic class. The adjusted Model 3 analysis after removal of the dioxin-by-current cigarette smoking interaction showed significant differences in posterior tibial pulse abnormalities between Comparisons and Ranch Hands in the high and low plus high dioxin categories (Table 15-26(f): p=0.031, Adj. RR=2.36 and p=0.050, Adj. RR=1.90). Further investigation of the interaction with categorized dioxin is displayed in Appendix Table K-2-19.

The unadjusted analyses for Models 4 through 6 did not show any significant associations between current dioxin and posterior tibial pulses (Table 15-26(g): p>0.61 for all unadjusted analyses). The adjusted analyses for Models 4 and 6 did not find any significant relationships between posterior tibial pulses and current dioxin (Table 15-26(h): p>0.17). Model 5, however, revealed a marginally significant positive association between current dioxin and posterior tibial pulses (Table 15-26(h): p=0.072, Adj. RR=1.23). Age, race, current cigarette smoking, body fat, and diabetic class were significant covariates in Models 4, 5, and 6.

Leg Pulses

The unadjusted and adjusted analyses of all leg pulses did not detect a significant overall difference between Ranch Hands and Comparisons for Model 1 (Table 15-27(a,b): p>0.13). However, stratifying the unadjusted analysis by occupation revealed a marginally significant association between group and leg pulses for the enlisted groundcrew (Table 15-27(a): p=0.083, Est. RR=1.51). Among the enlisted groundcrew, 10.8 percent of the Ranch Hands had an abnormal leg pulse index as compared to 7.4 percent of Comparisons. The final adjusted model contained the covariates age, lifetime cigarette smoking history, lifetime alcohol history, HDL cholesterol, body fat, and diabetic class.

The unadjusted Model 2 analysis of leg pulses did not show a significant association with initial dioxin (Table 15-27(c): p=0.930). Adjustment for covariates in Model 2 uncovered the interactions of initial dioxin-by-lifetime cigarette smoking history and initial dioxin-by-personality type (Table 15-27(d): p=0.035 and p=0.016 respectively). Occupation, age, and diabetic class also were significant covariates in the final model. After deleting the interactions from the model, the adjusted analyses did not detect a significant association between initial dioxin and leg pulses (Table 15-27(d): p=0.555). To investigate the interactions, stratified analyses were performed, and the results are presented in Appendix Table K-2-20. The unadjusted Model 3 analysis of leg pulses revealed a marginally significant difference between Comparisons and Ranch Hands in the high dioxin category (Table 15-27(e): p=0.099, Est. RR=1.46). The percentage of Ranch Hands with an abnormal leg pulse index in the high dioxin category was 11.2 percent as compared to 8.2 percent in the Comparison category. The adjusted Model 3 results were not statistically significant (Table 15-27(f): p>0.21 for all adjusted contrasts). However, after excluding HDL cholesterol, body fat, and diabetic class from the final adjusted model, a marginally significant difference was noted between Ranch Hands in the high dioxin category and Comparisons (Appendix Table K-3-22(b): p=0.054, Adj. RR=1.59).

Table 15-27.
Analysis of Leg Pulses

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	Group	n	Percent Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***938***	***9.6***	***1.27 (0.94,1.72)***	***0.132***
	Comparison	***1,261***	***7.7***		
Officer	Ranch Hand	360	8.3	1.22 (0.73,2.04)	0.523
	Comparison	491	6.9		
Enlisted Flyer	Ranch Hand	160	9.4	0.89 (0.44,1.79)	0.884
	Comparison	202	10.4		
Enlisted Groundcrew	Ranch Hand	418	10.8	1.51 (0.97,2.35)	0.083
	Comparison	568	7.4		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	***1.16 (0.85,1.60)***	***0.347***	AGE (p<0.001)
Officer	1.13 (0.67,1.90)	0.659	PACKYR (p<0.001) DRKYR (p=0.106)
Enlisted Flyer	0.83 (0.40,1.72)	0.615	HDL (p=0.025) BFAT (p<0.001)
Enlisted Groundcrew	1.39 (0.87,2.22)	0.171	DIAB (p<0.001)

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 15-27. (Continued)
Analysis of Leg Pulses

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	169	8.3	1.01 (0.81,1.26)	0.930
Medium	172	12.8		
High	171	8.2		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
511	0.92 (0.71,1.21)**	0.555**	INIT*PACKYR (p=0.035) INIT*PERS (p=0.016) OCC (p=0.003) AGE (p=0.018) DIAB (p<0.001)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interactions ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table K-2-20 for further analysis of these interactions.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 15-27. (Continued)
Analysis of Leg Pulses

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,045	8.2		
Background RH	370	9.7	1.16 (0.77,1.75)	0.483
Low RH	254	8.3	0.96 (0.58,1.59)	0.886
High RH	258	11.2	1.46 (0.93,2.30)	0.099
Low plus High RH	512	9.8	1.20 (0.83,1.74)	0.333

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,019			AGE (p=0.034) RACE (p=0.090) PACKYR (p=0.001) DRKYR (p=0.086) HDL (p=0.019) BFAT (p=0.034) DIAB (p=0.004)
Background RH	358	1.15 (0.75,1.76)	0.532	
Low RH	244	0.81 (0.47,1.38)	0.429	
High RH	246	1.36 (0.84,2.20)	0.215	
Low plus High RH	490	1.06 (0.71,1.57)	0.781	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 15-27. (Continued)
Analysis of Leg Pulses

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	9.6 (293)	8.2 (293)	11.5 (296)	1.00 (0.86,1.17)	0.986
5	10.1 (297)	8.2 (291)	10.9 (294)	1.00 (0.88,1.14)	0.962
6[c]	10.1 (296)	8.2 (291)	10.9 (294)	0.94 (0.75,1.19)	0.621

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	880	1.10 (0.93,1.30)	0.278	AGE (p=0.006) PACKYR (p=0.001) CHOL (p=0.106) BFAT (p=0.012) DIAB (p=0.002)
5	880	1.09 (0.94,1.26)	0.256	AGE (p=0.006) PACKYR (p=0.001) CHOL (p=0.088) BFAT (p=0.011) DIAB (p=0.002)
6[d]	879	1.09 (0.93,1.28)	0.272	AGE (p=0.007) PACKYR (p=0.001) BFAT (p=0.010) DIAB (p=0.001)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

The unadjusted and adjusted analyses of Models 4, 5, and 6 did not reveal any significant associations between leg pulses and current dioxin (Table 15-27(g,h): $p>0.25$ for unadjusted and adjusted analyses). Models 4 and 5 were adjusted for age, lifetime cigarette smoking history, total cholesterol, body fat, and diabetic class. For Model 6, age, lifetime cigarette smoking history, body fat, and diabetic class were significant in the final adjusted model.

Peripheral Pulses

All unadjusted and adjusted Model 1 analyses of the peripheral pulses index did not reveal any significant differences between Ranch Hands and Comparisons (Table 15-28(a,b): $p>0.18$ for unadjusted and adjusted results). The significant covariates in the adjusted analysis were age, occupation, lifetime cigarette smoking history, HDL cholesterol, body fat, and diabetic class.

The unadjusted analyses for Models 2 and 3 did not detect any significant associations between the peripheral pulse index and initial dioxin (Table 15-28(c,e): $p>0.15$). Interactions between initial dioxin and lifetime cigarette smoking history and between initial dioxin and personality type were revealed in the adjusted analysis for Model 2 (Table 15-28(d): $p=0.035$ and $p=0.016$). After removing the interactions, the adjusted analysis did not reveal a significant association between initial dioxin and the peripheral pulse index (Table 15-27(d): $p=0.555$). Stratified results of each interaction with initial dioxin are presented in Appendix Table K-2-21. The adjusted Model 3 analysis also did not detect any significant associations between the peripheral pulse index and categorized dioxin (Table 15-28(f): $p\geq0.23$ for adjusted analyses). Age, race, lifetime cigarette smoking history, current cigarette smoking, HDL cholesterol, body fat, and diabetic class were accounted for in the Model 3 adjusted analysis. After excluding HDL cholesterol, body fat, and diabetic class from the final model, a marginally significant difference between Comparisons and Ranch Hands in the high dioxin category was revealed (Appendix Table K-3-23(b): $p=0.061$, Adj. RR=1.55).

Models 4, 5, and 6 did not reveal any significant associations between the peripheral pulse index and current dioxin (Table 15-28(g,h): $p>0.32$ for unadjusted and adjusted analyses). Age, lifetime cigarette smoking history, total cholesterol, body fat, and diabetic class were accounted for in Models 4 and 5. Age, lifetime cigarette smoking history, body fat, and diabetic class were significant in the final adjusted model for Model 6.

Kidney, Urethra, and Bladder (KUB) X Ray (Excluding Kidney Stones)

Analysis of the KUB x ray did not reveal any significant differences between Ranch Hands and Comparisons in the unadjusted and adjusted analyses for Model 1 (Table 15-29(a,b): $p>0.10$ for unadjusted and adjusted results). The significant covariates in the adjusted analysis were age, occupation, lifetime alcohol history, current cigarette smoking, and diabetic class.

Table 15-28.
Analysis of Peripheral Pulses

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***938***	***9.7***	***1.22 (0.91,1.64)***	***0.213***
	Comparison	***1,261***	***8.1***		
Officer	Ranch Hand	360	8.6	1.23 (0.74,2.03)	0.503
	Comparison	491	7.1		
Enlisted Flyer	Ranch Hand	160	9.4	0.89 (0.44,1.79)	0.884
	Comparison	202	10.4		
Enlisted Groundcrew	Ranch Hand	418	10.8	1.37 (0.89,2.11)	0.187
	Comparison	568	8.1		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.16 (0.85,1.58)***	***0.352***	AGE (p<0.001) OCC (p=0.064) PACKYR (p<0.001) HDL (p=0.062) BFAT (p<0.001) DIAB (p<0.001)
Officer	1.14 (0.68,1.91)	0.620	
Enlisted Flyer	0.81 (0.39,1.69)	0.574	
Enlisted Groundcrew	1.35 (0.86,2.12)	0.193	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 15-28. (Continued)
Analysis of Peripheral Pulses

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	169	8.3	1.01 (0.81,1.26)	0.930
Medium	172	12.8		
High	171	8.2		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
511	0.92 (0.71,1.21)**	0.555**	INIT*PACKYR (p=0.035) INIT*PERS (p=0.016) AGE (p=0.018) OCC (p=0.003) DIAB (p<0.001)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interactions ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table K-2-21 for further analysis of these interactions.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 15-28. (Continued)
Analysis of Peripheral Pulses

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,045	8.7		
Background RH	370	10.0	1.12 (0.74,1.68)	0.597
Low RH	254	8.3	0.91 (0.55,1.50)	0.707
High RH	258	11.2	1.38 (0.88,2.17)	0.159
Low plus High RH	512	9.8	1.13 (0.79,1.64)	0.503

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,033			AGE (p=0.004) RACE (p=0.073) PACKYR (p=0.010) CSMOK (p=0.137) HDL (p=0.050) BFAT (p=0.091) DIAB (p=0.001)
Background RH	364	1.10 (0.72,1.67)	0.659	
Low RH	250	0.82 (0.49,1.38)	0.455	
High RH	253	1.34 (0.83,2.15)	0.230	
Low plus High RH	503	1.05 (0.72,1.55)	0.786	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 15-28. (Continued)
Analysis of Peripheral Pulses

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	9.9 (293)	8.2 (293)	11.5 (296)	0.99 (0.85,1.16)	0.936
5	10.4 (297)	8.2 (291)	10.9 (294)	1.00 (0.88,1.14)	0.966
6[c]	10.5 (296)	8.2 (291)	10.9 (294)	0.99 (0.86,1.14)	0.883

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	880	1.09 (0.92,1.29)	0.342	AGE (p=0.005) PACKYR (p=0.001) CHOL (p=0.146) BFAT (p=0.013) DIAB (p=0.001)
5	880	1.08 (0.93,1.25)	0.324	AGE (p=0.005) PACKYR (p=0.001) CHOL (p=0.126) BFAT (p=0.013) DIAB (p=0.001)
6[d]	879	1.08 (0.93,1.26)	0.326	AGE (p=0.005) PACKYR (p=0.001) BFAT (p=0.011) DIAB (p=0.001)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 15-29.
Analysis of Kidney, Urethra, and Bladder (KUB) X Ray (Excluding Kidney Stones)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***938***	***30.6***	***0.98 (0.82,1.18)***	***0.873***
	Comparison	***1,261***	***31.0***		
Officer	Ranch Hand	361	33.8	1.12 (0.84,1.50)	0.487
	Comparison	492	31.3		
Enlisted Flyer	Ranch Hand	159	35.2	1.17 (0.76,1.82)	0.551
	Comparison	202	31.7		
Enlisted Groundcrew	Ranch Hand	418	26.1	0.80 (0.61,1.07)	0.147
	Comparison	567	30.5		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***0.96 (0.79,1.16)***	***0.665***	AGE (p<0.001)
Officer	1.07 (0.79,1.46)	0.647	OCC (p=0.003) DRKYR (p=0.069)
Enlisted Flyer	1.19 (0.75,1.88)	0.461	CSMOK (p=0.103)
Enlisted Groundcrew	0.78 (0.58,1.06)	0.109	DIAB (p=0.095)

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 15-29. (Continued)
Analysis of Kidney, Urethra, and Bladder (KUB) X Ray (Excluding Kidney Stones)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	169	29.0	1.00 (0.86,1.15)	0.961
Medium	172	33.7		
High	171	28.7		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
498	1.09 (0.92,1.29)	0.305	AGE ($p<0.001$) RACE ($p=0.033$) PACKYR ($p=0.057$) DRKYR ($p=0.007$) PERS ($p=0.042$)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 15-29. (Continued)
Analysis of Kidney, Urethra, and Bladder (KUB) X Ray (Excluding Kidney Stones)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,045	32.3		
Background RH	370	31.1	1.00 (0.77,1.30)	0.974
Low RH	254	31.9	0.90 (0.67,1.21)	0.485
High RH	258	29.1	0.82 (0.60,1.11)	0.197
Low plus High RH	512	30.5	0.86 (0.68,1.08)	0.197

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,028			OCC (p=0.005) AGE (p<0.001) DRKYR (p=0.090) CSMOK (p=0.036)
Background RH	363	0.97 (0.73,1.28)	0.811	
Low RH	248	0.82 (0.59,1.12)	0.204	
High RH	251	0.90 (0.65,1.26)	0.537	
Low plus High RH	499	0.85 (0.67,1.10)	0.215	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin $\leq$ 10 ppt.
Background (Ranch Hand): Current Dioxin $\leq$ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin $\leq$ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 15-29. (Continued)
Analysis of Kidney, Urethra, and Bladder (KUB) X Ray (Excluding Kidney Stones)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	30.1 (292)	32.7 (294)	29.4 (296)	1.01 (0.91,1.11)	0.885
5	30.0 (297)	31.6 (291)	30.6 (294)	1.01 (0.93,1.10)	0.818
6[c]	30.1 (296)	31.6 (291)	30.6 (294)	0.99 (0.91,1.09)	0.892

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	862	****	****	CURR*RACE (p=0.010) AGE (p<0.001) CSMOK (p=0.126) DRKYR (p=0.008)
5	862	****	****	CURR*RACE (p=0.010) AGE (p<0.001) CSMOK (p=0.128) DRKYR (p=0.006)
6[d]	861	****	****	CURR*RACE (p=0.010) AGE (p<0.001) CSMOK (p=0.109) DRKYR (p=0.006)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

**** Log_2 (current dioxin + 1)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value not presented; refer to Appendix Table K-2-22 for further analysis of this interaction.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

The unadjusted and adjusted analyses of Models 2 and 3 did not detect any significant associations between KUB x ray and initial dioxin (Table 15-28(c-f): $p>0.19$ for all analyses). Age, race, lifetime cigarette smoking history, lifetime alcohol history, and personality type were significant in the final adjusted model for Model 2. Model 3 was adjusted for occupation, age, lifetime alcohol history, and current cigarette smoking.

Models 4, 5, and 6 did not reveal any significant associations between KUB x ray and current dioxin in the unadjusted analyses (Table 15-28(g): $p>0.81$ for all unadjusted analyses). Interactions between current dioxin and race were detected in the adjusted analyses of Models 4, 5, and 6 (Table 15-29(h): $p=0.010$ for each model). Models 4 through 6 also were adjusted for age, current cigarette smoking, and lifetime alcohol history. Stratified results of the current dioxin-by-race interactions for Models 4 through 6 are presented in Appendix Table K-2-22. Relative risks for non-Blacks were greater than one and significant; relative risks for Blacks were less than one and significant.

Intermittent Claudication and Vascular Insufficiency (ICVI) Index

The unadjusted and adjusted analyses of the intermittent claudication and vascular insufficiency index for Model 1 revealed a significant and a marginally significant overall difference between Ranch Hands and Comparisons (Table 15-30(a,b): $p=0.037$, Est. RR=1.77 and $p=0.074$, Adj. RR=1.63 respectively). An abnormal ICVI was found in 3.7 percent of the Ranch Hands and 2.1 percent of the Comparisons. However, analyses stratified by occupational category did not reveal any significant group differences ($p\geq0.13$). Age, current cigarette smoking, lifetime alcohol history, total cholesterol, HDL cholesterol, family history of heart disease, and diabetic class were accounted for in the final adjusted model.

Initial dioxin was not found to be significantly related to the ICVI index in the unadjusted analysis for Model 2 or 3 (Table 15-30(c,e): $p>0.12$ for all unadjusted analyses). The adjusted Model 2 analysis did not reveal any significant findings (Table 15-30(d): $p=0.745$). Age, current cigarette smoking, and diabetic class were significant in the final model. The adjusted analysis for Model 3 revealed a significant interaction between categorized dioxin and lifetime cigarette smoking history (Table 15-30(f): $p=0.035$). Stratified analyses of this interaction are presented in Appendix Table K-2-23. Significant covariates included in the final adjusted model were age, current cigarette smoking, lifetime alcohol history, total cholesterol, HDL cholesterol, family history of heart disease, and diabetic class. After deletion of the dioxin-by-lifetime cigarette smoking history interaction, the adjusted analysis did not detect any significant associations between categorized dioxin and the ICVI index ($p>0.38$). Excluding total cholesterol, HDL cholesterol, and diabetic class from the final model, however, revealed a marginally significant difference between Comparisons and Ranch Hands in the high dioxin category (Appendix Table K-3-25(b): $p=0.082$, Adj. RR=2.05).

The unadjusted and adjusted analyses of Models 4, 5, and 6 did not detect any significant associations between the ICVI index and current dioxin (Table 15-30(g,h): $p>0.10$ for unadjusted and adjusted analyses). The covariates age, current cigarette

Table 15-30.
Analysis of Intermittent Claudication and Vascular Insufficiency (ICVI) Index

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***940***	***3.7***	***1.77 (1.06,2.94)***	***0.037***
	Comparison	***1,259***	***2.1***		
Officer	Ranch Hand	361	3.9	1.94 (0.85,4.42)	0.163
	Comparison	491	2.0		
Enlisted Flyer	Ranch Hand	160	5.0	2.07 (0.67,6.47)	0.318
	Comparison	202	2.5		
Enlisted Groundcrew	Ranch Hand	419	3.1	1.48 (0.67,3.27)	0.445
	Comparison	566	2.1		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks**[a]
All	***1.63 (0.95,2.79)***	***0.074***	AGE (p=0.001) CSMOK (p=0.002)
Officer	1.96 (0.82,4.69)	0.130	DRKYR (p=0.107) CHOL (p<0.001)
Enlisted Flyer	1.87 (0.57,6.16)	0.304	HDL (p=0.017) HRTDIS (p=0.088)
Enlisted Groundcrew	1.28 (0.55,2.95)	0.563	DIAB (p=0.007)

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 15-30. (Continued)
Analysis of Intermittent Claudication and Vascular Insufficiency (ICVI) Index

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	169	3.6	1.02 (0.72,1.46)	0.899
Medium	172	4.1		
High	172	3.5		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
513	1.07 (0.72,1.58)	0.745	AGE (p=0.060) CSMOK (p=0.002) DIAB (p=0.059)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 15-30. (Continued)
Analysis of Intermittent Claudication and Vascular Insufficiency (ICVI) Index

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,043	2.4		
Background RH	371	3.2	1.31 (0.65,2.65)	0.456
Low RH	254	3.5	1.51 (0.70,3.29)	0.298
High RH	259	3.9	1.69 (0.80,3.59)	0.168
Low plus High RH	513	3.7	1.60 (0.87,2.95)	0.129

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,010			DXCAT*PACKYR (p=0.035) AGE (p=0.001) CSMOK (p=0.003) DRKYR (p=0.128) CHOL (p<0.001) HDL (p=0.003) HRTDIS (p=0.117) DIAB (p=0.001)
Background RH	354	1.24 (0.59,2.60)**	0.577**	
Low RH	239	1.26 (0.54,2.95)**	0.594**	
High RH	244	1.42 (0.62,3.25)**	0.400**	
Low plus High RH	483	1.34 (0.69,2.60)**	0.385**	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-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; refer to Appendix Table K-2-23 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 15-30. (Continued)
Analysis of Intermittent Claudication and Vascular Insufficiency (ICVI) Index

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	3.1 (293)	3.7 (294)	3.7 (297)	1.01 (0.79,1.29)	0.920
5	2.7 (298)	3.4 (291)	4.4 (295)	1.11 (0.90,1.37)	0.330
6[c]	2.7 (297)	3.4 (291)	4.4 (295)	0.94 (0.75,1.19)	0.621

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	883	1.11 (0.86,1.43)	0.447	AGE (p=0.030) CSMOK (p=0.026) BFAT (p=0.037) DIAB (p=0.047)
5	883	1.19 (0.96,1.49)	0.109	AGE (p=0.019) CSMOK (p=0.027) BFAT (p=0.024) DIAB (p=0.069)
6[d]	882	1.03 (0.81,1.32)	0.808	AGE (p=0.026) CSMOK (p=0.049) BFAT (p=0.019) DIAB (p=0.145)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

smoking, body fat, and diabetic class were significant in the adjusted analyses of Models 4, 5, and 6.

Longitudinal Analysis

Longitudinal analyses were conducted on systolic blood pressure and six pulse measurements—femoral, popliteal, dorsalis pedis, posterior tibial, leg, and peripheral pulses—to examine whether changes across time differed with respect to group membership (Model 1), initial dioxin (Model 2), and categorized dioxin (Model 3). Models 4, 5, and 6 were not examined in longitudinal analyses because current dioxin, the measure of exposure in these models, changes over time and is not available for all participants for 1982, 1985, or 1992.

The longitudinal analyses for systolic blood pressure, in both continuous and discrete forms, investigated the difference between the measures for the 1982 examination and the 1992 examination. Summary statistics are provided for reference purposes for the 1985 and 1987 examinations. Similarly, the longitudinal analyses of the six pulse measurements examined the difference between measurements for the 1985 and 1992 examinations because the Doppler assessment of pulses was conducted only at these two exams.

For the continuous variable systolic blood pressure, each of the three models used in the longitudinal analysis were adjusted for age and systolic blood pressure measured in 1982. The analyses of Models 2 and 3 also were adjusted for percent body fat at time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

The longitudinal analyses for the discrete variables (systolic blood pressure and the six pulses) examined relative risks at the 1992 examination for participants who were classified as normal at the earlier examination. Participants considered abnormal in 1982 (or 1985, as applicable) were excluded because the focus of the analyses was on investigating the temporal effects of dioxin during the period between 1982 or 1985 and 1992. Participants considered abnormal in 1982 or 1985 were already abnormal before this period; consequently, only participants considered normal at the 1982 or 1985 examination were considered to be at risk when the effects of dioxin over time were explored. The rate of abnormalities under this restriction approximates an incidence rate. All three models were adjusted for age; Models 2 and 3 also were adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

The results of the longitudinal analyses are presented in Tables 15-31 through 15-38. For the tables of discrete variables (Tables 15-32 through 15-38), the statistics in the upper portion of each table are provided to summarize the actual data (percent of abnormalities for each examination year). The statistics in the lower portion of each table are given to reflect the analyses conducted under the restriction of participants considered normal at the 1982 or 1985 examination.

Table 15-31.
Longitudinal Analysis of Systolic Blood Pressure (mm Hg)
(Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS								
Occupational Category	**Group**	**Mean/(n) Examination 1982**	**1985**	**1987**	**1992**	**Exam. Mean Change[a]**	**Difference of Exam. Mean Change**	**p-Value[b]**
All	***Ranch Hand***	132.35 (888)	119.01 (867)	127.51 (858)	121.79 (888)	-10.56	-1.38	0.098
	Comparison	132.04 (1,045)	119.80 (1,022)	127.85 (1,020)	122.86 (1,045)	-9.18		
Officer	Ranch Hand	132.72 (334)	119.80 (329)	127.51 (328)	124.24 (334)	-8.48	0.18	0.911
	Comparison	132.72 (394)	120.08 (386)	127.82 (382)	124.06 (394)	-8.66		
Enlisted Flyer	Ranch Hand	133.37 (156)	119.73 (154)	129.03 (151)	121.96 (156)	-11.41	-2.10	0.441
	Comparison	131.77 (174)	119.67 (171)	127.35 (173)	122.46 (174)	-9.31		
Enlisted Groundcrew	Ranch Hand	131.64 (398)	118.05 (384)	126.90 (379)	119.66 (398)	-11.98	-2.43	0.038
	Comparison	131.57 (477)	119.61 (465)	128.07 (465)	122.02 (477)	-9.55		

[a] Difference between 1992 and 1982 examination means.

[b] Results adjusted for systolic blood pressure in 1982 and age in 1992.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations.

Table 15-31. (Continued)
Longitudinal Analysis of Systolic Blood Pressure (mm Hg)
(Continuous)

b) MODEL 2: RANCH HANDS — INITIAL DIOXIN						
	Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[a]	
	Mean/(n) Examination					
Initial Dioxin	1982	1985	1987	1992	Adj. Slope (Std. Error)	p-Value
Low	133.23 (162)	120.25 (159)	128.81 (161)	122.07 (162)	0.050 (0.584)	0.932
Medium	133.26 (168)	120.35 (162)	126.01 (164)	123.71 (168)		
High	132.37 (167)	120.47 (165)	129.83 (161)	122.56 (167)		

[a] Results based on difference between systolic blood pressure in 1992 and systolic blood pressure in 1982 versus log_2 (initial dioxin); results adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to date of blood draw for dioxin, systolic blood pressure in 1982, and age in 1992.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations.

Table 15-31. (Continued)
Longitudinal Analysis of Systolic Blood Pressure (mm Hg)
(Continuous)

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY							
	Mean/(n) Examination						
Dioxin Category	1982	1985	1987	1992	Exam. Mean Change[a]	Difference of Exam. Mean Change[b]	p-Value[c]
Comparison	132.19 (901)	119.83 (890)	127.73 (891)	122.87 (901)	-9.32		
Background RH	131.37 (338)	117.33 (335)	126.46 (332)	120.98 (338)	-10.39	-1.07	0.527
Low RH	133.41 (244)	120.41 (238)	128.10 (242)	123.17 (244)	-10.24	-0.92	0.461
High RH	132.50 (253)	120.31 (248)	128.31 (244)	122.43 (253)	-10.07	-0.75	0.594
Low plus High RH	132.95 (497)	120.36 (486)	128.20 (486)	122.79 (497)	-10.16	-0.84	0.414

[a] Difference between 1992 and 1982 examination means.

[b] Difference between Ranch Hand dioxin category and Comparison category.

[c] Results adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, systolic blood pressure in 1982, and age in 1992.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations.

Table 15-32.
Longitudinal Analysis of Systolic Blood Pressure (Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS					
		Percent Abnormal/(n) Examination			
Occupational Category	Group	1982	1985	1987	1992
All	***Ranch Hand***	***18.7 (888)***	***6.7 (867)***	***19.7 (858)***	***15.4 (888)***
	Comparison	***20.5 (1,045)***	***7.1 (1,022)***	***22.6 (1,020)***	***16.6 (1,045)***
Officer	Ranch Hand	19.8 (334)	7.6 (329)	19.5 (328)	17.1 (334)
	Comparison	21.8 (394)	7.5 (386)	23.3 (382)	19.3 (394)
Enlisted Flyer	Ranch Hand	21.2 (156)	5.2 (154)	21.2 (151)	17.3 (156)
	Comparison	20.7 (174)	7.6 (171)	22.5 (173)	16.1 (174)
Enlisted Groundcrew	Ranch Hand	16.8 (398)	6.5 (384)	19.3 (379)	13.3 (398)
	Comparison	19.3 (477)	6.7 (465)	22.5 (465)	14.5 (477)

		Normal in 1982			
Occupational Category	Group	n in 1992	Percent Abnormal in 1992	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	***Ranch Hand***	***722***	***9.8***	***0.97 (0.69,1.35)***	***0.838***
	Comparison	***831***	***10.2***		
Officer	Ranch Hand	268	9.7	0.78 (0.46,1.33)	0.364
	Comparison	308	12.0		
Enlisted Flyer	Ranch Hand	123	7.3	0.57 (0.24,1.34)	0.197
	Comparison	138	12.3		
Enlisted Groundcrew	Ranch Hand	331	10.9	1.44 (0.87,2.39)	0.160
	Comparison	385	8.1		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1982 and 1992 results; results adjusted for age in 1992.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations. Statistical analyses are based only on participants who had normal systolic blood pressure in 1982 (see Chapter 7, Statistical Methods).

Table 15-32. (Continued)
Longitudinal Analysis of Systolic Blood Pressure (Discrete)

b) MODEL 2: RANCH HANDS – INITIAL DIOXIN				
	Percent Abnormal/(n) Examination			
Initial Dioxin	1982	1985	1987	1992
Low	22.2 (162)	5.7 (159)	23.0 (161)	16.7 (162)
Medium	20.2 (168)	6.2 (162)	15.9 (164)	17.3 (168)
High	17.4 (167)	9.7 (165)	23.6 (161)	17.4 (167)

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
	Normal in 1982			
Initial Dioxin	n in 1992	Percent Abnormal in 1992	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	126	11.9	1.08 (0.86,1.37)	0.510
Medium	134	9.0		
High	138	15.2		

[a] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and age in 1992.

[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations. Statistical analyses are based only on participants who had normal systolic blood pressure in 1982 (see Chapter 7, Statistical Methods).

Table 15-32. (Continued)
Longitudinal Analysis of Systolic Blood Pressure
(Discrete)

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY				
	Percent Abnormal/(n) Examination			
Dioxin Category	**1982**	**1985**	**1987**	**1992**
Comparison	20.6 (901)	7.1 (890)	22.1 (891)	16.9 (901)
Background RH	16.9 (338)	6.3 (335)	18.1 (332)	14.2 (338)
Low RH	20.9 (244)	5.9 (238)	21.5 (242)	16.8 (244)
High RH	19.0 (253)	8.5 (248)	20.1 (244)	17.4 (253)
Low plus High RH	19.9 (497)	7.2 (486)	20.8 (486)	17.1 (497)

	Normal in 1982			
Dioxin Category	**n in 1992**	**Percent Abnormal in 1992**	**Adj. Relative Risk (95% C.I.)[ab]**	**p-Value[b]**
Comparison	715	10.7		
Background RH	281	8.2	0.83 (0.50,1.38)	0.479
Low RH	193	10.9	0.86 (0.51,1.46)	0.576
High RH	205	13.2	1.31 (0.80,2.14)	0.280
Low plus High RH	398	12.1	1.07 (0.72,1.59)	0.743

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and age in 1992.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations. Statistical analyses are based only on participants who had normal systolic blood pressure in 1982 (see Chapter 7, Statistical Methods).

Table 15-33
Longitudinal Analysis of Femoral Pulses

a) MODEL 1: RANCH HANDS VS. COMPARISONS			
		Percent Abnormal/(n) Examination	
Occupational Category	Group	1985	1992
All	*Ranch Hand*	*0.4*	*1.2*
		(903)	*(903)*
	Comparison	*0.2*	*0.6*
		(1,134)	*(1,134)*
Officer	Ranch Hand	0.0	1.2
		(346)	(346)
	Comparison	0.5	0.5
		(434)	(434)
Enlisted Flyer	Ranch Hand	1.3	1.3
		(157)	(157)
	Comparison	0.0	1.6
		(188)	(188)
Enlisted Groundcrew	Ranch Hand	0.5	1.3
		(400)	(400)
	Comparison	0.0	0.4
		(512)	(512)

		Normal in 1985			
Occupational Category	Group	n in 1992	Percent Abnormal in 1992	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	*Ranch Hand*	*899*	*1.0*	*1.89 (0.67,5.35)*	*0.222*
	Comparison	*1,132*	*0.5*		
Officer	Ranch Hand	346	1.2	5.02 (0.56,45.11)	0.150
	Comparison	432	0.2		
Enlisted Flyer	Ranch Hand	155	0.6	0.40 (0.04,3.85)	0.429
	Comparison	188	1.6		
Enlisted Groundcrew	Ranch Hand	398	1.0	2.61 (0.48,14.38)	0.269
	Comparison	512	0.4		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1985 and 1992 results; results adjusted for age in 1992.

Note: Statistical analyses are based only on participants who had normal femoral pulses in 1985 (see Chapter 7, Statistical Methods).

Table 15-33. (Continued)
Longitudinal Analysis of Femoral Pulses

b) MODEL 2: RANCH HANDS - INITIAL DIOXIN		
	Percent Abnormal/(n) Examination	
Initial Dioxin	1985	1992
Low	0.0 (163)	3.7 (163)
Medium	0.6 (166)	1.2 (166)
High	1.2 (169)	0.6 (169)

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
	Normal in 1985			
Initial Dioxin	n in 1992	Percent Abnormal in 1992	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	163	3.7	0.35 (0.12,0.99)	0.015
Medium	165	0.6		
High	167	0.0		

[a] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and age in 1992.

[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.
Statistical analyses are based only on participants who had normal femoral pulses in 1985 (see Chapter 7, Statistical Methods).

Table 15-33. (Continued)
Longitudinal Analysis of Femoral Pulses

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY		
	Percent Abnormal/(n) Examination	
Dioxin Category	1985	1992
Comparison	0.2 (982)	0.5 (982)
Background RH	0.3 (358)	0.3 (358)
Low RH	0.0 (245)	2.9 (245)
High RH	1.2 (253)	0.8 (253)
Low plus High RH	0.6 (498)	1.8 (498)

	Normal in 1985			
Dioxin Category	n in 1992	Percent Abnormal in 1992	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
Comparison	980	0.4		
Background RH	357	0.3	0.67 (0.07,6.10)	0.722
Low RH	245	2.9	6.06 (1.72,21.30)	0.005
High RH	250	0.0	--	--
Low plus High RH	495	1.4	3.35 (0.95,11.80)	0.059

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and age in 1992.

--: Adjusted relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.
Statistical analyses are based only on participants who had normal femoral pulses in 1985 (see Chapter 7, Statistical Methods).

Table 15-34.
Longitudinal Analysis of Popliteal Pulses

a) MODEL 1: RANCH HANDS VS. COMPARISONS			
		Percent Abnormal/(n) Examination	
Occupational Category	Group	1985	1992
All	***Ranch Hand***	***0.7 (903)***	***2.0 (903)***
	Comparison	***0.5 (1,132)***	***0.9 (1,132)***
Officer	Ranch Hand	0.3 (346)	2.0 (346)
	Comparison	0.7 (433)	0.9 (433)
Enlisted Flyer	Ranch Hand	1.3 (157)	2.5 (157)
	Comparison	1.1 (187)	1.6 (187)
Enlisted Groundcrew	Ranch Hand	0.8 (400)	1.8 (400)
	Comparison	0.2 (512)	0.6 (512)

		Normal in 1985			
Occupational Category	Group	n in 1992	Percent Abnormal in 1992	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	***Ranch Hand***	***897***	***1.8***	***3.41 (1.33,8.79)***	***0.007***
	Comparison	***1,126***	***0.5***		
Officer	Ranch Hand	345	2.0	4.46 (0.92,21.69)	0.064
	Comparison	430	0.5		
Enlisted Flyer	Ranch Hand	155	1.9	1.81 (0.29,11.18)	0.522
	Comparison	185	1.1		
Enlisted Groundcrew	Ranch Hand	397	1.5	4.02 (0.82,20.06)	0.089
	Comparison	511	0.4		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1985 and 1992 results; results adjusted for age in 1992.

Note: Statistical analyses are based only on participants who had normal popliteal pulses in 1985 (see Chapter 7, Statistical Methods).

Table 15-34. (Continued)
Longitudinal Analysis of Popliteal Pulses
(Discrete)

b) MODEL 2: RANCH HANDS — INITIAL DIOXIN		
	Percent Abnormal/(n) Examination	
Initial Dioxin	1985	1992
Low	0.6 (163)	3.7 (163)
Medium	0.0 (166)	3.6 (166)
High	1.2 (169)	1.8 (169)

Initial Dioxin Category Summary Statistics Normal in 1985			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n in 1992	Percent Abnormal in 1992	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	162	3.1	0.94 (0.58,1.52)	0.793
Medium	166	3.6		
High	167	1.2		

[a] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and age in 1992.

[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.
Statistical analyses are based only on participants who had normal popliteal pulses in 1985 (see Chapter 7, Statistical Methods).

Table 15-34. (Continued)
Longitudinal Analysis of Popliteal Pulses

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY		
	Percent Abnormal/(n) Examination	
Dioxin Category	1985	1992
Comparison	0.5 (981)	1.0 (981)
Background RH	0.8 (358)	0.6 (358)
Low RH	0.4 (245)	2.9 (245)
High RH	0.8 (253)	3.2 (253)
Low plus High RH	0.6 (498)	3.0 (498)

	Normal in 1985			
Dioxin Category	n in 1992	Percent Abnormal in 1992	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
Comparison	976	0.6		
Background RH	355	0.6	0.76 (0.15,3.84)	0.740
Low RH	244	2.5	3.78 (1.19,12.10)	0.024
High RH	251	2.8	6.49 (2.08,20.20)	0.001
Low plus High RH	495	2.6	4.86 (1.80,13.10)	0.002

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and age in 1992.

Note: RH = Ranch Hand.
Comparison: Current Dioxin $\leq$ 10 ppt.
Background (Ranch Hand): Current Dioxin $\leq$ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin $\leq$ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.
Statistical analyses are based only on participants who had normal popliteal pulses in 1985 (see Chapter 7, Statistical Methods).

Table 15-35.
Longitudinal Analysis of Dorsalis Pedis Pulses

a) MODEL 1: RANCH HANDS VS. COMPARISONS			
		Percent Abnormal/(n) Examination	
Occupational Category	Group	1985	1992
All	***Ranch Hand***	***23.6***	***8.7***
		(899)	***(899)***
	Comparison	***21.5***	***7.0***
		(1,130)	***(1,130)***
Officer	Ranch Hand	27.8	8.1
		(345)	(345)
	Comparison	25.3	6.7
		(431)	(431)
Enlisted Flyer	Ranch Hand	21.7	8.3
		(157)	(157)
	Comparison	20.3	9.6
		(187)	(187)
Enlisted Groundcrew	Ranch Hand	20.7	9.3
		(397)	(397)
	Comparison	18.8	6.3
		(512)	(512)

		Normal in 1985			
Occupational Category	Group	n in 1992	Percent Abnormal in 1992	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	***Ranch Hand***	***687***	***5.5***	***1.62 (0.99,2.64)***	***0.053***
	Comparison	***887***	***3.6***		
Officer	Ranch Hand	249	4.8	1.39 (0.61,3.18)	0.436
	Comparison	322	3.7		
Enlisted Flyer	Ranch Hand	123	3.3	0.81 (0.22,2.95)	0.746
	Comparison	149	4.0		
Enlisted Groundcrew	Ranch Hand	315	7.0	2.29 (1.13,4.64)	0.021
	Comparison	416	3.4		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1985 and 1992 results; results adjusted for age in 1992.

Note: Statistical analyses are based only on participants who had normal dorsalis pedis pulses in 1985 (see Chapter 7, Statistical Methods).

Table 15-35. (Continued)
Longitudinal Analysis of Dorsalis Pedis Pulses

b) MODEL 2: RANCH HANDS - INITIAL DIOXIN		
	Percent Abnormal/(n) Examination	
Initial Dioxin	1985	1992
Low	21.5 (163)	8.0 (163)
Medium	22.3 (166)	10.8 (166)
High	20.4 (167)	7.8 (167)

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
	Normal in 1985			
Initial Dioxin	n in 1992	Percent Abnormal in 1992	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	128	5.5	1.04 (0.74,1.45)	0.827
Medium	129	7.8		
High	133	5.3		

[a] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and age in 1992.

[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.
Statistical analyses are based only on participants who had normal dorslis pedis pulses in 1985 (see Chapter 7, Statistical Methods).

Table 15-35. (Continued)
Longitudinal Analysis of Dorsalis Pedis Pulses

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY		
	Percent Abnormal/(n) Examination	
Dioxin Category	1985	1992
Comparison	21.3 (979)	7.7 (979)
Background RH	27.2 (357)	9.0 (357)
Low RH	20.0 (245)	8.2 (245)
High RH	22.7 (251)	9.6 (251)
Low plus High RH	21.4 (496)	8.9 (496)

	Normal in 1985			
Dioxin Category	n in 1992	Percent Abnormal in 1992	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
Comparison	770	3.9		
Background RH	260	4.6	1.21 (0.60,2.44)	0.595
Low RH	196	5.6	1.34 (0.65,2.76)	0.428
High RH	194	6.7	2.21 (1.10,4.45)	0.026
Low plus High RH	390	6.2	1.70 (0.96,2.99)	0.067

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and age in 1992.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.
Statistical analyses are based only on participants who had normal dorslis pedis pulses in 1985 (see Chapter 7, Statistical Methods).

Table 15-36.
Longitudinal Analysis of Posterior Tibial Pulses

a) MODEL 1: RANCH HANDS VS. COMPARISONS			
		Percent Abnormal/(n) Examination	
Occupational Category	Group	1985	1992
All	***Ranch Hand***	***1.8 (902)***	***3.8 (902)***
	Comparison	***1.8 (1,132)***	***2.3 (1,132)***
Officer	Ranch Hand	1.4 (346)	3.2 (346)
	Comparison	1.6 (433)	2.3 (433)
Enlisted Flyer	Ranch Hand	3.2 (157)	5.1 (157)
	Comparison	1.6 (187)	3.2 (187)
Enlisted Groundcrew	Ranch Hand	1.5 (399)	3.8 (399)
	Comparison	2.0 (512)	2.0 (512)

		Normal in 1985			
Occupational Category	Group	n in 1992	Percent Abnormal in 1992	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	***Ranch Hand***	***886***	***3.0***	***1.94 (1.06,3.58)***	***0.031***
	Comparison	***1,112***	***1.6***		
Officer	Ranch Hand	341	2.9	1.83 (0.68,4.91)	0.229
	Comparison	426	1.6		
Enlisted Flyer	Ranch Hand	152	3.3	1.24 (0.35,4.41)	0.741
	Comparison	184	2.7		
Enlisted Groundcrew	Ranch Hand	393	3.1	2.75 (1.00,7.51)	0.049
	Comparison	502	1.2		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1985 and 1992 results; results adjusted for age in 1992.

Note: Statistical analyses are based only on participants who had normal posterior tibial pulses in 1985 (see Chapter 7, Statistical Methods).

Table 15-36. (Continued)
Longitudinal Analysis of Posterior Tibial Pulses

b) MODEL 2: RANCH HANDS - INITIAL DIOXIN		
	Percent Abnormal/(n) Examination	
Initial Dioxin	1985	1992
Low	1.8 (163)	5.5 (163)
Medium	2.4 (166)	5.4 (166)
High	2.4 (169)	2.4 (169)

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
	Normal in 1985			
Initial Dioxin	n in 1992	Percent Abnormal in 1992	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	160	5.0	0.90 (0.59,1.36)	0.606
Medium	162	4.9		
High	165	1.8		

[a] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and age in 1992.

[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.
Statistical analyses are based only on participants who had normal posterior tibial pulses in 1985 (see Chapter 7, Statistical Methods).

Table 15-36. (Continued)
Longitudinal Analysis of Posterior Tibial Pulses

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY		
	Percent Abnormal/(n) Examination	
Dioxin Category	1985	1992
Comparison	1.7 (981)	2.3 (981)
Background RH	1.4 (358)	2.8 (358)
Low RH	2.0 (245)	4.1 (245)
High RH	2.4 (253)	4.7 (253)
Low plus High RH	2.2 (498)	4.4 (498)

	Normal in 1985			
Dioxin Category	n in 1992	Percent Abnormal in 1992	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
Comparison	964	1.7		
Background RH	353	1.7	0.80 (0.30,2.10)	0.646
Low RH	240	3.8	2.20 (0.93,5.17)	0.072
High RH	247	4.0	3.74 (1.61,8.73)	0.002
Low plus High RH	487	3.9	2.80 (1.39,5.65)	0.004

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and age in 1992.

Note: RH = Ranch Hand.
Comparison: Current Dioxin $\leq$10 ppt.
Background (Ranch Hand): Current Dioxin $\leq$10 ppt.
Low (Ranch Hand): Current Dioxin >10 ppt, 10 ppt < Initial Dioxin $\leq$143 ppt.
High (Ranch Hand): Current Dioxin >10 ppt, Initial Dioxin >143 ppt.
Statistical analyses are based only on participants who had normal posterior tibial pulses in 1985 (see Chapter 7, Statistical Methods).

Table 15-37.
Longitudinal Analysis of Leg Pulses
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS			
		Percent Abnormal/(n) Examination	
Occupational Category	Group	1985	1992
All	*Ranch Hand*	*24.6*	*9.6*
		(899)	*(899)*
	Comparison	*22.6*	*7.7*
		(1,130)	*(1,130)*
Officer	Ranch Hand	29.0	8.4
		(345)	(345)
	Comparison	25.8	7.0
		(431)	(431)
Enlisted Flyer	Ranch Hand	23.6	9.6
		(157)	(157)
	Comparison	20.9	10.2
		(187)	(187)
Enlisted Groundcrew	Ranch Hand	21.2	10.6
		(397)	(397)
	Comparison	20.5	7.4
		(512)	(512)

		Normal in 1985			
Occupational Category	Group	n in 1992	Percent Abnormal in 1992	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	*Ranch Hand*	*678*	*6.3*	*1.73 (1.09,2.77)*	*0.021*
	Comparison	*875*	*3.9*		
Officer	Ranch Hand	245	5.3	1.40 (0.63,3.10)	0.412
	Comparison	320	4.1		
Enlisted Flyer	Ranch Hand	120	4.2	0.90 (0.27,2.93)	0.857
	Comparison	148	4.7		
Enlisted Groundcrew	Ranch Hand	313	8.0	2.58 (1.29,5.16)	0.007
	Comparison	407	3.4		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1985 and 1992 results; results adjusted for age in 1992.

Note: Statistical analyses are based only on participants who had normal leg pulses in 1985 (see Chapter 7, Statistical Methods).

Table 15-37. (Continued)
Longitudinal Analysis of Leg Pulses

b) MODEL 2: RANCH HANDS — INITIAL DIOXIN		
	Percent Abnormal/(n) Examination	
Initial Dioxin	1985	1992
Low	22.1 (163)	8.6 (163)
Medium	24.7 (166)	12.0 (166)
High	21.0 (167)	8.4 (167)

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
	Normal in 1985			
Initial Dioxin	n in 1992	Percent Abnormal in 1992	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	127	6.3	1.03 (0.75,1.42)	0.858
Medium	125	8.0		
High	132	6.1		

[a] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and age in 1992.

[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.
Statistical analyses are based only on participants who had normal leg pulses in 1985 (see Chapter 7, Statistical Methods).

Table 15-37. (Continued)
Longitudinal Analysis of Leg Pulses

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY		
	Percent Abnormal/(n) Examination	
Dioxin Category	1985	1992
Comparison	22.4 (979)	8.3 (979)
Background RH	28.0 (357)	9.8 (357)
Low RH	21.2 (245)	8.6 (245)
High RH	23.9 (251)	10.8 (251)
Low plus High RH	22.6 (496)	9.7 (496)

	Normal in 1985			
Dioxin Category	n in 1992	Percent Abnormal in 1992	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
Comparison	760	4.1		
Background RH	257	5.4	1.31 (0.68,2.54)	0.426
Low RH	193	6.2	1.45 (0.72,2.91)	0.298
High RH	191	7.3	2.40 (1.21,4.74)	0.012
Low plus High RH	384	6.8	1.83 (1.06,3.18)	0.031

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and age in 1992.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.
Statistical analyses are based only on participants who had normal leg pulses in 1985 (see Chapter 7, Statistical Methods).

Table 15-38.
Longitudinal Analysis of Peripheral Pulses

a) MODEL 1: RANCH HANDS VS. COMPARISONS			
		Percent Abnormal/(n) Examination	
Occupational Category	Group	1985	1992
All	*Ranch Hand*	*24.7*	*9.7*
		(899)	*(899)*
	Comparison	*22.6*	*8.2*
		(1,128)	*(1,128)*
Officer	Ranch Hand	29.0	8.7
		(345)	(345)
	Comparison	25.8	7.2
		(431)	(431)
Enlisted Flyer	Ranch Hand	23.6	9.6
		(157)	(157)
	Comparison	21.4	10.2
		(187)	(187)
Enlisted Groundcrew	Ranch Hand	21.4	10.6
		(397)	(397)
	Comparison	20.4	8.2
		(510)	(510)

		Normal in 1985			
Occupational Category	Group	n in 1992	Percent Abnormal in 1992	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	*Ranch Hand*	*677*	*6.5*	*1.63 (1.03,2.57)*	*0.036*
	Comparison	*873*	*4.2*		
Officer	Ranch Hand	245	5.7	1.40 (0.65,3.03)	0.390
	Comparison	320	4.4		
Enlisted Flyer	Ranch Hand	120	4.2	0.89 (0.27,2.92)	0.854
	Comparison	147	4.8		
Enlisted Groundcrew	Ranch Hand	312	8.0	2.24 (1.15,4.37)	0.018
	Comparison	406	3.9		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1985 and 1992 results; results adjusted for age in 1992.

Note: Statistical analyses are based only on participants who had normal peripheral pulses in 1985 (see Chapter 7, Statistical Methods).

Table 15-38. (Continued)
Longitudinal Analysis of Peripheral Pulses

b) MODEL 2: RANCH HANDS - INITIAL DIOXIN		
	Percent Abnormal/(n) Examination	
Initial Dioxin	1985	1992
Low	22.7 (163)	8.6 (163)
Medium	24.7 (166)	12.0 (166)
High	21.0 (167)	8.4 (167)

Initial Dioxin Category Summary Statistics Normal in 1985			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n in 1992	Percent Abnormal in 1992	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	126	6.3	1.03 (0.75,1.42)	0.865
Medium	125	8.0		
High	132	6.1		

[a] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and age in 1992.

[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.
Statistical analyses are based only on participants who had normal peripheral pulses in 1985 (see Chapter 7, Statistical Methods).

Table 15-38. (Continued)
Longitudinal Analysis of Peripheral Pulses

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY		
	Percent Abnormal/(n) Examination	
Dioxin Category	1985	1992
Comparison	22.3 (977)	8.8 (977)
Background RH	28.0 (357)	10.1 (357)
Low RH	21.6 (245)	8.6 (245)
High RH	23.9 (251)	10.8 (251)
Low plus High RH	22.8 (496)	9.7 (496)

	Normal in 1985			
Dioxin Category	n in 1992	Percent Abnormal in 1992	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
Comparison	759	4.5		
Background RH	257	5.8	1.28 (0.67,2.42)	0.453
Low RH	192	6.3	1.31 (0.66,2.62)	0.440
High RH	191	7.3	2.20 (1.12,4.31)	0.022
Low plus High RH	383	6.8	1.67 (0.97,2.87)	0.063

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and age in 1992.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.
Statistical analyses are based only on participants who had normal peripheral pulses in 1985 (see Chapter 7, Statistical Methods).

Physical Examination Variables

Systolic Blood Pressure (Continuous)

Examination of the paired differences between 1982 and 1992 for systolic blood pressure in its continuous form uncovered a marginally significant overall group difference (Table 15-31(a): p=0.098, Diff. of Exam Mean Change=-1.38). Further analysis within each occupational stratum displayed a significant difference in the change in mean systolic blood pressure from 1982 to 1992 between Ranch Hands and Comparisons in the enlisted groundcrew stratum (p=0.038, Diff. of Exam Mean Change=-2.43). Systolic blood pressure decreased significantly more for Ranch Hands (Mean Change=-11.98) in the 10-year period than for Comparisons (Mean Change=-9.55).

The analyses of Models 2 and 3 did not find a significant association with initial dioxin or categorized dioxin (Table 15-31(b,c): p>0.41 for all analyses).

Systolic Blood Pressure (Discrete)

Longitudinal analyses for discretized systolic blood pressure were conditioned on participants without abnormally high systolic blood pressure (>140 mm Hg) in 1982. No statistically significant results were detected with respect to group differences, associations with initial dioxin, or associations with categorized dioxin (Table 15-32(a-c): p≥0.16 for all analyses).

Femoral Pulses

The longitudinal analysis for Model 1 did not find a significant group difference in the presence of abnormal femoral pulses for participants who had normal femoral pulse readings in 1985 (Table 15-33(a): p≥0.15 for all contrasts).

By contrast, Model 2 detected a significant negative association between discretized systolic blood pressure and initial dioxin (Table 15-33(b): p=0.015, Adj. RR=0.35). Of the Ranch Hand cohort with normal femoral pulses in 1985, 3.7 percent of the participants in the low category of initial dioxin had weak femoral pulses at the 1992 examination, while the percentages of weak pulses in the medium and high categories were 0.6 and 0.0 percent respectively.

The longitudinal analysis for Model 3 detected a significant relative risk for the low Ranch Hand category (Table 15-33(c): p=0.005, Adj. RR=6.06). Only 0.4 percent of Comparisons with normal femoral pulses in 1985 had abnormal femoral pulse readings at the 1992 examination, while 2.9 percent of Ranch Hands in the low dioxin category with normal femoral pulses in 1985 displayed abnormal femoral pulses in 1992. Although, there were no Ranch Hands in the high dioxin category (0.0%) who had normal femoral pulse readings in 1985 and abnormal femoral pulse readings in 1992, Ranch Hands in the low plus high dioxin category had a marginally higher percentage of diminished femoral pulses in 1992 (1.4%) than Comparisons (p=0.059, Adj. RR=3.35).

Popliteal Pulses

The longitudinal analysis for Model 1 detected a significant overall group difference in the prevalence of abnormal popliteal pulses at the 1992 examination for participants who had normal popliteal pulse readings in 1985 (Table 15-34(a): p=0.007, Adj. RR=3.41). Of the participants who had normal popliteal pulse measurements in 1985, 1.8 percent of the Ranch Hands and 0.5 percent of Comparisons had abnormal popliteal pulses in 1992. After stratifying the Model 1 analysis by occupation, a marginally significant difference between Ranch Hands and Comparisons was detected for the officer and enlisted groundcrew strata (p=0.064, Adj. RR=4.46 and p=0.089, Adj. RR=4.02). A higher percentage of Ranch Hands in both the officer and enlisted groundcrew strata had normal popliteal pulses in 1985 and abnormal popliteal pulses in 1992 (2.0% and 1.5%) than Comparisons (0.5% and 0.4%).

By contrast, Model 2 did not detect a significant association between the change in popliteal pulses from normal in 1985 to abnormal in 1992 and initial dioxin (Table 15-34(b): p=0.793).

The longitudinal analysis for Model 3 detected a significant relative risk for the low, high, and low plus high Ranch Hand categories (Table 15-34(c): p=0.024, Adj. RR=3.78; p=0.001, Adj. RR=6.49; and p=0.002, Adj. RR=4.86). Only 0.6 percent of Comparisons with normal popliteal pulses during the 1985 examination had abnormal popliteal pulse readings at the 1992 examination, while 2.5, 2.8, and 2.6 percent of Ranch Hands in the low, high, and low plus high dioxin categories respectively had similar popliteal pulse readings for the 1985 and 1992 examinations.

Dorsalis Pedis Pulses

The longitudinal analysis of dorsalis pedis pulses was conditioned on participants who had normal dorsalis pedis pulse measurements in 1985. The longitudinal analysis for Model 1 detected a marginally significant overall group difference in the percentage of abnormal dorsalis pedis pulses at the 1992 examination (Table 15-35(a): p=0.053, Adj. RR=1.62). Of the participants who had normal dorsalis pedis pulse measurements in 1985, 5.5 percent of the Ranch Hands and 3.6 percent of Comparisons had abnormal dorsalis pedis pulses in 1992. After stratifying the Model 1 analysis by occupation, a significant difference between Ranch Hands and Comparisons was detected for the enlisted groundcrew stratum (p=0.021, Adj. RR=2.29). Within this stratum, Ranch Hands were more than twice as likely as Comparisons to have abnormal dorsalis pedis pulse measurements at the 1992 examination (7.0% vs. 3.4%).

The Model 2 analysis did not detect a significant association between initial dioxin and dorsalis pedis pulses (Table 15-35(b): p=0.827). However, the Model 3 analysis of categorized dioxin detected significant and marginally significant relative risks for the high and low plus high dioxin categories (Table 15-35(c): p=0.026, Adj. RR=2.21 and p=0.067, Adj. RR=1.70). Ranch Hands in the high dioxin category (6.7%) and the low plus high current dioxin category (6.2%) had a higher percentage of abnormal dorsalis pedis pulses than Comparisons (3.9%).

Posterior Tibial Pulses

The longitudinal analysis for Model 1 detected a significant overall group difference in the percentage of abnormal posterior tibial pulses at the 1992 examination for participants who had normal posterior tibial pulse readings in 1985 (Table 15-36(a): p=0.031, Adj. RR=1.94). Of the participants who had normal posterior tibial pulse readings in 1985, 3.0 percent of Ranch Hands and 1.6 percent of Comparisons had abnormal popliteal pulses in 1992. After stratifying the Model 1 analysis by occupation, a significant difference between Ranch Hands and Comparisons was detected for the enlisted groundcrew stratum (p=0.049, Adj. RR=2.75). For this stratum, a higher percentage of Ranch Hands (3.1%) had normal posterior tibial pulses in 1985 and abnormal posterior tibial pulses in 1992 than Comparisons (1.2%).

By contrast, Model 2 did not detect a significant association between the change in posterior tibial pulses from normal in 1985 to abnormal in 1992 and initial dioxin (Table 15-36(b): p=0.606).

The longitudinal analysis for Model 3 detected a significant relative risk for the high and low plus high Ranch Hand categories (Table 15-36(c): p=0.002, Adj. RR=3.74 and p=0.004, Adj. RR=2.80). Ranch Hands in the high and low plus high dioxin categories had higher percentages of normal posterior tibial pulses at the 1985 examination and abnormal posterior tibial pulses during the 1992 examination (4.0% and 3.9%) than did Comparisons (1.7%).

Leg Pulses

The longitudinal analysis of leg pulses was conditioned on participants who had normal leg pulse indices in 1985. The longitudinal analysis for Model 1 detected a significant overall group difference in the percentage of abnormal leg pulse indices at the 1992 examination (Table 15-37(a): p=0.021, Adj. RR=1.73). Of the participants who had normal leg pulse indices in 1985, 6.3 percent of Ranch Hands and 3.9 percent of Comparisons had abnormal leg pulse indices in 1992. After stratifying the Model 1 analysis by occupation, a significant difference between Ranch Hands and Comparisons was detected for the enlisted groundcrew stratum (p=0.007, Adj. RR=2.58). Within this stratum, Ranch Hands were more than twice as likely than Comparisons to have abnormal leg pulse indices at the 1992 examination (8.0% vs. 3.4%).

The Model 2 analyses did not detect a significant association between initial dioxin and dorsalis pedis pulses (Table 15-37(b): p=0.858, Adj. RR=1.03). However, the Model 3 analysis of categorized dioxin detected significant relative risks for the high and low plus high dioxin categories (Table 15-37(c): p=0.012, Adj. RR=2.40 and p=0.031, Adj. RR=1.83). Ranch Hands in the high dioxin category (7.3%) and the low plus high dioxin category (6.8%) had a higher percentage of abnormal leg pulse indices than Comparisons (4.1%).

Peripheral Pulses

Similar to the longitudinal analyses for the other pulse variables, the Model 1 analysis of the peripheral pulse index detected a significant overall group difference in the percentage of abnormal peripheral pulse indices at the 1992 examination for participants who had a normal peripheral pulse index in 1985 (Table 15-38(a): p=0.036, Adj. RR=1.63). Of the participants who had normal peripheral pulse indices in 1985, 6.5 percent of the Ranch Hands and 4.2 percent of Comparisons had abnormal peripheral pulse indices in 1992. After stratifying the Model 1 analysis by occupation, a significant difference between Ranch Hands and Comparisons was detected for the enlisted groundcrew stratum (p=0.018, Adj. RR=2.24). For this stratum, a higher percentage of Ranch Hands (8.0%) had normal peripheral pulse indices in 1985 and abnormal peripheral pulse indices in 1992 than Comparisons (3.9%).

By contrast, Model 2 did not detect a significant association between the change in peripheral pulse indices from normal in 1985 to abnormal in 1992 and initial dioxin (Table 15-38(b): p=0.865).

The longitudinal analysis for Model 3 detected significant and marginally significant relative risks for the high and low plus high Ranch Hand categories (Table 15-38(c): p=0.022, Adj. RR=2.20 and p=0.063, Adj. RR=1.67). Only 4.5 percent of Comparisons with normal peripheral pulse indices during the 1985 examination had abnormal peripheral pulse indices at the 1992 examination as compared to 7.3 and 6.8 percent of Ranch Hands in the high and low plus high dioxin categories respectively.

DISCUSSION

Cardiovascular diseases are among the most common encountered by the primary care physician. The sources of the noninvasive data analyzed in this chapter occupy a time-honored place in cardiovascular practice. Specifically, the history, physical examination, chest x ray, and resting ECG remain highly reliable indices that can alert the clinician to the presence of underlying cardiovascular disease and indicate 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 systems will vary depending on the degree of development of collateral circulatory channels. While hemodynamically significant arterial disease of the lower extremities is usually 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 be present as "silent" myocardial ischemia (32). 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 arrhythmia, to an actual myocardial infarction. These imperfections highlight the importance of the type of medical record verification conducted in this study.

In the cardiovascular assessment particularly, the physical examination can provide valuable clues to the presence of asymptomatic but significant underlying disease. Steps were taken to simplify data collection and 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 over the carotid, abdominal, and femoral vessels.

The laboratory data relevant to this chapter included the resting ECG, the standard two-view chest x ray (discussed in Chapter 20, Pulmonary Assessment), a KUB flat film of the abdomen looking for vascular calcifications, and Doppler carotid arterial and peripheral vascular studies. In clinical 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 more sophisticated 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 ECG 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.

In the analyses of verified historical variables, the history of heart disease, hypertension, and myocardial infarction was similar in Ranch Hands and Comparisons. The analyses employing current and extrapolated initial serum dioxin yielded inconsistent results between endpoints. In several models, Ranch Hands appeared less at risk for the development of heart disease over time, and a highly significant inverse dose-response effect was noted in relationship to the current body burden of dioxin. In contrast, in the prevalence of hypertension, a highly significant positive dose-response effect was noted in Ranch Hands in all models employing current serum dioxin. Though lacking a plausible biologic explanation, these results are consistent with the results published in the Serum Dioxin Analysis Report for the 1987 Followup Examination (28).

Most but not all of the objective data collected during the physical examinations were consistent with the historical analyses cited above. In the unadjusted analyses, systolic and diastolic blood pressure in continuous form were positively associated with current serum dioxin levels though, across all exposure categories, the differences in the means were slight and not medically significant. In the adjusted analyses of the clinically more relevant discrete form, there was no evidence for a dose-response effect in either systolic or diastolic blood pressure.

In the enlisted flyer occupation category, Ranch Hands were more likely than Comparisons to have funduscopic abnormalities (11.3% vs. 5.5%). Though there was an apparent positive dose-response in some models employing current serum dioxin, the prevalence of abnormalities in those personnel most highly exposed, the enlisted groundcrew, was similar in Ranch Hands and Comparisons (6.7% vs. 6.5%).

In a few of the analyses (including the composite pulse indices) employing extrapolated initial serum dioxin, Ranch Hands were found to be at increased risk for the development of peripheral pulse abnormalities. In neither the unadjusted nor adjusted analyses, however, was there any consistent evidence for a dose-response effect in the prevalence of pulse deficits and the current body burden of dioxin. Similarly, though Ranch Hands were more likely than Comparisons to report subjective symptoms of intermittent claudication, there was no apparent dose-response effect.

Although the prevalence of ECG abnormalities was similar in the two cohorts, positive dose-response effects were noted in several of the indices, including RBBB, non-specific ST- and T-wave changes, and arrhythmias.

In contrast to the results of the 1987 examinations, Ranch Hands were more likely than Comparisons to have bradycardia. A consistent inverse dose-response relationship was noted in all models relating the presence of bradycardia to the current serum dioxin level.

With few exceptions, the dependent variable-covariate analyses confirmed associations well established in clinical practice. The classic risk factors of a positive family history, age, and cigarette use contributed consistently and significantly to a history of cardiovascular disease historically and by abnormalities detected during the physical examinations. In diabetics, hypertension and myocardial infarctions were much more common than in non-diabetics by history, on examination, and by ECG. Obesity proved to be a significant risk factor for the development of hypertension but not for myocardial infarction (by history or ECG) or for other forms of heart disease. The reduced prevalence of both the history of myocardial infarction and the evidence of prior myocardial infarction on the ECG provides evidence for the protective effects of an elevation in HDL cholesterol. Although alcohol consumption was associated with the development of hypertension, it appeared to reduce significantly the risk of myocardial infarction, a protective effect that may be mediated by an associated increase in the HDL fraction of cholesterol. The increased prevalence of symptoms of intermittent claudication and peripheral pulse deficits may have been mediated by concomitant cigarette use in participants with a history of heavy alcohol consumption. Finally, consistent with the results of the 1987 examinations, Type A personality traits were not found to be associated with an increased risk for the development of cardiovascular disease.

In the longitudinal analyses, Ranch Hands were slightly more likely than Comparisons to develop peripheral pulse deficits over time, especially in models using current dioxin levels. Dorsalis pedis pulse abnormalities were far more prevalent in both Ranch Hands and Comparisons in the 1985 than in the 1992 examinations, a variance that may relate to the use of different and more accurate Doppler instrumentation in the 1992 examinations. In both the Ranch Hands and Comparisons, a similar reduction in systolic blood pressure and the incidence of hypertension has occurred over the 10 years of observation, a trend that may reflect the beneficial effects of risk factor identification and life-style modification consequent to participation in this study.

In summary, consistent with the results of prior examinations, Ranch Hands were found to be at slightly greater risk than Comparisons for the development of selected peripheral pulse deficits. The findings based on the analysis of hypertension and ST- and T-wave changes, in conjunction with the increase in the number of deaths caused by diseases of the circulatory system among Ranch Hand nonflying enlisted personnel based on the 1994 AFHS mortality update, suggest some effects from dioxin. By all other objective and subjective indices, the prevalence of cardiovascular disease appears similar in the Ranch Hands and Comparisons with no consistent evidence for a dose-response effect related to prior dioxin exposure or current serum dioxin levels.

SUMMARY

The dependent variables listed in Table 15-1 were analyzed in the cardiovascular assessment. These 26 health endpoints were analyzed for associations with group (Model 1), initial dioxin (Model 2), categorized initial dioxin (Model 3), current lipid-adjusted dioxin (Model 4), and current whole-weight dioxin (Models 5 and 6). Of the 26 variables, all were examined in discrete form, and systolic and diastolic blood pressures also were analyzed in continuous form. In addition, 7 variables were examined longitudinally (systolic blood pressure—continuous and discrete—and six pulse indices). The results of the group, initial dioxin, and current dioxin analyses are summarized in Tables 15-39 through 15-42. A summary of group-by-covariate and dioxin-by-covariate interactions is found in Table 15-43.

The covariates body fat, total cholesterol, HDL, and diabetic class, which must be introduced in adjusted models, are all known risk factors for heart diseases; however, it is recognized that adjusting for them has the potential to over-adjust the model for the effects of dioxin exposure due to their relationship with dioxin. Consequently when these covariates and occupation (which is positively associated with dioxin and is a surrogate for education) were retained in final adjusted models, additional analyses were performed with these covariates removed from the final model. Examination of these contrasts suggests a dioxin association with some health endpoints mediated through body fat, total cholesterol, HDL, and diabetic class, or through occupation. Thus the associations between these conditions and dioxin may be secondary rather than direct in nature.

Questionnaire Variables

Three variables—essential hypertension, heart disease (excluding essential hypertension), and myocardial infarction—concerning cardiovascular disease were constructed from questionnaire information, augmented by physical examination determinations, and verified by medical records review.

Table 15-39.
Summary of Group Analyses (Model 1) for Cardiovascular Variables (Ranch Hands vs. Comparisons)

	UNADJUSTED			
Variable	**All**	**Officer**	**Enlisted Flyer**	**Enlisted Groundcrew**
Verified Medical Records				
Essential Hypertension (D)	NS	ns	NS	NS
Heart Disease (D)	NS	NS	NS*	NS
Myocardial Infarction (D)	NS	ns	NS	NS
Physical Examination: Central Cardiac Function				
Systolic Blood Pressure (C)	ns	NS	ns	ns
Systolic Blood Pressure (D)	ns	ns	NS	ns
Heart Sounds (D)	NS	NS	NS	ns
Overall Electrocardiograph (ECG) (D)	ns	ns	NS	ns
ECG: Right Bundle Branch Block (RBBB) (D)	ns	ns	NS	ns
ECG: Left Bundle Branch Block (LBBB) (D)	--	--	--	--
ECG: Non-specific ST- and T-Wave Changes (D)	ns	NS	NS	ns
ECG: Bradycardia (D)	NS	ns	+0.033	NS
ECG: Tachycardia (D)	--	--	--	--
ECG: Arrhythmia (D)	NS	ns	ns	NS
ECG: Evidence of Prior Myocardial Infarction (D)	NS	ns	NS	NS
ECG: Other Diagnoses (D)	NS	NS	NS	NS
Physical Examination: Peripheral Vascular Function				
Diastolic Blood Pressure (C)	ns	ns	ns	ns
Diastolic Blood Pressure (D)	ns	NS	NS	ns
Funduscopic Examination (D)	NS	NS	NS*	NS
Carotid Bruits (D)	NS	ns	NS	NS
Radial Pulses (D)	NS	NS	--	ns
Femoral Pulses (D)	NS	NS	ns	NS
Popliteal Pulses (D)	+0.035	NS	NS	NS

Table 15-39. (Continued)
Summary of Group Analyses (Model 1) for Cardiovascular Variables
(Ranch Hands vs. Comparisons)

	UNADJUSTED			
Variable	**All**	**Officer**	**Enlisted Flyer**	**Enlisted Groundcrew**
Dorsalis Pedis Pulses (D)	NS	NS	ns	NS
Posterior Tibial Pulses (D)	+0.049	NS	NS	NS*
Leg Pulses (D)	NS	NS	ns	NS*
Peripheral Pulses (D)	NS	NS	ns	NS
Kidney, Urethra, and Bladder (KUB) X Ray Excluding Kidney Stones (D)	ns	NS	NS	ns
Questionnaire: Peripheral Vascular Function				
Intermittent Claudication and Vascular Insufficiency (ICVI) Index (D)	+0.037	NS	NS	NS

C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥ 1.00.
--: Analysis not performed due to sparse number of abnormalities.
NS or ns: Not significant ($p>0.10$).
NS*: Marginally significant ($0.05<p\leq0.10$).
Note: P-value given if $p\leq0.05$.
A capital "NS" denotes a relative risk 1.00 or greater for discrete analysis or difference of means nonnegative for continuous analysis; a lower case "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

Table 15-39. (Continued)
Summary of Group Analyses (Model 1) for Cardiovascular Variables
(Ranch Hands vs. Comparisons)

	ADJUSTED			
Variable	**All**	**Officer**	**Enlisted Flyer**	**Enlisted Groundcrew**
Verified Medical Records				
Essential Hypertension (D)	ns	ns	NS	NS
Heart Disease (D)	**(NS)	**(NS)	**(NS*)	**(NS)
Myocardial Infarction (D)	**(ns)	**(ns)	**(NS)	**(NS)
Physical Examination: Central Cardiac Function				
Systolic Blood Pressure (C)	ns	ns	ns	ns
Systolic Blood Pressure (D)	**(ns)	**(ns)	**(NS)	**(NS)
Heart Sounds (D)	**(NS)	**(NS)	**(NS)	**(ns)
Overall Electrocardiograph (ECG) (D)	ns*	ns*	NS	ns
ECG: Right Bundle Branch Block (RBBB) (D)	**(ns)	**(ns)	**(NS)	**(ns)
ECG: Left Bundle Branch Block (LBBB) (D)	--	--	--	--
ECG: Non-specific ST- and T-Wave Changes (D)	ns	ns	NS	ns
ECG: Bradycardia (D)	NS	NS	+0.047	NS
ECG: Tachycardia (D)	--	--	--	--
ECG: Arrhythmia (D)	NS	ns	ns	NS
ECG: Evidence of Prior Myocardial Infarction (D)	**(ns)	**(ns)	**(NS)	**(NS)
ECG: Other Diagnoses (D)	NS*	NS	NS	NS
Physical Examination: Peripheral Vascular Function				
Diastolic Blood Pressure (C)	**(ns)	**(ns)	**(ns)	**(ns)
Diastolic Blood Pressure (D)	ns	NS	NS	ns
Funduscopic Examination (D)	NS	NS	NS*	NS
Carotid Bruits (D)	NS	ns	NS	NS
Radial Pulses (D)	--	--	--	--
Femoral Pulses (D)	NS	NS	ns	NS
Popliteal Pulses (D)	+0.022	NS	NS	NS*

Table 15-39. (Continued)
Summary of Group Analyses (Model 1) for Cardiovascular Variables (Ranch Hands vs. Comparisons)

	ADJUSTED			
Variable	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Dorsalis Pedis Pulses (D)	NS	NS	ns	NS*
Posterior Tibial Pulses (D)	NS*	NS	NS	NS*
Leg Pulses (D)	NS	NS	ns	NS
Peripheral Pulses (D)	NS	NS	ns	NS
Kidney, Urethra, and Bladder (KUB) X Ray Excluding Kidney Stones (D)	ns	NS	NS	ns
Questionnaire: Peripheral Vascular Function				
Intermittent Claudication and Vascular Insufficiency (ICVI) Index (D)	NS*	NS	NS	NS

C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥ 1.00.
--: Analysis not performed due to sparse number of abnormalities.
NS or ns: Not significant ($p>0.10$).
NS* or ns*: Marginally significant ($0.05<p\leq 0.10$).
**(NS) or **(ns): Group-by-covariate interaction ($p\leq 0.05$); not significant when interaction is deleted; refer to Appendix K-2 for further analysis of this interaction.
**(NS*): Group-by-covariate interaction ($p\leq 0.05$); marginally significant when interaction is deleted; refer to Appendix K-2 for further analysis of this interaction.
Note: P-value given if $p\leq 0.05$.
A capital "NS" denotes a relative risk 1.00 or greater for discrete analysis or difference of means nonnegative for continuous analysis; a lower case "ns" denotes relative risk less than 1.00 for discrete analysis.

Table 15-40.
Summary of Initial Dioxin Analyses (Model 2) for Cardiovascular Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Verified Medical Records		
Essential Hypertension (D)	NS	NS
Heart Disease (D)	-0.019	**(ns)
Myocardial Infarction (D)	NS	NS
Physical Examination: Central Cardiac Function		
Systolic Blood Pressure (C)	ns	****
Systolic Blood Pressure (D)	ns	NS
Heart Sounds (D)	ns	**(ns)
Overall Electrocardiograph (ECG) (D)	ns	**(ns)
ECG: Right Bundle Branch Block (RBBB) (D)	NS	**(NS)
ECG: Left Bundle Branch Block (LBBB) (D)	--	--
ECG: Non-specific ST- and T-Wave Changes (D)	ns	NS
ECG: Bradycardia (D)	ns	-0.030
ECG: Tachycardia (D)	--	--
ECG: Arrhythmia (D)	ns	**(NS)
ECG: Evidence of Prior Myocardial Infarction (D)	NS	**(NS)
ECG: Other Diagnoses (D)	NS	NS
Physical Examination: Peripheral Vascular Function		
Diastolic Blood Pressure (C)	NS	****
Diastolic Blood Pressure (D)	NS	NS
Funduscopic Examination (D)	NS	**(NS)
Carotid Bruits (D)	ns	**(ns)
Radial Pulses (D)	ns	--
Femoral Pulses (D)	ns*	-0.020
Popliteal Pulses (D)	ns	ns

Table 15-40. (Continued)
Summary of Initial Dioxin Analyses (Model 2) for Cardiovascular Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Dorsalis Pedis Pulses (D)	NS	**(ns)
Posterior Tibial Pulses (D)	ns	**(ns)
Leg Pulses (D)	NS	**(ns)
Peripheral Pulses (D)	NS	**(ns)
Kidney, Urethra, and Bladder (KUB) X Ray Excluding Kidney Stones (D)	NS	NS
Questionnaire: Peripheral Vascular Function		
Intermittent Claudication and Vascular Insufficiency (ICVI) Index (D)	NS	NS

C: Continuous analysis.
D: Discrete analysis.
-: Relative risk < 1.00 for discrete analysis.
--: Analysis not performed due to sparse number of abnormalities.
ns*: Marginally significant ($0.05 < p \leq 0.10$).
NS or ns: Not significant ($p > 0.10$).
**(NS) or **(ns): Log_2 (initial dioxin)-by-covariate interaction ($p \leq 0.05$); not significant when interaction is deleted; refer to Appendix K-2 for further analysis of this interaction.
**** Log_2 (initial dioxin)-by-covariate interaction ($p \leq 0.01$); refer to Appendix P-2 for further analysis of this interaction.
Note: P-value given if $p \leq 0.05$.
A capital "NS" denotes a relative risk 1.00 or greater for discrete analysis or slope nonnegative for continuous analysis; a lower case "ns" denotes relative risk less than 1.00 for discrete analysis or slope negative for continuous analysis.

Table 15-41.
Summary of Categorized Dioxin Analyses (Model 3) for Cardiovascular Variables (Ranch Hands vs. Comparisons)

Variable	UNADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Verified Medical Records				
Essential Hypertension (D)	NS	ns	NS	ns
Heart Disease (D)	NS	NS	-0.016	ns
Myocardial Infarction (D)	NS	ns	NS	NS
Physical Examination: Central Cardiac Function				
Systolic Blood Pressure (C)	ns	NS	ns	ns
Systolic Blood Pressure (D)	ns	ns	ns	ns
Heart Sounds (D)	NS	NS	NS	NS
Overall Electrocardiograph (ECG) (D)	-0.027	NS	-0.021	ns
ECG: Right Bundle Branch Block (RBBB) (D)	ns	NS	NS	NS
ECG: Left Bundle Branch Block (LBBB) (D)	--	--	--	--
ECG: Non-specific ST- and T-Wave Changes (D)	ns	NS	ns	ns
ECG: Bradycardia (D)	+0.023	NS	ns	NS
ECG: Tachycardia (D)	--	--	--	--
ECG: Arrhythmia (D)	ns	NS	NS	NS
ECG: Evidence of Prior Myocardial Infarction (D)	NS	ns	NS	NS
ECG: Other Diagnoses (D)	+0.040	NS	+0.004	+0.016
Physical Examination: Peripheral Vascular Function				
Diastolic Blood Pressure (C)	ns	ns	NS	ns
Diastolic Blood Pressure (D)	ns	ns	NS	ns
Funduscopic Examination (D)	NS	NS	NS*	NS
Carotid Bruits (D)	NS	NS	ns	NS
Radial Pulses (D)	NS	NS	--	ns
Femoral Pulses (D)	ns	+0.004	NS	+0.026
Popliteal Pulses (D)	ns	NS*	+0.024	+0.014

Table 15-41. (Continued)
Summary of Categorized Dioxin Analyses (Model 3) for Cardiovascular Variables (Ranch Hands vs. Comparisons)

Variable	UNADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Dorsalis Pedis Pulses (D)	NS	ns	NS	NS
Posterior Tibial Pulses (D)	NS	NS	+0.017	+0.022
Leg Pulses (D)	NS	ns	NS*	NS
Peripheral Pulses (D)	NS	ns	NS	NS
Kidney, Urethra, and Bladder (KUB) X Ray Excluding Kidney Stones (D)	NS	ns	ns	ns
Questionnaire: Peripheral Vascular Function				
Intermittent Claudication and Vascular Insufficiency Index (ICVI) (D)	NS	NS	NS	NS

C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥ 1.00 for discrete analysis.
-: Relative risk < 1.00 for discrete analysis.
--: Analysis not performed due to sparse number of abnormalities.
NS or ns: Not significant ($p>0.10$).
NS*: Marginally significant ($0.05<p\leq0.10$).
Note: P-value given if $p\leq0.05$.
A capital "NS" denotes a relative risk 1.00 or greater for discrete analysis or difference of means nonnegative for continuous analysis; a lower case "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

Table 15-41. (Continued)
Summary of Categorized Dioxin Analyses (Model 3) for Cardiovascular Variables (Ranch Hands vs. Comparisons)

Variable	ADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Verified Medical Records				
Essential Hypertension (D)	ns	ns	NS	NS
Heart Disease (D)	NS	NS	ns	ns
Myocardial Infarction (D)	**(NS)	**(ns)	**(NS)	**(NS)
Physical Examination: Central Cardiac Function				
Systolic Blood Pressure (C)	ns	ns	ns	ns
Systolic Blood Pressure (D)	ns	ns	NS	ns
Heart Sounds (D)	**(NS)	**(NS)	**(NS)	**(NS)
Overall Electrocardiograph (ECG) (D)	-0.003	ns	ns	ns
ECG: Right Bundle Branch Block (RBBB) (D)	**(ns)	**(ns)	**(NS)	**(NS)
ECG: Left Bundle Branch Block (LBBB) (D)	--	--	--	--
ECG: Non-specific ST- and T-Wave Changes (D)	**(ns*)	**(ns)	**(NS)	**(ns)
ECG: Bradycardia (D)	**(+0.021)	**(NS)	**(ns)	**(ns)
ECG: Tachycardia (D)	--	--	--	--
ECG: Arrhythmia (D)	**(ns)	**(NS)	**(NS)	**(NS)
ECG: Evidence of Prior Myocardial Infarction (D)	ns	ns	NS	NS
ECG: Other Diagnoses (D)	--	--	--	--
Physical Examination: Peripheral Vascular Function				
Diastolic Blood Pressure (C)	**(ns)	**(ns)	**(NS)	**(ns)
Diastolic Blood Pressure (D)	****	****	****	****
Funduscopic Examination (D)	NS	NS	NS	NS
Carotid Bruits (D)	**(NS)	**(NS)	**(NS)	**(NS)
Radial Pulses (D)	--	--	--	--
Femoral Pulses (D)	ns	+0.005	NS	+0.035

Table 15-41. (Continued)
Summary of Categorized Dioxin Analyses (Model 3) for Cardiovascular Variables (Ranch Hands vs. Comparisons)

	ADJUSTED			
Variable	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Popliteal Pulses (D)	ns	NS*	+0.016	+0.012
Dorsalis Pedis Pulses (D)	**(NS)	**(ns)	**(NS)	**(NS)
Posterior Tibial Pulses (D)	**(NS)	**(NS)	**(+0.031)	**(+0.050)
Leg Pulses (D)	NS	ns	NS	NS
Peripheral Pulses (D)	NS	ns	NS	NS
Kidney, Urethra, and Bladder (KUB) X Ray Excluding Kidney Stones (D)	ns	ns	ns	ns
Questionnaire: Peripheral Vascular Function				
Intermittent Claudication and Vascular Insufficiency Index (ICVI) (D)	**(NS)	**(NS)	**(NS)	**(NS)

C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥ 1.00 for discrete analysis.
-: Relative risk < 1.00 for discrete analysis.
--: Analysis not performed due to sparse number of abnormalities.
NS or ns: Not significant ($p>0.10$).
NS*: Marginally significant ($0.05<p\leq 0.10$).
**(NS) or **(ns): Categorized dioxin-by-covariate interaction ($0.01<p\leq 0.05$); not significant when interaction is deleted; refer to Appendix K-2 for further analysis of this interaction.
**(ns*): Categorized dioxin-by-covariate interaction ($0.01<p\leq 0.05$); marginally significant when interaction is deleted; refer to Appendix K-2 for further analysis of this interaction.
**(...): Categorized dioxin-by-covariate interaction ($0.01<p\leq 0.05$); significant when interaction is deleted and p-value is given in parentheses; refer to Appendix K-2 for further analysis of this interaction.
**** Categorized dioxin-by-covariate interaction ($p\leq 0.01$); refer to Appendix K-2 for further analysis of this interaction.
Note: P-value given if $p\leq 0.05$.
A capital "NS" denotes a relative risk 1.00 or greater for discrete analysis or difference of means nonnegative for continuous analysis; a lower case "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

Table 15-42.
Summary of Current Dioxin Analyses (Models 4, 5, and 6) for Cardiovascular Variables (Ranch Hands Only)

Variable	UNADJUSTED		
	Model 4: Lipid-Adjusted Current Dioxin	Model 5: Whole-Weight Current Dioxin	Model 6: Whole-Weight Current Dioxin Adjusted for Total Lipids
Verified Medical Records			
Essential Hypertension (D)	+<0.001	+<0.001	+0.005
Heart Disease (D)	-0.004	-0.004	-0.005
Myocardial Infarction (D)	NS	NS	NS
Physical Examination: Central Cardiac Function			
Systolic Blood Pressure (C)	NS*	+0.016	NS
Systolic Blood Pressure (D)	NS	NS*	NS
Heart Sounds (D)	NS	NS	NS
Overall Electrocardiograph (ECG) (D)	NS	NS	NS
ECG: Right Bundle Branch Block (RBBB) (D)	NS	NS	NS
ECG: Left Bundle Branch Block (LBBB) (D)	--	--	--
ECG: Non-specific ST- and T-Wave Changes (D)	NS	NS	NS
ECG: Bradycardia (D)	-0.012	-0.011	ns*
ECG: Tachycardia (D)	--	--	--
ECG: Arrhythmia (D)	NS	NS	NS
ECG: Evidence of Prior Myocardial Infarction (D)	NS	NS	NS
ECG: Other Diagnoses (D)	NS	NS	NS
Physical Examination: Peripheral Vascular Function			
Diastolic Blood Pressure (C)	+0.005	+0.001	+0.020
Diastolic Blood Pressure (D)	NS	NS	NS
Funduscopic Examination (D)	NS*	+0.045	NS
Carotid Bruits (D)	ns	ns	ns*
Radial Pulses (D)	ns	ns	ns
Femoral Pulses (D)	NS	NS	NS
Popliteal Pulses (D)	NS	NS	NS

Table 15-42. (Continued)
Summary of Current Dioxin Analyses (Models 4, 5, and 6) for Cardiovascular Variables (Ranch Hands Only)

	UNADJUSTED		
Variable	Model 4: Lipid-Adjusted Current Dioxin	Model 5: Whole-Weight Current Dioxin	Model 6: Whole-Weight Current Dioxin Adjusted for Total Lipids
Dorsalis Pedis Pulses (D)	NS	NS	NS
Posterior Tibial Pulses (D)	NS	NS	ns
Leg Pulses (D)	NS	NS	ns
Peripheral Pulses (D)	ns	NS	ns
Kidney, Urethra, and Bladder (KUB) X Ray Excluding Kidney Stones (D)	NS	NS	ns
Questionnaire: Peripheral Vascular Function			
Intermittent Claudication and Vascular Insufficiency Index (ICVI) (D)	NS	NS	ns

C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥ 1.00 for discrete analysis or slope nonnegative for continuous analysis.
-: Relative risk < 1.00 for discrete analysis.
--: Analysis not performed due to sparse number of abnormalities.
NS or ns: Not significant.
NS* or ns*: Marginally significant ($0.05 < p \leq 0.10$).
Note: P-value given if $p \leq 0.05$.
A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or slope nonnegative for continuous analysis; a lower case "ns" denotes relative risk less than 1.00 for discrete analysis.

Table 15-42. (Continued)
Summary of Current Dioxin Analyses (Models 4, 5, and 6) for Cardiovascular Variables (Ranch Hands Only)

Variable	ADJUSTED		
	Model 4: Lipid-Adjusted Current Dioxin	Model 5: Whole-Weight Current Dioxin	Model 6: Whole-Weight Current Dioxin Adjusted for Total Lipids
Verified Medical Records			
Essential Hypertension (D)	+0.021	+0.005	+0.049
Heart Disease (D)	ns*	ns*	ns*
Myocardial Infarction (D)	**(NS)	**(NS)	**(NS)
Physical Examination: Central Cardiac Function			
Systolic Blood Pressure (C)	**(NS)	NS	NS
Systolic Blood Pressure (D)	NS	NS	NS
Heart Sounds (D)	NS	NS	NS
Overall Electrocardiograph (ECG) (D)	NS	**(NS)	**(NS)
ECG: Right Bundle Branch Block (RBBB) (D)	NS*	NS*	+0.038
ECG: Left Bundle Branch Block (LBBB) (D)	--	--	--
ECG: Non-specific ST- and T-Wave Changes (D)	+0.017	+0.015	+0.028
ECG: Bradycardia (D)	**(ns*)	**(-0.020)	**(-0.049)
ECG: Tachycardia (D)	--	--	--
ECG: Arrhythmia (D)	NS*	**(NS*)	**(NS*)
ECG: Evidence of Prior Myocardial Infarction (D)	NS*	+0.020	NS
ECG: Other Diagnoses (D)	**(NS)	**(NS)	**(NS)
Physical Examination: Peripheral Vascular Function			
Diastolic Blood Pressure (C)	NS	NS	NS
Diastolic Blood Pressure (D)	NS	NS	NS
Funduscopic Examination (D)	NS*	+0.042	+0.037
Carotid Bruits (D)	****	****	****
Radial Pulses (D)	ns	ns	ns
Femoral Pulses (D)	NS	NS	NS

Table 15-42. (Continued)
Summary of Current Dioxin Analyses (Models 4, 5, and 6) for Cardiovascular Variables (Ranch Hands Only)

	ADJUSTED		
Variable	Model 4: Lipid-Adjusted Current Dioxin	Model 5: Whole-Weight Current Dioxin	Model 6: Whole-Weight Current Dioxin Adjusted for Total Lipids
Popliteal Pulses (D)	NS	****	**(NS)
Dorsalis Pedis Pulses (D)	NS	NS	NS
Posterior Tibial Pulses (D)	NS	NS*	NS
Leg Pulses (D)	NS	NS	NS
Peripheral Pulses (D)	NS	NS	NS
Kidney, Urethra, and Bladder (KUB) X Ray Excluding Kidney Stones (D)	****	****	****
Questionnaire: Peripheral Vascular Function			
Intermittent Claudication and Vascular Insufficiency Index (ICVI) (D)	NS	NS	NS

C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥ 1.00 for discrete analysis.
-: Relative risk < 1.00 for discrete analysis.
--: Analysis not performed due to sparse number of abnormalities.
NS or ns: Not significant.
NS* or ns*: Marginally significant ($0.05 < p \leq 0.10$).
**(NS): Log_2 (current dioxin+1)-by-covariate interaction ($p \leq 0.05$); not significant when interaction is deleted; refer to Appendix K-2 for further analysis of this interaction.
**(NS*) or **(ns*): Log_2 (current dioxin+1)-by-covariate interaction ($p \leq 0.05$); marginally significant when interaction is deleted; refer to Appendix K-2 for further analysis of this interaction.
**(....): Log_2 (current dioxin+1)-by-covariate interaction; significant when interaction is deleted and p-value is given in parentheses; refer to Appendix Table K-2 for further analysis of this interaction.
**** Log_2 (current dioxin+1)-by-covariate interaction ($p \leq 0.01$); refer to Appendix K-2 for further analysis of this interaction.
Note: P-value given if $p \leq 0.05$.
A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or slope nonnegative for continuous analysis; a lower case "ns" denotes relative risk less than 1.00 for discrete analysis.

Table 15-43.
Summary of Group-by-Covariate and Dioxin-by-Covariate Interactions from Adjusted Analyses of Cardiovascular Variables

Model	Variable	Covariate
1[a]	Heart Disease	Lifetime Alcohol History
	Myocardial Infarction	Body Fat
	Systolic Blood Pressure (D)	Total Cholesterol
	Heart Sounds	Age
	ECG: Right Bundle Branch Block	Diabetic Class, Current Cigarette Smoking
	ECG: Evidence of Prior Myocardial Infarction	Body Fat
	Diastolic Blood Pressure (C)	Age
2[b]	Heart Disease	Personality Type
	Systolic Blood Pressure (C)	Diabetic Class
	Heart Sounds	Age
	Overall Electrocardiograph	Total Cholesterol
	ECG: Right Bundle Branch Block	Lifetime Cigarette Smoking History
	ECG: Arrhythmia	Current Cigarette Smoking, HDL Cholesterol
	ECG: Evidence of Prior Myocardial Infarction	Diabetic Class
	Diastolic Blood Pressure (C)	Occupation
	Funduscopic Examination	Race
	Carotid Bruits	Lifetime Cigarette Smoking History, Family History of Heart Disease
	Dorsalis Pedis Pulses	Lifetime Cigarette Smoking History
	Posterior Tibial Pulses	Occupation, Lifetime Cigarette Smoking History, Family History of Heart Disease
	Leg Pulses	Lifetime Cigarette Smoking History, Personality Type
	Peripheral Pulses	Lifetime Cigarette Smoking History, Personality Type
3[c]	Myocardial Infarction	Body Fat
	Heart Sounds	Age
	ECG: Right Bundle Branch Block	Diabetic Class
	ECG: Non-specific ST- and T-Wave Changes	Lifetime Cigarette Smoking History
	ECG: Bradycardia	Personality Type
	ECG: Arrhythmia	HDL Cholesterol
	Diastolic Blood Pressure (C)	Family History of Heart Disease
	Diastolic Blood Pressure (D)	Family History of Heart Disease
	Carotid Bruits	Lifetime Alcohol History
	Dorsalis Pedis Pulses	Age
	Posterior Tibial Pulses	Current Cigarette Smoking
	Intermittent Claudication and Vascular Insufficiency Index	Lifetime Cigarette Smoking History
4[d]	Myocardial Infarction	Race
	Systolic Blood Pressure (C)	Diabetic Class
	ECG: Bradycardia	Personality Type, Diabetic Class
	ECG: Other Diagnoses	Occupation
	Carotid Bruits	Total Cholesterol
	Kidney, Urethra, & Bladder X Ray	Race

Table 15-43. (Continued)
Summary of Group-by-Covariate and Dioxin-by-Covariate Interactions from Adjusted Analyses of Cardiovascular Variables

Model	Variable	Covariate
5[e]	Myocardial Infarction	Race
	Overall Electrocardiograph	Total Cholesterol
	ECG: Bradycardia	Personality Type
	ECG: Arrhythmia	Current Cigarette Smoking
	ECG: Other Diagnoses	Occupation, Race
	Carotid Bruits	Family History of Heart Disease
	Popliteal Pulses	Occupation
	Kidney, Urethra, & Bladder X Ray	Race
6[f]	Myocardial Infarction	Race
	Overall Electrocardiograph	Total Cholesterol
	ECG: Bradycardia	Personality Type
	ECG: Arrhythmia	Current Cigarette Smoking
	ECG: Other Diagnoses	Occupation, Race
	Carotid Bruits	Family History of Heart Disease
	Popliteal Pulses	Occupation
	Kidney, Urethra, & Bladder X Ray	Race

C: Continuous analysis
D: Discrete analysis.

[a] Group Analysis (Ranch Hands vs. Comparison).
[b] Ranch Hands—Log_2 (Initial Dioxin)
[c] Categorized Dioxin.
[d] Ranch Hands—Log_2 (Current Lipid-Adjusted Dioxin + 1).
[e] Ranch Hands—Log_2 (Current Whole Weight Dioxin + 1).
[f] Ranch Hands—Log_2 (Current Whole Weight Dioxin + 1), Adjusted for Total Lipids.

Model 1: Group Analysis

Examination of the unadjusted and adjusted results from Model 1 showed no significant overall group differences among the three cardiovascular history variables. However, when the analyses were stratified by occupation, a marginally significant group difference was detected for heart disease in the enlisted flyer stratum (Adj. RR=1.51), with Ranch Hand enlisted flyers at a higher risk than comparison enlisted flyers.

Model 2: Initial Dioxin Analysis

In the unadjusted analyses of Model 2, verified heart disease exhibited a significant inverse relationship with initial dioxin. However, after adjusting for covariates, the association was no longer significant.

Model 3: Categorized Dioxin Analysis

In Model 3, the unadjusted analyses revealed significantly more comparisons with a history of heart disease than the Ranch Hands in the high dioxin category. However, after adjusting for covariates, the association was no longer significant.

Models 4, 5, and 6: Current Dioxin Analyses

The unadjusted and adjusted analyses of Models 4, 5, and 6 revealed significant positive associations between current dioxin and verified essential hypertension. In contrast, the analyses of verified heart disease uncovered significant inverse relationships with current dioxin for the Models 4 through 6, which became marginally significant after adjustment for covariates.

Physical Examination: Central Cardiac Function Variables

Variables analyzed in the evaluation of the central cardiac function included systolic blood pressure, heart sounds, and nine conditions associated with the ECG (overall ECG reading, RBBB, LBBB, nonspecific ST- and T-wave changes, bradycardia, tachycardia, arrhythmia, evidence of prior myocardial infarction and other diagnoses). However, only 1 Ranch Hand and 10 Comparisons had LBBB; thus, relative risks, confidence intervals, and p-values were not presented. Similarly, 3 Ranch Hands and 2 Comparisons had tachycardia; consequently, no analyses except Model 1 unadjusted analyses were performed on this cardiovascular endpoint.

Model 1: Group Analysis

The unadjusted analyses did not detect any overall group differences for the central cardiac function endpoints. The adjusted analyses revealed marginally significant associations between group and overall ECG (Adj. RR=0.82) and other ECG diagnoses (Adj. RR=2.68). Ranch Hands had fewer overall ECG abnormalities and more other ECG diagnoses then Comparisons.

Stratification by occupational category revealed that Ranch Hand officers had a marginally significantly higher prevalence of abnormal overall ECGs than the Comparison officers in the adjusted analysis. The enlisted flyer Ranch Hands had a significantly higher prevalence of bradycardia in both the unadjusted and adjusted analyses.

The longitudinal analyses of systolic blood pressure in continuous form uncovered a marginally significant overall group difference (Diff. of Exam Mean Change=-1.25). These analyses also revealed a significant difference in the change in mean systolic blood pressure from 1982 to 1992 between Ranch Hands and Comparisons in the enlisted groundcrew stratum. Systolic blood pressure decreased significantly more for Ranch Hands (Mean Change=-11.27) in the 10-year period than for Comparisons (Mean Change=-8.83) in the enlisted groundcrew stratum. Longitudinal analyses of discretized systolic blood pressure were not significant.

Model 2: Initial Dioxin Analysis

The unadjusted analyses did not detect any significant relationships between the central cardiac function variables and initial dioxin. The adjusted analyses revealed a significant inverse association between initial dioxin and bradycardia. Significant interactions with initial dioxin were revealed with a variety of covariates: age, current cigarette smoking, lifetime cigarette smoking history, total cholesterol, HDL cholesterol, and diabetic class.

The longitudinal analyses of systolic blood pressure did not find any significant associations with initial dioxin.

Model 3: Categorized Dioxin Analysis

The unadjusted analyses revealed significant differences in the prevalence of abnormal overall ECG readings between Comparisons and Ranch Hands in the background and high dioxin categories. In each case, the Comparisons had a greater percentage of abnormalities. After adjusting for covariates, only the contrast of the Comparisons and the background Ranch Hands remained significant (Adj. RR=0.62).

The unadjusted and adjusted analysis of bradycardia showed a higher percentage of bradycardia in the background Ranch Hands category than in the Comparisons (Adj. RR=2.15). The unadjusted analysis for other ECG diagnoses revealed a significantly higher percentage of abnormalities in the background, high, and low plus high Ranch Hand categories than in the Comparisons category. The adjusted analysis of other ECG diagnoses were not performed due to the sparse number of abnormalities.

The longitudinal analyses of systolic blood pressure did not find any significant associations with categorized dioxin.

Models 4, 5, and 6: Current Dioxin Analyses

Systolic blood pressure in its continuous form showed marginally significant and significant direct relationships with current dioxin in the unadjusted analyses of Models 4 and

5 respectively. After adjusting for covariates, the relationships were no longer significant except when HDL, body fat, and diabetic class were removed from the adjusted model. Systolic blood pressure in its discrete form showed a marginally significant positive relationship with current dioxin in the unadjusted analysis of Model 5; the association became nonsignificant after adjusting for covariates except when body fat and diabetic class were removed from the adjusted model. Consistent with a TCDD effect mediated through increases in these recognized risk factors for cardiovascular disease.

The adjusted analyses for RBBB, non-specific ST- and T-wave changes, and arrhythmia, all revealed significant or marginally significant positive relationships with current dioxin in Models 4 through 6. The analysis for bradycardia revealed a significant inverse relationship with current dioxin in both the unadjusted and adjusted analyses of Models 4, 5, and 6. The adjusted analyses of evidence of prior myocardial infarction revealed a marginally significant positive association with current dioxin for Model 4 and a significant positive association for Model 5.

Physical Examination: Peripheral Vascular Function Variables

The peripheral vascular function was assessed during the cardiovascular examination by the diastolic blood pressure; funduscopic examination of small vessels in the retina; the presence or absence of carotid bruits; and Doppler readings of the radial, femoral, popliteal, dorsalis pedis, and posterior tibial pulses. Two pulse indices were constructed from the above pulse measurements: leg pulses (femoral, popliteal, dorsalis pedis, and posterior tibial pulses) and peripheral pulses (radial and leg pulses). Both of these indices were considered normal if all components were normal and abnormal if one or more pulses were abnormal. In addition, the results of a kidney, urethra, and bladder x ray focusing on vascular calcification and a measure for detecting intermittent claudication and vascular insufficiency were analyzed.

Model 1: Group Analysis

In the unadjusted analyses of Model 1, popliteal pulses, posterior tibial pulses, and the ICVI index showed significant differences between Ranch Hands and Comparisons. Ranch Hands had a higher percentage of abnormalities than Comparisons for these three endpoints. The enlisted groundcrew Ranch Hands had a marginally significantly higher prevalence of abnormal posterior tibial and leg pulses than the enlisted groundcrew Comparisons. The enlisted flyer Ranch Hands had a marginally significantly higher prevalence of abnormal funduscopic examinations than the enlisted flyer Comparisons.

The adjusted analyses revealed a significant difference between groups for popliteal pulses and marginally significant difference between groups for posterior tibial pulses and the ICVI index with Ranch Hands having a higher percentage of abnormalities than Comparisons. Similar to the unadjusted analyses, the enlisted flyer Ranch Hands had a marginally significantly higher prevalence of abnormal funduscopic examinations than the enlisted flyer Comparisons and the enlisted groundcrew Ranch Hands had a marginally significantly higher prevalence of abnormal popliteal, dorsalis pedis, and posterior tibial pulses than the enlisted groundcrew Comparisons.

The longitudinal analyses of the six pulse endpoints—femoral, popliteal, dorsalis pedis, posterior tibial, leg, and peripheral—revealed significant and marginally significant overall differences between Ranch Hands and Comparisons for all of the pulses except femoral pulses. Specifically, enlisted groundcrew Ranch Hands who had normal pulse measurements in 1985 had higher percentages of diminished pulses in 1992 than their Comparisons.

Model 2: Initial Dioxin Analysis

The unadjusted analyses revealed a marginally significant inverse association between femoral pulses and initial dioxin that became significant after adjustment for covariates (Adj. RR=0.46). No other peripheral vascular function variables were significantly associated with initial dioxin. The adjusted analyses of the peripheral vascular function variables revealed significant interactions between initial dioxin and occupation, race, lifetime cigarette smoking history, personality type, and family history of heart disease.

The longitudinal analyses of the pulse variables did not detect any significant positive associations with initial dioxin.

Model 3: Categorized Dioxin Analysis

The unadjusted analyses of the funduscopic examination and leg pulses revealed a marginally significant higher percentage of abnormalities in the high Ranch Hand category than in the Comparison category. After adjusting for covariates, the associations were no longer significant except after removing occupation, HDL, body fat, and diabetic class from the adjusted model. The unadjusted and adjusted Model 3 analyses for femoral pulses revealed a significantly higher percentage of abnormalities in the low and low plus high Ranch Hand categories than in the Comparison category. Similarly, the unadjusted and adjusted analyses of popliteal pulses showed a significant or marginally significant difference between Comparisons and Ranch Hands in the low, high, and low plus high dioxin categories. For each contrast, Ranch Hands displayed a higher percentage of diminished pulses. Finally, the analyses of posterior tibial pulses showed significant differences between high Ranch Hands and Comparisons and between low plus high Ranch Hands and Comparisons with the Ranch Hands having a higher percentage of abnormal posterior tibial pulses than the Comparisons.

The longitudinal analyses showed significantly higher percentages of pulse abnormalities for Ranch Hands in the low dioxin category than for Comparisons for femoral and popliteal pulses. Similarly, the analyses showed a greater percentage of pulse deficits for Ranch Hands in the high dioxin category than for Comparisons for all pulse endpoints except femoral and corresponding differences between Ranch Hands in the low plus high dioxin category and Comparisons for all pulse endpoints.

Models 4, 5, and 6: Current Dioxin Analyses

The unadjusted analysis of diastolic blood pressure in continuous form detected significant positive associations with current dioxin for Models 4, 5, and 6. However, these associations became nonsignificant after adjustment for significant covariates. The unadjusted and adjusted analyses of the funduscopic examination results revealed marginally significant or significant positive associations with current dioxin in Models 4 through 6.

None of the unadjusted analyses of the pulse endpoints detected any significant associations with current dioxin in Models 4 through 6. The adjusted analyses of the pulse variables revealed a marginally significant positive relationship between current dioxin and posterior tibial pulses.

CONCLUSION

The cardiovascular evaluation found a marginally significant group difference for verified heart disease excluding essential hypertension for enlisted flyers with Ranch Hands having a higher history of post-SEA heart disease than Comparisons. However, similar to the 1987 study, verified heart disease significantly decreased for increasing levels of current dioxin. Ranch Hands also displayed an increased history of essential hypertension for increasing levels of current dioxin.

A few other central cardiac function endpoints including non-specific ST- and T-wave changes, RBBB, and prior ECG evidence of myocardial infarction displayed significant positive associations with current dioxin; however, none of these endpoints also displayed any group difference between Ranch Hands and Comparisons. These findings, in conjunction with the increase in the number of deaths caused by diseases of the circulatory system among Ranch Hand nonflying enlisted personnel based on the 1994 AFHS mortality update (29), may show potential associations with dioxin requiring further observation.

The analyses of the peripheral vascular function variables displayed significant group differences for the enlisted groundcrew stratum for a few of the pulse endpoints and significant differences between Ranch Hands in the high current dioxin category and Comparisons. However, none of these relationships were reinforced by a significant association with initial or current dioxin. Longitudinal analyses of the pulses endpoints also indicated that Ranch Hands in the enlisted groundcrew stratum and in the high initial dioxin category had a greater prevalence of pulse deficits since the 1985 examination than Comparisons. Again these relationships were not reinforced by a significant dose-response effect with initial dioxin.

In general, after reviewing the results of the cardiovascular assessment as a whole, the development of cardiovascular disease does not appear to be associated positively with dioxin. However, dioxin associations with selected endpoints, as discussed above, together with mortality results, point to the need for further evaluation in future studies.

CHAPTER 15
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