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AIR FORCE HEALTH STUDY

An Epidemiologic Investigation of
Health Effects in Air Force Personnel
Following Exposure to Herbicides

SAIC Team
William D. Grubbs, Ph.D.
Michael B. Lustik, M.S.
Amy S. Brockman, M.S.
Scott C. Henderson, M.S.
Frank R. Burnett, M.S.
Rebecca G. Land, M.S.
Dawn J. Osborne, M.S.
Vanessa K. Rocconi, B.S.
Margaret E. Schrieber, B.A.
David E. Williams, M.D., SCRF

Air Force Team
Col William H. Wolfe, M.D., M.P.H.
Joel E. Michalek, Ph.D.
Col Judson C. Miner, D.V.M., M.P.H.
Col Gary L. Henriksen, M.D., M.P.H.
Lt Col James A. Swaby, Ph.D., B.C.E.

Project Manager: Manager E.B. Owens, Ph.D.
Statistical Task Manager: W.D. Grubbs
SAIC Editor: Jean M. Ault, B.A.

Program Manager: R.W. Ogershok

SCIENCE APPLICATIONS INTERNATIONAL
1710 Goodridge Drive
McLean, Virginia 22102

in conjunction with:

SCRIPPS CLINIC & RESEARCH FOUNDATION,
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CHICAGO, ILLINOIS

EPIDEMIOLOGIC RESEARCH DIVISION
ARMSTRONG LABORATORY
HUMAN SYSTEMS CENTER (AFMC)
BROOKS AIR FORCE BASE, TEXAS 78235

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Armstrong Laboratory
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Brooks Air Force Base, Texas 78235

TABLE OF CONTENTS

VOLUME IV

	Page
CHAPTER 14 DERMATOLOGIC ASSESSMENT	14-1
INTRODUCTION	14-1
Background	14-1
Summary of Previous Analyses of the Air Force Health Study	14-2
1982 Baseline Study Summary Results	14-2
1985 Followup Study Summary Results	14-3
1987 Followup Study Summary Results	14-4
Serum Dioxin Analysis of 1987 Followup Study Summary Results	14-4
Parameters for the Dermatologic Assessment	14-5
Dependent Variables	14-5
Medical Records Data	14-5
Physical Examination Data	14-6
Covariates	14-6
Statistical Methods	14-7
RESULTS	14-7
Dependent Variable-Covariate Associations	14-7
Exposure Analysis	14-10
Verified Medical Records variables	14-11
Occurrence of Acne (Lifetime)	14-11
Acne Relative to SEA Time of Duty in SEA (Pre- and Post-SEA and Post-SEA vs Pre-SEA and None)	14-16
Acne Relative to Time of Duty in SEA (Post-SEA vs None)	14-16
Acne Relative to Time of Duty in SEA (Pre- and Post-SEA vs Pre-SEA)	14-25
Location of Acne (Post-SEA Only)	14-25
Location of Acne (Pre- and Post-SEA and Post-SEA)	14-35
Physical Examination Variables	14-35
Other Abnormalities	14-35
Dermatology Index	14-45
DISCUSSION	14-50
SUMMARY	14-52
Model 1: Group Analysis	14-52
Model 2: Initial Dioxin Analysis	14-52
Model 3: Categorized Dioxin Analysis	14-52
Models 4, 5, and 6: Current Dioxin Analysis	14-61
CONCLUSION	14-61
REFERENCES	14-62

LIST OF TABLES

		Page
Table 14-1.	Statistical Analyses for the Dermatologic Assessment	14-8
Table 14-2.	Number of Participants with Missing Data for the Dermatological Assessment	14-9
Table 14-3.	Analysis of Occurrence of acne	14-12
Table 14-4.	Analysis of Acne Relative to Time of Duty in SEA (Pre- and Post-SEA and Post-SEA vs Pre-SEA and None)	14-17
Table 14-5.	Analysis of Acne Relative to time of Duty (Post-SEA vs None)	14-21
Table 14-6.	Analysis of Acne Relative to SEA Tour of Duty (Pre- and Post-SEA vs Pre-SEA)	14-26
Table 14-7.	Number of Participants with, and Location of, Post-SEA Acne	14-30
Table 14-8.	Analysis of Location of Acne (Post-SEA)	14-31
Table 14-9.	Number of Participants with, and Location of, Pre- and Post-SEA and Post-SEA Acne	14-36
Table 14-10.	Analysis of Location of Acne (Pre- and Post-SEA and Post-SEA)	14-37
Table 14-11.	Analysis of Other Abnormalities	14-41
Table 14-12.	Analysis of Dermatology Index	14-46
Table 14-13.	Summary of Group Analyses (Model 1) for Dermatology Variables (Ranch Hands vs Comparisons)	14-53
Table 14-14.	Summary of Initial dioxin Analyses (Model 2) for Dermatology Variables (Ranch Hands Only)	14-55
Table 14-15.	Summary of Categorized Dioxin Analyses (Model 3) for Dermatology Variables (Ranch Hands vs Comparisons)	14-56
Table 14-16.	Summary of Group Analyses (Models 4, 5, and 6) for Dermatology Variables (Ranch Hands Only)	14-58
Table 14-17.	Summary Table of Group-by-Covariate and Dioxin-by-Covariate Interactions from Adjusted analyses of Dermatology Variables	14-60

TABLE OF CONTENTS

	Page
CHAPTER 15 CARDIOVASCULAR ASSESSMENT	15-1
INTRODUCTION	15-1
Background	15-1
Summary of Previous Analyses of the Air Force Health Study	15-2
1982 Baseline Study Summary Results	15-2
1985 Followup Study Summary Results	15-3
1987 Followup Study Summary Results	15-3
Serum Dioxin Analysis of 1987 Followup Study Summary Results	15-3
Parameters for the Cardiovascular Assessment	15-4
Dependent Variables	15-4
Medical Records Data	15-4
Physical Examination Data	15-4
Self-Reported Questionnaire Data	15-6
Associations of Coronary Heart Disease from Medical Records and Physical Examination Results	15-6
Covariates	15-6
Statistical Methods	15-8
Longitudinal Analysis	15-17
RESULTS	15-17
Dependent Variable-Covariate Associations	15-17
Association Between Cardiovascular Findings and Verified Essential Hypertension, Verified Heart Disease, and Verified Myocardial Infarction	15-22
Exposure Analysis	15-23
Verified Medical Records Variables	15-24
Essential Hypertension	15-24
Heart Disease (Excluding Hypertension)	15-29
Myocardial Infarction	15-34
Physical Examination Data	15-39
Systolic Blood Pressure (Continuous)	15-39
Systolic Blood Pressure (Discrete)	15-44
Heart Sounds	15-49
Overall Electrocardiograph (ECG)	15-49
Right Bundle Branch Block (RBBB)	15-58
Left Bundle Branch Block (LBBB)	15-63
Non-Specific ST- and T-Wave Changes	15-63
ECG: Bradycardia	15-70
ECG: Tachycardia	15-75
ECG: Arrhythmia	15-75
ECG: Evidence of Prior Myocardial Infarction	15-82
ECG: Other Diagnoses	15-82
Physical Examination: Peripheral Vascular Function Variables	15-91

TABLE OF CONTENTS (Continued)

Page

Diastolic Blood Pressure (Continuous) 15-91
Diastolic Blood Pressure (Discrete) 15-96
Funduscopic Examination 15-101
Carotid Bruits 15-106
Radial Pulses 15-106
Femoral Pulses 15-115
Popliteal Pulses 15-115
Dorsalis Pedis Pulses 15-124
Posterior Tibial Pulses 15-129
Leg Pulses 15-134
Peripheral Pulses 15-139
Kidney, Urethra, and Bladder (KUB) X-ray (Excluding Kidney Stones) 15-139
Intermittent Claudication and Vascular Insufficiency (ICVI) Index . 15-148
Longitudinal Analysis 15-153
Physical Examination Variables 15-178
Systolic Blood Pressure (Continuous) 15-178
Systolic Blood Pressure (Discrete) 15-178
Femoral Pulses 15-178
Popliteal Pulses 15-179
Dorsalis Pedis Pulses 15-179
Posterior Tibial Pulses 15-180
Leg Pulses 15-180
Peripheral Pulses 15-181
DISCUSSION 15-181
SUMMARY 15-184
Questionnaire Variables 15-184
Model 1: Group Analysis 15-201
Model 2: Initial Dioxin Analysis 15-201
Model 3: Categorized Dioxin Analysis 15-201
Model 4, 5, and 6: Current Dioxin Analyses 15-201
Physical Examination: Central Cardiac Function Variables 15-201
Model 1: Group Analysis 15-201
Model 2: Initial Dioxin Analysis 15-202
Model 3: Categorized dioxin Analysis 15-202
Model 4, 5, and 6: Current Dioxin Analyses 15-202
Physical Examination : Peripheral Vascular Function Variables 15-203
Model 1: Group Analysis 15-203
Model 2: Initial dioxin Analysis 15-204
Model 3: Categorized Dioxin Analysis 15-204
Model 4, 5, and 6: Current Dioxin Analyses 15-204
CONCLUSION 15-205
REFERENCES 15-206

LIST OF TABLES

		Page
Table 15-1.	Statistical Analyses for the Cardiovascular Assessment	15-9
Table 15-2.	Number of Participants with Missing Data for, or Excluded from, the Cardiovascular Assessment	15-15
Table 15-3.	Analysis of Verified Essential Hypertension	15-25
Table 15-4.	Analysis of Verified Heart Disease (Excluding Essential Hypertension)	15-30
Table 15-5.	Analysis of Verified Myocardial Infarction	15-35
Table 15-6.	Analysis of Systolic Blood Pressure (mm Hg) (Continuous)	15-40
Table 15-7.	Analysis of Systolic blood Pressure (Discrete)	15-45
Table 15-8.	Analysis of Heart Sounds	15-50
Table 15-9.	Analysis of Overall electrocardiograph (ECG)	15-54
Table 15-10.	Analysis of ECG: Right Bundle Branch Block (RBBB)	15-59
Table 15-11.	Analysis of ECG: Left Bundle Branch Block (LBBB)	15-64
Table 15-12.	Analysis of ECG: Non-Specific ST- and T-Wave Changes	15-66
Table 15-13.	Analysis of ECG: Bradycardia	15-71
Table 15-14.	Analysis of ECG: Tachycardia	15-76
Table 15-15.	Analysis of ECG: Arrhythmia	15-78
Table 15-16.	Analysis of ECG: Evidence of Prior Myocardial Infarction	15-83
Table 15-17.	Analysis of ECG: Other Diagnoses	15-87
Table 15-18.	Analysis of Diastolic Blood Pressure (mm Hg) (Continuous)	15-92
Table 15-19.	Analysis of Diastolic Blood Pressure (Discrete)	15-97
Table 15-20.	Analysis of Funduscopic Examination	15-102
Table 15-21.	Analysis of Carotid Bruits	15-107
Table 15-22.	Analysis of Radial Pulses	15-111
Table 15-23.	Analysis of Femoral Pulses	15-116
Table 15-24.	Analysis of Popliteal Pulses	15-120
Table 15-25.	Analysis of Dorsalis Pedis Pulses	15-125
Table 15-26.	Analysis of Posterior Tibial Pulses	15-130
Table 15-27.	Analysis of Leg Pulses	15-135
Table 15-28.	Analysis of Peripheral Pulses	15-140
Table 15-29.	Analysis of Kidney , Urethra, and Bladder (KUB) X-ray (Excluding Kidney Stones)	15-144
Table 15-30.	Analysis of Intermittent Claudication and Vascular Insufficiency (ICVI) Index	15-149
Table 15-31.	Longitudinal Analysis of Systolic Blood Pressure (mm Hg) (Continuous)	15-154
Table 15-32.	Longitudinal Analysis of Systolic Blood Pressure (Discrete)	15-157
Table 15-33.	Longitudinal Analysis of Femoral Pulses	15-160
Table 15-34.	Longitudinal Analysis of Popliteal Pulses	15-163
Table 15-35.	Longitudinal Analysis of dorsalis Pedis Pulses	15-166
Table 15-36.	Longitudinal Analysis of Posterior Tibial Pulses	15-169
Table 15-37.	Longitudinal Analysis of Leg Pulses (Discrete)	15-172
Table 15-38.	Longitudinal Analysis of Peripheral Pulses	15-175

LIST OF TABLES (Continued)

Page

Table 15-39. Summary of Group Analyses (Model 1) for Cardiovascular Variables (Ranch Hands vs Comparisons) 15-185
Table 15-40. Summary of Initial Dioxin Analyses (Model 2) for Cardiovascular Variables (Ranch Hands Only) 15-189
Table 15-41. Summary of Categorized Dioxin Analyses (Model 3) for Cardiovascular Variables (Ranch Hands vs Comparisons) 15-191
Table 15-42. Summary of Current Dioxin Analyses (Models 4, 5, and 6) for Cardiovascular Variables (Ranch Hands Only) 15-195
Table 15-43. Summary of Group-by-Covariate and Dioxin-by-Covariate Interactions from Adjusted Analyses of Cardiovascular Variables 15-199

TABLE OF CONTENTS

Page

CHAPTER 16 HEMATOLOGIC ASSESSMENT 16-1

INTRODUCTION 16-1
Background 16-1
Summary of Previous Analyses of the air Force Health Study 16-2
1982 Baseline Study Summary Results 16-2
1985 Followup Study Summary Results 16-3
1987 Followup Study Summary Results 16-3
Serum Dioxin Analysis of 1987 Followup Study Summary Results 16-4
Parameters for the Hematologic Assessment 16-4
Dependent Variables 16-4
Laboratory Examination Data 16-5
Covariates 16-5
Statistical Methods 16-6
Longitudinal Analysis 16-6
RESULTS 16-11
Dependent Variable-Covariate Associations 16-11
Exposure Analysis 16-14
Laboratory examination Variables 16-15
Red Blood Cell (RBC) Count (Continuous) 16-15
Red Blood Cell (RBC) Count (Discrete) 16-20
White Blood Cell (WBC) Count (Continuous) 16-20
White Blood Cell (WBC) Count (Discrete) 16-30
Hemoglobin (Continuous) 16-36
Hemoglobin (Discrete) 16-36
Hematocrit (Continuous) 16-46
Hematocrit (Discrete) 16-46
Platelet Count (Continuous) 16-55
Platelet Count (Discrete) 16-60
Prothrombin Time (Continuous) 16-60
Prothrombin Time (Discrete) 16-69
RBC Morphology 16-69
Absolute Neutrophils (segs) 16-78
Absolute Neutrophils (bands) 16-78
Absolute Lymphocytes 16-92
Absolute Monocytes 16-92
Absolute Eosinophils 16-101
Absolute Basophils 16-110
Longitudinal Analysis 16-119
Laboratory Examination Variables 16-119
Platelet Count (Continuous) 16-119
Platelet Count (Discrete) 16-123
DISCUSSION 16-123

TABLE OF CONTENTS (Continued)

Page

SUMMARY 16-128
Model 1: Group Analysis 16-128
Model 2: Initial dioxin Analysis 16-137
Model 3: Categorized Dioxin Analysis 16-137
Model 4, 5, and 6: Current Dioxin Analyses 16-138
CONCLUSION 16-138
REFERENCES 16-139

LIST OF TABLES

		Page
Table 16-1.	Statistical Analyses for the Hematologic Assessment	16-7
Table 16-2.	Number of Participants with Missing Data for, or Excluded from, the Hematologic Assessment	16-9
Table 16-3.	Analysis of Red blood Cell (RBC) Count (million/mm^3) (Continuous)	16-16
Table 16-4.	Analysis of Red Blood Cell (RBC) Count (Discrete)	16-21
Table 16-5.	Analysis of White blood Cell (WBC) Count (thousand/mm^3) (Continuous)	16-26
Table 16-6.	Analysis of White Blood Cell (WBC) Count (Discrete)	16-31
Table 16-7.	Analysis of Hemoglobin (gm/dl) (Continuous)	16-37
Table 16-8.	Analysis of Hemoglobin (Discrete)	16-41
Table 16-9.	Analysis of Hematocrit (percent) (Continuous)	16-47
Table 16-10.	Analysis of Hematocrit (Discrete)	16-51
Table 16-11.	Analysis of Platelet Count (thousand/mm^3) (Continuous)	16-56
Table 16-12.	Analysis of Platelet Count (Discrete)	16-61
Table 16-13.	Analysis of Prothrombin Time (seconds) (Continuous)	16-65
Table 16-14.	Analysis of Prothrombin Time (Discrete)	16-70
Table 16-15.	Analysis of RBC Morphology	16-74
Table 16-16.	Analysis of Absolute Neutrophils (segs) (thousand/mm^3)	16-79
Table 16-17.	Analysis of Absolute Neutrophils (bands) (Zero vs Nonzero)	16-84
Table 16-18.	Analysis of Absolute Lymphocytes (thousand/mm^3)	16-93
Table 16-19.	Analysis of Absolute Monocytes (thousand/mm^3)	16-97
Table 16-20.	Analysis of Absolute Eosinophils (Zero vs Nonzero)	16-102
Table 16-21.	Analysis of Absolute Basophils (Zero vs Nonzero)	16-111
Table 16-22.	Longitudinal Analysis of Platelet Count (thousand/mm^3) (Continuous)	16-120
Table 16-23.	Longitudinal Analysis of Platelet Count (Discrete)	16-124
Table 16-24.	Summary of Group Analyses (Model 1) for Hematology Variables (Ranch Hands Only)	16-129
Table 16-25.	Summary of Initial Dioxin Analyses (Model 2) for Hematology Variables (Ranch Hands Only)	16-131
Table 16-26.	Summary of Categorized dioxin Analyses (Model 3) for Hematology Variables (Ranch Hands vs Comparisons)	16-132
Table 16-27.	Summary of Current Dioxin Analyses (Models 4, 5, and 6) for Hematology variables (Ranch Hands Only)	16-134
Table 16-28.	Summary of Group-by-Covariate and Dioxin-by-Covariate Interactions from adjusted Analyses of Hematology variables	16-136

TABLE OF CONTENTS - REPORT

VOLUME I	EXECUTIVE SUMMARY
	ACKNOWLEDGEMENTS
	CHAPTER 1 - Introduction
	CHAPTER 2 - The Dioxin Assay
	CHAPTER 3 - Questionnaire Methodology
	CHAPTER 4 - Physical examination Methodology
	CHAPTER 5 - Study Selection and Participation
	CHAPTER 6 - Quality Control
	CHAPTER 7 - Statistical Methods
	CHAPTER 8 - Covariate Associations with Estimates of Dioxin Exposure
	CHAPTER 9 - General Health Assessment
VOLUME II	CHAPTER 10 - Neoplasia Assessment
	CHAPTER 11 - Neurological Assessment
VOLUME III	CHAPTER 12 - Psychological Assessment
	CHAPTER 13 - Gastrointestinal Assessment
VOLUME IV	CHAPTER 14 - Dermatologic Assessment
	CHAPTER 15 - Cardiovascular Assessment
	CHAPTER 16 - Hematologic Assessment
VOLUME V	CHAPTER 17 - Renal Assessment
	CHAPTER 18 - Endocrine Assessment
VOLUME VI	CHAPTER 19 - Immunologic Assessment
	CHAPTER 20 - Pulmonary Assessment
	CHAPTER 21 - Conclusions
	CHAPTER 22 - Future Directions
VOLUME VI	APPENDIX A - 1 through F-2
VOLUME VII	APPENDIX G - 1 through I-4
VOLUME IX	APPENDIX J - 1 through N-4
VOLUME X	APPENDIX 0 - 1 through R

CHAPTER 14

DERMATOLOGIC ASSESSMENT

INTRODUCTION

Background

Chloracne, a chronic acneiform eruption with a highly specific cutaneous distribution, was first described by Von Bettman in 1897 as an occupational disease in German industrial workers. It was not until 1957 that it became recognized as a very specific consequence of exposure to chlorophenols (1,2). A recent review article summarizes the unique clinical manifestations of this skin condition (3).

Early animal researchers employed the rabbit's ear as a model for assaying the effects of chloracnegenic compounds (4,5). Other experiments on hairless mice produced histopathologic changes similar to those that occur in humans exposed to tetrachlorodibenzo-p-dioxin (TCDD, or dioxin) including hyperkeratotic changes in the sebaceous follicle with plugging of the orifice, hyperkeratinization of the stratum corneum, and keratin cyst formation (6,7).

The earliest descriptions of chloracne-like disease date back to the turn of the century (8). It is a relatively rare dermatitis with fewer than 4,000 cases documented world-wide (9); most cases have occurred in chemical plant workers or in victims of industrial accidents (10-13). Chronic conditions associated with severe chloracne include actinic elastosis, acne scars, and hypertrichosis (14,15). Epidermoid inclusion cysts seen in biopsy specimens are considered pathognomonic (16). The occurrence and severity of chloracne appear to be dose-related but may depend on other factors including the route of administration, age, genetic predisposition, and the presence of acne vulgaris and other dermatoses (14,17,18). More recent studies in rats have documented that the extent of dermal absorption is inversely related to age (19). This observation may be relevant to the finding in the industrial explosion at Seveso, Italy, that most cases (170 of 193 exposed) of chloracne occurred in children (10,11,13).

Monkeys given lethal doses of TCDD develop acneiform lesions of the lips, retention cysts of the Meibomian glands of the eyelids, facial alopecia, and loss of eyelashes (20). Other studies have demonstrated that TCDD induced squamous cell carcinomas in hamsters (21) and also induced chloracne, hirsutism, and hyperpigmentation in association with suppression of selected androgens in rats (22). Domestic animals accidentally exposed to TCDD in contaminated soil have developed alopecia, mucous membrane inflammation, hyperkeratosis, and ulcerative dermatitis (23,24).

A genetic basis for the dermal responses to TCDD has been defined in selected laboratory animals. In one series of experiments, investigators found strain-specific differences in the cutaneous reactions of haired and hairless mice to the topical application of TCDD (25). The involvement of sebaceous glands and increased transglutamase activity

were noted in both strains, while epidermal proliferation and hyperkeratinization occurred in the responsive (haired) strain only. Furthermore, in a subsequent study from the same laboratory, these TCDD-induced dermal changes were associated with an increased density of Langerhans cells in mouse skin unique to the responsive strain (26). Based on these and other studies (27-29), it is clear that these strain-specific responses are determined genetically, and there is evidence that they may be mediated by the aryl hydrocarbon (Ah) receptor (30,31). Of the industrial compounds known to cause chloracne, TCDD is by far the most potent. Studies of the application of dioxin to the skin of human volunteers have defined the changes described earlier in animals (32). Chloracne is characterized by a maculopapular rash of active comedones conforming to an eyeglass or facial butterfly distribution, often accompanied by chest, back, or periorbital lesions (3,14,17,33). Clinically, the presence of chloracne, which can persist for more than 30 years after exposure (15), can be strongly suspected based on the history of cutaneous contact. Definitive diagnosis, however, requires biopsy and histologic confirmation particularly in light of reports that chloracne can occur after oral ingestion of chlorophenols (34).

The use of chloracne as a marker for the severity of TCDD exposure has been the subject of controversy. At issue is whether long-term consequences can occur at levels of exposure less than that required to produce chloracne. Earlier reports in subjects with chloracne found extreme variations in adipose tissue levels of TCDD (35-37), observations confirmed as well in serum levels from populations exposed in industrial accidents (11,38) and by occupation (39).

Although the high occurrence of dermatologic disease in Vietnam veterans has been well documented (40), there is no objective evidence to support an association with herbicide exposure. In a study of American Legion veterans (41), a higher prevalence of self-reported cutaneous disease was found in veterans who served in Vietnam when compared with controls, but no attempt was made to confirm the history by physical examination and the exposure indices have not been validated. In the Vietnam Experience Study (VES) conducted by the U.S. Centers for Disease Control (CDC), the occurrence of dermatologic disorders found upon physical examination was similar in Vietnam and non-Vietnam veterans (42).

Though initial examination cycles of the Air Force Health Study (AFHS) appeared to reveal an increased prevalence of basal cell and other sun-related skin cancers, the most recent analysis, using serum dioxin levels as the measure of exposure (43) did not find an association between these malignancies and TCDD.

Summary of Previous Analyses of the Air Force Health Study

1982 Baseline Study Summary Results

The 1982 Baseline clinical examination revealed an unexpected significant excess ($p=0.03$) of basal cell carcinoma in the Ranch Hand group. Risk factor data for skin cancer, including sun exposure, host factors of tannability, and complexion, were not collected in 1982. The 1982 examination focused on the diagnosis of chloracne both in historical terms by a detailed questionnaire and in contemporary terms via a comprehensive clinical assessment. The questionnaire data did not demonstrate anatomic, incidence, or onset-time

patterns of acne in the Ranch Hand group that might support an inference of past chloracne, nor did the physical examination detect a single case. Fourteen biopsies from 11 participants also did not document a chloracne diagnosis. A dermatology index (the number of clinically detected skin abnormalities per individual) was virtually identical between the Ranch Hand and Comparison groups. No exposure level associations were noted in any occupational category of the Ranch Hand group. The comprehensive dermatologic assessment did not reveal evidence of past or current chloracne in the Ranch Hand group.

1985 Followup Study Summary Results

Questionnaire data recaptured many of the acne parameters of the 1982 Baseline Questionnaire, and the physical examination parameters were similar to the 1982 Baseline examination. Particular emphasis was given to the diagnosis of basal cell carcinoma and to the collection of risk factor data, including skin color, hair color, reaction to sun exposure, and ethnicity (44).

Interval questionnaire data on the occurrence, time, and location of acne were analyzed to assess the possible historical diagnosis of chloracne. No significant difference was observed between groups for reported occurrence of acne. A marginally significant difference in the occurrence of post-1961 acne was found, with more Ranch Hands than Comparisons reporting acne. The duration of post-1961 acne was not significantly different between the two groups.

For participants with post-Southeast Asia (SEA) acne, the spatial eyeglass distribution of acne (suggesting chloracne) was observed to be similar for the Ranch Hand and Comparison groups, both for individual sites and the combination of acne on the eyelids, ears, and temples. This analysis suggested that the occurrence of skin disease compatible with chloracne was not different in the two groups.

Analyses of the 1985 followup physical examination data, as with the Baseline examination, placed primary emphasis on six dermatologic disorders: comedones, acneiform lesions, acneiform scars, inclusion cysts, depigmentation, and hyperpigmentation. Secondary emphasis was given to a composite variable consisting of 16 other minor conditions (generally not associated with chloracne). No significant difference was found for any of these variables in the unadjusted analyses. The adjusted analyses closely mirrored the unadjusted analyses, with no significant difference noted between groups for any variable. Exposure index analyses did support dose-response relationships for some of the variables in certain occupational strata, but did not reveal a strong pattern of results suggesting a relationship between skin disease and herbicide exposure.

Overall, the 1985 followup examination results paralleled the Baseline findings. Although the followup examination detected more dermatologic abnormalities than those present at Baseline, slightly more abnormalities were found in the Comparisons, and most relative risks approached unity.

1987 Followup Study Summary Results

With the exception of more Ranch Hands than Comparisons reporting at least one occurrence of acne during their lifetime, no significant group differences were detected in the Dermatologic Assessment. Subsequent analysis of the occurrence of acne indicated that, for participants with no history of acne before the start of the first SEA duty, a higher percentage of Ranch Hands than Comparisons reported the occurrence of acne after the start of the first SEA duty. However, the anatomic distribution of these lesions did not suggest chloracne as a cause. No cases of chloracne were diagnosed in the physical examination. Analyses were conducted on historical occurrence and duration of acne, six dermatologic disorders, a composite variable of other disorders, and a dermatology index of four disorders. All of these analyses found no significant group differences. The longitudinal analysis, based on the dermatology index, showed no significant differences between groups over time.

Serum Dioxin Analysis of 1987 Followup Study Summary Results

In general, the occurrence and location of acne were not associated with initial dioxin. However, in the stratified analysis of acne relative to duty in SEA, the association with initial dioxin showed a decreasing occurrence of post-SEA acne for increasing levels of initial dioxin in the stratum consisting of Ranch Hands without pre-SEA acne and an increasing occurrence of post-SEA acne for increasing levels of initial dioxin in the pre-SEA acne stratum. Of the physical examination variables, only hyperpigmentation had a significant positive association with initial dioxin under the maximal assumption.

The association between current dioxin and the occurrence of acne (lifetime), under the maximal assumption, differed between the time since SEA duty strata, with a positive association for Ranch Hands with a later duty in SEA and a negative association for those with an earlier duty in SEA. The same pattern was exhibited in the analysis of acne relative to time of duty in SEA. In the stratified analysis of acne relative to time of duty in SEA, the association with current dioxin, within the earlier duty stratum (greater than 18.6 years since duty in SEA), was similar to the association with initial dioxin—negative for Ranch Hands without pre-SEA acne and positive for those with pre-SEA acne.

Several of the physical examination variables also had significant or marginally significant positive associations with current dioxin in the later duty stratum (18.6 years or fewer since duty in SEA) but had nonsignificant associations in the earlier duty stratum. In contrast, the association between current dioxin and location of acne was negative in the later duty stratum and positive in the earlier duty stratum. No significant differences were found between the low and background current dioxin categories nor between the high and background categories for any of the variables. No cases of chloracne were defined, nor were there any dermatologic endpoints consistently related to the current body burden of dioxin. Also, the longitudinal analysis of the dermatology index showed no significant associations with dioxin. In summary, there was no consistent evidence in these data to suggest a dioxin effect on the dermatologic system.

Parameters for the Dermatologic Assessment

Dependent Variables

The dermatologic assessment was based on physical examination data and information regarding acne, as obtained in a face-to-face interview with the participant and subsequently verified by a medical records review.

Medical Records Data

During the health interview conducted as part of the questionnaire, each study participant was asked about occurrences of acne since the date of the last health interview. In addition, data regarding occurrence of acne were collected at the physical examination. This information was used to update data gathered through the 1987 examination, and was subsequently verified through a review of the participant's medical records. The definition of acne was expanded for the 1992 followup to include all reasonable conditions that could be confused with acne. This definition included the following conditions: erythemato-squamous dermatoses, toxic erythema-rosacea, unspecified erythematous, other dermatoses, diseases of hair and hair follicles, acne varioliformia, other acne, sebaceous cysts, specified and unspecified diseases of sebaceous glands, and other specified disorders of the skin. Information regarding the date and location of each acne occurrence also was collected and verified. The variables defined below were constructed from the acne data and analyzed in the dermatologic assessment.

- Occurrence of Acne (lifetime):
  - Yes: at least one occurrence of acne
  - No: no occurrences of acne.

- Acne Relative to Time of Duty in SEA:
  - Post-SEA: all occurrences were after the start of the first duty in SEA
  - Pre and post-SEA: multiple occurrences, both before and after the start of the first duty in SEA, or a case of acne that began before the start of the first duty in SEA and ended after starting duty in SEA
  - Pre-SEA: last occurrence was before the start of duty in SEA
  - None: no occurrences of acne.

- Location of Acne (post-SEA; post-SEA combined with pre- and post-SEA):
  - Temples
  - Eyes or eyelids
  - Ears
  - Temples and eyes
  - Eyes and ears
  - Temples and ears
  - Temples, eyes, and ears
  - Other sites (cheeks, nose, forehead, jaw or chin, chest, and back).

If an individual had multiple site involvement for one or more of the seven specified sites and for the category "other sites," then the specified site(s) category was assigned.

The analysis of the occurrence of acne was based on responses from all of the participants of the 1992 examination. Acne relative to the time of duty in SEA was analyzed for three strata of participants: (1) all participants of the 1992 examination, (2) participants of the 1992 examination without pre-SEA acne, and (3) participants of the 1992 examination with pre-SEA acne.

Location of acne was analyzed twice. The first analysis was limited to the participants who had all their acne after the start of the first duty in SEA (post-SEA). The second analysis was based on participants who had all their acne after the start of the first duty in SEA or who had multiple occurrences—both before and after the start of the first duty in SEA, or a case of acne that began before the start of the first duty in SEA and ended after starting duty in SEA (post-SEA combined with pre- and post-SEA). No participants were excluded for medical reasons from the analyses of these variables.

Physical Examination Data

Two composite variables from the physical examination data were analyzed in the dermatologic assessment: a dermatology index and a variable labeled "other abnormalities." The dermatology index was formed by examining the following conditions: comedones, acneiform lesions, acneiform scars, inclusion cysts, depigmentation, and hyperpigmentation. Depigmentation and hyperpigmentation are defined as areas of skin that are less or more pigmented relative to the rest of the skin. A participant was defined to be "abnormal" for this dermatology index if any of these conditions were present and defined as "normal" if none were present. The variable other abnormalities was coded as abnormal or normal. A participant was considered to be abnormal for this variable if any of the following disorders were detected in the physical examination: vitiligo, jaundice, spider angiomata, palmar erythema, palmar keratoses, actinic keratoses, petechiae, ecchymoses, conjunctival abnormality, oral mucosal abnormality, fingernail abnormality, toenail abnormality, dermatographia, cutis rhomboidalis, nevus, or other nonspecific abnormalities. Abnormalities relating to skin malignancies are discussed in Chapter 10, Neoplasia Assessment. No participants were excluded for medical reasons from the analyses of these variables.

Covariates

The covariates age, race, and military occupation were used in adjusted statistical analyses of the occurrence of acne and location of acne. Presence of pre-SEA acne (yes, no) was a stratification variable in the analysis of acne relative to time of duty in SEA. Time reference to SEA (pre- and post-SEA and post-SEA) was a stratification variable in the analysis of location of acne. The covariates age, race, occupation, and presence of pre-SEA acne were used in adjusted statistical analyses of both physical examination variables in the dermatologic assessment. Age was used in its continuous form for modeling purposes for all dependent variables and dichotomized for interaction summaries.

Statistical Methods

Chapter 7, Statistical Methods, describes basic statistical methods used throughout this report. Table 14-1 summarizes the statistical analyses performed for the Dermatologic 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 are summarized in Table 14-2.

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

The results of the analyses without occupation are presented in Appendix J-3 and are only discussed in the text if the level of significance differs from the original final adjusted model (significant versus nonsignificant).

RESULTS

Dependent Variable-Covariate Associations

Table J-1-1 in Appendix J presents the results of the following tests of association between the dermatology dependent variables and covariates.

Using pooled group data, the covariate tests of association detected a high association between the occurrence of acne and age ($p<0.001$). The percentage of participants with at least one occurrence of acne in their lifetime increased with age (81.7% for those participants born in or after 1942 and 89.0% for those participants born before 1942).

The association between the covariates and acne relative to time of duty in SEA for the primary stratum of pre- and post-SEA and post-SEA acne versus pre-SEA acne and none revealed highly significant associations with age ($p<0.001$) and presence of pre-SEA acne ($p<0.001$). Younger participants had a lower percentage of acne relative to time of duty in SEA than older participants (81.1% vs. 88.8%). Participants with a history of pre-SEA acne had a higher percentage of post-SEA acne (96.4%) than those with no pre-SEA acne (84.3%).

Table 14-1.
Statistical Analyses for the Dermatologic Assessment

Dependent Variables

Variable	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analysis
Occurrence of Acne (Lifetime)	MR-V	D	Yes No	AGE,RACE, OCC	U:LR,CS A:LR
Acne Relative to Time of Duty in SEA	MR-V and MIL	D	Pre-SEA Pre- & Post-SEA Post-SEA None	AGE,RACE, OCC,PRESEA	U:LR,CS A:LR
Location of Acne	MR-V	D	Temples Eyes Ears Other Sites	AGE,RACE, OCC,TIMESEA	U:LR,CS A:LR
Other Abnormalities	PE	D	Abnormal Normal	AGE,RACE, OCC,PRESEA	U:LR,CS A:LR
Dermatology Index	PE	D	Abnormal Normal	AGE,RACE, OCC,PRESEA	U:LR,CS A:LR

Covariates

Variable (Abbreviation)	Data Source	Data Form	Cutpoints
Age (AGE)	MIL	D/C	Born $\geq$ 1942 Born $<$ 1942
Race (RACE)	MIL	D	Black Non-Black
Occupation (OCC)	MIL	D	Officer Enlisted Flyer Enlisted Groundcrew
Time Reference to SEA (TIMESEA)	MR-V and MIL	D	Pre- & Post-SEA Post-SEA
Presence of Pre-SEA Acne (PRESEA)	MR-V and MIL	D	Yes No

Table 14-1. (Continued)
Statistical Analyses for the Dermatologic Assessment

Abbreviations

Data Source:	MIL	=	Air Force military records
	MR-V	=	Medical records (verified)
	PE	=	1992 physical examination
Data Form:	D	=	Discrete analysis only
	D/C	=	Appropriate form for analysis (either discrete or continuous)
Statistical Analyses:	U	=	Unadjusted analyses
	A	=	Adjusted analyses
Statistical Methods:	CS	=	Continuity-adjusted chi-square statistic
	LR	=	Logistic regression analysis

Table 14-2.
Number of Participants with Missing Data for the Dermatologic Assessment

		Group		Dioxin (Ranch Hands Only)		Categorized Dioxin	
Variable	Variable Use	Ranch Hand	Comparison	Initial	Current	Ranch Hand	Comparison
Location of Acne	DEP	2	1	2	2	2	1
Other Abnormalities	DEP	0	2	0	0	0	2
Dermatology Index	DEP	0	1	0	0	0	1

Abbreviations: DEP = Dependent variable.

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.

Investigation of the relationship between location of acne for participants with pre- and post-SEA and post-SEA acne and the covariates revealed highly significant associations with age ($p<0.001$) and race ($p<0.001$). Younger participants had a lower percentage of acne on the temples, eyes, and ears than older participants (38.7% vs. 51.1%). Blacks had a lower percentage of acne on the temples, eyes, and ears than non-Blacks (25.7% vs. 47.3%).

Statistically significant associations were found between the composite variable containing all other dermatologic abnormalities and age ($p<0.001$), occupation ($p=0.007$), race ($p=0.002$), and presence of pre-SEA acne ($p=0.001$). The percentage of other abnormalities increased with age. Of the younger participants, 74.0 percent had other abnormalities, while 89.2 percent of the older participants had abnormalities. The number of participants with other abnormalities was higher for the enlisted flyers (85.7%) than for the officers (84.6%) and enlisted groundcrew (79.9%). A higher percentage of non-Blacks than Blacks had other abnormalities (83.3% vs. 72.5%). Also, participants without pre-SEA acne had a higher percentage of other abnormalities (83.5%) than did those participants with pre-SEA acne (74.7%).

The dermatology index showed highly significant associations with the covariates occupation ($p<0.001$), race ($p<0.001$), and presence of pre-SEA acne ($p<0.001$). The percentage of participants with at least one abnormality was higher for enlisted flyers (49.5%) than for enlisted groundcrew (47.7%) and officers (39.1%). More Blacks had at least one abnormality than non-Blacks (64.1% vs. 43.5%). More participants with pre-SEA acne had at least one abnormality (59.1%) than those without pre-SEA acne (43.0%).

Exposure Analysis

The following section presents results of the statistical analyses of the dependent variables shown in Table 14-1. Dependent variables are grouped into two sections: those derived and verified from a review of medical records and data obtained during the 1992 physical examination.

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 (45). 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 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 investigations for group-by-covariate and dioxin-by-covariate interactions are referenced in the text, and tabular results are presented in Appendix J-2. As described previously, additional analyses are performed when occupation was retained in the final models for Models 2 through 6. Results excluding occupation from these models are tabled in Appendix J-3, and dioxin-by-covariate interactions with occupation excluded from these models are presented in Appendix J-4. Results from analyses excluding occupation are discussed in the text only if a meaningful change in the results occurred (that is, changes between significant results, marginally significant results, and nonsignificant results).

Verified Medical Records Variables

Occurrence of Acne (Lifetime)

Analysis of lifetime occurrence of acne did not find a significant difference between Ranch Hands and Comparisons in the unadjusted and adjusted analyses for Model 1 (Table 14-3(a,b): $p > 0.13$ for unadjusted and adjusted results). The final model in the adjusted analysis contained the covariate age. Stratifying the Model 1 analyses by occupation displayed a marginally significant association between group and occurrence of acne for enlisted groundcrew. In the unadjusted analysis, the percentage of enlisted groundcrew Ranch Hands with abnormalities (87.2%) was significantly greater than the percentage of enlisted groundcrew Comparisons with abnormalities (82.8%) (Table 14-3(a): $p=0.067$, Est. RR=1.42). The relative risk for the adjusted analysis of enlisted groundcrew was also marginally significant (Table 14-3(b): $p=0.051$, Adj. RR=1.43).

Models 2 and 3 did not find a significant association between initial or categorized dioxin and occurrence of acne for the unadjusted and adjusted analyses (Table 14-3(c-f): $p > 0.18$ for all analyses). The final adjusted model for Model 2 included age and occupation. Model 3 accounted for age in the adjusted analysis.

The unadjusted and adjusted analyses for Models 4 through 6 did not show significant associations between occurrence of acne and current dioxin (Table 14-3(g,h): $p > 0.51$ for all

Table 14-3.
Analysis of Occurrence of Acne (Lifetime)

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***	***952***	***87.2***	***1.21 (0.95,1.55)***	***0.134***
	Comparison	***1,281***	***84.9***		
Officer	Ranch Hand	367	88.0	1.21 (0.81,1.81)	0.410
	Comparison	502	85.9		
Enlisted Flyer	Ranch Hand	162	85.2	0.77 (0.42,1.42)	0.494
	Comparison	203	88.2		
Enlisted Groundcrew	Ranch Hand	423	87.2	1.42 (0.99,2.03)	0.067
	Comparison	576	82.8		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.21 (0.94,1.54)***	***0.135***	AGE ($p<0.001$)
Officer	1.18 (0.79,1.77)	0.428	
Enlisted Flyer	0.75 (0.41,1.39)	0.364	
Enlisted Groundcrew	1.43 (1.00,2.05)	0.051	

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

Table 14-3. (Continued)
Analysis of Occurrence of Acne (Lifetime)

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	174	87.9	0.93 (0.77,1.13)	0.487
Medium	173	87.9		
High	173	84.4		

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**
520	0.93 (0.74,1.18)	0.559	AGE ($p<0.001$) OCC ($p=0.010$)

[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] 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 14-3. (Continued)
Analysis of Occurrence of Acne (Lifetime)

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	1,063	86.1		
Background RH	374	88.2	1.28 (0.89,1.84)	0.180
Low RH	260	88.1	1.15 (0.76,1.74)	0.507
High RH	260	85.4	0.91 (0.62,1.35)	0.643
Low plus High RH	520	86.7	1.02 (0.75,1.39)	0.900

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	1,063			AGE ($p<0.001$)
Background RH	374	1.19 (0.83,1.72)	0.349	
Low RH	260	1.09 (0.72,1.66)	0.683	
High RH	260	1.04 (0.70,1.55)	0.829	
Low plus High RH	520	1.07 (0.78,1.46)	0.688	

[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 14-3. (Continued)
Analysis of Occurrence of Acne (Lifetime)

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	87.1 (295)	88.7 (300)	86.3 (299)	0.96 (0.84,1.10)	0.577
5	87.7 (300)	88.6 (297)	85.9 (297)	0.98 (0.87,1.10)	0.691
6[c]	87.6 (299)	88.6 (297)	85.9 (297)	0.96 (0.85,1.09)	0.514

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	894	0.97 (0.83,1.13)	0.687	AGE ($p<0.001$) OCC ($p=0.043$)
5	894	0.98 (0.86,1.12)	0.752	AGE ($p<0.001$) OCC ($p=0.045$)
6[d]	893	0.97 (0.84,1.12)	0.676	AGE ($p<0.001$) OCC ($p=0.043$)

[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.

analyses). Each of the adjusted analyses for Models 4 through 6 accounted for age and occupation.

Acne Relative to SEA Time of Duty in SEA (Pre- and Post-SEA and Post-SEA vs. Pre-SEA and None)

The Model 1 unadjusted and adjusted analyses of acne relative to time of duty in SEA revealed no significant overall differences in the history of post-SEA acne between groups (Table 14-4(a,b): $p > 0.14$ for unadjusted and adjusted analyses). However, after stratifying the Model 1 analyses by occupation, the association between group and acne was significant for the enlisted groundcrew. For the unadjusted analysis, the enlisted groundcrew Ranch Hands had a significantly higher prevalence of post- and pre- and post-SEA acne (87.2%) than the enlisted groundcrew Comparisons (82.3%) (Table 14-4(a): $p=0.042$, Est. $RR=1.47$). Similarly, the adjusted analysis displayed a significant relative risk for enlisted groundcrew (Table 14-4(b): $p=0.025$, Adj. $RR=1.51$). The Model 1 analysis was adjusted for age and presence of pre-SEA acne.

Examination of the unadjusted and adjusted results for Models 2 and 3 for acne relative to time of duty in SEA did not show a significant association with initial or categorized dioxin (Table 14-4(c-f): $p > 0.16$ for all analyses). The final models for both Models 2 and 3 were adjusted for age, occupation, and presence of pre-SEA acne.

The unadjusted and adjusted analyses for Models 4 through 6 did not display any significant associations between acne relative to time of duty in SEA and current dioxin (Table 14-4(g,h): $p > 0.47$ for all analyses) when Ranch Hands with acne before and after the start of their first duty in SEA (pre- and post-SEA) and Ranch Hands with acne only after the start of their first duty in SEA (post-SEA) were contrasted with Ranch Hands who did not have acne after the start of their duty in SEA (pre-SEA and none). Similar to Models 2 and 3, Models 4 through 6 accounted for the significant covariates of age, occupation, and presence of pre-SEA acne.

Acne Relative to Time of Duty in SEA (Post-SEA vs. None)

The Model 1 unadjusted and adjusted analyses of acne relative to time of duty in SEA for participants with no pre-SEA acne revealed no significant differences between groups combining all occupations (Table 14-5(a,b): $p > 0.11$ for unadjusted and adjusted analyses). However, stratifying by occupation revealed a difference between Ranch Hands and Comparisons for enlisted groundcrew. The unadjusted analysis showed a marginally significant higher percentage of post-SEA acne for Ranch Hands (85.8%) than for Comparisons (80.7%) (Table 14-5(a): $p=0.059$, Est. $RR=1.44$). The adjusted analysis also revealed a significant relative risk for enlisted groundcrew (Table 14-5(b): $p=0.041$, Adj. $RR=1.47$). Age was the only significant covariate for Model 1.

The unadjusted and adjusted analyses of acne relative to time of duty in SEA for participants with no pre-SEA acne for Models 2 and 3 were not statistically significant (Table 14-5(c-f): $p > 0.15$ for all analyses). The adjusted analysis of Model 2 accounted for the

Table 14-4.
Analysis of Acne Relative to Time of Duty in SEA
(Pre- and Post-SEA and Post-SEA vs. Pre-SEA and None)

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

Occupational Category	Group	n	Percent Pre-/ Post-SEA & Post-SEA	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***952***	***86.8***	***1.20 (0.94,1.53)***	***0.158***
	Comparison	***1,281***	***84.5***		
Officer	Ranch Hand	367	87.5	1.17 (0.79,1.74)	0.504
	Comparison	502	85.7		
Enlisted Flyer	Ranch Hand	162	84.0	0.70 (0.39,1.28)	0.311
	Comparison	203	88.2		
Enlisted Groundcrew	Ranch Hand	423	87.2	1.47 (1.03,2.10)	0.042
	Comparison	576	82.3		

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

Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	***1.20 (0.94,1.53)***	***0.145***	AGE ($p<0.001$) PRESEA ($p<0.001$)
Officer	1.15 (0.77,1.72)	0.507	
Enlisted Flyer	0.67 (0.36,1.23)	0.196	
Enlisted Groundcrew	1.51 (1.05,2.17)	0.025	

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

Note: Pre-/Post-SEA = multiple occurrences of acne, both before and after the start of the first duty in SEA, or a case of acne that began before the start of the first duty in SEA and ended after starting duty in SEA.

Table 14-4. (Continued)
Analysis of Acne Relative to Time of Duty in SEA
(Pre- and Post-SEA and Post-SEA vs. Pre-SEA and None)

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 Pre-/Post-SEA & Post-SEA**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	174	86.8	0.94 (0.78,1.13)	0.497
Medium	173	87.9		
High	173	83.8		

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**
520	0.92 (0.73,1.16)	0.470	AGE ($p<0.001$) OCC ($p=0.001$) PRESEA ($p=0.014$)

[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.
Pre-/Post-SEA = multiple occurrences of acne, both before and after the start of the first duty in SEA, or a case of acne that began before the start of the first duty in SEA and ended after starting duty in SEA.

Table 14-4. (Continued)
Analysis of Acne Relative to Time of Duty in SEA
(Pre- and Post-SEA and Post-SEA vs. Pre-SEA and None)

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

Dioxin Category	n	Percent Pre-/ Post-SEA & Post-SEA	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,063	85.7		
Background RH	374	88.0	1.29 (0.90,1.84)	0.168
Low RH	260	87.3	1.11 (0.74,1.66)	0.615
High RH	260	85.0	0.91 (0.62,1.34)	0.638
Low plus High RH	520	86.2	1.00 (0.74,1.36)	0.985

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	1,063			AGE ($p<0.001$) OCC ($p=0.119$) PRESEA ($p<0.001$)
Background RH	374	1.26 (0.87,1.84)	0.219	
Low RH	260	1.07 (0.71,1.61)	0.761	
High RH	260	1.00 (0.67,1.50)	0.995	
Low plus High RH	520	1.03 (0.75,1.41)	0.841	

[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.
Pre-/Post-SEA = multiple occurrences of acne, both before and after the start of the first duty in SEA, or a case of acne that began before the start of the first duty in SEA and ended after starting duty in SEA.

Table 14-4. (Continued)
Analysis of Acne Relative to Time of Duty in SEA
(Pre- and Post-SEA and Post-SEA vs. Pre-SEA and None)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Pre-/Post-SEA & Post-SEA/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	86.8 (295)	88.0 (300)	86.0 (299)	0.96 (0.84,1.09)	0.520
5	87.3 (300)	87.9 (297)	85.5 (297)	0.97 (0.87,1.09)	0.619
6[c]	87.3 (299)	87.9 (297)	85.5 (297)	0.96 (0.84.1.08)	0.470

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	894	0.95 (0.81,1.11)	0.513	AGE ($p<0.001$) OCC ($p=0.005$) PRESEA ($p=0.001$)
5	894	0.96 (0.84,1.10)	0.558	AGE ($p<0.001$) OCC ($p=0.005$) PRESEA ($p=0.001$)
6[d]	893	0.95 (0.82,1.11)	0.527	AGE ($p<0.001$) OCC ($p=0.005$) PRESEA ($p=0.001$)

[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.
Pre-/Post-SEA = multiple occurrences of acne, both before and after the start of the first duty in SEA, or a case of acne that began before the start of the first duty in SEA and ended after starting duty in SEA.

Table 14-5.
Analysis of Acne Relative to Time of Duty in SEA
(Post-SEA vs. None)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Post-SEA**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***859***	***85.8***	***1.23 (0.96,1.57)***	***0.116***
	Comparison	***1,149***	***83.1***		
Officer	Ranch Hand	335	86.9	1.24 (0.83,1.86)	0.350
	Comparison	450	84.2		
Enlisted Flyer	Ranch Hand	145	83.4	0.75 (0.41,1.38)	0.437
	Comparison	186	87.1		
Enlisted Groundcrew	Ranch Hand	379	85.8	1.44 (1.00,2.07)	0.059
	Comparison	513	80.7		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.22 (0.95,1.56)***	***0.116***	AGE ($p<0.001$)
Officer	1.19 (0.79,1.80)	0.401	
Enlisted Flyer	0.74 (0.40,1.37)	0.331	
Enlisted Groundcrew	1.47 (1.02,2.12)	0.041	

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

Table 14-5. (Continued)
Analysis of Acne Relative to Time of Duty in SEA
(Post-SEA vs. None)

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 Post-SEA**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	159	86.8	0.92 (0.76,1.12)	0.430
Medium	154	86.4		
High	157	82.8		

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**
470	0.93 (0.73,1.17)	0.525	AGE ($p<0.001$) OCC ($p=0.007$)

[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 14-5. (Continued)
Analysis of Acne Relative to Time of Duty in SEA
(Post-SEA vs. None)

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

Dioxin Category	n	Percent Post-SEA	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	946	84.4		
Background RH	337	86.9	1.31 (0.91,1.89)	0.150
Low RH	237	86.9	1.18 (0.77,1.79)	0.447
High RH	233	83.7	0.91 (0.62,1.35)	0.650
Low plus High RH	470	85.3	1.03 (0.76,1.41)	0.845

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	946			AGE ($p<0.001$)
Background RH	337	1.21 (0.83,1.75)	0.317	
Low RH	237	1.11 (0.73,1.70)	0.622	
High RH	233	1.07 (0.72,1.60)	0.735	
Low plus High RH	470	1.09 (0.80,1.50)	0.592	

[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 14-5. (Continued)
Analysis of Acne Relative to Time of Duty in SEA
(Post-SEA vs. None)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Post-SEA/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	85.7 (266)	87.5 (273)	84.7 (268)	0.96 (0.84,1.10)	0.563
5	86.3 (271)	87.4 (270)	84.2 (266)	0.98 (0.87,1.10)	0.695
6[c]	86.3 (271)	87.4 (270)	84.1 (266)	0.96 (0.84,1.09)	0.498

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	807	0.97 (0.82,1.14)	0.677	AGE ($p<0.001$) OCC ($p=0.030$)
5	807	0.98 (0.85,1.12)	0.734	AGE ($p<0.001$) OCC ($p=0.031$)
6[d]	807	0.97 (0.83,1.12)	0.670	AGE ($p<0.001$) OCC ($p=0.030$)

[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.

significant covariates of age and occupation. The final adjusted analysis for Model 3 revealed age as the only significant covariate.

For Models 4 through 6, the adjusted and unadjusted analyses did not show any significant associations between current dioxin and post-SEA acne for participants with no pre-SEA acne (Table 14-5(g,h): $p > 0.49$ for all analyses). The adjusted analysis of Models 4 through 6 each contained the significant covariates of age and occupation.

Acne Relative to Time of Duty in SEA (Pre- and Post-SEA vs. Pre-SEA)

The unadjusted analyses of acne relative to time of duty in SEA for participants with pre-SEA acne did not reveal a significant association between post-SEA acne and group (Table 14-6(a): $p > 0.38$ for all analyses). The adjusted analyses led to highly significant group-by-age and group-by-occupation interactions (Table 14-6(b): $p = 0.002$ and $p = 0.001$). Stratified results of these interactions are presented in Appendix Table J-2-1; the sparse number of individuals with pre-SEA acne only ($n = 8$) precluded meaningful analysis; therefore, the relative risks, confidence intervals, and p-values are not presented in Appendix Table J-2-1.

The unadjusted and adjusted analyses of Models 2 and 3 did not find a significant relationship between initial or categorized dioxin and post-SEA acne for participants with pre-SEA acne (Table 14-6(c-f): $p > 0.22$ for all analyses). For the Model 2 adjusted analyses, the sparse number of Ranch Hands with pre-SEA acne only ($n = 3$) precluded meaningful analysis; therefore, results are not presented. No covariates were retained in the final adjusted analyses for Model 3, therefore, the adjusted results are equivalent to the unadjusted results for this model.

Models 4 through 6 unadjusted analyses did not show any significant associations between current dioxin and post-SEA acne for participants with pre-SEA acne (Table 14-6(g): $p > 0.62$ for all unadjusted analyses). Similar to Model 2, the sparse number of Ranch Hands with pre-SEA acne only ($n = 4$) precluded meaningful adjusted analyses of these models.

Location of Acne (Post-SEA only)

The location of acne was analyzed for the participants with post-SEA acne only. Table 14-7 presents the spatial distribution of acne with primary emphasis on the temples, around the eyes, or on the ears. Due to the sparse number at individual sites, the analyses contrasted participants with acne on the temples, eyes, and ears, or a combination of these sites with participants with acne on other sites.

The Model 1 analysis of location of acne—temples, eyes, and ears versus other locations—for those participants with post-SEA acne did not uncover any statistically significant results (Table 14-8(a,b): $p > 0.13$ for all analyses). Covariate adjustment for Model 1 accounted for age and race.

Table 14-6.
Analysis of Acne Relative to Time of Duty in SEA
(Pre- and Post-SEA vs. Pre-SEA)

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

Occupational Category	Group	n	Percent Pre-/ Post-SEA	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***93***	***95.7***	***0.70 (0.17,2.85)***	***0.888***
	Comparison	***132***	***97.0***		
Officer	Ranch Hand	32	93.8	0.29 (0.03,3.38)	0.665
	Comparison	52	98.1		
Enlisted Flyer	Ranch Hand	17	88.2	0.18 (0.01,3.98)	0.466
	Comparison	17	100.0		
Enlisted Groundcrew	Ranch Hand	44	100.0	5.15 (0.26,102.22)	0.383
	Comparison	63	95.2		

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

Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	****	****	GROUP*AGE (p=0.002) GROUP*OCC (p=0.001)
Officer	****	****	
Enlisted Flyer	****	****	
Enlisted Groundcrew	****	****	

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

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

Note: Pre-/Post-SEA = multiple occurrences of acne, both before and after the start of the first duty in SEA, or a case of acne that began before the start of the first duty in SEA and ended after starting duty in SEA.

Table 14-6. (Continued)
Analysis of Acne Relative to Time of Duty in SEA
(Pre- and Post-SEA vs. Pre-SEA)

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 Pre-/ & Post-SEA	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	15	86.7	1.20 (0.44,3.29)	0.705
Medium	19	100.0		
High	16	93.8		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)			
n	Adj. Relative Risk (95% C.I.)	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.

--: Analysis not performed due to the sparse number of pre-SEA only occurrences of acne.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.
Pre-/Post-SEA = multiple occurrences of acne, both before and after the start of the first duty in SEA, or a case of acne that began before the start of the first duty in SEA and ended after starting duty in SEA.

Table 14-6. (Continued)
Analysis of Acne Relative to Time of Duty in SEA
(Pre- and Post-SEA vs. Pre-SEA)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Pre-/ Post-SEA	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	117	96.6		
Background RH	37	97.3	1.37 (0.14,13.90)	0.786
Low RH	23	91.3	0.32 (0.05,1.99)	0.222
High RH	27	96.3	0.82 (0.08,8.19)	0.865
Low plus High RH	50	94.0	0.48 (0.10,2.36)	0.367

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
Comparison	117			
Background RH	37	1.37 (0.14,13.90)	0.786	
Low RH	23	0.32 (0.05,1.99)	0.222	
High RH	27	0.82 (0.08,8.19)	0.865	
Low plus High RH	50	0.48 (0.10,2.36)	0.367	

[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.

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.
Pre-/Post-SEA = multiple occurrences of acne, both before and after the start of the first duty in SEA, or a case of acne that began before the start of the first duty in SEA and ended after starting duty in SEA.

Table 14-6. (Continued)
Analysis of Acne Relative to Time of Duty in SEA
(Pre- and Post-SEA vs. Pre-SEA)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Pre-/Post-SEA/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	96.6 (29)	92.6 (27)	96.8 (31)	0.88 (0.48,1.61)	0.671
5	96.6 (29)	92.6 (27)	96.8 (31)	0.88 (0.52,1.48)	0.625
6[c]	96.4 (28)	92.6 (27)	96.8 (31)	0.91 (0.50,1.66)	0.757

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model	n	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
4	--	--	--	
5	--	--	--	
6	--	--	--	

[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.

--: Analysis not performed due to the sparse number of pre-SEA only occurrences of acne.

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.
Pre-/Post-SEA = multiple occurrences of acne, both before and after the start of the first duty in SEA, or a case of acne that began before the start of the first duty in SEA and ended after starting duty in SEA.

Table 14-7.
Number of Participants with, and Location of, Post-SEA Acne

Location	Group	
	Ranch Hand	Comparison
Temples Only	222	271
Eyes Only	9	21
Ears Only	38	50
Temples and Eyes	19	15
Temples and Ears	43	53
Eyes and Ears	3	4
Temples, Eyes, and Ears	5	7
Other Sites	396	533

Location	Initial Dioxin	Current Dioxin
Temples Only	124	210
Eyes Only	4	9
Ears Only	14	31
Temples and Eyes	8	19
Temples and Ears	22	41
Eyes and Ears	0	3
Temples, Eyes, and Ears	5	5
Other Sites	222	374

Location	Current Dioxin Category				
	Comparison	Background RH	Low RH	High RH	Low plus High RH
Temples Only	233	86	67	57	124
Eyes Only	17	5	3	1	4
Ears Only	40	17	7	7	14
Temples and Eyes	12	11	4	4	8
Temples and Ears	45	19	12	10	22
Eyes and Ears	3	3	0	0	0
Temples, Eyes, and Ears	6	0	1	4	5
Other Sites	441	152	111	111	222

Table 14-8.
Analysis of Location of Acne (Post-SEA)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Temples/Eyes/Ears**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***735***	***46.1***	***1.08 (0.89,1.32)***	***0.443***
	Comparison	***954***	***44.1***		
Officer	Ranch Hand	291	48.1	1.06 (0.78,1.44)	0.777
	Comparison	379	46.7		
Enlisted Flyer	Ranch Hand	121	43.8	0.82 (0.51,1.31)	0.479
	Comparison	162	48.8		
Enlisted Groundcrew	Ranch Hand	323	45.2	1.24 (0.92,1.67)	0.175
	Comparison	413	40.0		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.07 (0.88,1.31)***	***0.474***	AGE ($p<0.001$) RACE ($p<0.001$)
Officer	1.04 (0.76,1.41)	0.821	
Enlisted Flyer	0.79 (0.49,1.27)	0.326	
Enlisted Groundcrew	1.26 (0.93,1.70)	0.139	

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

Note: Temples/Eyes/Ears = Temples, eyes, ears, temples and eyes, temples and ears, eyes and ears, or temples, eyes, and ears.

Table 14-8. (Continued)
Analysis of Location of Acne (Post-SEA)

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 Temples/Eyes/Ears	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	137	48.9	0.96 (0.82,1.11)	0.551
Medium	133	42.9		
High	129	41.1		

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
399	1.00 (0.86,1.18)	0.961	AGE (p=0.012) RACE (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.
Temples/Eyes/Ears = Temples, eyes, ears, temples and eyes, temples and ears, eyes and ears, or temples, eyes, and ears.

Table 14-8. (Continued)
Analysis of Location of Acne (Post-SEA)

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

Dioxin Category	n	Percent Temples/Eyes/Ears	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	797	44.7		
Background RH	293	48.1	1.17 (0.90,1.54)	0.246
Low RH	205	45.9	1.02 (0.75,1.39)	0.906
High RH	194	42.8	0.91 (0.66,1.26)	0.574
Low plus High RH	399	44.4	0.97 (0.76,1.23)	0.781

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	797			AGE ($p<0.001$) RACE ($p<0.001$)
Background RH	293	1.11 (0.84,1.46)	0.472	
Low RH	205	1.00 (0.73,1.37)	0.984	
High RH	194	1.01 (0.73,1.40)	0.936	
Low plus High RH	399	1.00 (0.78,1.29)	0.970	

[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.
Temples/Eyes/Ears = Temples, eyes, ears, temples and eyes, temples and ears, eyes and ears, or temples, eyes, and ears.

Table 14-8. (Continued)
Analysis of Location of Acne (Post-SEA)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Percent Temples/Eyes/Ears /(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) Est. Relative Risk (95% C.I.)[b]	p-Value
4	47.4 (228)	49.2 (238)	41.2 (226)	0.94 (0.84,1.04)	0.207
5	48.3 (234)	48.1 (235)	41.3 (223)	0.94 (0.86,1.03)	0.186
6[c]	48.3 (234)	48.1 (235)	41.3 (223)	0.93 (0.84,1.03)	0.144

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[a]	Analysis Results for Log_2 (Current Dioxin + 1) n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	692	0.97 (0.87,1.08)	0.607	AGE (p=0.001) RACE (p=0.005)
5	692	0.94 (0.84,1.04)	0.202	AGE (p<0.001) RACE (p=0.002) OCC (p=0.142)
6[d]	692	0.94 (0.84,1.05)	0.236	AGE (p<0.001) RACE (p=0.002) OCC (p=0.142)

[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.
Temples/Eyes/Ears = Temples, eyes, ears, temples and eyes, temples and ears, eyes and ears, or temples, eyes, and ears.

analyses of both Models 2 and 3 accounted for age and race. As presented in Table 14-8(g,h), the analyses for Models 4 through 6 did not detect a significant association between current dioxin and location of acne for participants with post-SEA acne ($p > 0.14$ for all analyses). The Model 4 adjusted analysis included the significant covariates of age and race. Models 5 and 6 each accounted for the covariates age, race, and occupation.

Location of Acne (Pre- and Post-SEA and Post-SEA)

The location of acne was also analyzed for participants with pre- and post-SEA and post-SEA acne. Table 14-9 presents the spatial distribution of acne for these participants with primary emphasis on the temples, around the eyes, or on the ears. Due to the sparse numbers at individual sites, the analyses contrasted participants with acne on the temples, eyes, and ears, or any combination of these sites, with participants with acne on other sites.

The analysis of location of acne on the eyes, ears, and temples versus other locations for those participants with pre- and post-SEA and post-SEA acne did not show a significant association with group (Table 14-10(a,b): $p > 0.18$ for all analyses). The covariates age and race were significant in the adjusted analysis.

Examination of the unadjusted and adjusted results for Models 2 and 3 of location of acne also did not disclose a statistically significant association with initial or categorized dioxin (Table 14-10(c-f): $p > 0.25$ for all analyses). After adjusting for covariates, Model 2 accounted for age, and Model 3 accounted for age and race.

The unadjusted and adjusted analyses for Models 4 through 6 showed no significant relationship between current dioxin and location of acne (Table 14-10(g,h): $p > 0.17$ for all analyses) for participants with pre- and post-SEA and post-SEA acne. The adjusted analyses for Models 4 through 6 each accounted for age, race, and occupation.

Physical Examination Variables

Other Abnormalities

The analyses performed in Model 1 found no significant difference between the composite variable containing all other dermatologic abnormalities and group (Table 14-11(a,b): $p > 0.31$ for all contrasts). The covariates age, race, occupation, and presence of pre-SEA acne were included in the final adjusted model.

The unadjusted analysis for Model 2 showed no significant relationship between other abnormalities and initial dioxin (Table 14-11(c): $p = 0.216$); however, the adjusted analysis detected a highly significant initial dioxin-by-presence of pre-SEA acne interaction (Table 14-11(d): $p = 0.001$) as well as the following interactions: presence of pre-SEA acne and age, presence of pre-SEA acne and race, presence of pre-SEA acne and occupation, and race and occupation. Further examination of the interaction with initial dioxin is presented in Appendix Table J-2-2. The association between initial dioxin and the occurrence of other abnormalities was positive and significant ($p = 0.012$) for Ranch Hands with pre-SEA acne and negative but nonsignificant for Ranch Hands with no history of pre-SEA acne. In Model

Table 14-9.
Number of Participants with, and Location of, Pre- and Post-SEA and Post-SEA Acne

Location	Group	
	Ranch Hand	Comparison
Temples Only	253	314
Eyes Only	10	27
Ears Only	41	52
Temples and Eyes	19	16
Temples and Ears	48	67
Eyes and Ears	4	6
Temples, Eyes, and Ears	9	12
Other Sites	440	588

Location	Initial Dioxin	Current Dioxin
Temples Only	138	238
Eyes Only	5	10
Ears Only	16	34
Temples and Eyes	8	19
Temples and Ears	24	46
Eyes and Ears	0	4
Temples, Eyes, and Ears	8	9
Other Sites	247	415

Location	Current Dioxin Category				
	Comparison	Background RH	Low RH	High RH	Low plus High RH
Temples Only	271	100	72	66	138
Eyes Only	23	5	3	2	5
Ears Only	42	18	7	9	16
Temples and Eyes	13	11	4	4	8
Temples and Ears	58	22	13	11	24
Eyes and Ears	5	4	0	0	0
Temples, Eyes, and Ears	11	1	2	6	8
Other Sites	487	168	125	122	247

Table 14-10.
Analysis of Location of Acne (Pre- and Post-SEA and Post-SEA)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Temples/Eyes/Ears**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***824***	***46.6***	***1.04 (0.87,1.25)***	***0.716***
	Comparison	***1,082***	***45.7***		
Officer	Ranch Hand	321	47.4	0.93 (0.70,1.25)	0.695
	Comparison	430	49.1		
Enlisted Flyer	Ranch Hand	136	44.9	0.92 (0.59,1.44)	0.801
	Comparison	179	46.9		
Enlisted Groundcrew	Ranch Hand	367	46.6	1.20 (0.91,1.58)	0.215
	Comparison	473	42.1		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.03 (0.86,1.24)***	***0.753***	AGE ($p<0.001$) RACE ($p<0.001$)
Officer	0.92 (0.69,1.23)	0.575	
Enlisted Flyer	0.88 (0.56,1.38)	0.577	
Enlisted Groundcrew	1.21 (0.91,1.59)	0.184	

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

Note: Temples/Eyes/Ears = Temples, eyes, ears, temples and eyes, temples and ears, eyes and ears, or temples, eyes, and ears.

Table 14-10. (Continued)
Analysis of Location of Acne (Pre- and Post-SEA and Post-SEA)

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 Temples/Eyes/Ears	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	150	46.7	1.02 (0.88,1.17)	0.804
Medium	152	43.4		
High	144	43.8		

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
446	1.09 (0.94,1.27)	0.252	AGE (p=0.002)

[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.
Temples/Eyes/Ears = Temples, eyes, ears, temples and eyes, temples and ears, eyes and ears, or temples, eyes, and ears.

Table 14-10. (Continued)
Analysis of Location of Acne (Pre- and Post-SEA and Post-SEA)

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

Dioxin Category	n	Percent Temples/Eyes/Ears	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	910	46.5		
Background RH	329	48.9	1.12 (0.87,1.44)	0.392
Low RH	226	44.7	0.91 (0.68,1.22)	0.537
High RH	220	44.5	0.92 (0.68,1.24)	0.594
Low plus High RH	446	44.6	0.92 (0.73,1.15)	0.457

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	910			AGE ($p<0.001$) RACE ($p<0.001$)
Background RH	329	1.06 (0.82,1.37)	0.665	
Low RH	226	0.89 (0.66,1.20)	0.446	
High RH	220	1.01 (0.75,1.37)	0.950	
Low plus High RH	446	0.95 (0.75,1.19)	0.646	

[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.
Temples/Eyes/Ears = Temples, eyes, ears, temples and eyes, temples and ears, eyes and ears, or temples, eyes, and ears.

Table 14-10. (Continued)
Analysis of Location of Acne (Pre- and Post-SEA and Post-SEA)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Temples/Eyes/Ears /(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	47.7 (256)	49.0 (263)	42.6 (256)	0.95 (0.86,1.05)	0.321
5	48.9 (262)	47.3 (260)	43.1 (253)	0.95 (0.88,1.04)	0.265
6[c]	48.7 (261)	47.3 (260)	43.1 (253)	0.95 (0.86,1.04)	0.226

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	775	0.94 (0.84,1.05)	0.265	AGE ($p<0.001$) RACE ($p=0.005$) OCC ($p=0.076$)
5	775	0.94 (0.85,1.03)	0.178	AGE ($p<0.001$) RACE ($p=0.005$) OCC ($p=0.063$)
6[d]	774	0.94 (0.85,1.04)	0.222	AGE ($p<0.001$) RACE ($p=0.006$) OCC ($p=0.067$)

[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.
Temples/Eyes/Ears = Temples, eyes, ears, temples and eyes, temples and ears, eyes and ears, or temples, eyes, and ears.

Table 14-11.
Analysis of Other Abnormalities

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***	***952***	***83.6***	***1.13 (0.90,1.41)***	***0.329***
	Comparison	***1,279***	***81.9***		
Officer	Ranch Hand	367	85.8	1.19 (0.81,1.73)	0.429
	Comparison	501	83.6		
Enlisted Flyer	Ranch Hand	162	84.6	0.85 (0.47,1.52)	0.683
	Comparison	202	86.6		
Enlisted Groundcrew	Ranch Hand	423	81.3	1.17 (0.85,1.61)	0.370
	Comparison	576	78.8		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.10 (0.88,1.39)***	***0.400***	AGE ($p<0.001$) RACE ($p=0.006$) OCC ($p=0.017$) PRESEA ($p=0.076$)
Officer	1.14 (0.77,1.68)	0.516	
Enlisted Flyer	0.81 (0.44,1.47)	0.482	
Enlisted Groundcrew	1.18 (0.85,1.64)	0.310	

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

Table 14-11. (Continued)
Analysis of Other Abnormalities

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	174	83.9	0.90 (0.75,1.07)	0.216
Medium	173	82.7		
High	173	80.9		

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
520	****	****	INIT*PRESEA (p=0.001) AGE*PRESEA (p=0.025) RACE*PRESEA (p=0.007) OCC*PRESEA (p=0.003) RACE*OCC (p=0.031)

[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 ($p \leq 0.01$); relative risk, confidence interval, and p-value not presented; refer to Appendix Table J-2-2 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.
INIT = Log_2 (initial dioxin).

Table 14-11. (Continued)
Analysis of Other Abnormalities

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	1,061	81.3		
Background RH	374	85.3	1.44 (1.04,2.01)	0.029
Low RH	260	84.6	1.20 (0.83,1.74)	0.342
High RH	260	80.4	0.89 (0.63,1.26)	0.519
Low plus High RH	520	82.5	1.03 (0.78,1.35)	0.849

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	1,061			AGE (p<0.001) OCC (p=0.005) RACE (p=0.002) PRESEA (p=0.037)
Background RH	374	1.41 (1.00,1.99)	0.052	
Low RH	260	1.13 (0.77,1.68)	0.525	
High RH	260	0.98 (0.67,1.41)	0.896	
Low plus High RH	520	1.05 (0.78,1.40)	0.749	

[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 14-11. (Continued)
Analysis of Other Abnormalities

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Percent Abnormal/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) Est. Relative Risk (95% C.I.)[b]	p-Value
4	86.4 (295)	83.7 (300)	80.9 (299)	0.89 (0.79,1.01)	0.062
5	85.7 (300)	83.5 (297)	81.8 (297)	0.93 (0.84,1.03)	0.180
6[c]	85.6 (299)	83.5 (297)	81.8 (297)	0.89 (0.79,0.99)	0.038

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[a]	Analysis Results for Log_2 (Current Dioxin + 1) n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	894	0.93 (0.81,1.07)	0.318	AGE ($p<0.001$) PRESEA ($p=0.104$) RACE*OCC ($p=0.032$)
5	894	0.97 (0.86,1.09)	0.566	AGE ($p<0.001$) PRESEA ($p=0.105$) RACE*OCC ($p=0.029$)
6[d]	893	0.93 (0.81,1.06)	0.264	AGE ($p<0.001$) PRESEA ($p=0.084$) RACE*OCC ($p=0.0228$)

[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.

Appendix Table J-2-2. The association between initial dioxin and the occurrence of other abnormalities was positive and significant ($p=0.012$) for Ranch Hands with pre-SEA acne and negative but nonsignificant for Ranch Hands with no history of pre-SEA acne. In Model 3, the unadjusted analysis exhibited a significantly higher percentage of other abnormalities in the background Ranch Hand category (85.3%) than in the Comparison category (81.3%) (Table 14-11(e): $p=0.029$, Est. RR=1.44) but no significant difference in the other dioxin categories. Similarly, the adjusted analysis showed a marginally significant difference between background Ranch Hands and Comparisons (Table 14-11(f): $p=0.052$, Adj. RR=1.41). The adjusted analysis for Model 3 contained the significant covariates age, occupation, race, and presence of pre-SEA acne.

The unadjusted analysis for Model 4 showed a marginally significant inverse association between other abnormalities and current lipid-adjusted dioxin (Table 14-11(g): $p=0.062$, Est. RR=0.89). The percentages of Ranch Hands with at least one other abnormality were 86.4 percent, 83.7 percent, and 80.9 percent for low, medium, and high current lipid-adjusted dioxin categories respectively. In the adjusted analysis for Model 4, no significant relationship was found between current dioxin and other abnormalities. Examination of the unadjusted and adjusted analyses of other abnormalities for Model 5 did not show any statistically significant results (Table 14-11(g,h): $p \geq 0.18$ for unadjusted and adjusted analyses). The unadjusted analysis for Model 6 revealed a statistically significant inverse association between current whole-weight dioxin and other abnormalities (Table 14-11(g): $p=0.038$, Est. RR=0.89). The percentage of Ranch Hands with at least one other dermatalogic abnormality index decreased over the low, medium, and high current whole-weight dioxin categories (85.6%, 83.5%, and 81.8%). The adjusted analysis for Model 6 did not detect any statistically significant results. Models 4, 5, and 6 accounted for age, presence of pre-SEA acne, and a race-by-occupation interaction in the adjusted final model.

Dermatology Index

Analysis of the dermatology index did not reveal a significant difference between Ranch Hands and Comparisons in the unadjusted analysis for Model 1 (Table 14-12(a): $p>0.10$ for all analyses). However, a highly significant group-by-age interaction was detected in the adjusted analysis (Table 14-12(b): $p=0.005$). Stratified results of the interaction are presented in Appendix Table J-2-3. There was not a significant association between group and the dermatology index for younger participants; however older Comparisons had a marginally significant higher percentage of an abnormal dermatology index than older Ranch Hands (Adj. RR=0.80, $p=0.58$). After further stratifying by occupation, there were still no significant differences between younger Ranch Hands and younger Comparisons for the dermatology index. For older participants, there was a significant difference between Ranch Hands and Comparisons for the enlisted flyer stratum ($p=0.034$). For this stratum, older enlisted flyer Ranch Hands had fewer occurrences of an abnormal dermatology index (45.2%) than older enlisted flyer Comparisons (53.8%). In addition to the group-by-age interaction, race, occupation, and presence of pre-SEA acne were significant in the final adjusted model.

The unadjusted analyses for Models 2 and 3 did not disclose a significant relationship between initial or categorized dioxin and the dermatology index (Table 14-12(c,e): $p>0.11$).

Table 14-12.
Analysis of Dermatology 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***	***952***	***43.8***	***0.94 (0.80,1.11)***	***0.505***
	Comparison	***1,280***	***45.3***		
Officer	Ranch Hand	367	38.1	0.93 (0.71,1.23)	0.664
	Comparison	502	39.8		
Enlisted Flyer	Ranch Hand	162	44.4	0.70 (0.46,1.06)	0.108
	Comparison	202	53.5		
Enlisted Groundcrew	Ranch Hand	423	48.5	1.05 (0.82,1.35)	0.746
	Comparison	576	47.2		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	****	****	GROUP*AGE (p=0.005)
Officer	****	****	RACE (p<0.001)
Enlisted Flyer	****	****	OCC (p<0.001)
Enlisted Groundcrew	****	****	PRESEA (p<0.001)

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

**** Group-by-covariate interaction ($p \leq 0.01$); relative risk, confidence interval, and p-value not presented; refer to Appendix Table J-2-3 for further analysis of this interaction.

Table 14-12. (Continued)
Analysis of Dermatology 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	174	37.9	1.03 (0.90,1.18)	0.673
Medium	173	45.7		
High	173	39.9		

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**
520	0.92 (0.79,1.07)	0.282	RACE (p=0.082) OCC (p=0.005) PRESEA (p=0.063)

[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 14-12. (Continued)
Analysis of Dermatology 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	1,062	44.8		
Background RH	374	46.8	1.13 (0.89,1.43)	0.332
Low RH	260	40.4	0.83 (0.63,1.09)	0.180
High RH	260	41.9	0.86 (0.65,1.13)	0.271
Low plus High RH	520	41.2	0.84 (0.68,1.04)	0.114

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	1,062			DXCAT*AGE (p=0.013) OCC (p<0.001) RACE (p=0.001) PRESEA (p<0.001)
Background RH	374	1.26 (0.98,1.61)**	0.070**	
Low RH	260	0.80 (0.60,1.06)**	0.124**	
High RH	260	0.77 (0.58,1.03)**	0.075**	
Low plus High RH	520	0.79 (0.63,0.98)**	0.031**	

[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 J-2-4 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, ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.
DXCAT=Categorized Dioxin.

Table 14-12. (Continued)
Analysis of Dermatology Index

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Percent Abnormal/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) Est. Relative Risk (95% C.I.)[b]	p-Value
4	48.1 (295)	39.7 (300)	42.8 (299)	0.94 (0.86,1.03)	0.167
5	46.7 (300)	42.4 (297)	41.4 (297)	0.94 (0.87,1.01)	0.099
6[c]	46.5 (299)	42.4 (297)	41.4 (297)	0.95 (0.88,1.04)	0.253

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[a]	Analysis Results for Log_2 (Current Dioxin + 1) n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	894	0.85 (0.77,0.95)	0.003	RACE (p=0.028) OCC (p=0.002) PRESEA (p=0.008)
5	894	0.87 (0.79,0.95)	0.002	RACE (p=0.030) OCC (p=0.002) PRESEA (p=0.009)
6[d]	893	0.87 (0.79,0.96)	0.006	RACE (p=0.031) OCC (p=0.002) PRESEA (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.

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 results of the adjusted analysis for Model 2, which accounted for race, occupation, and presence of pre-SEA acne in the final model, were also nonsignificant (Table 14-12(d): $p=0.282$). However, the adjusted analysis of Model 3 showed a significant categorized dioxin-by-age interaction (Table 14-12(f): $p=0.013$). The covariates occupation, race, and presence of pre-SEA acne were also significant in the final adjusted model. Stratified results of the dioxin-by-age interaction are displayed in Appendix Table J-2-3. Removing the interaction from the model revealed significant relative risks for the following contrasts: background Ranch Hands versus Comparisons ($p=0.070$, Adj. RR=1.26), high Ranch Hands versus Comparisons ($p=0.075$, Adj. RR=0.77), and low plus high Ranch Hands versus Comparisons ($p=0.031$, Adj. RR=0.79). After removing occupation from the model, none of the above contrasts were significant (Appendix Table J-3-7: $p>0.10$).

The unadjusted analyses for Models 4 and 6 did not detect a significant association between the dermatology index and current dioxin. However, the unadjusted analysis for Model 5 displayed a marginally significant inverse association between current whole-weight dioxin and the dermatology index (Table 14-12(g): $p=0.099$, Est. RR=0.94). The percentages of Ranch Hands with an abnormal dermatology index in the low, medium, and high current whole-weight dioxin categories for Model 5 were 46.7, 42.4, and 41.4 respectively. The adjusted analyses for Models 4, 5, and 6 all displayed a highly significant inverse relationship between the dermatology index and current dioxin (Table 14-12(h): $p=0.003$, Adj. RR=0.85; $p=0.002$, Adj. RR=0.87; $p=0.006$, Adj. RR=0.87). The covariates of race, occupation, and presence of pre-SEA acne were significant in the final adjusted model for Models 4, 5, and 6. However, after excluding occupation from the final models, the results for Models 4, 5, and 6 were no longer significant (Appendix Table J-3-7: $p>0.10$).

DISCUSSION

In the study of biological effects of herbicides in humans, the dermatologic examination assumes special importance. Of the organ systems analyzed in this report, only the skin has a clinical endpoint (chloracne) that has been related conclusively to dioxin exposure. Although the intact skin is an effective protective barrier to a wide range of industrial chemicals, it also can serve as a portal of entry across which other internal organ systems can be placed at risk for toxicity.

In dermatologic practice particularly, the history can be more important to accurate diagnosis than the physical examination findings. Chloracne, for example, apart from the characteristic cutaneous distribution, has no hallmark features that distinguish it from other more common acneiform eruptions. In the current study, examiners were strictly forbidden from taking any occupational history, a restriction considered essential to the elimination of observer bias. As in previous examination cycles, skin lesions felt to be suspicious for skin cancer were biopsied. Although blind to the participants' status, examiners performed a similar number of biopsies in the Ranch Hand (20 out of 952) and Comparison (34 out of 1,281) cohorts.

Because chloracne is rare, few dermatologists will encounter even a single case in a lifetime of clinical practice. Experimental dose-response studies in animals and humans have

confirmed that the topical concentrations of TCDD required to produce overt lesions are far greater than the concentrations to which participants in the current study were likely to have been exposed during service in SEA. It is therefore not surprising that, in the four examination cycles to date, no cases of chloracne have been detected. Recognizing the remote possibility that acute cases of chloracne might have occurred and resolved, several chronic complications of all forms of acne (scarring and hyperpigmentation) were included in the dermatology index as dependent variables in the comparative analyses. The prevalence of these complications of acne were similar in the two groups.

Most of the dependent variable-covariate associations documented would be expected in clinical practice. Age-related changes in the epidermis, stratum corneum, and corium layers of the skin are associated with thinning of the skin, an increase in capillary fragility, hyperkeratinization, dyshydrosis with wrinkling and scaling, and loss of elasticity. Hyperplasia of the epidermis is associated typically with keratoses (seborrheic and senile) and basal cell carcinomas. With the exception of typical acne, which is more common at an early age, an increase in most other forms of skin disease would be expected over time and were documented in the current study.

Several of the highly significant covariate associations can be explained on race-specific variations well established in dermatologic practice. Many of the components of the dermatology index, for example, occur far more commonly in Blacks than non-Blacks. Pseudofolliculitis barbae, a cutaneous inflammatory reaction to ingrown hair, occurs almost exclusively in Black males who shave. This highly prevalent condition, associated with hyperpigmentation, no doubt contributed to the highly significant association of an abnormal index in Blacks versus non-Blacks (64.1% vs. 43.5%, $p<0.001$). In contrast, the prevalence of the composite other abnormalities was significantly greater in non-Blacks (83.3% vs. 72.5%, $p=0.002$) and includes the components of dermatosis and actinic keratoses, which are rare in Blacks.

Although the lifetime occurrence of acne as self-reported by questionnaire was similar in both groups, Ranch Hand enlisted groundcrew, those most heavily exposed to TCDD, appeared to be at increased risk for the development of acne subsequent to time of duty in SEA. The possibility of bias associated with self-reporting is raised, however, in that on physical examination no group differences were defined.

In the analyses relating other abnormalities to the current and extrapolated initial body burden of dioxin, Ranch Hands with background levels of serum dioxin had a higher prevalence of certain dermatoses than Comparisons (85.3% vs. 81.3%, $p=0.029$). However, in all models employing current serum dioxin data, Ranch Hands with the highest levels of serum dioxin had fewer abnormalities on physical examination than those with medium and low levels (see Table 14-11). Although the differences were not statistically significant, these results provide evidence against a dose-response effect, as does the lower occurrence of an abnormal dermatology index in Ranch Hands with low and high levels of serum dioxin relative to Comparisons (41.9% vs. 44.8%, $p=0.031$).

In summary, consistent with prior examinations, there was no evidence to suggest a dioxin effect on the skin.

SUMMARY

The Dermatologic Assessment was based on the following health endpoints: occurrence of acne (lifetime and relative to time of duty in SEA); location of acne; other abnormalities (a composite of 16 dermatologic conditions); and a dermatology index based on the presence of comedones, acneiform lesions, acneiform scars, and inclusion cysts, depigmentation, and hyperpigmentation. Each of these variables was analyzed for associations with group (Model 1), initial dioxin (Model 2), categorized dioxin (Model 3), current lipid-adjusted dioxin (Model 4), and current whole-weight dioxin (Models 5 and 6). Tables 14-13, 14-14, 14-15, and 14-16 summarize the results. A summary of group-by-covariate and dioxin-by-covariate interactions is provided in Table 14-17.

Model 1: Group Analysis

In the unadjusted analyses of Model 1, none of the dermatology variables showed a significant relationship with group except for acne relative to time of duty in SEA. When enlisted groundcrew with post-SEA acne only or those who had acne both before and after the start of their time of duty in SEA (pre- and post-SEA) were contrasted with enlisted groundcrew who did not have acne after the start of their duty in SEA (pre-SEA and none), a significant direct association between group and post-SEA acne was found ($p=0.042$). This association exhibits an increased risk of post-SEA acne for the Ranch Hand enlisted groundcrew.

In the adjusted analysis of acne relative to time of duty in SEA, an association with group was found for the enlisted groundcrew for the pre- and post-SEA and post-SEA versus pre-SEA and none contrast ($p=0.025$, Adj. $RR=1.51$) and for the post-SEA acne versus none contrast ($p=0.041$, Adj. $RR=1.47$). Also, for the subset of participants with pre-SEA acne, there were significant interactions between group and age and between group and occupation. These interactions could have been caused by or affected by the small number of participants with only pre-SEA acne in each stratum. The dermatology index variable also showed a significant interaction between group and age in the adjusted analysis. For older participants, Ranch Hands in the low and high initial dioxin categories had significantly lower percentages of an abnormal dermatology index than Comparisons.

Model 2: Initial Dioxin Analysis

The unadjusted analyses of Model 2 did not find a significant association between any of the dependent variables and the continuous measure of initial dioxin in Ranch Hands. The adjusted analysis for other abnormalities detected a significant interaction between initial dioxin and presence of pre-SEA acne.

Model 3: Categorized Dioxin Analysis

In Model 3, the unadjusted analyses for categorized dioxin exhibited a significantly higher percentage of other abnormalities in the background Ranch Hands category than in the Comparisons category ($p=0.029$). Similarly, the adjusted analyses for other abnormalities detected a marginally significant higher occurrence of other abnormalities in the background

Table 14-13.
Summary of Group Analyses (Model 1) for Dermatology Variables
(Ranch Hands vs. Comparisons)

Variable	UNADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Questionnaire				
Occurrence of Acne (Lifetime)	NS	NS	ns	NS*
Acne Relative to Time of Duty in SEA				
Pre- & Post-SEA and Post-SEA vs. Pre-SEA and None	NS	NS	ns	+0.042
Post-SEA vs. None	NS	NS	ns	NS*
Pre- & Post-SEA vs. Pre-SEA	ns	ns	ns	NS
Location of Acne (Post-SEA)	NS	NS	ns	NS
Location of Acne (Pre- & Post-SEA and Post-SEA)	NS	ns	ns	NS
Physical Examination				
Other Abnormalities	NS	NS	ns	NS
Dermatology Index	ns	ns	ns	NS

+: Relative risk $\geq$ 1.00.
NS or ns: Not significant ($p > 0.10$).
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. A lower case "ns" denotes relative risk less than 1.00.

Table 14-13. (Continued)
Summary of Group Analyses (Model 1) for Dermatology Variables
(Ranch Hands vs. Comparisons)

Variable	ADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Questionnaire				
Occurrence of Acne (Lifetime)	NS	NS	ns	NS*
Acne Relative to Time of Duty in SEA				
Pre- & Post-SEA and Post-SEA vs. Pre-SEA and None	NS	NS	ns	+0.025
Post-SEA vs. None	NS	NS	ns	+0.041
Pre- & Post-SEA vs. Pre-SEA	****	****	****	****
Location of Acne (Post-SEA)	NS	NS	ns	NS
Location of Acne (Pre- & Post-SEA and Post-SEA)	NS	ns	ns	NS
Physical Examination				
Other Abnormalities	NS	NS	ns	NS
Dermatology Index	****	****	****	****

+: Relative risk $\geq$ 1.00.
NS or ns: Not significant ($p > 0.10$).
NS*: Marginally significant ($0.05 < p \leq 0.10$).
**** Group-by-covariate interaction ($p \leq 0.01$); refer to Appendix J-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. A lower case "ns" denotes relative risk less than 1.00.

Table 14-14.
Summary of Initial Dioxin Analyses (Model 2) for Dermatology Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Questionnaire		
Occurrence of Acne (Lifetime)	ns	ns
Acne Relative to Time of Duty in SEA		
Pre- & Post-SEA and Post-SEA vs. Pre-SEA and None	ns	ns
Post-SEA vs. None	ns	ns
Pre- & Post-SEA vs. Pre-SEA	NS	--
Location of Acne (Post-SEA)	ns	NS
Location of Acne (Pre- & Post-SEA and Post-SEA)	NS	NS
Physical Examination		
Other Abnormalities	ns	****
Dermatology Index	NS	ns

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

--: Adjusted analysis not performed due to sparseness of pre-SEA only occurrences of acne.

**** Log_2 (initial dioxin)-by-covariate interaction ($p \leq 0.01$); refer to Appendix J-2 for further analysis of this interaction.

Note: A capital "NS" denotes a relative risk of 1.00 or greater. A lower case "ns" denotes relative risk less than 1.00.

Table 14-15.
Summary of Categorized Dioxin Analyses (Model 3) for Dermatology 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
Questionnaire				
Occurrence of Acne (Lifetime)	NS	NS	ns	NS
Acne Relative to Time of Duty in SEA				
Pre- & Post-SEA and Post-SEA vs. Pre-SEA and None	NS	NS	ns	NS
Post-SEA vs. None	NS	NS	ns	NS
Pre- & Post-SEA vs. Pre-SEA	NS	ns	ns	ns
Location of Acne (Post-SEA)	NS	NS	ns	ns
Location of Acne (Pre- & Post-SEA and Post-SEA)	NS	ns	ns	ns
Physical Examination				
Other Abnormalities	+0.029	NS	ns	NS
Dermatology Index	NS	ns	ns	ns

+: Relative risk $\geq$ 1.00.
NS or ns: Not significant ($p > 0.10$).
Note: P-value given if $p \leq 0.05$.
A capital "NS" denotes a relative risk of 1.00 or greater. A lower case "ns" denotes relative risk less than 1.00.

Table 14-15. (Continued)
Summary of Categorized Dioxin (Model 3) for Dermatology 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
Questionnaire				
Occurrence of Acne (Lifetime)	NS	NS	NS	NS
Acne Relative to Time of Duty in SEA				
Pre- & Post-SEA and Post-SEA vs. Pre-SEA and None	NS	NS	NS	NS
Post-SEA vs. None	NS	NS	NS	NS
Pre- & Post-SEA vs. Pre-SEA	NS	ns	ns	ns
Location of Acne (Post-SEA)	NS	NS	NS	NS
Location of Acne (Pre- & Post-SEA and Post-SEA)	NS	ns	NS	ns
Physical Examination				
Other Abnormalities	NS*	NS	ns	NS
Dermatology Index	**(NS*)	**(ns)	**(ns*)	**(-0.031)

-: Relative risk < 1.00.
NS or ns: Not significant ($p > 0.10$).
NS* or ns*: Marginally significant ($0.05 < p \leq 0.10$).
**(ns): Categorized dioxin-by-covariate interaction ($0.01 < p \leq 0.05$); not significant when interaction is deleted; refer to Appendix J-2 for further analysis of this interaction.
**(NS*) or **(ns*): Categorized dioxin-by-covariate interaction ($0.01 < p \leq 0.05$); marginally significant when interaction is deleted; refer to Appendix J-2 for further analysis of this interaction.
**(-0.031): Categorized dioxin-by-covariate interaction ($0.01 < p \leq 0.05$); significant ($p = 0.031$) when interaction is deleted; refer to Appendix J-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. A lower case "ns" denotes relative risk less than 1.00.

Table 14-16.
Summary of Group Analyses (Models 4, 5, and 6) for Dermatology 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
Questionnaire			
Occurrence of Acne (Lifetime)	ns	ns	ns
Acne Relative to Time of Duty in SEA			
Pre- & Post-SEA and Post-SEA vs. Pre-SEA and None	ns	ns	ns
Post-SEA VS. None	ns	ns	ns
Pre- & Post-SEA vs. Pre-SEA	ns	ns	ns
Location of Acne (Post-SEA)	ns	ns	ns
Location of Acne (Pre- & Post-SEA and Post-SEA)	ns	ns	ns
Physical Examination			
Other Abnormalities	ns*	ns	-0.038
Dermatology Index	ns	ns*	ns

-: Relative risk < 1.00.
ns: Not significant ($p > 0.10$).
ns*: Marginally significant ($0.05 < p \leq 0.10$).
Note: P-value given if $p \leq 0.05$.
A lower case "ns" denotes relative risk less than 1.00.

Table 14-16. (Continued)
Summary of Group Analyses (Models 4, 5, and 6) for Dermatology 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
Questionnaire			
Occurrence of Acne (Lifetime)	ns	ns	ns
Acne Relative to Time of Duty in SEA			
Pre- & Post-SEA and Post-SEA vs. Pre-SEA and None	ns	ns	ns
Post-SEA vs. None	ns	ns	ns
Pre- & Post-SEA vs. Pre-SEA	--	--	--
Location of Acne (Post-SEA)	ns	ns	ns
Location of Acne (Pre- & Post-SEA and Post-SEA)	ns	ns	ns
Physical Examination			
Other Abnormalities	ns	ns	ns
Dermatology Index	-0.003	-0.002	-0.006

-: Relative risk < 1.00.
ns: Not significant ($p > 0.10$).
--: Adjusted analysis not performed due to sparseness of pre-SEA only occurrences of acne.
Note: P-value given if $p \leq 0.05$.
A lower case "ns" denotes relative risk less than 1.00.

Table 14-17.
Summary Table of Group-by-Covariate and Dioxin-by-Covariate Interactions from Adjusted Analyses of Dermatology Variables

Model	Variable	Covariate
1[a]	Acne Relative to Time of Duty in SEA (Pre- & Post-SEA vs. Pre-SEA)	Age, Occupation
	Dermatology Index	Age
2[b]	Other Abnormalities	Presence of Pre-SEA Acne
3[c]	Dermatology Index	Age

[a] Group analysis (Ranch Hand vs. Comparison).
[b] Ranch Hands - Log_2 (Initial Dioxin).
[c] Categorized Dioxin.

Ranch Hands than in Comparisons. The dermatology index variable showed a significant interaction between categorized dioxin and age in the adjusted analysis. When this interaction was removed from the adjusted model, the background Ranch Hands showed a marginally significant higher occurrence of an abnormal dermatology index than Comparisons ($p=0.070$), while the high Ranch Hands showed a marginally lower occurrence of an abnormal dermatology index. When Ranch Hands in the low and high initial dioxin categories were combined and contrasted with Comparisons, Ranch Hands displayed a significantly lower occurrence of an abnormal dermatology index ($p=0.031$).

Models 4, 5, and 6: Current Dioxin Analysis

The unadjusted analyses of both Models 4 and 6 showed marginal and significant inverse associations between other abnormalities and current dioxin ($p=0.062$ and $p=0.038$ respectively). However, after adjusting for age, occupation, and presence of pre-SEA acne, these associations were no longer significant. In addition, the unadjusted analysis of Model 5 detected a marginally significant inverse relationship between current whole-weight dioxin and the dermatology index ($p=0.099$). In Models 4, 5, and 6, the adjusted analyses also detected a highly significant inverse association between current dioxin and the dermatology index ($p=0.003$, $p=0.002$, $p=0.006$, respectively; Adj. RR < 0.88 for all analyses).

CONCLUSION

In general, the dermatology variables showed no significant differences between Ranch Hands and Comparisons except for a few significant results for acne for enlisted groundcrew participants. In these significant analyses, Ranch Hands had higher occurrences of acne than Comparisons.

The analyses of categorized initial dioxin indicated a marginally significant positive difference between background Ranch Hands and Comparisons for the composite variable other abnormalities. The analyses of categorized initial dioxin also indicated a significantly lower occurrence of dermatology index abnormalities for Ranch Hands in the low plus high category than for Comparisons. However, the background Ranch Hands showed a marginally significant higher occurrence of dermatology index abnormalities than Comparisons.

The analysis of dermatology index exhibited a significant negative association with current dioxin in Models 4, 5, and 6. Also, all other results for Models 4, 5, and 6, although nonsignificant, displayed a negative association between current dioxin and the dermatology variables.

In summary, there is no consistent evidence in these data to suggest an adverse dioxin effect on the dermatologic system at doses received by U.S. military personnel in SEA.

CHAPTER 14
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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" ($\leq$140 mm Hg) and "abnormal" ($>$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" ($\leq$90 mm Hg) and "abnormal" ($>$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

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

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		Dioxin (Ranch Hands Only)		Categorized Dioxin	
		Ranch Hand	Comparison	Initial	Current	Ranch Hand	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 Myo-cardial 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

Variable	Variable Use	Group		Dioxin (Ranch Hands Only)		Categorized Dioxin	
		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 ($p<0.001$)
Officer	0.83 (0.61,1.13)	0.245	RACE ($p=0.028$)
Enlisted Flyer	1.35 (0.85,2.12)	0.202	DIAB ($p<0.001$)
Enlisted Groundcrew	1.03 (0.77,1.38)	0.837	DRKYR ($p<0.001$)
			HRTDIS ($p<0.001$)
			CHOL ($p=0.060$)
			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 $\leq$ 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 15-3. (Continued)
Analysis of Verified Essential Hypertension

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Percent Yes/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) 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

Model[a]	Analysis Results for Log_2 (Current Dioxin+1) 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. $RR \geq 1.14$). 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. $RR \geq 1.11$). 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

Model[a]	Current Dioxin Category Percent Yes/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) 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

Model[a]	n	Analysis Results for Log_2 (Current Dioxin+1) 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): $p\leq0.005$, 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): $p\geq0.70$ 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)
Officer	0.71 (0.39,1.30)**	0.269**	OCC (p=0.020)
Enlisted Flyer	1.23 (0.58,2.61)**	0.580**	AGE (p<0.001)
Enlisted Groundcrew	1.08 (0.62,1.85)**	0.793**	PACKYR (p=0.010)
			HRTDIS (p<0.001)
			HDL (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 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

Model[a]	Current Dioxin Category Percent Yes/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) 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

Model[a]	n	Analysis Results for Log_2 (Current Dioxin + 1) 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)
	Comparison	489	126.66			DIAB (p<0.001)
Enlisted Flyer	Ranch Hand	155	125.36	-0.45 (-3.98,3.08)	0.802	CHOL (p=0.010)
	Comparison	198	125.81			HDL (p=0.004)
Enlisted Groundcrew	Ranch Hand	416	125.44	-1.13 (-3.27,1.00)	0.297	BPMED (p<0.001)
	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

Model[a]	Current Dioxin Category Mean/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) 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

Model[a]	Current Dioxin Category Adjusted Mean/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) 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)
Officer	0.79 (0.53,1.16)**	0.224**	AGE (p<0.001)
Enlisted Flyer	1.15 (0.63,2.08)**	0.649**	DIAB (p=0.002)
Enlisted Groundcrew	1.00 (0.67,1.48)**	0.990**	BFAT (p<0.001) HDL (p=0.055) 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 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 $\leq$ 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 15-7. (Continued)
Analysis of Systolic Blood Pressure
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Percent Abnormal/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) 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

Model[a]	Analysis Results for Log_2 (Current Dioxin + 1) 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

Model[a]	Current Dioxin Category Percent Abnormal/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) 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

Model[a]	Analysis Results for Log_2 (Current Dioxin + 1) 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 ($p<0.001$)
Officer	0.76 (0.55,1.05)	0.099	RACE ($p=0.006$)
Enlisted Flyer	1.07 (0.65,1.73)	0.801	PACKYR ($p=0.054$)
Enlisted Groundcrew	0.79 (0.56,1.12)	0.185	BFAT ($p=0.044$) DIAB ($p=0.010$)

[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

Model[a]	Current Dioxin Category Percent Abnormal/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) 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

Model[a]	Analysis Results for Log_2 (Current Dioxin + 1) 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 ($0.01 < p \leq 0.05$); 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: 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): $p\geq0.13$). 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) AGE (p<0.001) RACE (p<0.001) CHOL (p=0.146) BFAT (p=0.011) DIAB (p=0.043)
Background RH	369	0.68 (0.46,1.01)**	0.057**	
Low RH	254	0.95 (0.64,1.40)**	0.778**	
High RH	259	1.04 (0.69,1.57)**	0.860**	
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 ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table K-2-8 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

Model[a]	Current Dioxin Category Percent Abnormal/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) 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

Model[a]	Analysis Results for Log_2 (Current Dioxin + 1) 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

Model[a]	Current Dioxin Category Percent Abnormal/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) 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

Model[a]	Analysis Results for Log_2 (Current Dioxin + 1) 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 ($0.01 < p \leq 0.05$); 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: 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

Model[a]	Current Dioxin Category Percent Abnormal/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) 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

Model[a]	Analysis Results for Log_2 (Current Dioxin + 1) 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): $p \geq 0.44$ 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)
Officer	0.75 (0.36,1.56)**	0.440**	AGE (p<0.001)
Enlisted Flyer	1.13 (0.38,3.36)**	0.822**	PERS (p=0.090)
Enlisted Groundcrew	1.06 (0.47,2.35)**	0.896**	CSMOK (p=0.050)
			HRTDIS (p=0.076)
			HDL (p=0.003)

[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

Model[a]	Current Dioxin Category Percent Abnormal/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) 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

Model[a]	n	Analysis Results for Log_2 (Current Dioxin + 1) 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

Model[a]	Current Dioxin Category Percent Abnormal/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) 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

Model[a]	Analysis Results for Log_2 (Current Dioxin) 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): $p\geq0.17$ 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)
High	172	****				BFAT (p=0.012)
						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

Model[a]	Current Dioxin Category Mean/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) 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

Model[a]	Current Dioxin Category Adjusted Mean/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) 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)
Officer	1.02 (0.46,2.26)	0.963	PACKYR (p=0.001)
Enlisted Flyer	1.41 (0.42,4.78)	0.581	BFAT (p=0.004)
Enlisted Groundcrew	0.58 (0.26,1.28)	0.177	CHOL (p=0.022)
			BPMED (p=0.064)

[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

Model[a]	Current Dioxin Category Percent Abnormal/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) 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

Model[a]	Analysis Results for Log_2 (Current Dioxin + 1) 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 ($p\leq 0.002$). 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

Model[a]	Current Dioxin Category Percent Abnormal/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) 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

Model[a]	Analysis Results for Log_2 (Current Dioxin + 1) 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): $p \leq 0.035$, $RR > 3.4$). 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)
Officer	2.40 (0.41,14.06)	0.333	CHOL (p=0.088)
Enlisted Flyer	0.79 (0.12,5.01)	0.803	HDL (p=0.075)
Enlisted Groundcrew	3.16 (0.58,17.23)	0.183	BFAT (p=0.015)
			DIAB (p<0.001)

[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 ≤ 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 15-23. (Continued)
Analysis of Femoral Pulses

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Percent Abnormal/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) 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

Model[a]	Analysis Results for Log_2 (Current Dioxin + 1) 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 ($p<0.001$)
Enlisted Flyer	0.76 (0.35,1.65)	0.492	HDL ($p=0.040$)
Enlisted Groundcrew	1.53 (0.93,2.50)	0.091	BFAT ($p=0.002$)
			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 ($p<0.001$)
Officer	1.18 (0.49,2.84)	0.718	RACE ($p=0.098$)
Enlisted Flyer	1.65 (0.53,5.13)	0.391	CSMOK ($p<0.001$)
Enlisted Groundcrew	2.14 (0.93,4.88)	0.073	BFAT ($p<0.001$) DIAB ($p<0.001$)

[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 ($p<0.001$)
Enlisted Flyer	0.83 (0.40,1.72)	0.615	DRKYR ($p=0.106$)
Enlisted Groundcrew	1.39 (0.87,2.22)	0.171	HDL ($p=0.025$)
			BFAT ($p<0.001$)
			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 ($p<0.001$)
Officer	1.14 (0.68,1.91)	0.620	OCC ($p=0.064$)
Enlisted Flyer	0.81 (0.39,1.69)	0.574	PACKYR ($p<0.001$)
Enlisted Groundcrew	1.35 (0.86,2.12)	0.193	HDL ($p=0.062$)
			BFAT ($p<0.001$)
			DIAB ($p<0.001$)

[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 ($p=0.003$)
Enlisted Flyer	1.19 (0.75,1.88)	0.461	DRKYR ($p=0.069$)
Enlisted Groundcrew	0.78 (0.58,1.06)	0.109	CSMOK ($p=0.103$)
			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 ≤ 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 15-29. (Continued)
Analysis of Kidney, Urethra, and Bladder (KUB) X Ray (Excluding Kidney Stones)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Percent Abnormal/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) 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

Model[a]	Analysis Results for Log_2 (Current Dioxin + 1) 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 ($p\geq 0.13$). 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) DRKYR (p=0.107) CHOL (p<0.001) HDL (p=0.017) HRTDIS (p=0.088) DIAB (p=0.007)
Officer	1.96 (0.82,4.69)	0.130	
Enlisted Flyer	1.87 (0.57,6.16)	0.304	
Enlisted Groundcrew	1.28 (0.55,2.95)	0.563	

[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

Model[a]	Current Dioxin Category Percent Abnormal/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) 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

Model[a]	Analysis Results for Log_2 (Current Dioxin + 1) 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 Mean/(n) Examination				Analysis Results for Log_2 (Initial Dioxin)[a]	
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 $\leq$ 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.
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

Occupational Category	Group	Percent Abnormal/(n) Examination			
		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)

Occupational Category	Group	Normal in 1982		Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
		n in 1992	Percent Abnormal in 1992		
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 (903)***	***1.2 (903)***
	Comparison	***0.2 (1,134)***	***0.6 (1,134)***
Officer	Ranch Hand	0.0 (346)	1.2 (346)
	Comparison	0.5 (434)	0.5 (434)
Enlisted Flyer	Ranch Hand	1.3 (157)	1.3 (157)
	Comparison	0.0 (188)	1.6 (188)
Enlisted Groundcrew	Ranch Hand	0.5 (400)	1.3 (400)
	Comparison	0.0 (512)	0.4 (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			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	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 ≤ 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 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

Occupational Category	Group	Percent Abnormal/(n) Examination 1985	1992
All	***Ranch Hand***	***23.6 (899)***	***8.7 (899)***
	Comparison	***21.5 (1,130)***	***7.0 (1,130)***
Officer	Ranch Hand	27.8 (345)	8.1 (345)
	Comparison	25.3 (431)	6.7 (431)
Enlisted Flyer	Ranch Hand	21.7 (157)	8.3 (157)
	Comparison	20.3 (187)	9.6 (187)
Enlisted Groundcrew	Ranch Hand	20.7 (397)	9.3 (397)
	Comparison	18.8 (512)	6.3 (512)

Occupational Category	Group	Normal in 1985: n in 1992	Normal in 1985: 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

Occupational Category	Group	Percent Abnormal/(n) Examination 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)

Occupational Category	Group	Normal in 1985: n in 1992	Normal in 1985: 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 ≤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 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 (899)***	***9.6 (899)***
	Comparison	***22.6 (1,130)***	***7.7 (1,130)***
Officer	Ranch Hand	29.0 (345)	8.4 (345)
	Comparison	25.8 (431)	7.0 (431)
Enlisted Flyer	Ranch Hand	23.6 (157)	9.6 (157)
	Comparison	20.9 (187)	10.2 (187)
Enlisted Groundcrew	Ranch Hand	21.2 (397)	10.6 (397)
	Comparison	20.5 (512)	7.4 (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 (899)***	***9.7 (899)***
	Comparison	***22.6 (1,128)***	***8.2 (1,128)***
Officer	Ranch Hand	29.0 (345)	8.7 (345)
	Comparison	25.8 (431)	7.2 (431)
Enlisted Flyer	Ranch Hand	23.6 (157)	9.6 (157)
	Comparison	21.4 (187)	10.2 (187)
Enlisted Groundcrew	Ranch Hand	21.4 (397)	10.6 (397)
	Comparison	20.4 (510)	8.2 (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			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	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): $p \geq 0.16$ 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): $p \geq 0.15$ 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)

Variable	UNADJUSTED			
	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)

Variable	UNADJUSTED			
	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 $\geq$ 1.00.
--: Analysis not performed due to sparse number of abnormalities.
NS or ns: Not significant ($p > 0.10$).
NS*: Marginally significant ($0.05 < p \leq 0.10$).
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 15-39. (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)

Variable	ADJUSTED			
	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 $\geq$ 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 $\geq$ 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 ($0.05 < p \leq 0.10$).
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 15-41. (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)

Variable	ADJUSTED			
	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 $\geq$ 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)

Variable	UNADJUSTED		
	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 $\geq$ 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)

Variable	ADJUSTED		
	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 $\geq$ 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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CHAPTER 16

HEMATOLOGIC ASSESSMENT

INTRODUCTION

Background

Experiments in laboratory animals have demonstrated that 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD, or dioxin) is directly toxic to the hematopoietic system in several species. In one study, TCDD administered in low doses to monkeys resulted in elevated neutrophil counts while higher doses were associated with lympho- and thrombocytopenia (1). A decrease in overall cellularity and an increase in the myeloid-erythroid ratio were noted in approximately half of the sternal bone marrow samples examined at the conclusion of the experiment.

Other animal studies have shown that the toxic effects of TCDD on the hematopoietic system vary depending on the dose employed and the species examined. In many reports, it is difficult to distinguish primary effects from those occurring secondary to systemic toxicity. One study in rats using gavage doses of TCDD varying from 0.001 to 1.0 μg/kg noted depressed red blood cell counts and packed cell volumes in the high-dose group (2). In another rat experiment, elevated erythrocyte, reticulocyte, and neutrophil counts were noted with reduction in mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), platelet counts, and clot retraction times—effects that the authors felt could be attributed to systemic toxicity with terminal dehydration (3). In another multispecies study, mice and guinea pigs were found to have dose-dependent reductions in leukocytes with relative lymphocytopenia within 1 week of TCDD administration while thrombocytopenia and hemoconcentration were found in rats (4).

More recent animal research relevant to the hematopoietic system has focused on the altered cellular differentiation associated with TCDD toxicity. In mice, progenitor cells were suppressed following exposure to TCDD in doses as low as 1.0 μg/kg of body weight, and in vitro studies demonstrated that myelotoxicity occurs by a direct inhibition of proliferating stem cells (5). A subsequent study from the same laboratory demonstrated a direct effect of TCDD on cultured lymphocytes resulting in a selective inhibition of B-cell differentiation into antibody-secretive cells (6). In these and other studies (7), the authors cite evidence for the role of the aryl hydrocarbon (Ah) receptor in mediating these myelo- and lymphotoxic effects. In another report, the presence of the Ah receptor was defined in the spleens of numerous primate species (8). Though Ah receptors have been isolated in the tissue of several human organs (9-14), the relevance of these observations to dioxin toxicity remains to be proven (15).

In general, human observational studies have shown fewer and less consistent hematologic findings than the structured animal experiments. A case report of dichlorophenoxyacetic acid (2,4-D) intoxication with marked neurological findings described transient bone marrow depression with peripheral leukopenia and granulocytopenia (16). In two industrial accidents involving significant contamination with TCDD associated with

chloracne, temporary depression of peripheral leukocyte and lymphocyte formation was observed (17,18).

Several human morbidity studies have included routine, complete blood counts in examination protocols (19,20). A clinical epidemiologic study was conducted 30 years after the Nitro, West Virginia, tricholrophenol explosion. The study compared 204 highly exposed employees (86% of whom had developed chloracne) with 163 employees who were not exposed (20). No significant differences were found in the standard hematologic indices.

Numerous studies have been conducted on cohorts exposed to TCDD by environmental contamination of the soil in the Quail Run (21-23) and Times Beach (24) residential areas of Missouri. With one exception, no differences were found in any of the hematologic parameters examined. In the Times Beach study, a statistically significant increase in the mean platelet count was noted in the exposed cohort relative to the unexposed, but the difference (281,927/mm^3 vs. 249,061/mm^3) was not clinically significant. A more recent study, the first to report clinical indices in relation to tissue levels of dioxin (25), found no abnormalities in the complete blood count related to the body burden of TCDD.

In previous reports of the Air Force Health Study (AFHS) (26-28), Ranch Hand participants were found to have slightly higher mean platelet counts than Comparisons and, in the 1987 followup examination (28), a significantly greater percentage of abnormally high platelet counts as well. In the most recent serum dioxin analysis of the 1987 followup examination (29), Ranch Hands with the highest current serum dioxin levels had higher mean platelet and total white blood cell counts (WBC) than Comparisons with background levels of dioxin. Though the differences in the means between the cohorts (270,050/mm^3 vs. 259,010/mm^3 for platelets and 7,124/mm^3 vs. 6,668/mm^3 for WBCs) cannot be considered clinically significant, these results are consistent with a dose-response effect and, along with the elevation in the erythrocyte sedimentation rate (see Chapter 9, General Health), raise the possibility of a chronic inflammatory response associated with dioxin exposure.

Summary of Previous Analyses of the Air Force Health Study

1982 Baseline Study Summary Results

The functional integrity of the hematopoietic system was assessed at the Baseline examination by the measurement of eight peripheral blood variables: red blood cell (RBC) count, WBC, hemoglobin, hematocrit, MCV, MCH, mean corpuscular hemoglobin concentration (MCHC), and platelet count. These variables were analyzed in the discrete form to detect differences in the percentages of values outside the designed laboratory range, as well as analyzed in the continuous form to detect shifts in mean values between the Ranch Hand and Comparison groups.

The Ranch Hand group had a significantly higher adjusted mean MCV and MCH than the Comparison group ($p=0.05$ and $p=0.04$ respectively), although the magnitude of the difference was small in each case. The Ranch Hand adjusted mean values for six other parameters (i.e., RBC, WBC, hemoglobin, hematocrit, MCHC, and platelet count) were nearly identical to the adjusted mean values of the Comparison group, and all were well

within normal range. The percent of abnormal values for these eight variables, as established by the upper and lower limits of normal, did not differ significantly between the two groups.

The 1982 report concluded that the overall statistical findings were generally consistent, and that adverse health effects related to herbicides were not present.

1985 Followup Study Summary Results

The same eight peripheral blood variables (i.e., RBC, WBC, hemoglobin, hematocrit, MCV, MCH, MCHC, and platelet count) were analyzed in the 1985 followup. The unadjusted discrete analysis of the percent abnormal values, both low and high, showed no statistically significant difference between the Ranch Hand and Comparison groups for any of the hematologic variables. Similarly, in the adjusted discrete analyses, none of the adjusted relative risks was significant.

As no subgroup demonstrated consistent patterns of hematologic impairment, biologic relevance was not assigned to the interactions. The significant group differences found for MCV and MCH at the Baseline examination were not present in the 1985 followup analyses. The covariate effects of age, race, occupation, and lifetime smoking history were highly significant for many of the hematologic variables.

The longitudinal analyses of MCV, MCH, and platelet count found a significant difference for platelet count, with the Ranch Hands having an average decrease in platelet count between examinations and the Comparisons having an average increase. As a result, the Baseline group difference (nonsignificant) in mean values closed to near equivalence at the followup examination.

In conclusion, none of the eight hematologic variables was found to differ significantly between the Ranch Hand and Comparison groups. The expected effects of age, race, and smoking were demonstrated with most of the hematologic variables. The longitudinal analyses also suggested that neither group manifested an impairment of the hematopoietic system. Exposure index analyses did not support a plausible dose-response relationship for any of the hematologic variables.

1987 Followup Study Summary Results

The hematologic status of the Ranch Hand and Comparison groups was assessed by the examination of the same eight variables used in the two previous examinations: RBC, WBC, hemoglobin, hematocrit, MCV, MCH, MCHC, and platelet count. There were no statistically significant differences between the Ranch Hand and Comparison groups for RBC count, hemoglobin, hematocrit, MCV, MCH, and MCHC, in analyses either unadjusted or adjusted for the covariates of age, race, occupation, current cigarette smoking, and lifetime cigarette smoking history. For WBC count, the mean level was significantly greater in Ranch Hands than in Comparisons. The difference was not statistically significant after adjustment for covariates, nor were significant differences detected in the percentage of individuals with abnormal values.

Mean platelet counts also were significantly greater in Ranch Hands than in Comparisons, as was the percentage of individuals with abnormally high platelet counts. While these differences remained significant after adjustment for covariates, no platelet count was above 595,000/mm^3. Longitudinal analyses detected a significantly greater decrease in the mean platelet count in Ranch Hands than in Comparisons, despite the higher overall mean count, from the Baseline examination to the 1987 followup examination.

Serum Dioxin Analysis of 1987 Followup Study Summary Results

Several variables showed an association with initial dioxin in the unadjusted model, but when the model was adjusted for covariates, the associations became nonsignificant. Hemoglobin and hematocrit were positively associated with current dioxin when time since duty in Southeast Asia (SEA) was no more than 18.6 years and negatively associated with current dioxin when time since duty in SEA was greater than 18.6 years. For the discrete RBC count analysis, the risk of an abnormally low count was less than 1 when time since duty in SEA did not exceed 18.6 years and was greater than 1 when time since duty in SEA was more than 18.6 years. Since a low RBC count was considered abnormal for the purpose of these statistical analyses, the trend in relation to current dioxin was similar to that in the continuous analyses of hemoglobin and hematocrit. In the discrete analysis of prothrombin time, the trend in relation to current dioxin also was similar to that in the continuous analyses of hemoglobin and hematocrit. In the categorized current dioxin analyses, whenever the overall contrast showed significant, or marginally significant, differences among the categories, the mean level or percent abnormal in the three categories of Ranch Hands (i.e., officers, enlisted flyers, and enlisted groundcrew) tended to exceed the corresponding mean level or percent abnormal in the background category that consisted of Comparisons.

The longitudinal analyses of MCV, MCH, and platelet count displayed no significant associations with dioxin.

In summary, the results of the previous analysis reveal no evidence for hematopoietic toxicity secondary to dioxin exposure. Statistical analyses of two variables (WBC and platelet count) raised the possibility of subtle biologic effects that cannot be considered clinically significant but do point to the need for followup in future examination cycles. The increased platelet and WBC counts, in addition to the elevation of erythrocyte sedimentation rates (in the general health assessment) may indicate the presence of a chronic inflammatory response to dioxin exposure.

Parameters for the Hematologic Assessment

Dependent Variables

The analysis of the hematologic assessment consisted of data from the laboratory examination only. No questionnaire or physical examination data were analyzed as part of the hematologic assessment.

Laboratory Examination Data

A total of 13 hematology variables were measured at the laboratory as part of the 1992 followup examination and analyzed statistically. These variables include 5 cell counts, 1 RBC cell morphology, 6 measures of absolute blood counts, and a coagulation measure (prothrombin time). These variables were determined by routine hematologic procedures. In particular, the cell count indices were performed on the Coulter S Plus® automated instrument, and prothrombin time was measured on the MLA Electra 1000-C® instrument. All dependent variables were analyzed in the continuous form, except for the RBC morphology. RBC count, WBC count, hemoglobin, hematocrit, platelet count, prothrombin time, and the RBC morphology also were analyzed in their discrete form, using Scripps Clinic and Research Foundation (SCRF) normal ranges as cutpoints. RBC count, WBC count, hemoglobin, hematocrit, and platelet count were trichotomized as abnormal low, normal, and abnormal high. However, due to the sparse number of participants with abnormally high hematocrit values, the abnormal high category was combined with the normal category, resulting in contrasts of "normal or abnormal high" versus "abnormal low." Likewise, due to the sparse number of participants with abnormally low platelet counts, the discrete analysis of platelet counts contrasts "abnormal low or normal" versus "abnormal high."

The RBC morphology dependent variable was constructed from a number of laboratory conditions, many of which were minor abnormalities. These conditions were rouleaux, slight rouleaux, few Burr cells, few macrocytes, few ovalocytes, few target cells, moderate macrocytes, moderate stomatocytes, moderate anisocytosis, slight anisocytosis, slight polychromasia, slight baso-strippling, moderate microcytes, few Howell-Jolly bodies, and few schistocytes.

The SCRF laboratory coefficients of variation for the cell counts and indices meet or exceed requirements due to the precision of the Coulter S Plus® automated instrument, in conjunction with fast initial response cumulative sum (FIR CUSUM) quality control techniques. The SCRF laboratory normal values varied to some extent from the Kelsey-Seybold Clinic norms used at the Baseline examination. The SCRF laboratory normal values for all variables subsequently are shown.

Participants testing positive for the human immunosuppressant virus (HIV) (3 Ranch Hands and 1 Comparison) were excluded from the analysis of all variables. Participants with a fever (body temperature greater than or equal to 100° Fahrenheit) at the time of the examination were excluded from the analysis of all variables except prothrombin time. Participants taking an anticoagulant (Coumadin®) or aspirin at the time of the examination also were excluded from the analysis of prothrombin time.

Covariates

Age, race, military occupation, current level of cigarette smoking (cigarettes/day), and lifetime cigarette smoking history (pack-years) were used as candidate covariates in adjusted statistical analyses evaluating the hematologic dependent variables. 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. The smoking covariates were used in their continuous form for logistic regression and general linear models analyses and were discretized as necessary for tabular presentations of interactions between these covariates and exposure.

Statistical Methods

Table 16-1 summarizes the statistical analyses performed for the hematologic assessment. The first part of this table describes the dependent variables analyzed. The second part of this table provides a further description of the candidate covariates examined. Abbreviations used in the body of the table are defined at the end of the table. Chapter 7, Statistical Methods, describes the basic statistical analysis methods used in the Hematologic Assessment. Table 16-2 provides the number of participants with missing dependent variable and covariate data and those excluded due to medical conditions.

The variables absolute neutrophils (bands), absolute eosinophils, and absolute basophils had a substantial number of measurements equal to 0 counts per mm^3. The nonzero measurements exhibited a positively skewed distribution, and a logarithmic transformation enhanced the assumption of a normal distribution for these measurements. However, the logarithmic transformation cannot be applied to the measurements equal to 0 counts per mm^3. Consequently these variables were analyzed in two forms: (1) a discrete analysis of the proportion of zero measurements and (2) a continuous analysis of the nonzero measurements.

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

The results of the analyses without occupation are presented in Appendix L-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

Longitudinal analyses on platelet count were conducted to evaluate the association of exposure to changes between the 1982 Baseline examination and the 1992 followup examination.

Table 16-1.
Statistical Analyses for the Hematologic Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analyses
Red Blood Cell (RBC) Count (million/mm^3)	LAB	D/C	Abnormal Low: <4.3 Normal: 4.3-5.9 Abnormal High: >5.9	AGE,RACE, OCC,CSMOK, PACKYR	U:PR,CS, GLM,TT A:PR,GLM
White Blood Cell (WBC) Count (thousand/mm^3)	LAB	D/C	Abnormal Low: <4.5 Normal: 4.5-11.0 Abnormal High: >11.0	AGE,RACE, OCC,CSMOK, PACKYR	U:PR,CS, GLM,TT A:PR,GLM
Hemoglobin (gm/dl)	LAB	D/C	Abnormal Low: <13.9 Normal: 13.9-18.0 Abnormal High: >18.0	AGE,RACE, OCC,CSMOK, PACKYR	U:PR,CS, GLM,TT A:PR,GLM
Hematocrit (percent)	LAB	D/C	Abnormal Low: <39.0 Normal or Abnormal High: ≥39.0	AGE,RACE, OCC,CSMOK, PACKYR	U:LR,CS, GLM,TT A:LR,GLM
Platelet Count (thousand/mm^3)	LAB	D/C	Abnormal High: >400.0 Abnormal Low or Normal: ≤400.0	AGE,RACE, OCC,CSMOK, PACKYR	U:LR,CS, GLM,TT A:LR,GLM L:LR,GLM
Prothrombin Time (seconds)	LAB	D/C	High: >13.2 Normal: ≤13.2	AGE,RACE, OCC,CSMOK, PACKYR	U:LR,CS, GLM,TT A:LR,GLM
RBC Morphology	LAB	D	Abnormal Normal	AGE,RACE, OCC,CSMOK, PACKYR	U:LR,CS A:LR
Absolute Neutrophils (segs) (thousand/mm^3)	LAB	C	--	AGE,RACE, OCC,CSMOK, PACKYR	U:GLM,TT A:GLM
Absolute Neutrophils (bands) (thousand/mm^3)	LAB	D/C	Zero Nonzero	AGE,RACE, OCC,CSMOK, PACKYR	U:LR,CS, GLM,TT A:GLM
Absolute Lymphocytes (thousand/mm^3)	LAB	C	--	AGE,RACE, OCC,CSMOK, PACKYR	U:GLM,TT A:GLM
Absolute Monocytes (thousand/mm^3)	LAB	C	--	AGE,RACE, OCC,CSMOK, PACKYR	U:GLM,TT A:GLM
Absolute Eosinophils (thousand/mm^3)	LAB	D/C	Zero Nonzero	AGE,RACE, OCC,CSMOK, PACKYR	U:LR,CS, GLM,TT A:GLM
Absolute Basophils (thousand/mm^3)	LAB	D/C	Zero Nonzero	AGE,RACE, OCC,CSMOK, PACKYR	U:LR,CS, GLM,TT A:GLM

Table 16-1. (Continued)
Statistical Analyses for the Hematologic 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
Current Cigarette Smoking (CSMOK) (cigarettes/day)	Q-SR	D/C	0-Never 0-Former >0-20 >20
Lifetime Cigarette Smoking History (PACKYR) (pack-years)	Q-SR	D/C	0 >0-10 >10

Abbreviations

Data Source:
- LAB = 1992 laboratory results
- MIL = Air Force military records
- Q-SR = Health questionnaires (self-reported)

Data Form:
- C = Continuous analysis only
- 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 2x2 tables)
- GLM = General linear models analysis
- LR = Logistic regression analysis
- PR = Polychotomous logistic regression analysis
- TT = Two-sample t-test

Table 16-2.
Number of Participants with Missing Data for, or Excluded from, the Hematologic Assessment

Variable	Variable Use	Group		Dioxin (Ranch Hands Only)		Categorized Dioxin	
		Ranch Hand	Comparison	Initial	Current	Ranch Hand	Comparison
Red Blood Cell (RBC) Count	DEP	0	1	0	0	0	0
White Blood Cell (WBC) Count	DEP	0	1	0	0	0	0
Hemoglobin	DEP	0	1	0	0	0	0
Hematocrit	DEP	0	1	0	0	0	0
Platelet Count	DEP	0	2	0	0	0	1
Prothrombin Time	DEP	0	1	0	0	0	0
RBC Morphology	DEP	0	1	0	0	0	0
Absolute Neutrophils (segs)	DEP	0	1	0	0	0	0
Absolute Neutrophils (bands)	DEP	0	1	0	0	0	0
Absolute Lymphocytes	DEP	0	1	0	0	0	0
Absolute Monocytes	DEP	0	1	0	0	0	0
Absolute Eosinophils	DEP	0	1	0	0	0	0
Absolute Basophils	DEP	0	1	0	0	0	0
Current Cigarette Smoking	COV	0	2	0	0	0	2
Lifetime Cigarette Smoking History	COV	1	2	0	1	1	2
HIV Positive	EXC	3	1	2	3	3	1

Table 16-2. (Continued)
Number of Participants with Missing Data for, or Excluded from, the Hematologic Assessment

Variable	Variable Use	Group		Dioxin (Ranch Hands Only)		Categorized Dioxin	
		Ranch Hand	Comparison	Initial	Current	Ranch Hand	Comparison
Body Temperature Greater than or Equal to 100° Fahrenheit	EXC	3	1	1	3	3	1
Participants Taking an Anticoagulant or Aspirin	EXC	80	103	44	75	75	83

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.

RESULTS

Dependent Variable-Covariate Associations

Results of the tests of association between the hematology dependent variables and covariates are presented in Appendix Table L-1-1. These associations are based on combined group data. Participants who tested positive for HIV were excluded from the analyses of all variables; participants with a fever at the time of the examination were excluded from the analyses of all variables except prothrombin time; participants who were taking an anticoagulant or aspirin at the time of the examination also were excluded from the analysis of prothrombin time.

Examining the association between the covariates and RBC count, in continuous form, revealed significant associations with age ($p<0.001$), race ($p=0.021$), occupation ($p<0.001$), and current cigarette smoking ($p<0.001$). RBC count decreased with age ($r=-0.143$). Blacks had a higher mean RBC count (5.11 million/mm^3) than non-Blacks (5.01 million/mm^3). Mean RBC count was highest for enlisted groundcrew (5.07 million/mm^3), followed by enlisted flyers (5.02 million/mm^3) and officers (4.96 million/mm^3). RBC count was positively associated with current cigarette smoking; that is, RBC count tended to increase as the number of cigarettes per day increased ($r=0.083$).

RBC count, in discrete form, was significantly associated with age ($p=0.047$), race ($p<0.001$), and occupation ($p=0.029$). The percentage of older participants with abnormally low RBC counts (3.5%) was greater than the percentage of younger participants with abnormally low RBC counts (1.8%). The percentages of older and younger participants with abnormally high RBC counts were equal (1.3%). The percentage of Blacks with abnormally high RBC counts (5.3%) was significantly greater than the percentage of non-Blacks with abnormally high RBC counts (1.1%). Percentages of Blacks and non-Blacks with abnormally low RBC counts were similar (3.1% for Blacks and 2.8% for non-Blacks). The percentage of participants with abnormally high RBC counts was greater for enlisted flyers and enlisted groundcrew (1.7% for both categories) than for officers (0.7%); the percentage of participants with abnormally low RBC counts was greater for officers (3.9%) than for enlisted personnel (1.9% for enlisted flyers and 2.1% for enlisted groundcrew).

Highly significant associations were found between WBC count, in continuous form, and race ($p<0.001$), occupation ($p<0.001$), current cigarette smoking ($p<0.001$), and lifetime cigarette smoking history ($p<0.001$). In contrast to RBC count, non-Blacks had a higher mean WBC count (7.43 thousand/mm^3) than Blacks (6.58 thousand/mm^3). Enlisted personnel had higher mean WBC counts (7.62 thousand/mm^3 for enlisted groundcrew, 7.77 thousand/mm^3 for enlisted flyers) than officers (6.95 thousand/mm^3). WBC count increased as current cigarette smoking increased ($r=0.438$) and lifetime cigarette smoking history increased ($r=0.245$).

WBC count in discrete form also was significantly associated with race ($p<0.001$), occupation ($p=0.002$), current cigarette smoking ($p<0.001$), and lifetime cigarette smoking history ($p<0.001$). The percentage of participants with abnormally low WBC counts was greater for Blacks (13.0%) than for non-Blacks (3.1%), while the percentage with

abnormally high WBC counts was greater for non-Blacks (5.7%) than Blacks (3.1%). The percentage of participants with abnormally low WBC counts was 4.1, 4.1, and 3.2 percent for officers, enlisted flyers, and enlisted groundcrew. The percentage of participants with abnormally high WBC counts was 3.4, 8.8, and 6.3 percent for officers, enlisted flyers, and enlisted groundcrew. The percentage of participants with abnormally low WBC counts decreased as the levels of current and lifetime cigarette smoking increased, while the percentage with abnormally high WBC counts increased as the levels of smoking increased.

Hemoglobin, in continuous form, was significantly associated with age ($p<0.001$), race ($p<0.001$), occupation ($p=0.007$), current cigarette smoking ($p<0.001$), and lifetime cigarette smoking history ($p=0.007$). The association between hemoglobin and age was negative ($r=-0.089$). The hemoglobin mean was greater for non-Blacks (15.89 gm/dl) than for Blacks (15.41 gm/dl) and increased from officers (15.78 gm/dl) to enlisted flyers (15.90 gm/dl) and enlisted groundcrew (15.93 gm/dl). Hemoglobin was positively associated with current cigarette smoking ($r=0.227$) and lifetime cigarette smoking history ($r=0.057$).

In discrete form, hemoglobin was significantly associated only with race ($p=0.001$) and current cigarette smoking ($p<0.001$). A greater percentage of Blacks had abnormally low hemoglobin levels (7.6%) than non-Blacks (2.3%), while a smaller percentage of Blacks had abnormally high levels (0.8%) than non-Blacks (1.9%). The percentage of participants with abnormally low hemoglobin levels decreased as current cigarette smoking increased, while the percentage of participants with abnormally high levels increased as current smoking increased.

Similar to hemoglobin, hematocrit in continuous form was significantly associated with all of the candidate covariates ($p<0.003$ for all covariates) and was significantly associated only with race ($p=0.048$) and current cigarette smoking ($p=0.032$) in discrete form. The association with hematocrit in continuous form was negative for age ($r=-0.067$) and was positive for current cigarette smoking ($r=0.239$) and lifetime cigarette smoking history ($r=0.072$). The hematocrit mean was greater for non-Blacks (46.33 percent) than for Blacks (45.48 percent) and increased from officers (45.98 percent) to enlisted flyers (46.42 percent) and enlisted groundcrew (46.49 percent). The percentage of Blacks with abnormally low hematocrit levels (3.8%) was greater than the percentage of non-Blacks (1.3%) and the percentage of non-smokers with abnormally low hematocrit levels (1.6% for participants who never smoked and 2.0% for former smokers) was greater than the percentage of smokers (0.3% for >0-20 cigarettes/day and 0.0% for >20 cigarettes/day).

Platelet count, in continuous form, was negatively associated with age ($p<0.001$, $r=-0.114$) and positively associated with current cigarette smoking ($p<0.001$, $r=0.109$) and lifetime cigarette smoking history ($p<0.001$, $r=0.091$). Platelet count also was significantly associated with occupation ($p<0.001$), where the platelet count means increased from officers (243.9 thousand/mm^3) to enlisted flyers (251.9 thousand/mm^3) and enlisted groundcrew (257.6 thousand/mm^3).

Platelet count, in discrete form, was associated only with occupation ($p=0.040$) and current cigarette smoking ($p=0.011$). Within each occupation category, the percentage of participants with abnormally high platelet counts were 0.5 percent for officers, 1.1 percent

for enlisted flyers, and 1.7 percent for enlisted groundcrew. The percentage of participants with abnormally high platelet counts increased with the levels of current cigarette smoking (0.8% for current non-smokers, 1.4% for >0-20 cigarettes/day, and 3.3% for >20 cigarettes/day).

Race, current cigarette smoking, and lifetime cigarette smoking history were significantly associated with prothrombin time in continuous form ($p=0.018$, $p<0.001$, and $p=0.007$ respectively). Blacks had a greater mean prothrombin time (12.09 seconds) than non-Blacks (11.93 seconds). The associations of prothrombin time with current cigarette smoking and lifetime cigarette smoking history were negative ($r=-0.140$ and $r=-0.060$). Discretized prothrombin time was significantly associated with age only, where 1.1 percent of the older participants had abnormally high prothrombin times while only 0.2 percent of the younger participants had abnormally high prothrombin times ($p=0.033$).

RBC morphology was significantly associated with age ($p<0.001$), race ($p=0.012$), and occupation ($p=0.046$). The percentage of older participants with abnormal RBC morphology measurements (50.5%) was greater than the percentage of younger participants (38.8%). A greater percentage of Blacks (56.5%) had abnormal RBC morphology measurements than did non-Blacks (44.8%). The percentage of participants with abnormal RBC morphology measurements within each occupation category was 47.3 percent for officers, 49.0 percent for enlisted flyers, and 42.7 percent for enlisted groundcrew.

Significant associations with absolute neutrophils (segs) were found for race, occupation, current cigarette smoking, and lifetime cigarette smoking history ($p<0.001$ for all associations). Mean absolute neutrophil (segs) counts were greater for non-Blacks (4.28 thousand/mm^3) than for Blacks (3.54 thousand/mm^3). Absolute neutrophil (segs) means were 3.96 thousand/mm^3 for officers, 4.45 thousand/mm^3 for enlisted flyers, and 4.40 thousand/mm^3 for enlisted groundcrew. The associations of absolute neutrophils (segs) with current cigarette smoking and lifetime cigarette smoking history were positive ($r=0.426$ and $r=0.242$ respectively).

Absolute neutrophils (bands), restricted to non-zero values, were significantly associated with race ($p=0.003$), current cigarette smoking ($p<0.001$, $r=0.229$), and lifetime cigarette smoking history ($p<0.001$, $r=0.129$). The mean absolute neutrophil (bands) count was greater for non-Blacks (0.261 thousand/mm^3) than for Blacks (0.185 thousand/mm^3). When contrasting zero versus non-zero absolute neutrophil (bands) measurements, a significant association was found with race ($p<0.001$). The percentage of Blacks with 0 absolute neutrophils (bands) per mm^3 was 32.8 percent in contrast to 15.7 percent of non-Blacks.

Absolute lymphocytes was significantly associated with occupation ($p<0.001$), current cigarette smoking ($p<0.001$, $r=0.164$), and lifetime cigarette smoking history ($p<0.001$, $r=0.087$). Mean absolute lymphocyte counts were 1.94 thousand/mm^3 for officers, 2.24 thousand/mm^3 for enlisted flyers, and 2.16 thousand/mm^3 for enlisted groundcrew.

For absolute monocytes, significant positive associations were found with current cigarette smoking ($p<0.001$, $r=0.184$) and lifetime cigarette smoking history ($p<0.001$, $r=0.109$).

Restricted to nonzero counts, absolute eosinophils was significantly associated with race ($p=0.021$), current cigarette smoking ($p<0.001$, $r=0.147$), and lifetime cigarette smoking history ($p<0.001$, $r=0.080$). The mean absolute eosinophil count was greater for non-Blacks (0.220 thousand/mm^3) than for Blacks (0.189 thousand/mm^3). Discretized absolute eosinophil values (zero versus nonzero) were not significantly associated with any of the candidate covariates.

For absolute basophils, restricted to nonzero values, significant positive associations were found with current cigarette smoking ($p<0.001$, $r=0.199$) and lifetime cigarette smoking history ($p<0.001$, $r=0.105$).

Exposure Analysis

The following section presents the results of the statistical analyses of the dependent variables shown in Table 16-1. Dependent variables are based on data derived from the laboratory portion of the 1992 followup examination.

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 level 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 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 (30). 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 percent body fat at the participant's time of duty in SEA and the change in the percent 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 investigations for group-by-covariate and dioxin-by-covariate interactions are referenced in the text, and tabular results are presented in Appendix L-2. As described previously, additional analyses were performed when occupation was retained in the final model for Models 2 through 6. Results excluding occupation from these models are tabled in Appendix L-3, and dioxin-by-covariate interactions with occupation excluded from these models are presented in Appendix L-4. Results from analyses excluding occupation are discussed in the text only if a meaningful change in the results occurred (that is, changes between significant results, marginally significant results, and nonsignificant results.

Laboratory Examination Variables

Red Blood Cell (RBC) Count (Continuous)

The unadjusted Model 1 analysis of RBC count in its continuous form revealed nonsignificant results (Table 16-3(a): $p>0.10$ for all contrasts). A highly significant interaction between group and current cigarette smoking was disclosed in the adjusted analysis (Table 16-3(b): $p=0.006$). Appendix Table L-2-1 shows stratified results from further analysis on the interaction. The results of the analysis displayed in Appendix Table L-2-1 showed a marginally significantly higher mean for Comparison former smokers than for Ranch Hand former smokers ($p=0.070$, Ranch Hand: 5.000 million/mm^3 and Comparison 5.044 million/mm^3). For heavy current smokers (>20 cigarettes/day), the Ranch Hand mean was marginally significantly higher than the Comparison mean ($p=0.076$, Ranch Hand: 5.163 million/mm^3 and Comparison: 5.070 million/mm^3). Additional covariates retained in the adjusted analysis included age, race, occupation, and lifetime cigarette smoking history.

Results from both the unadjusted and adjusted Model 2 analyses of RBC count were nonsignificant (Table 16-3(c,d): $p>0.12$ for both analyses). Race, lifetime cigarette smoking history, and the age-by-current cigarette smoking interaction were retained in the adjusted analysis. In the unadjusted Model 3 analysis, significant differences between Comparisons and the four Ranch Hand categories were not evident (Table 16-3(e): $p>0.17$ for all contrasts). The adjusted analysis showed a significant interaction between categorized dioxin and current cigarette smoking (Table 16-3(f): $p=0.027$). Stratified results from the investigation of the categorized dioxin-by-current smoking interaction are found in Appendix Table L-2-1. Analysis with this interaction removed revealed marginally significant differences between Comparisons and high Ranch Hands and low plus high Ranch Hands, with Comparisons having a higher mean RBC count than Ranch Hands ($p=0.095$, Diff. of Adj. Means=-0.045 for high Ranch Hands vs. Comparisons, and $p=0.065$, Diff. of Adj. Means=-0.038 for low plus high Ranch Hands vs. Comparisons). Covariates retained in the adjusted analysis were age, race, occupation, and lifetime cigarette smoking history. Without occupation in the final model, all contrasts became nonsignificant (Appendix Table L-3-1: $p>0.15$ for all contrasts).

Current dioxin displayed a marginally significant relationship with RBC count in the unadjusted Model 4 analysis (Table 16-3(g): $p=0.072$, Slope=0.0162). However, after adjusting for race, lifetime cigarette smoking history, and the age-by-current cigarette smoking interaction, the association was no longer significant (Table 16-3(h): $p=0.190$).

Table 16-3.
Analysis of Red Blood Cell (RBC) Count (million/mm^3)
(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***	***946***	***5.009***	***-0.019 (-0.052,0.013)***	***0.243***
	Comparison	***1,278***	***5.028***		
Officer	Ranch Hand	364	4.956	-0.007 (-0.059,0.044)	0.779
	Comparison	501	4.964		
Enlisted Flyer	Ranch Hand	162	4.986	-0.064 (-0.140,0.013)	0.105
	Comparison	201	5.050		
Enlisted Groundcrew	Ranch Hand	420	5.063	-0.014 (-0.062,0.035)	0.585
	Comparison	576	5.076		

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***	***945***	****	****	****	GROUP*CSMOK (p=0.006)
	Comparison	***1,276***	****			AGE (p<0.001)
Officer	Ranch Hand	363	****	****	****	RACE (p=0.071)
	Comparison	501	****			OCC (p=0.004)
Enlisted Flyer	Ranch Hand	162	****	****	****	PACKYR (p=0.038)
	Comparison	201	****			
Enlisted Groundcrew	Ranch Hand	420	****	****	****	
	Comparison	574	****			

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

**** Group-by-covariate interaction ($p \leq 0.01$); adjusted mean, difference of adjusted means, confidence interval, and p-value not presented; refer to Appendix Table L-2-1 for further analysis this interaction.

Table 16-3. (Continued)
Analysis of Red Blood Cell (RBC) Count (million/mm^3)
(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	174	4.974	4.980	0.021	0.0201 (0.0130)	0.122
Medium	172	5.015	5.017			
High	171	5.042	5.035			

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	174	5.046	0.055	0.0127 (0.0135)	0.347	RACE (p=0.073) PACKYR (p=0.089) AGE*CSMOK (p=0.021)
Medium	172	5.067				
High	171	5.071				

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

Table 16-3. (Continued)
Analysis of Red Blood Cell (RBC) Count (million/mm^3)
(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	1,061	5.025	5.025		
Background RH	371	4.988	5.000	-0.025 (-0.070,0.021)	0.289
Low RH	259	4.990	4.989	-0.036 (-0.088,0.016)	0.175
High RH	258	5.031	5.018	-0.007 (-0.059,0.045)	0.801
Low plus High RH	517	5.010	5.003	-0.021 (-0.062,0.019)	0.299

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	1,059	5.060**			DXCAT*CSMOK (p=0.027) AGE (p=0.001) RACE (p=0.041) OCC (p=0.019) PACKYR (p=0.015)
Background RH	370	5.057**	-0.003 (-0.049,0.043)**	0.897**	
Low RH	259	5.030**	-0.030 (-0.082,0.021)**	0.246**	
High RH	258	5.015**	-0.045 (-0.098,0.008)**	0.095**	
Low plus High RH	517	5.023**	-0.038 (-0.078,0.002)**	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] 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 L-2-1 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 16-3. (Continued)
Analysis of Red Blood Cell (RBC) Count (million/mm^3)
(Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Mean/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Slope (Std. Error)	p-Value
4	4.986 (292)	4.973 (299)	5.044 (297)	0.004	0.0162 (0.0089)	0.072
5	4.979 (297)	4.980 (297)	5.045 (294)	0.005	0.0157 (0.0077)	0.042
6[b]	4.988 (296)	4.980 (297)	5.035 (294)	0.008	0.0109 (0.0083)	0.188

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[a]	Current Dioxin Category Adjusted Mean/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Adj. Slope (Std. Error)	p-Value	Covariate Remarks
4	5.040 (291)	5.040 (299)	5.080 (297)	0.058	0.0118 (0.0090)	0.190	RACE (p=0.033) PACKYR (p=0.004) AGE*CSMOK (p=0.005)
5	5.033 (296)	5.044 (297)	5.083 (294)	0.059	0.0130 (0.0077)	0.089	RACE (p=0.032) PACKYR (p=0.004) AGE*CSMOK (p=0.005)
6[c]	5.050 (295)	5.050 (297)	5.072 (294)	0.064	0.0063 (0.0083)	0.445	RACE (p=0.022) PACKYR (p=0.003) AGE*CSMOK (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] 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.

The Model 5 unadjusted analysis of RBC count disclosed a significant relationship with current whole-weight dioxin (Table 16-3(g): $p=0.042$, Slope=0.0157). The relationship became marginally significant after adjusting for covariate information (Table 16-3(h): $p=0.089$, Slope=0.0130). Results from both the unadjusted and adjusted Model 6 analyses were not significant ($p>0.18$ for both analyses). Race, lifetime cigarette smoking history, and the age-by-current cigarette smoking interaction were retained in the Model 5 and 6 adjusted analyses.

Red Blood Cell (RBC) Count (Discrete)

Both unadjusted and adjusted Model 1 analyses of RBC count revealed marginally significant differences overall between Ranch Hands and Comparisons for the abnormal low RBC count versus normal contrasts (Table 16-4(a,b): $p=0.087$, Est. RR=1.56 and $p=0.092$, Adj. RR=1.55 respectively). All other Model 1 contrasts were nonsignificant (Table 16-4(a,b): $p\geq0.16$ for all remaining contrasts). Age and race were significant covariates in the final adjusted model.

All Model 2 results examining the association between discrete RBC counts and initial dioxin were nonsignificant in the unadjusted and adjusted analyses (Table 16-4(c,d): $p>0.33$ for each contrast). Race was included in the final adjusted model.

Model 3 analysis of RBC count revealed a significant difference between background Ranch Hands and Comparisons from the unadjusted abnormal low versus normal RBC count contrast (Table 16-4(e): $p=0.049$, Est. RR=1.91). The difference was marginally significant for the analogous contrast in the adjusted analysis (Table 16-4(f): $p=0.084$, Adj. RR=1.77). The unadjusted low Ranch Hands versus Comparisons contrast was marginally significant for the examination of abnormal low versus normal RBC counts (Table 16-4(e): $p=0.063$, Est. RR=1.95). All other contrasts in Model 3 were nonsignificant (Table 16-4(e,f): $p>0.10$ for each remaining contrast). The age-by-race interaction was significant in the final adjusted model.

All results from Models 4, 5, and 6 analyzing the association between discrete RBC counts and current dioxin were nonsignificant for both the unadjusted and adjusted analyses (Table 16-4(g,h): $p>0.26$ for each contrast). Each model adjusted for the covariate effects of race, current cigarette smoking, and lifetime cigarette smoking history.

White Blood Cell (WBC) Count (Continuous)

While the unadjusted Model 1 analysis of WBC count yielded only nonsignificant results (Table 16-5(a): $p>0.28$), the adjusted analysis led to a significant group-by-race interaction (Table 16-5(b): $p=0.023$). Appendix Table L-2-2 presents results for Ranch Hands versus Comparisons stratified by race. Differences between Ranch Hands and Comparisons in mean WBC count, computed after removing the interaction, were not significant ($p>0.55$ for all contrasts). Age, lifetime cigarette smoking history, and the current cigarette smoking-by-occupation interaction were included in the final model.

Table 16-4.
Analysis of Red Blood Cell (RBC) Count
(Discrete)

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

Occupational Category	Group	n	Percent Abnormal Low	Percent Normal	Percent Abnormal High	Abnormal Low vs. Normal Est. Relative Risk (95% C.I.)	Abnormal Low vs. Normal p-Value	Abnormal High vs. Normal Est. Relative Risk (95% C.I.)	Abnormal High vs. Normal p-Value
All	***Ranch Hand***	***946***	***3.5***	***95.2***	***1.3***	***1.56 (0.94,2.58)***	***0.087***	***0.97 (0.46,2.03)***	***0.926***
	Comparison	***1,278***	***2.3***	***96.4***	***1.3***				
Officer	Ranch Hand	364	4.7	94.8	0.6	1.39 (0.70,2.76)	0.345	0.70 (0.13,3.82)	0.676
	Comparison	501	3.4	95.8	0.8				
Enlisted Flyer	Ranch Hand	162	2.5	96.9	0.6	1.64 (0.36,7.43)	0.522	0.25 (0.03,2.11)	0.201
	Comparison	201	1.5	96.0	2.5				
Enlisted Groundcrew	Ranch Hand	420	2.9	95.0	2.1	1.87 (0.78,4.48)	0.161	1.58 (0.61,4.13)	0.354
	Comparison	576	1.6	97.1	1.4				

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

Occupational Category	Abnormal Low vs. Normal Adj. Relative Risk (95% C.I.)	Abnormal Low vs. Normal p-Value	Abnormal High vs. Normal Adj. Relative Risk (95% C.I.)	Abnormal High vs. Normal p-Value	Covariate Remarks[a]
All	***1.55 (0.93,2.57)***	***0.092***	***0.96 (0.46,2.03)***	***0.919***	AGE ($p<0.001$) RACE ($p=0.004$)
Officer	1.37 (0.69,2.74)	0.366	0.68 (0.12,3.72)	0.654	
Enlisted Flyer	1.62 (0.36,7.39)	0.530	0.25 (0.03, 2.21)	0.213	
Enlisted Groundcrew	1.87 (0.78,4.51)	0.160	1.59 (0.61,4.18)	0.346	

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

Table 16-4. (Continued)
Analysis of Red Blood Cell (RBC) Count
(Discrete)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED

Initial Dioxin Category Summary Statistics					Analysis Results for Log_2 (Initial Dioxin)[a]			
		Percent			Abnormal Low vs. Normal		Abnormal High vs. Normal	
Initial Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)[b]	p-Value	Est. Relative Risk (95% C.I.)[b]	p-Value
Low	174	4.6	94.8	0.6	0.80 (0.52,1.22)	0.305	1.03 (0.59,1.79)	0.918
Medium	172	2.9	94.2	2.9				
High	171	1.8	97.7	0.6				

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)[c]					
	Abnormal Low vs. Normal		Abnormal Low vs. Normal		
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
517	0.81 (0.53,1.24)	0.333	1.06 (0.60,1.90)	0.833	RACE (p=0.122)

[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 16-4. (Continued)
Analysis of Red Blood Cell (RBC) Count
(Discrete)

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

Dioxin Category	n	Percent Abnormal Low	Percent Normal	Percent Abnormal High	Abnormal Low vs. Normal Est. Relative Risk (95% C.I.)[ab]	Abnormal Low vs. Normal p-Value	Abnormal High vs. Normal Est. Relative Risk (95% C.I.)[ab]	Abnormal High vs. Normal p-Value
Comparison	1,061	2.4	96.3	1.3				
Background RH	371	4.3	94.9	0.8	1.91 (1.00,3.65)	0.049	0.77 (0.22,2.73)	0.686
Low RH	259	4.6	93.8	1.5	1.95 (0.96,3.95)	0.063	1.06 (0.33,3.38)	0.919
High RH	258	1.6	97.3	1.2	0.64 (0.22,1.86)	0.410	0.66 (0.18,2.39)	0.525
Low plus High RH	517	3.1	95.6	1.4	1.29 (0.68,2.45)	0.436	0.84 (0.33,2.17)	0.722

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

Dioxin Category	n	Abnormal Low vs. Normal Adj. Relative Risk (95% C.I.)[ac]	Abnormal Low vs. Normal p-Value	Abnormal High vs. Normal Adj. Relative Risk (95% C.I.)[ac]	Abnormal High vs. Normal p-Value	Covariate Remarks
Comparison	1,061					AGE*RACE (p=0.040)
Background RH	371	1.77 (0.93,3.39)	0.084	0.79 (0.22,2.84)	0.723	
Low RH	259	1.80 (0.88,3.66)	0.107	0.98 (0.31,3.15)	0.974	
High RH	258	0.75 (0.26,2.20)	0.603	0.75 (0.20,2.77)	0.668	
Low plus High RH	517	1.33 (0.70,2.54)	0.383	0.87 (0.34,2.24)	0.769	

[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 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 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 16-4. (Continued)
Analysis of Red Blood Cell (RBC) Count
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category	n	Current Dioxin Category Summary Statistics: Percent Abnormal Low	Percent Normal	Percent Abnormal High	Analysis Results for Log_2 (Current Dioxin + 1): Abnormal Low vs. Normal Est. Relative Risk (95% C.I.)[b]	Abnormal Low vs. Normal p-Value	Abnormal High vs. Normal Est. Relative Risk (95% C.I.)[b]	Abnormal High vs. Normal p-Value
4	Low	292	4.1	94.9	1.0	0.87 (0.67,1.12)	0.285	1.18 (0.79,1.77)	0.423
	Medium	299	4.4	95.3	0.3				
	High	297	2.4	95.6	2.0				
5	Low	297	4.0	95.0	1.0	0.89 (0.72,1.09)	0.268	1.16 (0.81,1.67)	0.417
	Medium	297	4.4	95.0	0.7				
	High	294	2.4	95.9	1.7				
6[c]	Low	296	4.1	94.9	1.0	0.90 (0.73,1.12)	0.359	1.20 (0.82,1.75)	0.356
	Medium	297	4.4	95.0	0.7				
	High	294	2.4	95.9	1.7				

[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.

Table 16-4. (Continued)
Analysis of Red Blood Cell (RBC) Count
(Discrete)

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED						
		Analysis Results for Log_2 (Current Dioxin + 1)				
		Abnormal Low vs. Normal		Abnormal High vs. Normal		
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	887	0.88 (0.68,1.15)	0.349	1.21 (0.79,1.86)	0.377	RACE (p=0.026) CSMOK (p=0.092) PACKYR (p=0.027)
5	887	0.90 (0.73,1.11)	0.331	1.20 (0.82,1.76)	0.354	RACE (p=0.025) CSMOK (p=0.090) PACKYR (p=0.027)
6[c]	886	0.92 (0.73,1.15)	0.447	1.23 (0.82,1.84)	0.308	RACE (p=0.031) CSMOK (p=0.095) PACKYR (p=0.024)

[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 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 16-5.
Analysis of White Blood Cell (WBC) Count (thousand/mm^3)
(Continuous)

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

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***946***	***7.15***	***0.09 --***	***0.305***
	Comparison	***1,278***	***7.06***		
Officer	Ranch Hand	364	6.75	0.04 --	0.704
	Comparison	501	6.70		
Enlisted Flyer	Ranch Hand	162	7.37	0.02 --	0.924
	Comparison	201	7.35		
Enlisted Groundcrew	Ranch Hand	420	7.43	0.14 --	0.282
	Comparison	576	7.29		

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

Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]	Covariate Remarks[d]
All	***Ranch Hand***	***945***	***6.66****	***0.03 --****	0.690**	GROUP*RACE (p=0.023)
	Comparison	***1,276***	***6.63****			AGE (p<0.001)
Officer	Ranch Hand	363	6.37**	0.03 --**	0.771**	PACKYR (p=0.002)
	Comparison	501	6.34**			CSMOK*OCC (p=0.025)
Enlisted Flyer	Ranch Hand	162	6.66**	-0.08 --**	0.656**	
	Comparison	201	6.73**			
Enlisted Groundcrew	Ranch Hand	420	6.93**	0.06 --**	0.551**	
	Comparison	574	6.87**			

[a] Transformed from the natural logarithm scale.

[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

[c] P-values based on difference of means on natural logarithm scale.

[d] 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, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table L-2-2 for further analysis of this interaction.

Table 16-5. (Continued)
Analysis of White Blood Cell (WBC) Count (thousand/mm^3)
(Continuous)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	174	6.87	6.88	0.012	0.0161 (0.0097)	0.100
Medium	172	7.40	7.42			
High	171	7.34	7.31			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ad]	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
Low	174	6.50**	0.283**	0.0019 (0.0098)**	0.846**	INIT*RACE (p=0.008) INIT*OCC (p=0.028) CSMOK (p<0.001) PACKYR (p=0.018)
Medium	172	6.68**				
High	171	6.60**				

[a] Transformed from natural logarithm scale.

[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] Slope and standard error based on natural logarithm of WBC count versus log_2 (initial dioxin).

[d] 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 mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table L-2-2 for further analysis of these interactions.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.
INIT = Log_2 (initial dioxin).

Table 16-5. (Continued)
Analysis of White Blood Cell (WBC) Count (thousand/mm^3)
(Continuous)

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

Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,061	7.05	7.05		
Background RH	371	7.00	7.03	-0.02 --	0.838
Low RH	259	7.06	7.05	0.00 --	0.999
High RH	258	7.34	7.31	0.26 --	0.058
Low plus High RH	517	7.20	7.18	0.13 --	0.221

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

Dioxin Category	n	Adj. Mean[ae]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]	Covariate Remarks
Comparison	1,059	6.62			PACKYR (p<0.001) AGE*RACE (p=0.007) CSMOK*OCC (p=0.016)
Background RH	370	6.64	0.03 --	0.792	
Low RH	259	6.66	0.04 --	0.726	
High RH	258	6.64	0.02 --	0.828	
Low plus High RH	517	6.65	0.03 --	0.713	

[a] Transformed from natural logarithm scale.

[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] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on natural logarithm scale.

[d] P-value is based on difference of means on natural logarithm scale.

[e] 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 16-5. (Continued)
Analysis of White Blood Cell (WBC) Count (thousand/mm^3)
(Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[b]	Current Dioxin Category Mean[a]/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Slope (Std. Error)[c]	p-Value
4	6.99 (292)	7.02 (299)	7.34 (297)	0.002	0.0093 (0.0066)	0.162
5	6.95 (297)	7.02 (297)	7.39 (294)	0.003	0.0086 (0.0057)	0.130
6[d]	7.02 (296)	7.02 (297)	7.30 (294)	0.013	0.0035 (0.0061)	0.571

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[b]	Current Dioxin Category Adjusted Mean[a]/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
4	6.53** (291)	6.53** (299)	6.57** (297)	0.263	0.0013 (0.0067)**	0.850**	CURR*RACE (p=0.041) PACKYR (p=0.011) AGE*RACE (p=0.032) CSMOK*OCC (p=0.022)
5	6.50** (296)	6.52** (297)	6.62** (294)	0.264	0.0014 (0.0056)**	0.803**	CURR*RACE (p=0.019) PACKYR (p=0.011) AGE*RACE (p=0.030) CSMOK*OCC (p=0.022)
6[e]	6.53** (295)	6.54** (297)	6.59** (294)	0.265	-0.0009 (0.0061)**	0.879**	CURR*RACE (p=0.019) PACKYR (p=0.014) AGE*RACE (p=0.025) CSMOK*OCC (p=0.031)

[a] Transformed from natural logarithm scale.

[b] 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.

[c] Slope and standard error based on natural logarithm of WBC count versus log_2 (current dioxin + 1).

[d] Adjusted for log_2 total lipids.

[e] 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 L-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 = Log_2 (current dioxin + 1).

A marginally significant dose-response relationship between initial dioxin and WBC count was disclosed in the unadjusted Model 2 analysis (Table 16-5(c): $p=0.100$, Slope=0.0161). Adjusting for covariates caused the association to become nonsignificant (Table 16-5(d): $p=0.846$). Two significant initial dioxin interactions involving race and occupation were retained in the adjusted analysis ($p=0.008$ and $p=0.028$ respectively) as were the covariates of current cigarette smoking and lifetime cigarette smoking history. Appendix Table L-2-2 contains information on the association between WBC count and initial dioxin stratified by race and occupation. Results cited for the final adjusted model reflect removal of the initial dioxin-by-race and initial dioxin-by-occupation interactions.

The Model 3 unadjusted analysis revealed that Ranch Hands in the high category possess a marginally significantly greater mean WBC count level than do Comparisons (Table 16-5(e): $p=0.058$, Diff. of Adj. Mean=0.26). Other contrasts between Ranch Hands and Comparisons examined in the unadjusted analysis were nonsignificant ($p>0.22$). Furthermore, no significant results were found after adjusting for lifetime cigarette smoking history and the age-by-race and current cigarette smoking-by-occupation interactions (Table 16-5(f): $p>0.71$ for all contrasts).

Unadjusted and adjusted results examining the relationship between WBC count and current dioxin were nonsignificant for each of Models 4, 5, and 6 (Table 16-5(g,h): $p\geq0.13$ for all analyses). Each adjusted analysis retained the current dioxin-by-race interaction as well as lifetime cigarette smoking history and the age-by-race and current cigarette smoking-by-occupation interactions. Final adjusted model results are based on the exclusion of the current dioxin-by-race interaction. Results stratified by race that examine the association between current dioxin and WBC count are found in Appendix Table L-2-2. When occupation was removed from the final model, the association between current dioxin and WBC count became marginally significant in Models 4 and 5 (Appendix Table L-3-2: $p=0.061$, Slope=0.0111 for Model 4; $p=0.058$, Slope=0.0096 for Model 5).

White Blood Cell (WBC) Count (Discrete)

Each unadjusted and adjusted analysis of discrete WBC counts was nonsignificant for all contrasts and associations examined in Models 1, 2, and 3 (Table 16-6(a-f): $p>0.12$ for each contrast). Each model adjusted for age, race, occupation, and current cigarette smoking in the final adjusted model. However, after excluding occupation from the Model 2 adjusted analysis, the association with initial dioxin was marginally significant for the abnormal high versus normal contrast (Table L-3-3: $p=0.096$, Adj. RR=0.74), showing a decrease in the percentage of abnormally high WBC counts as initial dioxin increased.

Adjusted analyses of discrete WBC counts in Models 4 and 6 revealed a significant inverse relationship between abnormally high WBC counts and current dioxin (Table 16-6(h): $p=0.029$, Adj. RR=0.79 and $p=0.034$, Adj. RR=0.83 respectively). Results were marginally significant for the Model 5 adjusted analysis (Table 16-6(h): $p=0.081$, Adj. RR=0.87). All other unadjusted and adjusted analyses were nonsignificant (Table 16-6(g,h): $p>0.22$ for all remaining contrasts). Each model adjusted for the significant covariate effects of occupation and lifetime cigarette smoking history as well as the current dioxin-by-race and age-by-race interactions. Each adjusted analysis is based on the final model after

Table 16-6.
Analysis of White Blood Cell (WBC) Count
(Discrete)

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

Occupational Category	Group	n	Percent Abnormal Low	Percent Normal	Percent Abnormal High	Abnormal Low vs. Normal Est. Relative Risk (95% C.I.)	Abnormal Low vs. Normal p-Value	Abnormal High vs. Normal Est. Relative Risk (95% C.I.)	Abnormal High vs. Normal p-Value
All	***Ranch Hand***	***946***	***3.8***	***90.0***	***6.2***	***1.07 (0.69,1.67)***	***0.756***	***1.24 (0.87,1.79)***	***0.237***
	Comparison	***1,278***	***3.6***	***91.3***	***5.1***				
Officer	Ranch Hand	364	3.9	92.3	3.9	0.92 (0.46,1.84)	0.819	1.29 (0.62,2.71)	0.498
	Comparison	501	4.2	92.8	3.0				
Enlisted Flyer	Ranch Hand	162	5.6	85.2	9.3	1.93 (0.67,5.56)	0.221	1.14 (0.55,2.36)	0.728
	Comparison	201	3.0	88.6	8.5				
Enlisted Groundcrew	Ranch Hand	420	3.1	89.8	7.1	0.95 (0.46,1.95)	0.891	1.26 (0.76,2.11)	0.370
	Comparison	576	3.3	91.0	5.7				

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

Occupational Category	Abnormal Low vs. Normal Adj. Relative Risk (95% C.I.)	Abnormal Low vs. Normal p-Value	Abnormal High vs. Normal Adj. Relative Risk (95% C.I.)	Abnormal High vs. Normal p-Value	Covariate Remarks[a]
All	***1.11 (0.70,1.75)***	***0.654***	***1.18 (0.80,1.74)***	***0.400***	AGE (p=0.002)
Officer	0.92 (0.46,1.85)	0.815	1.33 (0.60,2.95)	0.480	RACE (p<0.001)
Enlisted Flyer	1.95 (0.66,5.77)	0.226	0.97 (0.44,2.10)	0.931	OCC (p=0.005)
Enlisted Groundcrew	1.05 (0.50,2.20)	0.903	1.24 (0.72,2.13)	0.443	CSMOK (p<0.001)

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

Table 16-6. (Continued)
Analysis of White Blood Cell (WBC) Count
(Discrete)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED

Initial Dioxin Category Summary Statistics					Analysis Results for Log_2 (Initial Dioxin)[a]			
		Percent			Abnormal Low vs. Normal		Abnormal High vs. Normal	
Initial Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)[b]	p-Value	Est. Relative Risk (95% C.I.)[b]	p-Value
Low	174	6.3	87.4	6.3	0.94 (0.67,1.33)	0.740	0.90 (0.67,1.20)	0.457
Medium	172	2.9	90.1	7.0				
High	171	3.5	91.8	4.7				

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)[c]					
	Abnormal Low vs. Normal		Abnormal High vs. Normal		
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
517	0.94 (0.60,1.46)	0.778	0.75 (0.52,1.08)	0.127	AGE (p=0.007) RACE (p=0.018) OCC (p=0.130) CSMOK (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 16-6. (Continued)
Analysis of White Blood Cell (WBC) Count
(Discrete)

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

Dioxin Category	n	Percent Abnormal Low	Percent Normal	Percent Abnormal High	Abnormal Low vs. Normal Est. Relative Risk (95% C.I.)[ab]	Abnormal Low vs. Normal p-Value	Abnormal High vs. Normal Est. Relative Risk (95% C.I.)[ab]	Abnormal High vs. Normal p-Value
Comparison	1,061	3.3	91.4	5.3				
Background RH	371	3.5	90.6	5.9	0.95 (0.49,1.83)	0.884	1.07 (0.64,1.78)	0.808
Low RH	259	4.6	88.4	7.0	1.51 (0.77,2.97)	0.232	1.41 (0.81,2.45)	0.223
High RH	258	3.9	91.1	5.0	1.31 (0.64,2.70)	0.462	1.01 (0.54,1.87)	0.987
Low plus High RH	517	4.3	89.8	6.0	1.41 (0.82,2.45)	0.217	1.21 (0.77,1.90)	0.418

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

Dioxin Category	n	Abnormal Low vs. Normal Adj. Relative Risk (95% C.I.)[ac]	Abnormal Low vs. Normal p-Value	Abnormal High vs. Normal Adj. Relative Risk (95% C.I.)[ac]	Abnormal High vs. Normal p-Value	Covariate Remarks
Comparison	1,059					AGE (p=0.011) RACE (p<0.001) OCC (p=0.099) CSMOK (p<0.001)
Background RH	371	1.06 (0.54,2.11)	0.861	1.11 (0.63,1.96)	0.709	
Low RH	259	1.26 (0.62,2.58)	0.521	1.53 (0.86,2.75)	0.151	
High RH	258	1.37 (0.63,3.00)	0.431	0.79 (0.41,1.52)	0.477	
Low plus High RH	517	1.31 (0.73,2.34)	0.369	1.11 (0.69,1.80)	0.664	

[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 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 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 16-6. (Continued)
Analysis of White Blood Cell (WBC) Count
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

	Current Dioxin Category Summary Statistics					Analysis Results for Log_2 (Current Dioxin + 1)			
			Percent			Abnormal Low vs. Normal		Abnormal High vs. Normal	
Model[a]	Current Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)[b]	p-Value	Est. Relative Risk (95% C.I.)[b]	p-Value
4	Low	292	3.8	90.4	5.8	1.00 (0.79,1.26)	0.984	0.88 (0.73,1.08)	0.224
	Medium	299	4.4	89.0	6.7				
	High	297	3.7	90.9	5.4				
5	Low	297	3.7	90.9	5.4	1.00 (0.82,1.22)	0.982	0.93 (0.79,1.09)	0.380
	Medium	297	4.7	88.2	7.1				
	High	294	3.4	91.2	5.4				
6[c]	Low	296	3.7	90.9	5.4	1.02 (0.82,1.25)	0.873	0.91 (0.76,1.07)	0.259
	Medium	297	4.7	88.2	7.1				
	High	294	3.4	91.2	5.4				

[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.

Table 16-6. (Continued)
Analysis of White Blood Cell (WBC) Count
(Discrete)

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED						
		Analysis Results for Log_2 (Current Dioxin + 1)				
		Abnormal Low vs. Normal		Abnormal High vs. Normal		
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	887	1.04 (0.77,1.39)**	0.821**	0.79 (0.65,0.98)**	0.029**	CURR*RACE (p=0.044) OCC (p=0.019) PACKYR (p<0.001) AGE*RACE (p=0.009)
5	887	1.06 (0.82,1.37)**	0.660**	0.87 (0.74,1.02)**	0.081**	CURR*RACE (p=0.036) OCC (p=0.023) PACKYR (p<0.001) AGE*RACE (p=0.007)
6[c]	886	1.04 (0.80,1.36)**	0.769**	0.83 (0.70,0.99)**	0.034**	CURR*RACE (p=0.026) OCC (p=0.027) PACKYR (p<0.001) AGE*RACE (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 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 L-2-3 for further analysis of this interaction.

deletion of the current dioxin-by-race interaction. Results stratified by race for each model are presented in Appendix Table L-2-3. After excluding occupation from each final adjusted model for Models 4, 5, and 6, all contrasts were nonsignificant (Appendix Table L-3-3: $p>0.10$ for each contrast).

Hemoglobin (Continuous)

None of the contrasts examining differences in mean hemoglobin for Ranch Hands versus Comparisons were significant in the Model 1 analyses (Table 16-7(a,b): $p>0.38$ for all contrasts). Two significant group interactions involving current cigarette smoking and lifetime cigarette smoking history were disclosed in the adjusted analysis (Table 16-7(b): $p=0.008$ and $p=0.036$ respectively). Appendix Table L-2-4 shows results from separate analyses on these interactions, stratified by the levels of each covariate. Results were nonsignificant after removal of the group-by-covariate interactions from the model ($p>0.50$ for all contrasts). Other significant covariates in the adjusted analysis included age, race, and the lifetime cigarette smoking history-by-occupation interaction.

Mean levels of hemoglobin increased significantly with initial dioxin in the unadjusted Model 2 analysis (Table 16-7(c): $p=0.029$, Slope=0.0792). However, adjustment for race and the age-by-current cigarette smoking interaction caused this finding to become nonsignificant (Table 16-7(d): $p=0.179$).

All associations with hemoglobin from the Model 3 categorized dioxin unadjusted and adjusted analyses were nonsignificant (Table 16-7(e,f): $p>0.12$) although, analogous to Model 1, two group interactions involving current cigarette smoking and lifetime cigarette smoking history were retained in the adjusted analysis ($p=0.007$ and $p=0.019$). Stratified results from additional analyses of these terms are shown in Appendix Table L-2-4. Final adjusted results were calculated with the interactions excluded from the final model. Age, race, and the current cigarette smoking-by-occupation interaction also were retained in the adjusted analysis.

No significant associations between current dioxin and hemoglobin were disclosed in the unadjusted and adjusted analyses for Model 4, 5, and 6 (Table 16-7(g,h): $p>0.23$ for all analyses). Race, lifetime cigarette smoking history, and the age-by-current cigarette smoking interaction were significant in each of the adjusted analyses.

Hemoglobin (Discrete)

Except for the adjusted abnormal high versus normal contrast among officers in Model 1, all unadjusted and adjusted analyses of hemoglobin in discrete form revealed nonsignificant results (Table 16-8(a-h): $p>0.11$ for each contrast). Within the officer stratum, the Model 1 adjusted analysis revealed a marginally significant difference in the percentage of Ranch Hands with abnormally high hemoglobin levels versus Comparisons (Table 16-8(b): $p=0.095$, Adj. RR=2.33). Models 1 and 3 adjusted for the covariate effects of current cigarette smoking and the age-by-race interaction. Model 2 adjusted for current cigarette smoking only, and Models 4, 5, and 6 each adjusted for the race-by-current cigarette smoking interaction.

Table 16-7.
Analysis of Hemoglobin (gm/dl)
(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***	***946***	***15.87***	***0.01 (-0.08,0.10)***	***0.818***
	Comparison	***1,278***	***15.86***		
Officer	Ranch Hand	364	15.81	0.04 (-0.09,0.18)	0.527
	Comparison	501	15.76		
Enlisted Flyer	Ranch Hand	162	15.87	-0.07 (-0.29,0.16)	0.553
	Comparison	201	15.93		
Enlisted Groundcrew	Ranch Hand	420	15.93	0.01 (-0.12,0.14)	0.912
	Comparison	576	15.92		

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***	***945***	***15.62*****	***-0.00 (-0.09,0.08)*****	0.944**	GROUP*CSMOK (p=0.008)
	Comparison	***1,276***	***15.63*****			GROUP*PACKYR (p=0.036)
Officer	Ranch Hand	363	15.61**	0.05 (-0.09,0.18)**	0.509**	AGE (p=0.014)
	Comparison	501	15.57**			RACE (p<0.001)
Enlisted Flyer	Ranch Hand	162	15.60**	-0.09 (-0.30,0.11)**	0.384**	PACKYR*OCC (p=0.004)
	Comparison	201	15.69**			
Enlisted Groundcrew	Ranch Hand	420	15.63**	-0.01 (-0.14,0.11)**	0.849**	
	Comparison	574	15.64**			

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

** Group-by-covariate interactions ($p \leq 0.05$); adjusted mean, difference of adjusted means, confidence interval, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table L-2-4 for further analysis of these interactions.

Table 16-7. (Continued)
Analysis of Hemoglobin (gm/dl)
(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	174	15.74	15.74	0.009	0.0792 (0.0361)	0.029
Medium	172	15.83	15.83			
High	171	16.00	16.01			

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	174	15.64	0.071	0.0496 (0.0369)	0.179	RACE (p=0.037) AGE*CSMOK (p=0.026)
Medium	172	15.63				
High	171	15.81				

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

[b] Adjusted for percent body fat at the time of duty in the SEA, change in percent body fat from the time of duty in the 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 16-7. (Continued)
Analysis of Hemoglobin (gm/dl)
(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	1,061	15.86	15.86		
Background RH	371	15.86	15.87	0.01 (-0.11,0.13)	0.876
Low RH	259	15.75	15.75	-0.11 (-0.24,0.03)	0.128
High RH	258	15.97	15.96	0.10 (-0.04,0.24)	0.159
Low plus High RH	517	15.85	15.85	0.00 (-0.11,0.10)	0.941

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	1,059	15.65**			DXCAT*CSMOK (p=0.007) DXCAT*PACKYR (p=0.019) AGE (p=0.060) RACE (p<0.001) PACKYR*OCC (p=0.002)
Background RH	370	15.68**	0.03 (-0.09,0.15)**	0.615**	
Low RH	259	15.57**	-0.08 (-0.21,0.06)**	0.259**	
High RH	258	15.66**	0.01 (-0.13,0.15)**	0.863**	
Low plus High RH	517	15.62**	-0.03 (-0.14,0.07)**	0.544**	

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

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

** Categorized dioxin-by-covariate interactions ($p \leq 0.05$); adjusted mean, difference of adjusted means, confidence interval, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table L-2-4 for further analysis of these interactions.

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 16-7. (Continued)
Analysis of Hemoglobin (gm/dl)
(Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Mean/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Slope (Std. Error)	p-Value
4	15.88 (292)	15.75 (299)	15.95 (297)	0.001	0.0237 (0.0244)	0.332
5	15.85 (297)	15.77 (297)	15.95 (294)	0.002	0.0250 (0.0209)	0.232
6[b]	15.85 (296)	15.77 (297)	15.95 (294)	0.008	0.0088 (0.0225)	0.696

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[a]	Current Dioxin Category Adjusted Mean/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Adj. Slope (Std. Error)	p-Value	Covariate Remarks
4	15.71 (291)	15.63 (299)	15.75 (297)	0.095	0.0166 (0.0239)	0.487	RACE (p=0.010) PACKYR (p=0.004) AGE*CSMOK (p=0.032)
5	15.69 (296)	15.95 (297)	15.75 (294)	0.095	0.0202 (0.0204)	0.322	RACE (p=0.010) PACKYR (p=0.004) AGE*CSMOK (p=0.030)
6[c]	15.75 (295)	15.66 (297)	15.72 (294)	0.099	0.0048 (0.0221)	0.826	RACE (p=0.015) PACKYR (p=0.003) AGE*CSMOK (p=0.028)

[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.

Table 16-8.
Analysis of Hemoglobin
(Discrete)

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

Occupational Category	Group	n	Percent Abnormal Low	Percent Normal	Percent Abnormal High	Abnormal Low vs. Normal Est. Relative Risk (95% C.I.)	Abnormal Low vs. Normal p-Value	Abnormal High vs. Normal Est. Relative Risk (95% C.I.)	Abnormal High vs. Normal p-Value
All	***Ranch Hand***	***946***	***3.0***	***94.7***	***2.3***	***1.24 (0.74,2.08)***	***0.419***	***1.59 (0.85,2.95)***	***0.144***
	Comparison	***1,278***	***2.4***	***96.1***	***1.5***				
Officer	Ranch Hand	364	2.5	94.5	3.0	0.69 (0.31,1.56)	0.374	2.17 (0.83,5.67)	0.112
	Comparison	501	3.6	95.0	1.4				
Enlisted Flyer	Ranch Hand	162	3.7	94.4	1.9	2.57 (0.63,10.47)	0.186	3.86 (0.40,37.64)	0.245
	Comparison	201	1.5	98.0	0.5				
Enlisted Groundcrew	Ranch Hand	420	3.1	95.0	1.9	1.81 (0.79,4.16)	0.164	1.01 (0.40,2.54)	0.980
	Comparison	576	1.7	96.4	1.9				

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

Occupational Category	Abnormal Low vs. Normal Adj. Relative Risk (95% C.I.)	Abnormal Low vs. Normal p-Value	Abnormal High vs. Normal Adj. Relative Risk (95% C.I.)	Abnormal High vs. Normal p-Value	Covariate Remarks[a]
All	***1.26 (0.75,2.13)***	***0.386***	***1.56 (0.83,2.93)***	***0.170***	CSMOK (p<0.001) AGE*RACE (p=0.001)
Officer	0.68 (0.30,1.54)	0.355	2.33 (0.86,6.31)	0.095	
Enlisted Flyer	2.59 (0.63,10.65)	0.187	3.44 (0.34,35.03)	0.297	
Enlisted Groundcrew	1.95 (0.83,4.55)	0.123	0.97 (0.39,2.46)	0.955	

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

Table 16-8. (Continued)
Analysis of Hemoglobin
(Discrete)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED

Initial Dioxin Category Summary Statistics					Analysis Results for Log_2 (Initial Dioxin)[a]			
		Percent			Abnormal Low vs. Normal		Abnormal High vs. Normal	
Initial Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)[b]	p-Value	Est. Relative Risk (95% C.I.)[b]	p-Value
Low	174	2.9	94.8	2.3	0.91 (0.59,1.40)	0.669	1.09 (0.71,1.67)	0.689
Medium	172	2.9	95.9	1.2				
High	171	1.8	95.3	2.9				

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)[c]					
	Abnormal Low vs. Normal		Abnormal High vs. Normal		
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
517	0.93 (0.61,1.42)	0.732	1.07 (0.68,1.68)	0.765	CSMOK (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 16-8. (Continued)
Analysis of Hemoglobin
(Discrete)

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

		Percent			Abnormal Low vs. Normal		Abnormal High vs. Normal	
Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)[ab]	p-Value	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,061	2.3	96.2	1.5				
Background RH	371	3.5	94.6	1.9	1.63 (0.81,3.25)	0.170	1.44 (0.58,3.55)	0.434
Low RH	259	3.9	94.2	1.9	1.65 (0.78,3.51)	0.192	1.25 (0.45,3.46)	0.667
High RH	258	1.2	96.5	2.3	0.49 (0.15,1.67)	0.256	1.37 (0.53,3.58)	0.516
Low plus High RH	517	2.5	95.4	2.1	1.08 (0.54,2.14)	0.835	1.31 (0.60,2.87)	0.493

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

		Abnormal Low vs. Normal		Abnormal High vs. Normal		
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,059					CSMOK ($p<0.001$) AGE*RACE ($p=0.006$)
Background RH	371	1.59 (0.79,3.19)	0.197	1.26 (0.48,3.28)	0.635	
Low RH	259	1.38 (0.64,2.98)	0.414	1.24 (0.43,3.53)	0.691	
High RH	258	0.58 (0.17,1.98)	0.382	1.49 (0.56,3.98)	0.423	
Low plus High RH	517	1.05 (0.52,2.12)	0.897	1.37 (0.61,3.04)	0.446	

[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 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 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 16-8. (Continued)
Analysis of Hemoglobin
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category	n	Current Dioxin Category Summary Statistics: Percent Abnormal Low	Percent Normal	Percent Abnormal High	Analysis Results for Log_2 (Current Dioxin + 1): Abnormal Low vs. Normal Est. Relative Risk (95% C.I.)[b]	Abnormal Low vs. Normal p-Value	Abnormal High vs. Normal Est. Relative Risk (95% C.I.)[b]	Abnormal High vs. Normal p-Value
4	Low	292	3.8	94.2	2.1	0.92 (0.70,1.21)	0.542	1.13 (0.83,1.54)	0.448
	Medium	299	3.3	94.7	2.0				
	High	297	1.7	96.3	2.0				
5	Low	297	3.4	95.0	1.7	0.92 (0.73,1.16)	0.477	1.14 (0.86,1.50)	0.359
	Medium	297	3.7	94.3	2.0				
	High	294	1.7	95.9	2.4				
6[c]	Low	296	3.4	94.9	1.7	0.94 (0.74,1.20)	0.634	1.15 (0.86,1.53)	0.340
	Medium	297	3.7	94.3	2.0				
	High	294	1.7	95.9	2.4				

[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.

Table 16-8. (Continued)
Analysis of Hemoglobin
(Discrete)

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED						
		Analysis Results for Log_2 (Current Dioxin + 1)				
		Abnormal Low vs. Normal		Abnormal High vs. Normal		
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	888	0.91 (0.68,1.23)	0.548	1.20 (0.88,1.65)	0.242	RACE*CSMOK (p=0.002)
5	888	0.91 (0.70,1.18)	0.486	1.19 (0.90,1.56)	0.219	RACE*CSMOK (p=0.002)
6[c]	887	0.93 (0.71,1.22)	0.610	1.23 (0.92,1.64)	0.165	RACE*CSMOK (p=0.002)

[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 in addition to covariates specified under "Covariate Remarks" column.

Hematocrit (Continuous)

For Ranch Hands versus Comparisons, no significant differences in mean hematocrit levels were disclosed in the Model 1 unadjusted analysis (Table 16-9(a): $p>0.42$ for all contrasts). In the adjusted analysis, two group interactions were retained, one involving current cigarette smoking and the other involving lifetime cigarette smoking history (Table 16-9(b): $p=0.006$ and $p=0.015$). When these terms were deleted from the final model, differences between the two groups were nonsignificant ($p>0.42$ for all contrasts). Race and the lifetime cigarette smoking history-by-occupation interaction were additionally significant in the adjusted analysis. Appendix Table L-2-5 presents stratified results for the two group interaction terms.

The Model 2 unadjusted analysis revealed a significant positive association between hemoglobin and initial dioxin (Table 16-9(c): $p=0.015$, Slope=0.2647). The association was marginally significant after adjusting for the age-by-current cigarette smoking interaction (Table 16-9(d): $p=0.057$, Slope=0.2117). In the unadjusted Model 3 analysis, Ranch Hands in the low category possessed a marginally significant lower mean level of hematocrit (45.89 percent) than Comparisons (46.25 percent), (Table 16-9(e): $p=0.100$, Diff. of Adj. Means= -0.36). Results were nonsignificant in the adjusted analysis (Table 16-9(f): $p>0.13$ for all contrasts). The categorized dioxin-by-current cigarette smoking and the categorized dioxin-by-lifetime cigarette smoking history interactions were significant in the adjusted analysis ($p=0.002$ and $p=0.008$). Final adjusted results reflect analyses omitting these interactions. Further investigation of the interactions was performed and results are found in Appendix Table L-2-5.

Current dioxin and hematocrit were not significantly associated in the Model 4, 5, and 6 unadjusted and adjusted analyses (Table 16-9(g,h): $p>0.18$ for all analyses). Each of the final models were adjusted for lifetime cigarette smoking history and the age-by-current cigarette smoking interaction.

Hematocrit (Discrete)

The unadjusted and adjusted Model 1 analyses of hematocrit, in discrete form, displayed no significant differences between Ranch Hands and Comparisons (Table 16-10(a,b): $p>0.15$). Covariates retained in the adjusted model were age, race, current cigarette smoking, and lifetime cigarette smoking history.

Analyses of Model 2 found no significant association between hematocrit and initial dioxin (Table 16-10(c,d): $p>0.28$ for both analyses). Age and lifetime cigarette smoking history were retained in the final adjusted model. The unadjusted Model 3 analysis of hematocrit showed a marginally significant difference between background Ranch Hands and Comparisons (Table 16-10(e): $p=0.096$, Est. RR=2.31). However, after adjusting for the effect of covariates, the contrast became nonsignificant (Table 16-10(f): $p=0.106$). All other contrasts were nonsignificant in the unadjusted and adjusted analyses ($p>0.48$ for all remaining contrasts). Covariates retained in the adjusted model were age, race, current cigarette smoking, and lifetime cigarette smoking history.

Table 16-9.
Analysis of Hematocrit (percent)
(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***	***946***	***46.30***	***0.03 (-0.24,0.29)***	***0.839***
	Comparison	***1,278***	***46.27***		
Officer	Ranch Hand	364	46.08	0.18 (-0.26,0.61)	0.426
	Comparison	501	45.90		
Enlisted Flyer	Ranch Hand	162	46.32	-0.19 (-0.86,0.49)	0.585
	Comparison	201	46.51		
Enlisted Groundcrew	Ranch Hand	420	46.48	-0.03 (-0.42,0.36)	0.888
	Comparison	576	46.51		

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***	***945***	***45.82*****	***-0.02 (-0.28,0.24)*****	***0.879*****	GROUP*CSMOK (p=0.006) GROUP*PACKYR (p=0.015) RACE (p<0.001) PACKYR*OCC (p<0.001)
	Comparison	***1,276***	***45.84*****			
Officer	Ranch Hand	363	45.73**	0.16 (-0.26,0.57)**	0.451**	
	Comparison	501	45.57**			
Enlisted Flyer	Ranch Hand	162	45.75**	-0.26 (-0.89,0.38)**	0.423**	
	Comparison	201	46.01**			
Enlisted Groundcrew	Ranch Hand	420	45.90**	-0.09 (-0.47,0.30)**	0.658**	
	Comparison	574	45.99**			

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

** Group-by-covariate interactions ($p \leq 0.05$); adjusted mean, difference of adjusted means, confidence interval, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table L-2-5 for further analysis of these interactions.

Table 16-9. (Continued)
Analysis of Hematocrit (percent)
(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	174	45.82	45.82	0.011	0.2647 (0.1085)	0.015
Medium	172	46.16	46.16			
High	171	46.70	46.71			

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	174	45.96	0.062	0.2117 (0.1110)	0.057	AGE*CSMOK (p=0.038)
Medium	172	46.07				
High	171	46.65				

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

Table 16-9. (Continued)
Analysis of Hematocrit (percent)
(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	1,061	46.25	46.25		
Background RH	371	46.26	46.29	0.04 (-0.33,0.41)	0.835
Low RH	259	45.90	45.89	-0.36 (-0.78,0.07)	0.100
High RH	258	46.55	46.52	0.27 (-0.15,0.70)	0.209
Low plus High RH	517	46.22	46.21	-0.04 (-0.37,0.29)	0.802

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	1,059	45.88**			DXCAT*CSMOK (p=0.002) DXCAT*PACKYR (p=0.008) RACE (p=0.002) CSMOK*OCC (p=0.047) PACKYR*OCC (p<0.001)
Background RH	370	45.98**	0.10 (-0.27,0.47)**	0.591**	
Low RH	259	45.56**	-0.31 (-0.72,0.10)**	0.138**	
High RH	258	45.89**	0.02 (-0.41,0.44)**	0.935**	
Low plus High RH	517	45.73**	-0.15 (-0.47,0.18)**	0.370**	

[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 interactions ($p \leq 0.05$); adjusted mean, difference of adjusted means, confidence interval, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table L-2-5 for further analysis of these interactions.

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 16-9. (Continued)
Analysis of Hematocrit (percent)
(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	46.29 (292)	45.91 (299)	46.51 (297)	0.001	0.0827 (0.0747)	0.268
5	46.22 (297)	45.96 (297)	46.54 (294)	0.002	0.0827 (0.0640)	0.197
6[b]	46.22 (296)	45.96 (297)	46.54 (294)	0.006	0.0397 (0.0691)	0.565

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	46.27 (291)	46.02 (299)	46.43 (297)	0.091	0.0783 (0.0731)	0.285	PACKYR (p=0.004) AGE*CSMOK (p=0.017)
5	46.22 (296)	46.05 (297)	46.45 (294)	0.091	0.0824 (0.0624)	0.187	PACKYR (p=0.004) AGE*CSMOK (p=0.016)
6[c]	46.30 (295)	46.06 (297)	46.35 (294)	0.094	0.0414 (0.0678)	0.542	PACKYR (p=0.003) AGE*CSMOK (p=0.014)

[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.

Table 16-10.
Analysis of Hematocrit
(Discrete)

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

Occupational Category	Group	n	Percent Abnormal Low	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***946***	***1.7***	***1.36 (0.68,2.73)***	***0.496***
	Comparison	***1,278***	***1.3***		
Officer	Ranch Hand	364	1.7	0.75 (0.27,2.04)	0.746
	Comparison	501	2.2		
Enlisted Flyer	Ranch Hand	162	2.5	5.06 (0.56,45.75)	0.250
	Comparison	201	0.5		
Enlisted Groundcrew	Ranch Hand	420	1.4	2.07 (0.58,7.39)	0.409
	Comparison	576	0.7		

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

Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	***1.42 (0.70,2.88)***	***0.330***	AGE ($p<0.001$) RACE ($p=0.012$) CSMOK ($p=0.002$) PACKYR ($p=0.072$)
Officer	0.77 (0.28,2.12)	0.615	
Enlisted Flyer	4.97 (0.55,45.30)	0.155	
Enlisted Groundcrew	2.28 (0.63,8.27)	0.208	

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

Table 16-10. (Continued)
Analysis of Hematocrit
(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 Low**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	174	1.2	1.22 (0.74,2.01)	0.439
Medium	172	1.2		
High	171	1.8		

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**
517	1.33 (0.79,2.24)	0.287	AGE (p=0.089) PACKYR (p=0.014)

[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 16-10. (Continued)
Analysis of Hematocrit
(Discrete)

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

Dioxin Category	n	Percent Abnormal Low	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,061	0.9		
Background RH	371	1.9	2.31 (0.86,6.19)	0.096
Low RH	259	1.5	1.51 (0.47,4.89)	0.489
High RH	258	1.2	1.11 (0.30,4.09)	0.880
Low plus High RH	517	1.4	1.31 (0.49,3.48)	0.592

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	1,059			AGE (p=0.005) RACE (p=0.081) CSMOK (p=0.012) PACKYR (p=0.123)
Background RH	370	2.27 (0.84,6.14)	0.106	
Low RH	259	1.40 (0.43,4.56)	0.580	
High RH	258	1.38 (0.36,5.32)	0.638	
Low plus High RH	517	1.39 (0.51,3.76)	0.516	

[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 16-10. (Continued)
Analysis of Hematocrit
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal Low/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	1.7 (292)	1.7 (299)	1.4 (297)	1.16 (0.82,1.64)	0.417
5	1.4 (297)	2.0 (297)	1.4 (294)	1.08 (0.80,1.48)	0.608
6[c]	1.4 (296)	2.0 (297)	1.4 (294)	1.22 (0.87,1.71)	0.247

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	888	1.16 (0.82,1.65)	0.404	CSMOK (p=0.014)
5	888	1.10 (0.79,1.51)	0.582	CSMOK (p=0.014)
6[d]	887	1.21 (0.86,1.70)	0.282	CSMOK (p=0.020)

[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.

No significant association between hematocrit and current dioxin was found in the unadjusted and adjusted analyses of Models 4, 5, and 6 (Table 16-10(g,h): $p>0.24$ for all analyses). Current cigarette smoking was the only significant covariate in each of the adjusted models.

Platelet Count (Continuous)

Overall, Ranch Hands possessed a significantly greater mean platelet count than Comparisons in the Model 1 unadjusted analysis (Table 16-11(a): $p=0.030$, Diff. of Means=5.1). Mean platelet count for Ranch Hands was 251.3 thousand/mm^3 in contrast to 246.2 thousand/mm^3 for Comparisons. Stratifying this analysis by occupation disclosed significant differences between Ranch Hands and Comparisons in both the enlisted flyer and enlisted groundcrew categories ($p=0.016$, Diff. of Means=14.1 for enlisted flyers and $p=0.011$, Diff. of Means=9.2 for enlisted groundcrew). Mean platelet count in the enlisted flyer stratum was 256.6 thousand/mm^3 for Ranch Hands and 242.5 thousand/mm^3 for Comparisons. In the enlisted groundcrew category, mean platelet count for Ranch Hands and Comparisons was 259.8 thousand/mm^3 and 250.7 thousand/mm^3 respectively. In the adjusted analysis, the interaction of group and occupation was significant (Table 16-11(b): $p=0.010$). Comparable to the unadjusted analysis, the Ranch Hands and Comparisons differed significantly overall and within the enlisted flyer and enlisted groundcrew strata (Table 16-11(b): $p=0.036$, Diff. of Adj. Mean=4.8; $p=0.014$, Diff. of Adj. Mean=13.9; and $p=0.010$, Diff. of Adj. Means=8.9 respectively). In each case, Ranch Hands possessed a greater mean level of platelet count than Comparisons. Age, current cigarette smoking, and lifetime cigarette smoking were included in the final model.

In the unadjusted Model 2 analysis, mean platelet count levels increased significantly with initial dioxin (Table 16-11(c): $p=0.025$, Slope=0.1270). However, adjustment for age, current cigarette smoking, and the lifetime cigarette smoking history-by-race interaction yielded nonsignificant results (Table 16-11(d): $p=0.267$).

In the Model 3 unadjusted analysis, the differences for the high Ranch Hand and the low plus high Ranch Hand categories versus the Comparison group were highly significant (Table 16-11(e): $p<0.001$, Diff. of Means=15.1 and $p=0.004$, Diff. of Mean=8.3 respectively). Mean platelet counts for the high and low plus high Ranch Hand categories were 260.8 and 254.0 thousand/mm^3 in contrast to only 245.7 thousand/mm^3 for Comparisons. These differences remained highly significant in the adjusted analysis. The adjusted mean platelet count was 258.5 thousand/mm^3 for high Ranch Hands, 253.1 thousand/mm^3 for low plus high Ranch Hands, and 245.8 thousand/mm^3 for Comparisons (Table 16-11(f): $p<0.001$ for high Ranch Hands vs. Comparisons and $p=0.010$ for low plus high Ranch Hands vs. Comparisons). The adjusted analysis retained age, current cigarette smoking, and lifetime cigarette smoking history.

Significant positive relationships between platelet count and current dioxin were found to exist in the Model 4, 5, and 6 unadjusted analyses (Table 16-11(g): $p=0.033$ Slope=0.0845, for Model 4; $p=0.018$, Slope=0.0800 for Model 5; and $p=0.045$, Slope= 0.0734, for Model 6). However, after adjusting for lifetime cigarette smoking history and the age-by-occupation interaction, the associations became nonsignificant and, in the case of

Table 16-11.
Analysis of Platelet Count (thousand/mm^3)
(Continuous)

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

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***946***	***251.3***	***5.1 --***	***0.030***
	Comparison	***1,277***	***246.2***		
Officer	Ranch Hand	364	239.3	-3.3 --	0.343
	Comparison	500	242.6		
Enlisted Flyer	Ranch Hand	162	256.6	14.1 --	0.016
	Comparison	201	242.5		
Enlisted Groundcrew	Ranch Hand	420	259.8	9.2 --	0.011
	Comparison	576	250.7		

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

Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]	Covariate Remarks[d]
All	***Ranch Hand***	***945***	***251.0****	***4.8 --****	***0.036****	GROUP*OCC (p=0.010)
	Comparison	***1,275***	***246.1****			AGE (p<0.001)
Officer	Ranch Hand	363	242.6	-3.6 --	0.324	CSMOK (p=0.036)
	Comparison	500	246.2			PACKYR (p<0.001)
Enlisted Flyer	Ranch Hand	162	256.2	13.9 --	0.014	
	Comparison	201	242.2			
Enlisted Groundcrew	Ranch Hand	420	256.7	8.9 --	0.010	
	Comparison	574	247.8			

[a] Transformed from the square root scale.

[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.

[c] P-values based on difference of means on square root scale.

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

** Group-by-covariate interaction ($p \leq 0.05$); adjusted mean, difference of adjusted means, and p-value derived from a model fitted after deletion of this interaction.

Table 16-11. (Continued)
Analysis of Platelet Count (thousand/mm^3)
(Continuous)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	174	245.9	245.8	0.029	0.1270 (0.0566)	0.025
Medium	172	252.9	252.4			
High	171	258.8	259.4			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ad]	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
Low	174	257.4	0.086	0.0645 (0.0580)	0.267	AGE ($p<0.001$)
Medium	172	259.6				CSMOK ($p=0.135$)
High	171	265.1				PACKYR*RACE ($p=0.029$)

[a] Transformed from square root scale.

[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] Slope and standard error based on square root of platelet count versus log_2 (initial dioxin).

[d] 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 16-11. (Continued)
Analysis of Platelet Count (thousand/mm^3)
(Continuous)

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

Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,060	245.7	245.7		
Background RH	371	247.2	245.1	-0.6 --	0.855
Low RH	259	245.8	247.3	1.6 --	0.669
High RH	258	259.2	260.8	15.1 --	<0.001
Low plus High RH	517	252.4	254.0	8.3 --	0.004

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

Dioxin Category	n	Adj. Mean[ae]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]	Covariate Remarks
Comparison	1,058	245.8			AGE (p<0.001) CSMOK (p=0.105) PACKYR (p<0.001)
Background RH	370	246.0	0.2 --	0.949	
Low RH	259	247.8	2.1 --	0.575	
High RH	258	258.5	12.7 --	<0.001	
Low plus High RH	517	253.1	7.3 --	0.010	

[a] Transformed from square root scale.

[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] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on square root scale.

[d] P-value is based on difference of means on square root scale.

[e] 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 16-11. (Continued)
Analysis of Platelet Count (thousand/mm^3)
(Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[b]	Current Dioxin Category Mean[a]/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Slope (Std. Error)[c]	p-Value
4	247.2 (292)	245.7 (299)	258.0 (297)	0.005	0.0845 (0.0395)	0.033
5	245.6 (297)	248.9 (297)	256.4 (294)	0.006	0.0800 (0.0339)	0.018
6[d]	246.3 (296)	248.9 (297)	255.4 (294)	0.009	0.0734 (0.0366)	0.045

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[b]	Current Dioxin Category Adjusted Mean[a]/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
4	250.3 (291)	246.8 (299)	250.8 (297)	0.056	-0.0093 (0.0452)	0.836	PACKYR ($p<0.001$) AGE*OCC ($p=0.042$)
5	248.6 (296)	249.9 (297)	249.3 (294)	0.056	0.0105 (0.0380)	0.782	PACKYR ($p<0.001$) AGE*OCC ($p=0.048$)
6[e]	249.7 (295)	250.1 (297)	247.5 (294)	0.058	-0.0050 (0.0415)	0.904	PACKYR ($p=0.001$) AGE*OCC ($p=0.046$)

[a] Transformed from square root scale.

[b] 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.

[c] Slope and standard error based on square root of platelet count versus log_2 (current dioxin + 1).

[d] Adjusted for log_2 total lipids.

[e] 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 and 6, negative (Table 16-11(h): p=0.836 for Model 4, p=0.782 for Model 5, and p=0.904 for Model 6).

Platelet Count (Discrete)

All unadjusted and adjusted analyses of platelet count in discrete form were nonsignificant in Models 1 and 2 (Table 16-12(a-d): p>0.16 for each analysis). Covariates in the final adjusted model for Model 1 were age, occupation, and current cigarette smoking. Model 2 adjusted for age only.

The unadjusted and adjusted analyses of platelet count in Model 3 revealed a significant difference between the high Ranch Hand category and the Comparison group (Table 16-12(e,f): p=0.027, Est. RR=3.12 and p=0.029, Adj. RR=3.10). Both analyses indicated that Ranch Hands in the high dioxin category had a greater percentage of abnormally high platelet counts than Comparisons (2.7% versus 0.9%). All other contrasts in Model 3 were nonsignificant (p>0.14 for each remaining contrast). Current cigarette smoking was the only significant covariate in the adjusted model.

Unadjusted analyses of platelet count in Models 4, 5, and 6 each displayed a significant positive association with current dioxin (Table 16-12(g): p=0.014, Est. RR=1.63; p=0.017, Est. RR=1.55; and p=0.016, Est. RR=1.60 respectively). The adjusted results in Model 4 are identical to the unadjusted results due to the absence of any significant covariate in the final adjusted model. The association with current dioxin was marginally significant in Model 5 after adjustment for age (Table 16-12(h): p=0.062, Adj. RR=1.42) and was nonsignificant in Model 6 after adjustment for current cigarette smoking (p=0.377).

Prothrombin Time (Continuous)

All contrasts investigating differences between Ranch Hands and Comparisons in the Model 1 analyses of prothrombin time were nonsignificant (Table 16-13(a,b): p>0.15 for all contrasts). The final model was adjusted for current cigarette smoking and the lifetime cigarette smoking history-by-race interaction.

Prothrombin time did not increase significantly with initial dioxin in the unadjusted Model 2 analysis (Table 16-13(c): p=0.337). However, in the adjusted analysis, a highly significant dose-response relationship between prothrombin time and initial dioxin was disclosed (Table 16-13(d): p=0.019, Slope=0.0033). Adjusted means for the low, medium, and high initial dioxin categories were 11.93, 11.96, and 11.98 seconds. Race, current cigarette smoking, and the age-by-lifetime cigarette smoking history interaction were retained in the final adjusted model. No significant differences between Ranch Hands and Comparisons were found in the unadjusted and adjusted analyses of prothrombin time for Model 3 (Table 16-13(e,f): p>0.13). The categorized dioxin-by-age interaction, race, occupation, and current cigarette smoking were significant in the adjusted analysis. Adjusted results are based on analysis after the deletion of the categorized dioxin-by-age interaction. Appendix Table L-2-6 contains results from further analysis on the categorized dioxin-by-age interaction.

Table 16-12.
Analysis of Platelet Count
(Discrete)

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

Occupational Category	Group	n	Percent Abnormal High	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***946***	***1.4***	***1.47 (0.67,3.23)***	***0.449***
	Comparison	***1,277***	***0.9***		
Officer	Ranch Hand	364	0.3	0.46 (0.05,4.41)	0.851
	Comparison	500	0.6		
Enlisted Flyer	Ranch Hand	162	1.2	1.24 (0.17,8.93)	0.999
	Comparison	201	1.0		
Enlisted Groundcrew	Ranch Hand	420	2.4	1.98 (0.75,5.25)	0.248
	Comparison	576	1.2		

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

Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	***1.45 (0.65,3.20)***	***0.362***	AGE (p=0.142) OCC (p=0.019) CSMOK (p=0.014)
Officer	0.47 (0.05,4.58)	0.517	
Enlisted Flyer	1.17 (0.16,8.42)	0.875	
Enlisted Groundcrew	1.95 (0.76,4.99)	0.167	

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

Table 16-12. (Continued)
Analysis of Platelet Count
(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 High**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	174	0.6	1.38 (0.88,2.16)	0.174
Medium	172	1.7		
High	171	2.9		

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**
517	1.17 (0.71,1.93)	0.550	AGE (p=0.037)

[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 16-12. (Continued)
Analysis of Platelet Count
(Discrete)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Abnormal High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,060	0.9		
Background RH	371	0.3	0.33 (0.04,2.66)	0.300
Low RH	259	0.8	0.86 (0.19,4.04)	0.853
High RH	258	2.7	3.12 (1.14,8.55)	0.027
Low plus High RH	517	1.7	1.97 (0.77,5.03)	0.156

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	1,058			CSMOK (p=0.006)
Background RH	371	0.34 (0.04,2.70)	0.306	
Low RH	259	0.91 (0.19,4.29)	0.905	
High RH	258	3.10 (1.13,8.54)	0.029	
Low plus High RH	517	2.02 (0.78,5.21)	0.145	

[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 16-12. (Continued)
Analysis of Platelet Count
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Percent Abnormal High/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) Est. Relative Risk (95% C.I.)[b]	p-Value
4	0.3 (292)	0.3 (299)	2.7 (297)	1.63 (1.11,2.39)	0.014
5	0.3 (297)	0.7 (297)	2.4 (294)	1.55 (1.09,2.20)	0.017
6[c]	0.3 (296)	0.7 (297)	2.4 (294)	1.60 (1.09,2.34)	0.016

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[a]	n	Analysis Results for Log_2 (Current Dioxin + 1) Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	888	1.63 (1.11,2.39)	0.014	
5	888	1.42 (0.98,2.05)	0.062	AGE (p=0.073)
6[d]	887	0.76 (0.42,1.38)	0.377	CSMOK (p=0.077)

[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 16-13.
Analysis of Prothrombin Time (seconds)
(Continuous)

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

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***869***	***11.93***	***0.01 --***	***0.765***
	Comparison	***1,176***	***11.92***		
Officer	Ranch Hand	336	11.93	0.02 --	0.504
	Comparison	457	11.90		
Enlisted Flyer	Ranch Hand	145	11.97	0.06 --	0.479
	Comparison	182	11.91		
Enlisted Groundcrew	Ranch Hand	388	11.92	-0.03 --	0.358
	Comparison	537	11.95		

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

Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]	Covariate Remarks[d]
All	***Ranch Hand***	***868***	***12.05***	***0.01 --***	0.662	CSMOK ($p<0.001$) PACKYR*RACE ($p<0.001$)
	Comparison	***1,174***	***12.04***			
Officer	Ranch Hand	335	12.02	0.02 --	0.582	
	Comparison	457	12.00			
Enlisted Flyer	Ranch Hand	145	12.10	0.08 --	0.155	
	Comparison	182	12.02			
Enlisted Groundcrew	Ranch Hand	388	12.04	-0.02 --	0.481	
	Comparison	535	12.07			

[a] Transformed from the natural logarithm scale.

[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

[c] P-values based on difference of means on natural logarithm scale.

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

Table 16-13. (Continued)
Analysis of Prothrombin Time (seconds)
(Continuous)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	157	11.90	11.91	0.040	0.0013 (0.0014)	0.337
Medium	157	11.90	11.91			
High	160	11.90	11.89			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ad]	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
Low	157	11.93**	0.113	0.0033 (0.0014)**	0.019**	CSMOK (p=0.001) RACE (p=0.088) AGE*PACKYR (p=0.028)
Medium	157	11.96**				
High	160	11.98**				

[a] Transformed from natural logarithm scale.

[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] Slope and standard error based on natural logarithm of prothromobin time versus log_2 (initial dioxin).

[d] 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 16-13. (Continued)
Analysis of Prothrombin Time (seconds)
(Continuous)

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

Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	979	11.92	11.92		
Background RH	342	11.94	11.95	0.03 --	0.328
Low RH	234	11.88	11.88	-0.05 --	0.171
High RH	240	11.92	11.91	-0.01 --	0.662
Low plus High RH	474	11.90	11.89	-0.03 --	0.245

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

Dioxin Category	n	Adj. Mean[ae]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]	Covariate Remarks
Comparison	977	11.97**			DXCAT*AGE (p=0.004) RACE (p=0.015) OCC (p=0.101) CSMOK (p<0.001)
Background RH	341	12.01**	0.04 --**	0.157**	
Low RH	234	11.92**	-0.05 --**	0.131**	
High RH	240	11.95**	-0.02 --**	0.590**	
Low plus High RH	474	11.93**	-0.03 --**	0.188**	

[a] Transformed from natural logarithm scale.

[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] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on natural logarithm scale.

[d] P-value is based on difference of means on natural logarithm scale.

[e] 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 ($p \leq 0.05$); adjusted mean, difference of adjusted means, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table L-2-6 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 16-13. (Continued)
Analysis of Prothrombin Time (seconds)
(Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[b]	Current Dioxin Category Mean[a]/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Slope (Std. Error)[c]	p-Value
4	11.93 (269)	11.92 (270)	11.90 (277)	<0.001	-0.0002 (0.0009)	0.819
5	11.94 (271)	11.91 (273)	11.89 (272)	0.001	-0.0007 (0.0008)	0.412
6[d]	11.92 (270)	11.91 (273)	11.92 (272)	0.011	0.0002 (0.0009)	0.814

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[b]	Current Dioxin Category Adjusted Mean[a]/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
4	11.92 (268)	11.91 (270)	11.91 (277)	0.041	0.0001 (0.0009)	0.910	CSMOK (p<0.001) AGE*PACKYR (p=0.009)
5	11.94 (270)	11.90 (273)	11.91 (272)	0.041	-0.0004 (0.0008)	0.633	CSMOK (p<0.001) AGE*PACKYR (p=0.010)
6[e]	11.92 (269)	11.90 (273)	11.93 (272)	0.048	0.0004 (0.0009)	0.626	CSMOK (p<0.001) AGE*PACKYR (p=0.014)

[a] Transformed from natural logarithm scale.

[b] 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.

[c] Slope and standard error based on natural logarithm of prothrombin time versus log_2 (current dioxin + 1).

[d] Adjusted for log_2 total lipids.

[e] 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.

Prothrombin time and current dioxin were not significantly associated in any of the Model 4, 5, and Model 6 unadjusted and adjusted analyses (Table 16-13(g,h): $p>0.41$). Each adjusted analysis retained current cigarette smoking and the age-by-lifetime cigarette smoking history interaction.

Prothrombin Time (Discrete)

Ranch Hands and Comparisons did not display significantly different percentages of abnormally high prothrombin time in either the unadjusted or adjusted Model 1 analyses (Table 16-14(a,b): $p>0.39$). Age was the only covariate retained in the adjusted analysis.

All results from the Model 2 and Model 3 analyses exploring associations between prothrombin time and dioxin were nonsignificant (Table 16-14(c-f): $p>0.10$ for all analyses). Age was retained in each adjusted analysis and the occupation-by-lifetime cigarette smoking history interaction also was retained in Model 3.

Prothrombin time was not significantly associated with current dioxin in the Model 4, 5, and 6 unadjusted and adjusted analyses (Table 16-14(g,h): $p>0.38$ for all analyses). The Model 4 adjusted analysis contained a significant interaction between current dioxin and lifetime cigarette smoking history (Table 16-14(h): $p=0.047$). Final adjusted results are based upon analyses without the interaction. Further analysis of the interaction was performed and results are shown in Appendix Table L-2-7. Covariates retained in the final models included current cigarette smoking and the age-by-lifetime cigarette smoking history interaction for Model 4, age and current cigarette smoking history for Model 5, and age, current cigarette smoking, and lifetime cigarette smoking history for Model 6.

RBC Morphology

Results from the Model 1 group analyses of RBC morphology were nonsignificant (Table 16-15(a,b): $p>0.14$ for all analyses). Significant covariates included age and the race-by-occupation interaction.

Neither the unadjusted nor adjusted Model 2 analyses of RBC morphology revealed a significant association with initial dioxin (Table 16-15(c,d): $p>0.68$). Age and the race-by-lifetime cigarette smoking history interaction were retained in the adjusted analysis. Unadjusted analysis results for Model 3 were nonsignificant (Table 16-15(e): $p\geq0.11$ for all contrasts). In the adjusted analysis, a significant negative association between background Ranch Hands and Comparisons was disclosed (Table 16-15(f): $p=0.049$, Adj. RR=0.78). All other contrasts between Ranch Hands and Comparisons were nonsignificant ($p>0.46$). The final model was adjusted for age and the race-by-occupation interaction.

Each of the unadjusted Model 4, 5, and 6 analyses of RBC morphology were not significant (Table 16-15(g): $p>0.41$ for all analyses). After adjusting for age and the race-by-occupation interaction, positive associations between current dioxin and RBC morphology for each final model were either significant or marginally significant (Table 16-15(h): $p=0.083$, Adj. RR=1.10 for Model 4; $p=0.090$, Adj. RR=1.08 for Model 5; and $p=0.045$, Adj. RR=1.11 for Model 6). However, after removing occupation from the final

Table 16-14.
Analysis of Prothrombin Time
(Discrete)

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

Occupational Category	Group	n	Percent High	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***869***	***0.9***	***1.55 (0.56,4.30)***	***0.555***
	Comparison	***1,176***	***0.6***		
Officer	Ranch Hand	336	1.2	1.36 (0.34,5.50)	0.937
	Comparison	457	0.9		
Enlisted Flyer	Ranch Hand	145	1.4	1.26 (0.18,9.05)	0.999
	Comparison	182	1.1		
Enlisted Groundcrew	Ranch Hand	388	0.5	2.78 (0.25,30.74)	0.777
	Comparison	537	0.2		

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

Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	***1.56 (0.56,4.34)***	***0.393***	AGE ($p<0.001$)
Officer	1.41 (0.35,5.73)	0.628	
Enlisted Flyer	1.18 (0.16,8.62)	0.868	
Enlisted Groundcrew	2.77 (0.25,30.72)	0.406	

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

Table 16-14. (Continued)
Analysis of Prothrombin Time
(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 High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	157	1.3	0.47 (0.16,1.38)	0.101
Medium	157	1.3		
High	160	0.0		

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
474	0.58 (0.16,2.12)	0.346	AGE (p=0.004)

[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 16-14. (Continued)
Analysis of Prothrombin Time
(Discrete)

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

Dioxin Category	n	Percent High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	979	0.4		
Background RH	342	0.9	2.80 (0.61,12.78)	0.184
Low RH	234	1.3	2.50 (0.54,11.49)	0.239
High RH	240	0.4	0.79 (0.09,7.21)	0.832
Low plus High RH	474	0.8	1.62 (0.40,6.65)	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	977			AGE (p=0.028) OCC*PACKYR (p=0.037)
Background RH	341	2.38 (0.49,11.52)	0.280	
Low RH	234	1.81 (0.36,9.14)	0.474	
High RH	240	1.29 (0.10,16.11)	0.846	
Low plus High RH	474	1.67 (0.36,7.69)	0.513	

[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 16-14. (Continued)
Analysis of Prothrombin Time
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Percent High/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) Est. Relative Risk (95% C.I.)[b]	p-Value
4	0.7 (269)	1.5 (270)	0.4 (277)	0.82 (0.48,1.41)	0.462
5	0.7 (271)	1.5 (273)	0.4 (272)	0.83 (0.55,1.25)	0.386
6[c]	0.7 (270)	1.5 (273)	0.4 (272)	0.92 (0.58,1.46)	0.712

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[a]	Analysis Results for Log_2 (Current Dioxin + 1) n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	815	0.88 (0.46,1.68)**	0.698**	CURR*PACKYR (p=0.047) CSMOK (p=0.111) AGE*PACKYR (p=0.036)
5	816	0.82 (0.48,1.42)	0.483	AGE (p=0.011) CSMOK (p=0.064)
6[d]	814	0.98 (0.54,1.78)	0.950	AGE (p=0.058) CSMOK (p=0.053) PACKYR (p=0.117)

[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 L-2-7 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 16-15.
Analysis of RBC Morphology

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***	***946***	***44.6***	***0.94 (0.79,1.11)***	***0.493***
	Comparison	***1,278***	***46.2***		
Officer	Ranch Hand	364	47.3	1.00 (0.76,1.31)	0.999
	Comparison	501	47.3		
Enlisted Flyer	Ranch Hand	162	50.6	1.12 (0.74,1.70)	0.663
	Comparison	201	47.8		
Enlisted Groundcrew	Ranch Hand	420	40.0	0.83 (0.64,1.07)	0.164
	Comparison	576	44.6		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***0.93 (0.79,1.11)***	***0.436***	AGE ($p<0.001$) RACE*OCC ($p=0.006$)
Officer	0.99 (0.75,1.30)	0.945	
Enlisted Flyer	1.13 (0.74,1.73)	0.558	
Enlisted Groundcrew	0.82 (0.64,1.07)	0.144	

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

Table 16-15. (Continued)
Analysis of RBC Morphology

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	174	45.4	0.97 (0.85,1.11)	0.681
Medium	172	47.1		
High	171	44.4		

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
517	1.02 (0.89,1.17)	0.773	AGE (p=0.075) RACE*PACKYR (p=0.032)

[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 16-15. (Continued)
Analysis of RBC Morphology

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	1,061	46.7		
Background RH	371	41.5	0.82 (0.65,1.05)	0.110
Low RH	259	46.3	0.96 (0.73,1.27)	0.788
High RH	258	45.0	0.93 (0.71,1.23)	0.618
Low plus High RH	517	45.7	0.95 (0.77,1.17)	0.618

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	1,061			AGE ($p<0.001$) RACE*OCC ($p=0.007$)
Background RH	371	0.78 (0.61,1.00)	0.049	
Low RH	259	0.90 (0.68,1.19)	0.469	
High RH	258	1.05 (0.79,1.40)	0.749	
Low plus High RH	517	0.97 (0.78,1.20)	0.779	

[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 16-15. (Continued)
Analysis of RBC Morphology

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	44.5 (292)	42.5 (299)	44.8 (297)	1.02 (0.93,1.12)	0.619
5	44.1 (297)	42.1 (297)	45.6 (294)	1.02 (0.95,1.11)	0.578
6[c]	43.9 (296)	42.1 (297)	45.6 (294)	1.04 (0.95,1.13)	0.417

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	888	1.10 (0.99,1.22)	0.083	AGE (p=0.008) RACE*OCC (p=0.022)
5	888	1.08 (0.99,1.19)	0.090	AGE (p=0.009) RACE*OCC (p=0.021)
6[d]	887	1.11 (1.00,1.22)	0.045	AGE (p=0.008) RACE*OCC (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.

adjusted model, all three models become nonsignificant (Appendix Table L-3-9: $p>0.11$ for all models).

Absolute Neutrophils (segs)

Significant differences between Ranch Hands and Comparisons did not exist in the Model 1 unadjusted and adjusted analyses of absolute neutrophils (segs) (Table 16-16(a,b): $p>0.31$ for all analyses). The adjusted analysis retained four interactions: age-by-race, current cigarette smoking-by-occupation, current cigarette smoking-by-race, and lifetime cigarette smoking history-by-race.

Initial dioxin and absolute neutrophils (segs) were not significantly associated in the Model 2 unadjusted analysis (Table 16-16(c): $p=0.151$). A significant interaction between initial dioxin and race was disclosed in the adjusted analysis (Table 16-16(d): $p=0.038$). Results stratified by race are found in Appendix Table L-2-8. After deleting the interaction from the final model, the association between initial dioxin and absolute neutrophils (segs) remained nonsignificant ($p=0.962$). Covariates included in the adjusted analysis were occupation, current cigarette smoking, and lifetime cigarette smoking history. The unadjusted Model 3 analysis revealed a marginally significant difference in mean absolute neutrophils (segs) for high Ranch Hands versus Comparisons (Table 16-16(e): $p=0.063$, Diff. of Mean=0.189). The adjusted mean (adjusted for body fat measures) for the Ranch Hand category was 4.145 thousand/mm^3 compared to only 3.956 thousand/mm^3 for Comparisons. All contrasts were nonsignificant after adjusting for lifetime cigarette smoking history and the age-by-race and current cigarette smoking-by-occupation interactions (Table 16-16(f): $p>0.68$ for all contrasts).

Results from the Model 4 through 6 unadjusted analysis of absolute neutrophils (segs) were nonsignificant (Table 16-16(g): $p>0.10$ for all analyses). In each of the adjusted analyses, the interaction of current dioxin and race was significant (Table 16-16(h): $p=0.034$ for Model 4, $p=0.011$ for Model 5, and $p=0.012$ for Model 6). After excluding these interactions from each of the final models, no significant associations between current dioxin and absolute neutrophils (segs) were revealed ($p>0.45$ for all analyses). Also retained in each adjusted analysis were age, lifetime cigarette smoking history, and the current cigarette smoking-by-occupation interaction. Appendix Table L-2-8 contains results stratified by race for further analysis on the current dioxin interaction. After occupation was removed from the final models, the current dioxin effect became significant in Models 4 and 5 (Appendix Table L-3-10(c): $p=0.029$, Slope=0.0174 for Model 4 and $p=0.036$, Slope=0.0143 for Model 5) and marginally significant in Model 6 ($p=0.068$, Slope=0.0135). These results also reflect the exclusion of the current dioxin-by-race interactions.

Absolute Neutrophils (bands)

Because a substantial number of measurements (372/2,224 or 16.7%) for absolute neutrophils (bands) were equal to 0 counts per mm^3, this variable was analyzed in two forms. A discrete analysis was first performed on the proportion of zero measurements and a second continuous analysis was performed on the nonzero measurements.

Table 16-16.
Analysis of Absolute Neutrophils (segs) (thousand/mm^3)

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

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***946***	***4.012***	***0.062 --***	***0.315***
	Comparison	***1,278***	***3.951***		
Officer	Ranch Hand	364	3.779	0.053 --	0.534
	Comparison	501	3.726		
Enlisted Flyer	Ranch Hand	162	4.119	-0.022 --	0.903
	Comparison	201	4.141		
Enlisted Groundcrew	Ranch Hand	420	4.183	0.094 --	0.320
	Comparison	576	4.089		

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

Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]	Covariate Remarks[d]
All	***Ranch Hand***	***945***	***3.568***	***0.025 --***	***0.608***	AGE*RACE (p=0.017)
	Comparison	***1,276***	***3.543***			CSMOK*OCC (p=0.035)
Officer	Ranch Hand	363	3.397	0.044 --	0.561	CSMOK*RACE (p=0.009)
	Comparison	501	3.354			PACKYR*RACE (p=0.047)
Enlisted Flyer	Ranch Hand	162	3.524	-0.084 --	0.490	
	Comparison	201	3.607			
Enlisted Groundcrew	Ranch Hand	420	3.750	0.050 --	0.519	
	Comparison	574	3.700			

[a] Transformed from the natural logarithm scale.

[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

[c] P-values based on difference of means on natural logarithm scale.

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

Table 16-16. (Continued)
Analysis of Absolute Neutrophils (segs) (thousand/mm^3)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	174	3.910	3.917	0.018	0.0184 (0.0128)	0.151
Medium	172	4.105	4.118			
High	171	4.153	4.132			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ad]	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
Low	174	3.573**	0.223	0.0006 (0.0132)**	0.962**	INIT*RACE (p=0.038)
Medium	172	3.540**				OCC (p=0.078)
High	171	3.544**				CSMOK (p<0.001)
						PACKYR (p=0.016)

[a] Transformed from natural logarithm scale.

[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] Slope and standard error based on natural logarithm of absolute neutrophils (segs) versus log_2 (initial dioxin).

[d] 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 mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table L-2-8 for further analysis of this interaction.

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

Table 16-16. (Continued)
Analysis of Absolute Neutrophils (segs) (thousand/mm^3)

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

Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,061	3.957	3.956		
Background RH	371	3.907	3.928	-0.028 --	0.738
Low RH	259	3.947	3.938	-0.018 --	0.848
High RH	258	4.163	4.145	0.189 --	0.063
Low plus High RH	517	4.054	4.041	0.085 --	0.281

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

Dioxin Category	n	Adj. Mean[ae]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]	Covariate Remarks
Comparison	1,059	3.561			PACKYR (p=0.009) AGE*RACE (p=0.015) CSMOK*OCC (p=0.010)
Background RH	370	3.559	-0.002 --	0.974	
Low RH	259	3.578	0.017 --	0.836	
High RH	258	3.595	0.034 --	0.681	
Low plus High RH	517	3.586	0.025 --	0.686	

[a] Transformed from natural logarithm scale.

[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] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on natural logarithm scale.

[d] P-value is based on difference of means on natural logarithm scale.

[e] 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 16-16. (Continued)
Analysis of Absolute Neutrophils (segs) (thousand/mm^3)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[b]	Current Dioxin Category Mean[a]/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Slope (Std. Error)[c]	p-Value
4	3.904 (292)	3.909 (299)	4.167 (297)	0.003	0.0135 (0.0086)	0.116
5	3.889 (297)	3.913 (297)	4.183 (294)	0.003	0.0120 (0.0074)	0.104
6[d]	3.925 (296)	3.917 (297)	4.132 (294)	0.010	0.0069 (0.0079)	0.387

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[b]	Current Dioxin Category Adjusted Mean[a]/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
4	3.413** (291)	3.413** (299)	3.516** (297)	0.208	0.0068 (0.0090)**	0.451**	CURR*RACE (p=0.034) AGE (p=0.028) PACKYR (p=0.090) CSMOK*OCC (p=0.014)
5	3.405** (296)	3.423** (297)	3.518** (294)	0.210	0.0051 (0.0076)**	0.498**	CURR*RACE (p=0.011) AGE (p=0.028) PACKYR (p=0.089) CSMOK*OCC (p=0.014)
6[e]	3.413** (295)	3.426** (297)	3.509** (294)	0.209	0.0042 (0.0083)**	0.615**	CURR*RACE (p=0.012) AGE (p=0.033) PACKYR (p=0.098) CSMOK*OCC (p=0.018)

[a] Transformed from natural logarithm scale.
[b] 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.
[c] Slope and standard error based on natural logarithm of absolute neutrophils (segs) versus log_2 (current dioxin + 1).
[d] Adjusted for log_2 total lipids.
[e] 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 L-2-8 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.

No significant association between group and the proportion of zero measurements for absolute neutrophils (bands) was disclosed in the Model 1 analyses (Table 16-17(a1-b1): $p \geq 0.50$ for all contrasts). Race and current cigarette smoking were significant covariates. The continuous analysis investigating associations between group and nonzero measurements of absolute neutrophils (bands) revealed only one statistically significant difference between Ranch Hands and Comparisons. In the adjusted analysis, the adjusted mean of the absolute neutrophils (bands) for Ranch Hands in the enlisted flyer category was significantly lower than that of the Comparisons (Table 16-17(b2): $p=0.038$, Diff. of Adj. Mean=-0.024). The final model adjusted for age, current cigarette smoking, and the occupation-by-race interaction.

The proportion of zero measurements of absolute neutrophils (bands) did not display a significant association with initial dioxin in the Model 2 analyses (Table 16-17(c1-d1): $p > 0.33$ for unadjusted and adjusted analyses). Race and the initial dioxin-by-lifetime cigarette smoking history interaction ($p=0.018$) were significant in the adjusted analysis. The final adjusted model reflects results after removing the initial dioxin-by-lifetime cigarette smoking history interaction. Appendix Table L-2-9(a) contains additional information on the interaction. No significant relationship between initial dioxin and the nonzero measurements of absolute neutrophils (bands) was disclosed in the unadjusted and adjusted continuous Model 2 analyses (Table 16-17(c2-d2): $p \geq 0.49$ for both analyses). The initial dioxin-by-occupation interaction was significant in the adjusted analysis ($p=0.021$). Results stratified by occupation are found in Appendix Table L-2-9(b). Current cigarette smoking and the interaction of race and occupation also were significant in this analysis.

All unadjusted Model 3 contrasts for zero versus nonzero measurements of absolute neutrophils (bands) were nonsignificant (Table 16-17(e1): $p > 0.58$ for each contrast). In the adjusted analysis, the categorized dioxin-by-lifetime cigarette smoking history interaction was highly significant (Table 16-17(f1): $p < 0.001$). Analyses stratified by each lifetime cigarette smoking history category are presented in Appendix Table L-2-9(c). Race was additionally retained in the adjusted analysis. Nonzero measurements of absolute neutrophils (bands) for Ranch Hands in the four dioxin categories were not significantly different than those of the Comparisons (Table 16-17(e2-f2): $p > 0.82$ for all contrasts). Age and the race-by-occupation and current cigarette smoking-by-race interactions were significant in the final adjusted model.

Current dioxin and the proportion of zero measurements for absolute neutrophils (bands) were not significantly associated in the unadjusted analyses for Models 4, 5, and 6 (Table 16-17(g1): $p > 0.58$ for each analysis). Each adjusted analysis retained race and a highly significant current dioxin-by-lifetime cigarette smoking history interaction (Table 16-17(h1): $p=0.001$ for Model 4, $p=0.003$ for Model 5, and $p=0.002$ for Model 6). Appendix Table L-2-9(d-f) shows results stratified by the levels of lifetime cigarette smoking history. The association between current dioxin and nonzero absolute neutrophils (bands) measurements was nonsignificant in Models 4, 5, and 6 (Table 16-17(g2-h2): $p > 0.18$ for all analyses). Each adjusted analysis retained age, current cigarette smoking, occupation, and race.

Table 16-17.
Analysis of Absolute Neutrophils (bands)
(Zero versus Nonzero)

a1) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Percent Zero	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***946***	***16.9***	***1.02 (0.82,1.28)***	***0.884***
	Comparison	***1,278***	***16.6***		
Officer	Ranch Hand	364	16.2	1.12 (0.77,1.62)	0.629
	Comparison	501	14.8		
Enlisted Flyer	Ranch Hand	162	15.4	0.81 (0.46,1.41)	0.543
	Comparison	201	18.4		
Enlisted Groundcrew	Ranch Hand	420	18.1	1.04 (0.75,1.44)	0.885
	Comparison	576	17.5		

b1) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	***1.03 (0.82,1.29)***	***0.817***	RACE ($p<0.001$) CSMOK ($p=0.055$)
Officer	1.11 (0.76,1.61)	0.587	
Enlisted Flyer	0.82 (0.47,1.44)	0.500	
Enlisted Groundcrew	1.05 (0.75,1.46)	0.791	

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

Table 16-17. (Continued)
Analysis of Absolute Neutrophils (bands) (thousand/mm^3)
(Nonzero Measurements)

a2) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Mean[a]**	**Difference of Means (95% C.I.)[b]**	**p-Value[c]**
All	***Ranch Hand***	***786***	***0.188***	***0.001 --***	***0.860***
	Comparison	***1,066***	***0.186***		
Officer	Ranch Hand	305	0.190	0.011 --	0.312
	Comparison	427	0.178		
Enlisted Flyer	Ranch Hand	137	0.174	-0.028 --	0.110
	Comparison	164	0.202		
Enlisted Groundcrew	Ranch Hand	344	0.192	0.003 --	0.762
	Comparison	475	0.189		

b2) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED						
Occupational Category	**Group**	**n**	**Adj. Mean[a]**	**Difference of Adj. Means (95% C.I.)[b]**	**p-Value[c]**	**Covariate Remarks[d]**
All	***Ranch Hand***	***786***	***0.169***	***-0.001 --***	0.916	AGE (p=0.003) CSMOK (p<0.001) OCC*RACE (p=0.014)
	Comparison	***1,064***	***0.169***			
Officer	Ranch Hand	305	0.227	0.014 --	0.272	
	Comparison	427	0.213			
Enlisted Flyer	Ranch Hand	137	0.124	-0.024 --	0.038	
	Comparison	164	0.148			
Enlisted Groundcrew	Ranch Hand	344	0.161	0.001 --	0.946	
	Comparison	473	0.160			

[a] Transformed from the natural logarithm scale.

[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

[c] P-values based on difference of means on natural logarithm scale.

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

Table 16-17. (Continued)
Analysis of Absolute Neutrophils (bands)
(Zero versus Nonzero)

c1) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Zero	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	174	19.5	0.92 (0.76,1.10)	0.332
Medium	172	16.3		
High	171	15.8		

d1) 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
517	0.93 (0.78,1.12)**	0.448**	INIT*PACKYR (p=0.018) RACE (p=0.085)

[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 L-2-9 for further analysis of this interaction.

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

Table 16-17. (Continued)
Analysis of Absolute Neutrophils (bands) (thousand/mm^3)
(Nonzero Measurements)

c2) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	140	0.171	0.171	<0.001	0.0035 (0.0304)	0.909
Medium	144	0.203	0.203			
High	144	0.188	0.188			

d2) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ad]	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
Low	140	0.141**	0.140	-0.0228 (0.0330)**	0.490**	INIT*OCC (p=0.021)
Medium	144	0.157**				CSMOK (p<0.001)
High	144	0.144**				RACE*OCC (p=0.021)

[a] Transformed from natural logarithm scale.

[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] Slope and standard error based on natural logarithm of absolute neutrophils (bands) versus log_2 (initial dioxin).

[d] 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 mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table L-2-9 for further analysis of this interaction.

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

Table 16-17. (Continued)
Analysis of Absolute Neutrophils (bands)
(Zero versus Nonzero)

e1) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Zero	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,061	16.5		
Background RH	371	17.0	1.05 (0.76,1.44)	0.782
Low RH	259	17.8	1.11 (0.77,1.58)	0.583
High RH	258	16.7	0.99 (0.69,1.44)	0.974
Low plus High RH	517	17.2	1.05 (0.79,1.39)	0.739

f1) 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	1,059			DXCAT*PACKYR ($p<0.001$) RACE ($p<0.001$)
Background RH	370	****	****	
Low RH	259	****	****	
High RH	258	****	****	
Low plus High RH	517	****	****	

[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 L-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 16-17. (Continued)
Analysis of Absolute Neutrophils (bands) (thousand/mm^3)
(Nonzero Measurements)

e2) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	886	0.188	0.188		
Background RH	308	0.189	0.189	0.001 --	0.962
Low RH	213	0.188	0.188	0.000 --	0.990
High RH	215	0.186	0.187	-0.001 --	0.905
Low plus High RH	428	0.187	0.187	-0.001 --	0.932

f2) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Mean[ae]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]	Covariate Remarks
Comparison	884	0.171			AGE (p=0.002) RACE*OCC (p=0.001) CSMOK*RACE (p=0.008)
Background RH	308	0.169	-0.002 --	0.828	
Low RH	213	0.172	0.001 --	0.902	
High RH	215	0.170	-0.001 --	0.927	
Low plus High RH	428	0.171	0.000 --	0.985	

[a] Transformed from natural logarithm scale.

[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] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on natural logarithm scale.

[d] P-value is based on difference of means on natural logarithm scale.

[e] 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 16-17. (Continued)
Analysis of Absolute Neutrophils (bands)
(Zero versus Nonzero)

g1) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Zero/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	16.8 (292)	18.7 (299)	15.8 (297)	1.01 (0.90,1.14)	0.876
5	17.9 (297)	18.2 (297)	15.3 (294)	1.00 (0.91,1.11)	0.933
6[c]	17.9 (296)	18.2 (297)	15.3 (294)	1.03 (0.92,1.15)	0.589

h1) 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	887	****	****	CURR*PACKYR (p=0.001) RACE (p<0.001)
5	887	****	****	CURR*PACKYR (p=0.003) RACE (p<0.001)
6[d]	886	****	****	CURR*PACKYR (p=0.002) RACE (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 ($p \leq 0.01$); adjusted relative risk, confidence interval, and p-value not presented; refer to Appendix Table L-2-9 for further analyses 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 16-17. (Continued)
Analysis of Absolute Neutrophils (bands) (thousand/mm^3)
(Nonzero Measurements)

g2) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[b]	Current Dioxin Category Mean[a]/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Slope (Std. Error)[c]	p-Value
4	0.192 (243)	0.184 (243)	0.188 (250)	<0.001	-0.0108 (0.0201)	0.592
5	0.192 (244)	0.173 (243)	0.199 (249)	<0.001	-0.0071 (0.0171)	0.679
6[d]	0.197 (243)	0.174 (243)	0.194 (249)	0.008	-0.0246 (0.0185)	0.185

h2) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[b]	Current Dioxin Category Adjusted Mean[a]/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
4	0.150 (243)	0.150 (243)	0.155 (250)	0.076	0.0053 (0.0226)	0.814	AGE (p=0.072) CSMOK (p<0.001) OCC (p=0.114) RACE (p=0.003)
5	0.151 (244)	0.143 (243)	0.166 (249)	0.076	0.0052 (0.0188)	0.782	AGE (p=0.073) CSMOK (p<0.001) OCC (p=0.113) RACE (p=0.003)
6[e]	0.154 (243)	0.144 (243)	0.164 (249)	0.079	-0.0078 (0.0207)	0.707	AGE (p=0.093) CSMOK (p<0.001) OCC (p=0.144) RACE (p=0.004)

[a] Transformed from natural logarithm scale.

[b] 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.

[c] Slope and standard error based on natural logarithm of absolute neutrophils (bands) versus log_2 (current dioxin + 1).

[d] Adjusted for log_2 total lipids.

[e] 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.

Absolute Lymphocytes

Model 1 analyses investigating group differences in mean absolute lymphocytes between Ranch Hands and Comparisons did not reveal any significant results (Table 16-18(a,b): $p > 0.36$ for all contrasts). Current cigarette smoking history, occupation, and lifetime cigarette smoking history were retained in the adjusted analysis.

Results from the unadjusted and adjusted Model 2 analysis of absolute lymphocytes were nonsignificant (Table 16-18(c,d): $p > 0.31$ for both analyses). Significant covariates included current cigarette smoking and the age-by-race and the race-by-occupation interactions. All results investigating associations between categorized dioxin and absolute lymphocytes for Model 3 were nonsignificant (Table 16-18(e,f): $p > 0.45$). Lifetime cigarette smoking history and the current cigarette smoking-by-occupation interaction were retained in the final adjusted model.

None of the Model 4 through 6 unadjusted and adjusted analyses revealed significant results (Table 16-18(g,h): $p > 0.38$ for all analyses). Lifetime cigarette smoking and the age-by-race, occupation-by-race, and current cigarette smoking-by-occupation interactions were retained in all adjusted analyses.

Absolute Monocytes

The unadjusted and adjusted Model 1 results for absolute monocytes were nonsignificant (Table 16-19(a,b): $p \geq 0.39$ for all contrasts). The interaction of group and race was significant in the adjusted analysis. Results stratified by race are found in Appendix Table L-2-10. Adjusted results are based on a final model after deletion of this interaction. Additional covariates retained in the adjusted analysis included current cigarette smoking and lifetime cigarette smoking history.

A positive marginally significant association between initial dioxin and absolute monocytes was revealed in the Model 2 unadjusted analysis (Table 16-19(c): $p=0.069$, Slope$=0.0107$). Adjustment for race, current cigarette smoking, and lifetime cigarette smoking history, however, caused the association to become nonsignificant (Table 16-19(d): $p=0.104$). Both the unadjusted and adjusted Model 3 analyses revealed marginally significant differences between high Ranch Hands and Comparisons, with high Ranch Hands possessing the greater mean level of absolute monocytes (Table 16-19(e,f): $p=0.064$, Diff. of Mean$=0.032$ for the unadjusted analysis and $p=0.079$, Diff. of Adj. Mean$=0.030$ for the adjusted analysis). The remaining unadjusted and adjusted contrasts for Ranch Hands and Comparisons were nonsignificant ($p > 0.26$).

All results from the Model 4, 5, and 6 analyses of absolute monocytes were nonsignificant (Table 16-19(g,h): $p \geq 0.12$ for all analyses). Current cigarette smoking, lifetime cigarette smoking history, and the age-by-race interaction were retained in the adjusted analysis.

Table 16-18.
Analysis of Absolute Lymphocytes (thousand/mm^3)

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

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***946***	***1.937***	***-0.009 --***	***0.771***
	Comparison	***1,278***	***1.946***		
Officer	Ranch Hand	364	1.814	-0.024 --	0.585
	Comparison	501	1.837		
Enlisted Flyer	Ranch Hand	162	1.972	-0.052 --	0.541
	Comparison	201	2.024		
Enlisted Groundcrew	Ranch Hand	420	2.036	0.019 --	0.679
	Comparison	576	2.017		

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

Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]	Covariate Remarks[d]
All	***Ranch Hand***	***945***	***1.934***	***-0.019 --***	0.517	CSMOK ($p<0.001$)
	Comparison	***1,276***	***1.953***			OCC ($p<0.001$)
Officer	Ranch Hand	363	1.850	-0.025 --	0.577	PACKYR ($p=0.098$)
	Comparison	501	1.875			
Enlisted Flyer	Ranch Hand	162	1.931	-0.066 --	0.364	
	Comparison	201	1.997			
Enlisted Groundcrew	Ranch Hand	420	2.008	0.005 --	0.918	
	Comparison	574	2.003			

[a] Transformed from the natural logarithm scale.

[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

[c] P-values based on difference of means on natural logarithm scale.

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

Table 16-18. (Continued)
Analysis of Absolute Lymphocytes (thousand/mm^3)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	174	1.870	1.874	0.006	0.0129 (0.0129)	0.318
Medium	172	1.952	1.952			
High	171	1.990	1.986			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ad]	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
Low	174	1.782	0.094	0.0041 (0.0144)	0.773	CSMOK ($p<0.001$) AGE*RACE ($p=0.017$) RACE*OCC ($p=0.009$)
Medium	172	1.790				
High	171	1.823				

[a] Transformed from natural logarithm scale.

[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] Slope and standard error based on natural logarithm of absolute lymphocytes versus log_2 (initial dioxin).

[d] 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 16-18. (Continued)
Analysis of Absolute Lymphocytes (thousand/mm^3)

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

Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,061	1.931	1.930		
Background RH	371	1.905	1.909	-0.021 --	0.608
Low RH	259	1.907	1.909	-0.021 --	0.660
High RH	258	1.966	1.960	0.030 --	0.539
Low plus High RH	517	1.936	1.934	0.004 --	0.911

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

Dioxin Category	n	Adj. Mean[ae]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]	Covariate Remarks
Comparison	1,059	1.931			PACKYR (p=0.114) CSMOK*OCC (p=0.036)
Background RH	370	1.932	0.001 --	0.970	
Low RH	259	1.910	-0.021 --	0.662	
High RH	258	1.897	-0.034 --	0.484	
Low plus High RH	517	1.904	-0.027 --	0.459	

[a] Transformed from natural logarithm scale.

[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] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on natural logarithm scale.

[d] P-value is based on difference of means on natural logarithm scale.

[e] 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 16-18. (Continued)
Analysis of Absolute Lymphocytes (thousand/mm^3)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[b]	Current Dioxin Category Mean[a]/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Slope (Std. Error)[c]	p-Value
4	1.890 (292)	1.929 (299)	1.950 (297)	<0.001	0.0052 (0.0086)	0.549
5	1.882 (297)	1.934 (297)	1.954 (294)	0.001	0.0055 (0.0074)	0.461
6[d]	1.900 (296)	1.936 (297)	1.931 (294)	0.006	0.0006 (0.0080)	0.939

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[b]	Current Dioxin Category Adjusted Mean[a]/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
4	1.855 (291)	1.868 (299)	1.799 (297)	0.115	-0.0061 (0.0095)	0.524	PACKYR (p=0.083) AGE*RACE (p=0.006) OCC*RACE (p=0.020) CSMOK*OCC (p=0.011)
5	1.845 (296)	1.867 (297)	1.809 (294)	0.115	-0.0035 (0.0080)	0.660	PACKYR (p=0.081) AGE*RACE (p=0.007) OCC*RACE (p=0.020) CSMOK*OCC (p=0.010)
6[e]	1.865 (295)	1.874 (297)	1.794 (294)	0.116	-0.0075 (0.0087)	0.388	PACKYR (p=0.103) AGE*RACE (p=0.006) OCC*RACE (p=0.019) CSMOK*OCC (p=0.015)

[a] Transformed from natural logarithm scale.

[b] 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.

[c] Slope and standard error based on natural logarithm of absolute lymphocytes versus log_2 (current dioxin + 1).

[d] Adjusted for log_2 total lipids.

[e] 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 16-19.
Analysis of Absolute Monocytes (thousand/mm^3)

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

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***946***	***0.462***	***0.009 --***	***0.390***
	Comparison	***1,278***	***0.453***		
Officer	Ranch Hand	364	0.461	0.014 --	0.416
	Comparison	501	0.447		
Enlisted Flyer	Ranch Hand	162	0.456	-0.003 --	0.900
	Comparison	201	0.459		
Enlisted Groundcrew	Ranch Hand	420	0.466	0.009 --	0.549
	Comparison	576	0.457		

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

Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]	Covariate Remarks[d]
All	***Ranch Hand***	***945***	***0.450****	***0.006 --****	0.527**	GROUP*RACE (p=0.034)
	Comparison	***1,276***	***0.444****			CSMOK (p<0.001)
Officer	Ranch Hand	363	0.459**	0.013 --**	0.426**	PACKYR (p=0.081)
	Comparison	501	0.446**			
Enlisted Flyer	Ranch Hand	162	0.435**	-0.007 --**	0.780**	
	Comparison	201	0.442**			
Enlisted Groundcrew	Ranch Hand	420	0.451**	0.006 --**	0.696**	
	Comparison	574	0.445**			

[a] Transformed from the square root scale.

[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.

[c] P-values based on difference of means on square root scale.

[d] 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, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table L-2-10 for further analysis of this interaction.

Table 16-19. (Continued)
Analysis of Absolute Monocytes (thousand/mm^3)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	174	0.439	0.441	0.014	0.0107 (0.0059)	0.069
Medium	172	0.471	0.472			
High	171	0.486	0.482			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ad]	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
Low	174	0.414	0.066	0.0094 (0.0058)	0.104	CSMOK (p=0.006) PACKYR (p=0.017) RACE (p=0.054)
Medium	172	0.430				
High	171	0.449				

[a] Transformed from square root scale.

[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] Slope and standard error based on square root of absolute monocytes versus log_2 (initial dioxin).

[d] 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 16-19. (Continued)
Analysis of Absolute Monocytes (thousand/mm^3)

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

Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,061	0.448	0.448		
Background RH	371	0.459	0.462	0.014 --	0.348
Low RH	259	0.447	0.446	-0.002 --	0.895
High RH	258	0.482	0.480	0.032 --	0.064
Low plus High RH	517	0.465	0.463	0.015 --	0.266

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

Dioxin Category	n	Adj. Mean[ae]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]	Covariate Remarks
Comparison	1,059	0.449			AGE (p=0.107) CSMOK (p<0.001) PACKYR (p=0.025)
Background RH	370	0.461	0.012 --	0.430	
Low RH	259	0.445	-0.004 --	0.789	
High RH	258	0.479	0.030 --	0.079	
Low plus High RH	517	0.462	0.013 --	0.332	

[a] Transformed from square root scale.

[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] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on square root scale.

[d] P-value is based on difference of means on square root scale.

[e] 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 16-19. (Continued)
Analysis of Absolute Monocytes (thousand/mm^3)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED						
	Current Dioxin Category Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)		
Model[b]	Low	Medium	High	R^2	Slope (Std. Error)[c]	p-Value
4	0.461 (292)	0.442 (299)	0.484 (297)	0.002	0.0054 (0.0041)	0.191
5	0.462 (297)	0.438 (297)	0.488 (294)	0.002	0.0046 (0.0035)	0.190
6[d]	0.463 (296)	0.438 (297)	0.488 (294)	0.002	0.0040 (0.0038)	0.297

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED							
	Current Dioxin Category Adjusted Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)			
Model[b]	Low	Medium	High	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
4	0.446 (291)	0.428 (299)	0.470 (297)	0.047	0.0065 (0.0041)	0.120	CSMOK (p=0.001) PACKYR (p=0.023) AGE*RACE (p=0.015)
5	0.449 (296)	0.425 (297)	0.474 (294)	0.047	0.0053 (0.0035)	0.134	CSMOK (p=0.001) PACKYR (p=0.023) AGE*RACE (p=0.014)
6[e]	0.446 (295)	0.423 (297)	0.476 (294)	0.048	0.0058 (0.0038)	0.133	CSMOK (p=0.001) PACKYR (p=0.020) AGE*RACE (p=0.016)

[a] Transformed from square root scale.

[b] 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.

[c] Slope and standard error based on square root of absolute monocytes versus log_2 (current dioxin + 1).

[d] Adjusted for log_2 total lipids.

[e] 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.

Absolute Eosinophils

A sizable number of absolute eosinophil measurements collected at the laboratory examination were equal to 0 counts per mm^3 (259/2,224 or 11.6%). Consequently, this variable was analyzed in two ways. First, the proportion of zero measurements was analyzed for associations with exposure in a discrete analysis and secondly, nonzero measurements were investigated for an association with exposure in a continuous analysis.

In the Model 1 unadjusted analysis of zero versus nonzero measurements of absolute eosinophils, a significant overall difference between Ranch Hands and Comparisons was disclosed (Table 16-20(a1): $p=0.050$, Est. RR=0.76). A larger percentage of Comparisons possessed zero-valued measurements than Ranch Hands (12.8% vs. 10.0%). Analyses stratified by occupation revealed similar results in the officer category ($p=0.018$, Est. RR=0.59), where 15.0% of absolute eosinophil measurements for Comparisons equaled zero in contrast to only 9.3% for Ranch Hands. Contrasts in the enlisted flyer and enlisted groundcrew categories were nonsignificant ($p>0.29$). Results were identical in the adjusted analysis because no covariates were retained in the final model. In the continuous analyses of the nonzero-valued measurements for absolute eosinophils, no significant differences between Ranch Hands and Comparisons were observed (Table 16-20(a2-b2): $p>0.13$ for each analysis). Race, current cigarette smoking, and the age-by-lifetime cigarette smoking history interaction were significant.

The Model 2 analyses of the proportion of zero measurements for absolute eosinophils found no significant associations with initial dioxin (Table 16-20(c1-d1): $p>0.62$). Two significant initial dioxin interactions involving age and occupation were retained in the adjusted analysis ($p=0.026$ and $p<0.001$ respectively). Stratified results for each interaction are located in Appendix Table L-2-11(a-b). The final model also adjusted for race. Model 2 analyses on the nonzero measurements of absolute eosinophils also found no significant associations with initial dioxin (Table 16-20(c2-d2): $p\geq0.89$). Current cigarette smoking was retained in the final model.

The proportion of zero measurements was not significantly different between Ranch Hands and Comparisons in the Model 3 analyses of absolute eosinophils (Table 16-20(e1-f1): $p>0.27$ for each contrast). The age-by-current cigarette smoking interaction was retained in the adjusted analysis. The Model 3 adjusted analysis of the nonzero measurements of absolute eosinophils revealed a marginally significant negative difference between the low plus high Ranch Hand category and Comparisons (Table 16-20(f2): $p=0.098$, Diff. of Adj. Mean=-0.011). The remaining unadjusted and adjusted contrasts were nonsignificant (Table 16-20(e2-f2): $p>0.10$ for each contrast). Race, current cigarette smoking, and lifetime cigarette smoking history were retained in the adjusted analysis.

The unadjusted Model 4 analysis of zero versus nonzero measurements of absolute eosinophils revealed no significant association with current dioxin (Table 16-20(g1): $p=0.116$). Adjustment for the race-by-current cigarette smoking interaction led to a marginally significant positive association (Table 16-20(h1): $p=0.082$, Adj. RR=1.14). Marginally significant associations between the proportion of zero absolute eosinophil measurements and current dioxin also were observed in both the unadjusted and adjusted

Table 16-20.
Analysis of Absolute Eosinophils
(Zero versus Nonzero)

a1) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Zero**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***946***	***10.0***	***0.76 (0.58,0.99)***	***0.050***
	Comparison	***1,278***	***12.8***		
Officer	Ranch Hand	364	9.3	0.59 (0.38,0.90)	0.018
	Comparison	501	15.0		
Enlisted Flyer	Ranch Hand	162	8.0	0.64 (0.32,1.31)	0.293
	Comparison	201	11.9		
Enlisted Groundcrew	Ranch Hand	420	11.4	1.01 (0.68,1.51)	0.999
	Comparison	576	11.3		

b1) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks**
All	***0.76 (0.58,0.99)***	***0.050***	
Officer	0.59 (0.38,0.90)	0.018	
Enlisted Flyer	0.64 (0.32,1.31)	0.293	
Enlisted Groundcrew	1.01 (0.68,1.51)	0.999	

Table 16-20. (Continued)
Analysis of Absolute Eosinophils (thousand/mm^3)
(Nonzero Measurements)

a2) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Mean[a]**	**Difference of Means (95% C.I.)[b]**	**p-Value[c]**
All	***Ranch Hand***	***851***	***0.169***	***-0.004 --***	***0.502***
	Comparison	***1,114***	***0.172***		
Officer	Ranch Hand	330	0.167	-0.003 --	0.720
	Comparison	426	0.170		
Enlisted Flyer	Ranch Hand	149	0.163	-0.018 --	0.200
	Comparison	177	0.182		
Enlisted Groundcrew	Ranch Hand	372	0.172	0.001 --	0.873
	Comparison	511	0.171		

b2) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED						
Occupational Category	**Group**	**n**	**Adj. Mean[a]**	**Difference of Adj. Means (95% C.I.)[b]**	**p-Value[c]**	**Covariate Remarks[d]**
All	***Ranch Hand***	***850***	***0.158***	***-0.004 --***	0.373	RACE (p=0.026) CSMOK (p<0.001) AGE*PACKYR (p=0.034)
	Comparison	***1,112***	***0.162***			
Officer	Ranch Hand	329	0.159	-0.004 --	0.661	
	Comparison	426	0.162			
Enlisted Flyer	Ranch Hand	149	0.149	-0.018 --	0.133	
	Comparison	177	0.168			
Enlisted Groundcrew	Ranch Hand	372	0.160	0.000 --	0.999	
	Comparison	509	0.160			

[a] Transformed from the natural logarithm scale.

[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

[c] P-values based on difference of means on natural logarithm scale.

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

Table 16-20. (Continued)
Analysis of Absolute Eosinophils
(Zero versus Nonzero)

c1) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Zero	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	174	11.5	1.05 (0.86,1.29)	0.625
Medium	172	11.1		
High	171	9.9		

d1) 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
517	1.04 (0.82,1.31)**	0.769**	INIT*AGE (p=0.026) INIT*OCC (p<0.001) RACE (p=0.080)

[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 L-2-11 for further analysis of these interactions.

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

Table 16-20. (Continued)
Analysis of Absolute Eosinophils (thousand/mm^3)
(Nonzero Measurements)

c2) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	154	0.163	0.163	0.006	0.0036 (0.0271)	0.894
Medium	153	0.167	0.167			
High	154	0.158	0.158			

d2) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ad]	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
Low	154	0.166	0.041	-0.0037 (0.0267)	0.890	CSMOK ($p<0.001$)
Medium	153	0.165				
High	154	0.157				

[a] Transformed from natural logarithm scale.

[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] Slope and standard error based on natural logarithm of absolute eosinophils versus log_2 (initial dioxin).

[d] 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 16-20. (Continued)
Analysis of Absolute Eosinophils
(Zero versus Nonzero)

e1) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Percent Zero	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,061	11.8		
Background RH	371	9.2	0.81 (0.54,1.21)	0.305
Low RH	259	11.2	0.90 (0.59,1.39)	0.643
High RH	258	10.5	0.83 (0.53,1.29)	0.409
Low plus High RH	517	10.8	0.87 (0.62,1.21)	0.404

f1) 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	1,059			AGE*CSMOK (p=0.014)
Background RH	371	0.80 (0.53,1.20)	0.276	
Low RH	259	0.91 (0.59,1.40)	0.653	
High RH	258	0.83 (0.53,1.29)	0.400	
Low plus High RH	517	0.87 (0.62,1.21)	0.401	

[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 16-20. (Continued)
Analysis of Absolute Eosinophils (thousand/mm^3)
(Nonzero Measurements)

e2) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	936	0.173	0.173		
Background RH	337	0.175	0.175	0.002 --	0.785
Low RH	230	0.165	0.164	-0.009 --	0.316
High RH	231	0.161	0.161	-0.012 --	0.171
Low plus High RH	461	0.163	0.163	-0.010 --	0.126

f2) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Mean[ae]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]	Covariate Remarks
Comparison	934	0.162			RACE (p=0.034)
Background RH	336	0.164	0.002 --	0.797	CSMOK (p<0.001)
Low RH	230	0.154	-0.008 --	0.354	PACKYR (p=0.100)
High RH	231	0.149	-0.013 --	0.103	
Low plus High RH	461	0.151	-0.011 --	0.098	

[a] Transformed from natural logarithm scale.

[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] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on natural logarithm scale.

[d] P-value is based on difference of means on natural logarithm scale.

[e] 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 16-20. (Continued)
Analysis of Absolute Eosinophils
(Zero versus Nonzero)

g1) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Percent Zero/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) Est. Relative Risk (95% C.I.)[b]	p-Value
4	9.6 (292)	10.0 (299)	10.8 (297)	1.13 (0.97,1.30)	0.116
5	9.4 (297)	10.4 (297)	10.5 (294)	1.12 (0.98,1.27)	0.085
6[c]	9.5 (296)	10.4 (297)	10.5 (294)	1.11 (0.97,1.27)	0.144

h1) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[a]	Analysis Results for Log_2 (Current Dioxin + 1) n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	888	1.14 (0.99,1.32)	0.082	RACE*CSMOK (p=0.014)
5	888	1.13 (0.99,1.28)	0.065	RACE*CSMOK (p=0.015)
6[d]	887	1.12 (0.96,1.32)**	0.155**	CURR*OCC (p=0.043) RACE*CSMOK (p=0.026)

[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 L-2-11 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 16-20. (Continued)
Analysis of Absolute Eosinophils (thousand/mm^3)
(Nonzero Measurements)

g2) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[b]	Current Dioxin Category Mean[a]/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Slope (Std. Error)[c]	p-Value
4	0.174 (264)	0.167 (269)	0.163 (265)	0.002	-0.0243 (0.0181)	0.180
5	0.173 (269)	0.170 (266)	0.161 (263)	0.002	-0.0206 (0.0154)	0.182
6[d]	0.174 (268)	0.171 (266)	0.159 (263)	0.003	-0.0264 (0.0166)	0.113

h2) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[b]	Current Dioxin Category Adjusted Mean[a]/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
4	0.160 (263)	0.153 (269)	0.149 (265)	0.046	-0.0221 (0.0178)	0.213	RACE (p=0.060) CSMOK (p<0.001) PACKYR (p=0.044)
5	0.159 (268)	0.156 (266)	0.146 (263)	0.046	-0.0191 (0.0151)	0.205	RACE (p=0.058) CSMOK (p<0.001) PACKYR (p=0.042)
6[e]	0.159 (267)	0.156 (266)	0.146 (263)	0.046	-0.0212 (0.0164)	0.197	RACE (p=0.063) CSMOK (p<0.001) PACKYR (p=0.048)

[a] Transformed from natural logarithm scale.

[b] 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.

[c] Slope and standard error based on natural logarithm of absolute eosinophils versus log_2 (current dioxin + 1).

[d] Adjusted for log_2 total lipids.

[e] 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.

analyses for Model 5 (Table 16-20(g1-h1): p=0.085, Est. RR=1.12 and p=0.065, Adj. RR=1.13 respectively). The final model included the race-by-current cigarette smoking interaction. No significant associations with current dioxin were disclosed in the Model 6 analyses ($p > 0.14$). The adjusted analysis retained the current dioxin-by-occupation interaction (p=0.043). Results stratified by occupation are presented in Appendix Table L-2-11(c). When occupation was removed from this model, a marginally significant association between the proportion of zero measurements and current dioxin was observed (Table L-3-13: p=0.095, Adj. RR=1.13). In Models 4 through 6, all results from the continuous analyses of the nonzero measurements of absolute eosinophils were nonsignificant (Table 16-20(g2-h2): $p > 0.11$ for all analyses). Each final model adjusted for race, current cigarette smoking, and lifetime cigarette smoking history.

Absolute Basophils

Comparable to absolute neutrophils (bands) and absolute eosinophils, the substantial number of measurements equal to 0 thousand/mm^3 for absolute basophils (1,005/2,224 or 45.2%) necessitated two types of analyses: a discrete analysis on the proportion of zero measurements and a continuous analysis on the nonzero measurements.

No significant results were found in the Model 1 analyses investigating associations between group and the proportion of zero measurements for absolute basophils (Table 16-21(a1-b1): $p \geq 0.58$ for all analyses). Age, current cigarette smoking, and the race-by-lifetime cigarette smoking history interaction were retained in the final adjusted model. Model 1 results from the continuous unadjusted analysis of nonzero measurements for absolute basophils were nonsignificant (Table 16-21(a2): $p > 0.18$). In the adjusted analysis based on nonzero measurements, Ranch Hands in the enlisted flyer category possessed a marginally significant lower mean level of absolute basophils than Comparisons (Table 16-21(b2): p=0.094, Diff. of Adj. Means=-0.008). Race and current cigarette smoking were significant in the final adjusted model.

The Model 2 analyses examining zero versus nonzero measurements of absolute basophils revealed nonsignificant results (Table 16-21(c1-d1): $p > 0.66$). The adjusted analysis duplicated the unadjusted analysis because no covariates were retained in the final model. The unadjusted Model 2 analysis of absolute basophil measurements greater than 0 thousand/mm^3 disclosed a significant positive association with initial dioxin (Table 16-21(c2): p=0.037, Slope=0.0429). After adjusting for current cigarette smoking, the association with initial dioxin was marginally significant (Table 16-21(d2): p=0.092, slope=0.0334).

All results from the Model 3 analyses of zero versus nonzero measurements of absolute basophils were nonsignificant (Table 16-21(e1-f1): $p \geq 0.53$ for all analyses). Current cigarette smoking was retained in the adjusted analysis. Similarly, Model 3 continuous analyses on the nonzero measurements of absolute basophils were nonsignificant (Table 16-21(e2-f2): $p > 0.26$ for all analyses). Race, current cigarette smoking, and lifetime cigarette smoking history were retained.

The proportion of zero measurements for absolute basophils did not display a significant association with current dioxin in the Model 4, 5, and 6 unadjusted analyses (Table

Table 16-21.
Analysis of Absolute Basophils
(Zero versus Nonzero)

a1) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Zero**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***946***	***45.0***	***0.99 (0.84,1.17)***	***0.932***
	Comparison	***1,278***	***45.3***		
Officer	Ranch Hand	364	44.0	0.95 (0.72,1.24)	0.744
	Comparison	501	45.3		
Enlisted Flyer	Ranch Hand	162	43.2	0.92 (0.61,1.40)	0.774
	Comparison	201	45.3		
Enlisted Groundcrew	Ranch Hand	420	46.7	1.06 (0.82,1.36)	0.719
	Comparison	576	45.3		

b1) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***0.99 (0.83,1.17)***	***0.875***	AGE (p=0.065)
Officer	0.95 (0.72,1.25)	0.713	CSMOK (p=0.011)
Enlisted Flyer	0.89 (0.58,1.35)	0.580	RACE*PACKYR (p=0.012)
Enlisted Groundcrew	1.06 (0.82,1.36)	0.672	

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

Table 16-21. (Continued)
Analysis of Absolute Basophils (thousand/mm^3)
(Nonzero Measurements)

a2) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***520***	***0.091***	***0.002 --***	***0.500***
	Comparison	***699***	***0.089***		
Officer	Ranch Hand	204	0.088	0.003 --	0.348
	Comparison	274	0.085		
Enlisted Flyer	Ranch Hand	92	0.089	-0.008 --	0.186
	Comparison	110	0.097		
Enlisted Groundcrew	Ranch Hand	224	0.093	0.003 --	0.318
	Comparison	315	0.090		

b2) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]	Covariate Remarks[d]
All	***Ranch Hand***	***520***	***0.085***	***0.001 --***	***0.653***	RACE (p=0.011)
	Comparison	***698***	***0.084***			CSMOK (p<0.001)
Officer	Ranch Hand	204	0.083	0.003 --	0.360	
	Comparison	274	0.080			
Enlisted Flyer	Ranch Hand	92	0.081	-0.008 --	0.094	
	Comparison	110	0.089			
Enlisted Groundcrew	Ranch Hand	224	0.086	0.003 --	0.386	
	Comparison	314	0.083			

[a] Transformed from the natural logarithm scale.

[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

[c] P-values based on difference of means on natural logarithm scale.

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

Table 16-21. (Continued)
Analysis of Absolute Basophils
(Zero versus Nonzero)

c1) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Zero	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	174	45.4	0.97 (0.85,1.11)	0.669
Medium	172	41.3		
High	171	46.8		

d1) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[a]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
517	0.97 (0.85,1.11)	0.669	

[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.

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

Table 16-21. (Continued)
Analysis of Absolute Basophils (thousand/mm^3)
(Nonzero Measurements)

c2) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	95	0.084	0.084	0.016	0.0429 (0.0204)	0.037
Medium	101	0.087	0.087			
High	91	0.095	0.095			

d2) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ad]	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
Low	95	0.086	0.093	0.0334 (0.0197)	0.092	CSMOK ($p<0.001$)
Medium	101	0.087				
High	91	0.094				

[a] Transformed from natural logarithm scale.

[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] Slope and standard error based on natural logarithm of absolute basophils versus log_2 (initial dioxin).

[d] 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 16-21. (Continued)
Analysis of Absolute Basophils
(Zero versus Nonzero)

e1) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Percent Zero	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,061	46.1		
Background RH	371	45.8	0.98 (0.77,1.25)	0.876
Low RH	259	44.4	0.93 (0.70,1.22)	0.587
High RH	258	44.6	0.95 (0.72,1.25)	0.725
Low plus High RH	517	44.5	0.94 (0.76,1.16)	0.561

f1) 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	1,059			CSMOK (p=0.042)
Background RH	371	0.98 (0.77,1.25)	0.869	
Low RH	259	0.93 (0.71,1.22)	0.595	
High RH	258	0.94 (0.71,1.24)	0.659	
Low plus High RH	517	0.93 (0.76,1.16)	0.530	

[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 16-21. (Continued)
Analysis of Absolute Basophils (thousand/mm^3)
(Nonzero Measurements)

e2) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	572	0.089	0.089		
Background RH	201	0.091	0.092	0.003 --	0.370
Low RH	144	0.085	0.085	-0.004 --	0.262
High RH	143	0.093	0.092	0.003 --	0.333
Low plus High RH	287	0.089	0.088	-0.001 --	0.918

f2) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Mean[ae]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]	Covariate Remarks
Comparison	571	0.084			RACE (p=0.057) CSMOK (p<0.001) PACKYR (p=0.117)
Background RH	200	0.087	0.003 --	0.304	
Low RH	144	0.081	-0.003 --	0.316	
High RH	143	0.086	0.002 --	0.653	
Low plus High RH	287	0.083	-0.001 --	0.719	

[a] Transformed from natural logarithm scale.

[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] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on natural logarithm scale.

[d] P-value is based on difference of means on natural logarithm scale.

[e] 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 16-21. (Continued)
Analysis of Absolute Basophils
(Zero versus Nonzero)

g1) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Zero/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	44.5 (292)	46.5 (299)	44.1 (297)	0.98 (0.90,1.08)	0.715
5	44.4 (297)	46.8 (297)	43.9 (294)	0.99 (0.91,1.07)	0.767
6[c]	44.3 (296)	46.8 (297)	43.9 (294)	0.98 (0.90,1.07)	0.673

h1) 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	888	0.98 (0.90,1.08)	0.715	
5	888	0.99 (0.91,1.07)	0.767	
6[c]	887	0.98 (0.90,1.07)	0.673	

[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.

Table 16-21. (Continued)
Analysis of Absolute Basophils (thousand/mm^3)
(Nonzero Measurements)

g2) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[b]	Current Dioxin Category Mean[a]/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Slope (Std. Error)[c]	p-Value
4	0.090 (162)	0.087 (160)	0.091 (166)	<0.001	0.0056 (0.0143)	0.695
5	0.089 (165)	0.087 (158)	0.093 (165)	<0.001	0.0060 (0.0123)	0.624
6[d]	0.091 (165)	0.087 (158)	0.091 (165)	0.013	-0.0062 (0.0132)	0.640

h2) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[b]	Current Dioxin Category Adjusted Mean[a]/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
4	0.083 (162)	0.081 (160)	0.082 (166)	0.067	0.0014 (0.0139)	0.921	RACE (p=0.014) CSMOK (p<0.001)
5	0.081** (165)	0.081** (158)	0.083** (165)	0.077	0.0020 (0.0119)**	0.869**	CURR*RACE (p=0.023) CSMOK (p<0.001)
6[e]	0.083** (165)	0.082** (158)	0.082** (165)	0.086	-0.0079 (0.0128)**	0.537**	CURR*RACE (p=0.019) CSMOK (p<0.001)

[a] Transformed from natural logarithm scale.

[b] 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.

[c] Slope and standard error based on natural logarithm of absolute basophils versus log_2 (current dioxin + 1).

[d] Adjusted for log_2 total lipids.

[e] 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 L-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.

16-21(g1): $p>0.67$). The adjusted analysis was identical to the unadjusted analysis because no covariates were retained in the final model. All results from the Model 4, 5, and 6 continuous analyses of nonzero measurements for absolute basophils were nonsignificant (Table 16-21(g2-h2): $p>0.53$ for all analyses). The Model 5 and Model 6 adjusted analyses retained a significant interaction between current dioxin and race. Appendix Table L-2-12 shows results from these two models stratified by race. Current cigarette smoking was retained in all three adjusted analyses, and race was additionally retained in the Model 4 analysis.

Longitudinal Analysis

Laboratory Examination Variables

Longitudinal analyses were conducted on platelet count, both in the continuous form and discretized as abnormally high versus normal and abnormal low combined. The purpose of these analyses were to examine whether changes over 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 the longitudinal analyses because current dioxin is the measure of exposure in these models. Current dioxin changes over time and is not available for all participants for 1982 and 1992.

Longitudinal analyses for the continuous form of platelet count examined the paired difference between the measurements from 1982 and 1992. These paired differences measured the change in the ratio over time. Each of the three models used in the longitudinal analysis was adjusted for age and the platelet count measured in 1982. The analyses of 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.

For the discretized longitudinal analysis of platelet count, relative risks at the 1992 examination were examined for participants who were classified as "normal" or "abnormal low" at the 1982 examination. Participants classified as "abnormal" at the 1982 examination were excluded because the focus of the analyses was on investigating the temporal effects of dioxin during the period between 1982 and 1992. Participants classified as "abnormal" in 1982 already were abnormal before this period; consequently, only participants classified as "normal" or "abnormal low" at the 1982 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 between 1982 and 1992. 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.

Platelet Count (Continuous)

Platelet count group differences of examination mean change (from 1982 to 1992) overall and within the enlisted flyer and enlisted groundcrew strata were nonsignificant (Table 16-22(a): $p>0.44$ for each analysis). The officer stratum displayed a marginally

Table 16-22.
Longitudinal Analysis of Platelet Count (thousand/mm^3)
(Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Mean[a]/(n) Examination 1982	1985	1987	1992	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
All	*Ranch Hand*	*273.9 (891)*	*268.1 (866)*	*261.1 (859)*	*250.7 (891)*	*-23.1*	*-5.2*	*0.444*
	Comparison	*262.9 (1,058)*	*264.4 (1,033)*	*255.4 (1,027)*	*244.9 (1,058)*	*-18.0*		
Officer	Ranch Hand	263.0 (335)	258.8 (328)	253.6 (328)	238.9 (335)	-24.1	-7.1	0.068
	Comparison	258.2 (401)	262.5 (393)	252.7 (387)	241.1 (401)	-17.1		
Enlisted Flyer	Ranch Hand	281.8 (158)	272.6 (156)	265.2 (153)	256.0 (158)	-25.9	-4.5	0.576
	Comparison	261.8 (174)	257.0 (171)	246.6 (172)	240.5 (174)	-21.4		
Enlisted Groundcrew	Ranch Hand	280.0 (398)	274.4 (382)	266.0 (378)	258.8 (398)	-21.2	-3.7	0.830
	Comparison	267.1 (483)	268.6 (469)	260.8 (468)	249.6 (483)	-17.5		

[a] Transformed from square root scale.

[b] Difference between 1992 and 1982 examination means after transformation to original scale.

[c] P-value is based on analysis of square root of platelet count; results adjusted for square root of platelet count 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 16-22. (Continued)
Longitudinal Analysis of Platelet Count (thousand/mm^3)
(Continuous)

b) MODEL 2: RANCH HANDS — INITIAL DIOXIN						
	Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]	
	Mean[a]/(n) Examination					
Initial Dioxin	1982	1985	1987	1992	Adj. Slope (Std. Error)	p-Value
Low	264.6 (167)	263.5 (163)	254.7 (165)	245.2 (167)	0.0224 (0.0442)	0.612
Medium	281.3 (168)	271.3 (162)	266.9 (164)	253.0 (168)		
High	279.3 (165)	271.9 (162)	266.1 (159)	258.3 (165)		

[a] Transformed from square root scale.

[b] Results based on difference between square root of platelet count in 1992 and square root of platelet count 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 the date of the blood draw for dioxin, square root of 1982 platelet count, 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 16-22. (Continued)
Longitudinal Analysis of Platelet Count (thousand/mm^3)
(Continuous)

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY							
Dioxin Category	Mean[a]/(n) Examination 1982	1985	1987	1992	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
Comparison	261.6 (912)	263.4 (899)	254.4 (898)	244.4 (912)	-17.2		
Background RH	271.0 (337)	266.3 (333)	259.2 (331)	246.9 (337)	-24.1	-7.0	0.097
Low RH	268.4 (249)	264.4 (242)	257.1 (246)	245.6 (249)	-22.8	-5.6	0.510
High RH	281.7 (251)	273.3 (245)	268.0 (242)	258.7 (251)	-23.0	-5.8	0.755
Low plus High RH	275.0 (500)	268.9 (487)	262.5 (488)	252.1 (500)	-22.9	-5.7	0.819

[a] Transformed from square root scale.

[b] Difference between 1992 and 1982 examination means after transformation to original scale.

[c] P-value is based on analysis of square root of platelet count; 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, square root of platelet count in 1982, 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.
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.

significant difference of examination mean change between Ranch Hands and Comparisons ($p=0.068$, Diff. of Exam. Mean Change= -7.1).

The Model 2 longitudinal analysis of platelet count in continuous form was not significant (Table 16-22(b): $p=0.612$). For Model 3, the difference of examination mean change between background Ranch Hands and Comparisons was marginally significant (Table 16-22(c): $p=0.097$, Diff. of Exam. Mean Change= -7.0). The background Ranch Hands exhibited a larger decrease in platelet count means from 1982 to 1992 than Comparisons. The remaining Model 3 contrasts were not significant (Table 16-22(c): $p \geq 0.51$ for each analysis).

Platelet Count (Discrete)

The longitudinal analysis of platelet count in discrete form was conditioned on participants who had either low or normal platelet counts in 1982. The longitudinal analysis for Model 1 did not detect a significant difference between Ranch Hands and Comparisons in the percentage of participants with normal or low platelet counts in 1982 and abnormally high platelet counts in 1992 (Table 16-23(a): $p > 0.52$ for all analyses).

Model 2 did not show a significant relationship between initial dioxin and abnormally high platelet counts in 1992, conditioned on normal or low platelet counts in 1982 (Table 16-23(b): $p=0.272$).

The Model 3 longitudinal analysis of abnormally high platelet counts detected a marginally significant relative risk for the high Ranch Hand category (Table 16-23(c): $p=0.072$, Adj. RR=3.24). Among Ranch Hands in the high dioxin category with either low or normal platelet counts during the 1982 examination, 2.0 percent had abnormally high platelet counts in 1992, while only 0.6 percent of Comparisons with either low or normal platelet counts during the 1982 examination had abnormally high platelet counts at the 1992 examination. The remaining contrasts in Model 3 were nonsignificant ($p > 0.25$).

DISCUSSION

The variables analyzed in this chapter serve as indices of the three peripheral blood lines (erythrocytes, leukocytes, and platelets). These variables are heavily relied upon to reflect disease of the hematopoietic system and also to alert the clinician to the presence of disease in other organ systems. The total WBC count varies across a broad range of disease states. Though lacking specificity, leukocytosis or leukopenia can serve as a sensitive clue to the presence of a host of infections, inflammatory and neoplastic disorders, and can point to the need for further investigation.

As elements essential to normal coagulation, the platelets have a short half-life and are most subject to decreased survival in the presence of a wide range of diseases, toxic chemical exposure, and numerous prescription and over-the-counter medications. The normal range ($130{,}000/mm^3$ to $400{,}000/mm^3$) allows subtle changes in platelet survival to occur and not be identified as abnormal. Furthermore, small differences in the total platelet count do not have a clinically significant effect on clotting mechanisms.

Table 16-23.
Longitudinal Analysis of Platelet Count
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Percent Abnormal High/(n) Examination			
		1982	1985	1987	1992
All	***Ranch Hand***	***0.8 (891)***	***1.8 (866)***	***2.2 (859)***	***1.2 (891)***
	Comparison	***1.0 (1,058)***	***1.6 (1,033)***	***1.5 (1,027)***	***1.0 (1,058)***
Officer	Ranch Hand	0.6 (335)	2.1 (328)	1.8 (328)	0.3 (335)
	Comparison	0.5 (401)	1.0 (393)	1.3 (387)	0.7 (401)
Enlisted Flyer	Ranch Hand	0.6 (158)	1.9 (156)	3.3 (153)	1.3 (158)
	Comparison	1.7 (174)	1.8 (171)	0.6 (172)	1.1 (174)
Enlisted Groundcrew	Ranch Hand	1.0 (398)	1.6 (382)	2.1 (378)	2.0 (398)
	Comparison	1.0 (483)	2.1 (469)	1.9 (468)	1.0 (483)

Occupational Category	Group	Abnormal Low or Normal in 1982			
		n in 1992	Percent Abnormal High in 1992	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	***Ranch Hand***	***884***	***0.8***	***1.18 (0.41,3.39)***	***0.752***
	Comparison	***1,048***	***0.7***		
Officer	Ranch Hand	333	0.0	--	--
	Comparison	399	0.5		
Enlisted Flyer	Ranch Hand	157	1.3	2.19 (0.20,24.45)	0.523
	Comparison	171	0.6		
Enlisted Groundcrew	Ranch Hand	394	1.3	1.53 (0.41,5.69)	0.529
	Comparison	478	0.8		

[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.

--: Adjusted relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities.

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 abnormal low or normal platelet counts in 1982 (see Chapter 7, Statistical Methods).

Table 16-23. (Continued)
Longitudinal Analysis of Platelet Count
(Discrete)

b) MODEL 2: RANCH HANDS — INITIAL DIOXIN

Initial Dioxin	Percent Abnormal High/(n) Examination			
	1982	1985	1987	1992
Low	0.6 (167)	1.2 (163)	2.4 (165)	0.6 (167)
Medium	0.6 (168)	1.2 (162)	3.1 (164)	1.8 (168)
High	0.6 (165)	1.9 (162)	2.5 (159)	3.0 (165)

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
	Abnormal Low or Normal in 1982			
Initial Dioxin	n in 1992	Percent Abnormal High in 1992	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	166	0.0	1.41 (0.77,2.57)	0.272
Medium	167	1.2		
High	164	2.4		

[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 abnormal low or normal platelet counts in 1982 (see Chapter 7, Statistical Methods).

Table 16-23. (Continued)
Longitudinal Analysis of Platelet Count
(Discrete)

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY				
	Percent Abnormal High/(n) Examination			
Dioxin Category	1982	1985	1987	1992
Comparison	0.9 (912)	1.6 (899)	1.3 (898)	0.8 (912)
Background RH	1.2 (337)	2.1 (333)	1.8 (331)	0.3 (337)
Low RH	0.4 (249)	1.2 (242)	2.0 (246)	0.8 (249)
High RH	0.8 (251)	1.6 (245)	3.3 (242)	2.8 (251)
Low plus High RH	0.6 (500)	1.4 (487)	2.7 (488)	1.8 (500)

	Abnormal Low or Normal in 1982			
Dioxin Category	n in 1992	Percent Abnormal High in 1992	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
Comparison	904	0.6		
Background RH	333	0.0	--	--
Low RH	248	0.4	0.71 (0.08,6.15)	0.755
High RH	249	2.0	3.24 (0.90,11.70)	0.072
Low plus High RH	497	1.2	2.00 (0.60,6.66)	0.258

[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 $\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.
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 abnormal low or normal platelet counts in 1982 (see Chapter 7, Statistical Methods).

Of the 13 laboratory variables examined, only the analyses of the platelet count yielded significant positive results. In the enlisted flyer and enlisted groundcrew occupational categories, mean platelet counts in continuous (but not discrete) form were significantly higher in Ranch Hands than in Comparisons; though the difference in the means (14,100/mm^3 and 9,200/mm^3 for enlisted flyers and enlisted groundcrew respectively) cannot be considered clinically significant.

Very few of the serum dioxin analyses yielded significant results. By both unadjusted and adjusted analysis, Ranch Hands with high extrapolated initial levels of serum dioxin had significantly higher mean platelet counts than Comparisons. In the unadjusted continuous analyses of the three models employing current serum dioxin and in a pattern consistent with a positive dose-response, mean platelet counts were increased in Ranch Hands with higher levels of serum dioxin. When adjusted for covariates, however, the findings were no longer significant. In the unadjusted discrete analyses, Ranch Hands with the highest levels of current serum dioxin were most at risk for an elevated platelet count and in Model 4 (lipid-adjusted current dioxin), the findings remained significant after adjustment for covariates. Although of uncertain biologic significance, these results are consistent with those noted in the 1987 Followup Report, and the Serum Dioxin Analysis Report.

In the 1987 examinations, the mean WBC and platelet counts and the erythrocyte sedimentation rates (ESR) were higher in Ranch Hands than in Comparisons, raising the possibility of a subclinical inflammatory response associated with prior dioxin exposure. In the current study, no group differences were noted in either the WBC or, as reported in Chapter 9, General Health, the ESR. Furthermore, in the current study, current serum dioxin was inversely related to the prevalence of abnormally elevated WBC counts.

Dependent variable-covariate associations confirmed numerous observations that have been well established in clinical practice. In cigarette smokers, cellular hypoxia related to carboxyhemoglobin formation and systemic arterial desaturation in obstructive airway disease combine to raise the hemoglobin and hematocrit in comparison to non-smokers. The increased incidence of chronic bronchitis in smokers is often associated with an elevation in the total WBC count. Older participants were found to have statistically significant reductions in the total RBC count, hemoglobin, and hematocrit, associations that may reflect the increased incidence of chronic disease associated with age.

Race-related associations also were noted. When compared to non-Black participants, Black participants had statistically significant reductions in the RBC indices, findings that may relate to the increased incidence of glucose-6-phosphate dehydrogenase (G-6-PD) deficiency and of hemoglobin variants (S and C) associated with heterozygous sickling disorders. Blacks were found to have a greater prevalence of abnormally low WBC counts than non-Blacks (13.0% versus 3.1%), though the difference in the means (6,580/mm^3 vs. 7,430/mm^3) is not likely of clinical significance.

The longitudinal analyses documented a gradual reduction in the total platelet count in each cohort and across all occupational strata. As in the 1987 followup report, Ranch Hands continue to have a greater reduction in the total platelet count over time than do Comparisons, although the current means (250,700/mm^3 vs. 244,900/mm^3) are nearly equal.

In summary, the results of the current study reveal no evidence for any hematopoietic toxicity associated with prior dioxin exposure. Based on the analyses of three indices noted above (WBC, ESR, and total platelet count), there is no longer evidence that a subclinical inflammatory reaction may be present in Ranch Hands.

SUMMARY

The assessment of the hematologic system comprised analyses on 13 dependent laboratory endpoints. Associations with group (Model 1), initial dioxin (Model 2), categorized dioxin (Model 3), and current dioxin (Models 4, 5, and 6) were examined for each variable. Continuous and discrete analyses were performed for each cell count variable as well as for prothrombin time. In addition, due to the large number of nonzero measurements for absolute neutrophils (bands), absolute eosinophils, and absolute basophils, investigations on these variables incorporated two analyses. First, a discrete analysis was executed on the proportion of zero measurements and secondly, a continuous analysis was performed on the nonzero measurements. Summarized results from the analyses are presented in Tables 16-24 through 16-27. Significant group-by-covariate and dioxin-by-covariate interactions found in the six exposure analyses are listed in Table 16-28.

Model 1: Group Analysis

Analyses on the hematologic cell count variables disclosed significant group effects for platelet count only. Mean platelet count levels were significantly greater for Ranch Hands than for Comparisons in the enlisted flyer and enlisted groundcrew strata of the unadjusted analysis and in the overall, enlisted flyer, and enlisted groundcrew strata of the adjusted analysis. In the unadjusted and adjusted RBC count analyses of all participants, Ranch Hands possessed a marginally significantly greater percentage of abnormally low levels of RBC count than did Comparisons. Analysis restricted to officers detected a marginally greater percentage of abnormally high hemoglobin levels in Ranch Hands than in Comparisons. In the group analyses of the cell count variables, several group-by-covariate interactions were retained, most of which involved one of the smoking risk factors.

Few significant results were observed in the group analyses of the absolute blood count variables. In the adjusted analysis of enlisted flyers, the difference between Ranch Hands and Comparisons in mean levels of nonzero absolute neutrophil (bands) and absolute basophil measurements were significant and marginally significant respectively, with Ranch Hands having a lower mean than Comparisons. Also, the proportion of nonzero measurements for absolute eosinophils was significantly greater for Comparisons than for Ranch Hands for all participants and within the officer category.

Means and abnormality percentages for the remaining hematology variables, prothrombin time, and RBC morphology did not differ significantly between Ranch Hands and Comparisons.

Table 16-24.
Summary of Group Analyses (Model 1) for Hematology Variables (Ranch Hands vs. Comparisons)

Variable	UNADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Laboratory				
Red Blood Cell (RBC) Count (C)	ns	ns	ns	ns
Red Blood Cell (RBC) Count (D)				
Abnormal Low vs. Normal	NS*	NS	NS	NS
Abnormal High vs. Normal	ns	ns	ns	NS
White Blood Cell (WBC) Count (C)	NS	NS	NS	NS
White Blood Cell (WBC) Count (D)				
Abnormal Low vs. Normal	NS	ns	NS	ns
Abnormal High vs. Normal	NS	NS	NS	NS
Hemoglobin (C)	NS	NS	ns	NS
Hemoglobin (D)				
Abnormal Low vs. Normal	NS	ns	NS	NS
Abnormal High vs. Normal	NS	NS	NS	NS
Hematocrit (C)	NS	NS	ns	ns
Hematocrit (D)	NS	ns	NS	NS
Platelet Count (C)	NS	ns	+0.016	+0.011
Platelet Count (D)	NS	ns	NS	NS
Prothrombin Time (C)	NS	NS	NS	ns
Prothrombin Time (D)	NS	NS	NS	NS
RBC Morphology (D)	ns	NS	NS	ns
Absolute Neutrophils (segs) (C)	NS	NS	ns	NS
Absolute Neutrophils (bands) (Zero vs. Nonzero) (D)	NS	NS	ns	NS
Absolute Neutrophils (bands) (Nonzero Measurements) (C)	NS	NS	ns	NS
Absolute Lymphocytes (C)	ns	ns	ns	NS
Absolute Monocytes (C)	NS	NS	ns	NS
Absolute Eosinophils (Zero vs. Nonzero) (D)	-0.050	-0.018	ns	NS
Absolute Eosinophils (Nonzero Measurements) (C)	ns	ns	ns	NS
Absolute Basophils (Zero vs. Nonzero) (D)	ns	ns	ns	NS
Absolute Basophils (Nonzero Measurements) (C)	NS	NS	ns	NS

C: Continuous analysis.
D: Discrete analysis.
+: Difference of means nonnegative.
-: Relative risk < 1.00.
NS or ns: Not significant ($p > 0.10$).
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 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 16-24. (Continued)
Summary of Group Analyses (Model 1) for Hematology Variables
(Ranch Hands vs. Comparisons)

Variable	ADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Laboratory				
Red Blood Cell (RBC) Count (C)	****	****	****	****
Red Blood Cell (RBC) Count (D)				
Abnormal Low vs. Normal	NS*	NS	NS	NS
Abnormal High vs. Normal	ns	ns	ns	NS
White Blood Cell (WBC) Count (C)	**(NS)	**(NS)	**(ns)	**(NS)
White Blood Cell (WBC) Count (D)				
Abnormal Low vs. Normal	NS	ns	NS	NS
Abnormal High vs. Normal	NS	NS	ns	NS
Hemoglobin (C)	**(ns)	**(NS)	**(ns)	**(ns)
Hemoglobin (D)				
Abnormal Low vs. Normal	NS	ns	NS	NS
Abnormal High vs. Normal	NS	NS*	NS	ns
Hematocrit (C)	**(ns)	**(NS)	**(ns)	**(ns)
Hematocrit (D)	NS	ns	NS	NS
Platelet Count (C)	**(+0.036)	ns	+0.014	+0.010
Platelet Count (D)	NS	ns	NS	NS
Prothrombin Time (C)	NS	NS	NS	ns
Prothrombin Time (D)	NS	NS	NS	NS
RBC Morphology (D)	ns	ns	NS	ns
Absolute Neutrophils (segs) (C)	NS	NS	ns	NS
Absolute Neutrophils (bands) (Zero vs. Nonzero) (D)	NS	NS	ns	NS
Absolute Neutrophils (bands) (Nonzero Measurements) (C)	ns	NS	-0.038	NS
Absolute Lymphocytes (C)	ns	ns	ns	NS
Absolute Monocytes (C)	**(NS)	**(NS)	**(ns)	**(NS)
Absolute Eosinophils (Zero vs. Nonzero) (D)	-0.050	-0.018	ns	NS
Absolute Eosinophils (Nonzero Measurements) (C)	ns	ns	ns	NS
Absolute Basophils (Zero vs. Nonzero) (D)	ns	ns	ns	NS
Absolute Basophils (Nonzero Measurements) (C)	NS	NS	ns*	NS

C: Continuous analysis.
D: Discrete analysis.
+: Difference of means nonnegative.
-: Relative risk < 1.00.
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 L-2 for further analysis of this interaction.
**(+0.036): Group-by-covariate interaction ($0.01 < p \leq 0.05$); significant when interaction is deleted and p-value is given in parentheses; refer to Appendix L-2 for further analysis of this interaction.
**** Group-by-covariate interaction ($p \leq 0.01$); refer to Appendix L-2 for further analysis of this interaction.
Note: 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 16-25.
Summary of Initial Dioxin Analyses (Model 2) for Hematology Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Laboratory		
Red Blood Cell (RBC) Count (C)	NS	NS
Red Blood Cell (RBC) Count (D)		
Abnormal Low vs. Normal	ns	ns
Abnormal High vs. Normal	NS	NS
White Blood Cell (WBC) Count (C)	NS*	**(NS)
White Blood Cell (WBC) Count (D)		
Abnormal Low vs. Normal	ns	ns
Abnormal High vs. Normal	ns	ns
Hemoglobin (C)	+0.029	NS
Hemoglobin (D)		
Abnormal Low vs. Normal	ns	ns
Abnormal High vs. Normal	NS	NS
Hematocrit (C)	+0.015	NS*
Hematocrit (D)	NS	NS
Platelet Count (C)	+0.025	NS
Platelet Count (D)	NS	NS
Prothrombin Time (C)	NS	**(+0.019)
Prothrombin Time (D)	ns	ns
RBC Morphology (D)	ns	NS
Absolute Neutrophils (segs) (C)	NS	**(NS)
Absolute Neutrophils (bands) (Zero vs. Nonzero) (D)	ns	**(ns)
Absolute Neutrophils (Nonzero Measurements) (bands) (C)	NS	**(ns)
Absolute Lymphocytes (C)	NS	NS
Absolute Monocytes (C)	NS*	NS
Absolute Eosinophils (Zero vs. Nonzero) (D)	NS	**(NS)
Absolute Eosinophils (Nonzero Measurements) (C)	NS	ns
Absolute Basophils (Zero vs. Nonzero) (D)	ns	ns
Absolute Basophils (Nonzero Measurements) (C)	+0.037	NS*

C: Continuous analysis.
D: Discrete analysis.
+: Slope nonnegative.
NS or ns: Not significant ($p > 0.10$).
NS*: Marginally significant ($0.05 < p \leq 0.10$).
**(NS) or **(ns): Log_2 (initial dioxin)-by-covariate interaction ($p \leq 0.05$); not significant when interaction is deleted; refer to Appendix L-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 16-26.
Summary of Categorized Dioxin Analyses (Model 3) for Hematology 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
Laboratory				
Red Blood Cell (RBC) Count (C)	ns	ns	ns	ns
Red Blood Cell (RBC) Count (D)				
Abnormal Low vs. Normal	+0.049	NS*	ns	NS
Abnormal High vs. Normal	ns	NS	ns	ns
White Blood Cell (WBC) Count (C)	ns	NS	NS*	NS
White Blood Cell (WBC) Count (D)				
Abnormal Low vs. Normal	ns	NS	NS	NS
Abnormal High vs. Normal	NS	NS	NS	NS
Hemoglobin (C)	NS	ns	NS	NS
Hemoglobin (D)				
Abnormal Low vs. Normal	NS	NS	ns	NS
Abnormal High vs. Normal	NS	NS	NS	NS
Hematocrit (C)	NS	ns*	NS	ns
Hematocrit (D)	NS*	NS	NS	NS
Platelet Count (C)	ns	NS	+<0.001	+0.004
Platelet Count (D)	ns	ns	+0.027	NS
Prothrombin Time (C)	NS	ns	ns	ns
Prothrombin Time (D)	NS	NS	ns	NS
RBC Morphology (D)	ns	ns	ns	ns
Absolute Neutrophils (segs) (C)	ns	ns	NS*	NS
Absolute Neutrophils (bands) (Zero vs. Nonzero) (D)	NS	NS	ns	NS
Absolute Neutrophils (bands) (Nonzero Measurements) (C)	NS	NS	ns	ns
Absolute Lymphocytes (C)	ns	ns	NS	NS
Absolute Monocytes (C)	NS	ns	NS*	NS
Absolute Eosinophils (Zero vs. Nonzero) (D)	ns	ns	ns	ns
Absolute Eosinophils (Nonzero Measurements) (C)	NS	ns	ns	ns
Absolute Basophils (Zero vs. Nonzero) (D)	ns	ns	ns	ns
Absolute Basophils (Nonzero Measurements) (C)	NS	ns	NS	ns

C: Continuous analysis.
D: Discrete analysis.
+: Relative risk $\geq$ 1.00 for discrete analysis or difference of means nonnegative for continuous analysis.
NS or ns: Not significant ($p > 0.10$).
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 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 16-26. (Continued)
Summary of Categorized Dioxin Analyses (Model 3) for Hematology 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
Laboratory				
Red Blood Cell (RBC) Count (C)	**(ns)	**(ns)	**(ns*)	**(ns*)
Red Blood Cell (RBC) Count (D)				
Abnormal Low vs. Normal	NS*	NS	ns	NS
Abnormal High vs. Normal	ns	ns	ns	ns
White Blood Cell (WBC) Count (C)	NS	NS	NS	NS
White Blood Cell (WBC) Count (D)				
Abnormal Low vs. Normal	NS	NS	NS	NS
Abnormal High vs. Normal	NS	NS	ns	NS
Hemoglobin (C)	**(NS)	**(ns)	**(NS)	**(ns)
Hemoglobin (D)				
Abnormal Low vs. Normal	NS	NS	ns	NS
Abnormal High vs. Normal	NS	NS	NS	NS
Hematocrit (C)	**(NS)	**(ns)	**(NS)	**(ns)
Hematocrit (D)	NS	NS	NS	NS
Platelet Count (C)	NS	NS	+<0.001	+0.010
Platelet Count (D)	ns	ns	+0.029	NS
Prothrombin Time (C)	**(NS)	**(ns)	**(ns)	**(ns)
Prothrombin Time (D)	NS	NS	NS	NS
RBC Morphology (D)	-0.049	ns	NS	ns
Absolute Neutrophils (segs) (C)	ns	NS	NS	NS
Absolute Neutrophils (bands) (Zero vs. Nonzero) (D)	****	****	****	****
Absolute Neutrophils (bands) (Nonzero Measurements) (C)	ns	NS	ns	NS
Absolute Lymphocytes (C)	NS	ns	ns	ns
Absolute Monocytes (C)	NS	ns	NS*	NS
Absolute Eosinophils (Zero vs. Nonzero) (D)	ns	ns	ns	ns
Absolute Eosinophils (Nonzero Measurements) (C)	NS	ns	ns	ns*
Absolute Basophils (Zero vs. Nonzero) (D)	ns	ns	ns	ns
Absolute Basophils (Nonzero Measurements) (C)	NS	ns	NS	ns

C: Continuous analysis.
D: Discrete analysis.
+: Relative risk $\geq$ 1.00 for discrete analysis or difference of means nonnegative for continuous analysis.
-: Difference of means negative.
NS or ns: Not significant ($p > 0.10$).
NS* or ns*: Marginally significant ($0.05 < p \leq 0.10$).
**(NS) or **(ns): Categorized dioxin-by-covariate interaction ($p \leq 0.05$); not significant when interaction is deleted; refer to Appendix L-2 for further analysis of this interaction.
**(ns*): Categorized dioxin-by-covariate interaction ($p \leq 0.05$); marginally significant when interaction is deleted; refer to Appendix L-2 for further analysis of this interaction.
**** Categorized dioxin-by-covariate interaction ($p \leq 0.01$); refer to Appendix L-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 16-27.
Summary of Current Dioxin Analyses (Models 4, 5, and 6) for Hematology 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
Laboratory			
Red Blood Cell (RBC) Count (C)	NS*	+0.042	NS
Red Blood Cell (RBC) Count (D)			
Abnormal Low vs. Normal	ns	ns	ns
Abnormal High vs. Normal	NS	NS	NS
White Blood Cell (WBC) Count (C)	NS	NS	NS
White Blood Cell (WBC) Count (D)			
Abnormal Low vs. Normal	NS	NS	NS
Abnormal High vs. Normal	ns	ns	ns
Hemoglobin (C)	NS	NS	NS
Hemoglobin (D)			
Abnormal Low vs. Normal	ns	ns	ns
Abnormal High vs. Normal	NS	NS	NS
Hematocrit (C)	NS	NS	NS
Hematocrit (D)	NS	NS	NS
Platelet Count (C)	+0.033	+0.018	+0.045
Platelet Count (D)	+0.014	+0.017	+0.016
Prothrombin Time (C)	ns	ns	NS
Prothrombin Time (D)	ns	ns	ns
RBC Morphology (D)	NS	NS	NS
Absolute Neutrophils (segs) (C)	NS	NS	NS
Absolute Neutrophils (bands) (Zero vs. Nonzero) (D)	NS	NS	NS
Absolute Neutrophils (bands) (Nonzero Measurements) (C)	ns	ns	ns
Absolute Lymphocytes (C)	NS	NS	NS
Absolute Monocytes (C)	NS	NS	NS
Absolute Eosinophils (Zero vs. Nonzero) (D)	NS	NS*	NS
Absolute Eosinophils (Nonzero Measurements) (C)	ns	ns	ns
Absolute Basophils (Zero vs. Nonzero) (D)	ns	ns	ns
Absolute Basophils (Nonzero Measurements) (C)	NS	NS	ns

C: Continuous analysis.
D: Discrete analysis.
+: Relative risk $\geq$ 1.00 for discrete analysis or slope nonnegative for continuous analysis.
NS or ns: Not significant ($p > 0.10$).
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 or slope negative for continuous analysis.

Table 16-27. (Continued)
Summary of Current Dioxin Analyses (Models 4, 5, and 6) for Hematology 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
Laboratory			
Red Blood Cell (RBC) Count (C)	NS	NS*	NS
Red Blood Cell (RBC) Count (D)			
Abnormal Low vs. Normal	ns	ns	ns
Abnormal High vs. Normal	NS	NS	NS
White Blood Cell (WBC) Count (C)	**(NS)	**(NS)	**(ns)
White Blood Cell (WBC) Count (D)			
Abnormal Low vs. Normal	**(NS)	**(NS)	**(NS)
Abnormal High vs. Normal	**(-0.029)	**(ns*)	**(-0.034)
Hemoglobin (C)	NS	NS	NS
Hemoglobin (D)			
Abnormal Low vs. Normal	ns	ns	ns
Abnormal High vs. Normal	NS	NS	NS
Hematocrit (C)	NS	NS	NS
Hematocrit (D)	NS	NS	NS
Platelet Count (C)	ns	NS	ns
Platelet Count (D)	+0.014	NS*	ns
Prothrombin Time (C)	NS	ns	NS
Prothrombin Time (D)	**(ns)	ns	ns
RBC Morphology (D)	NS*	NS*	+0.045
Absolute Neutrophils (segs) (C)	**(NS)	**(NS)	**(NS)
Absolute Neutrophils (bands) (Zero vs. Nonzero) (D)	****	****	****
Absolute Neutrophils (bands) (Nonzero Measurements) (C)	NS	NS	ns
Absolute Lymphocytes (C)	ns	ns	ns
Absolute Monocytes (C)	NS	NS	NS
Absolute Eosinophils (Zero vs. Nonzero) (D)	NS*	NS*	**(NS)
Absolute Eosinophils (Nonzero Measurements) (C)	ns	ns	ns
Absolute Basophils (Zero vs. Nonzero) (D)	ns	ns	ns
Absolute Basophils (Nonzero Measurements) (C)	ns	**(NS)	**(ns)

C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥ 1.00.
-: Relative risk < 1.00.
NS or ns: Not significant ($p > 0.10$).
NS*: Marginally significant ($0.05 < p \leq 0.10$).
**(NS) or **(ns): Log_2 (current dioxin + 1)-by-covariate interaction ($p \leq 0.05$); not significant when interaction is deleted; refer to Appendix L-2 for further analysis of this interaction.
**(ns*): Log_2 (current dioxin + 1)-by-covariate interaction ($p \leq 0.05$); marginally significant when interaction is deleted; refer to Appendix L-2 for further analysis of this interaction.
**** Log_2 (current dioxin + 1)-by-covariate interaction ($p \leq 0.01$); refer to Appendix L-2 for a detailed description 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 a nonnegative slope for continuous analysis; a lower case "ns" denotes relative risk less than 1.00 for discrete analysis or slope negative for continuous analysis.

Table 16-28.
Summary of Group-by-Covariate and Dioxin-by-Covariate Interactions from Adjusted Analyses of Hematology Variables

Model	Variable	Covariate
1[a]	Red Blood Cell (RBC) Count (C)	Current Cigarette Smoking
	White Blood Cell (WBC) Count (C)	Race
	Hemoglobin (C)	Current Cigarette Smoking, Lifetime Cigarette Smoking History
	Hematocrit (C)	Current Cigarette Smoking, Lifetime Cigarette Smoking History
	Platelet Count (C)	Occupation
	Absolute Monocytes (C)	Race
2[b]	White Blood Cell (WBC) Count (C)	Race, Occupation
	Absolute Neutrophils (segs) (C)	Race
	Absolute Neutrophils (bands) (C)	Lifetime Cigarette Smoking History
	Absolute Neutrophils (bands) (C)	Occupation
	Absolute Eosinophils (C)	Age, Occupation
3[c]	Red Blood Cell (RBC) Count (C)	Current Cigarette Smoking
	Hemoglobin (C)	Current Cigarette Smoking, Lifetime Cigarette Smoking History
	Hematocrit (C)	Current Cigarette Smoking, Lifetime Cigarette Smoking History
	Prothrombin Time (C)	Age
	Absolute Neutrophils (bands) (C)	Lifetime Cigarette Smoking History
4[d]	White Blood Cell (WBC) Count (C)	Race
	White Blood Cell (WBC) Count (D)	Race
	Prothrombin Time (D)	Lifetime Cigarette Smoking History
	Absolute Neutrophils (segs) (C)	Race
	Absolute Neutrophils (bands) (C)	Lifetime Cigarette Smoking History
5[e]	White Blood Cell (WBC) Count (C)	Race
	White Blood Cell (WBC) Count (D)	Race
	Absolute Neutrophils (segs) (C)	Race
	Absolute Neutrophils (bands) (C)	Lifetime Cigarette Smoking History
	Absolute Basophils (C)	Race
6[f]	White Blood Cell (WBC) Count (C)	Race
	White Blood Cell (WBC) Count (D)	Race
	Absolute Neutrophils (segs) (C)	Race
	Absolute Neutrophils (bands) (C)	Lifetime Cigarette Smoking History
	Absolute Eosinophils (C)	Occupation
	Absolute Basophils (C)	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 2: Initial Dioxin Analysis

In the unadjusted analysis of the cell count variables, hemoglobin, hematocrit, and platelet count displayed significant associations with initial dioxin, which indicated a positive dose-response relationship. However, adjustment for covariate information caused the dioxin effect for both platelet count and hemoglobin to become nonsignificant. Adjusted analysis results for hematocrit became marginally significant. Analyses on the remaining cell count endpoints disclosed nonsignificant associations with initial dioxin.

Nonzero measurements of absolute basophils increased significantly with initial dioxin in the unadjusted Model 2 analyses; the adjusted slope was only marginally significant. A marginally significant positive association between initial dioxin and absolute monocytes was found in the unadjusted analysis.

Analyses on the remaining hematology variables detected a significant positive relationship between continuously measured prothrombin time and initial dioxin in the adjusted analysis.

Model 3: Categorized Dioxin Analysis

Significant results from the categorized dioxin analyses of the cell count variables were seen mainly in the analyses of platelet count. Measured continuously, mean levels of platelet count in the high and low plus high Ranch Hand categories were significantly greater than those of the Comparisons in both the unadjusted and adjusted analyses. Additionally, the percentage of abnormally high platelet count levels was greater in high Ranch Hands than Comparisons. Adjusted RBC count means displayed marginally significant inverse associations in the analyses of high Ranch Hands and low plus high Ranch Hands versus Comparisons. The inverse associations indicate that mean levels of RBC count in the aforementioned Ranch Hand categories were lower than the mean levels of RBC count in the Comparison group. Analyzed discretely, the percentage of abnormally low RBC counts in background Ranch Hands was significantly greater than that of the Comparisons in the unadjusted analysis and marginally significant in the adjusted analysis. Several cell count variables displayed marginally significant associations with categorized dioxin in the unadjusted analyses that became nonsignificant after covariate adjustment (i.e., abnormal low RBC counts, continuously measured WBC counts, continuously measured hematocrit, and abnormal low hematocrit levels).

Only marginally significant results were disclosed in the categorized dioxin analyses of the absolute blood count variables. Unadjusted means for absolute neutrophils (segs) and absolute monocytes were greater in high Ranch Hands than Comparisons. However, this result remained marginally significant only for absolute monocytes after covariate adjustment. Adjusted mean levels of nonzero absolute eosinophil measurements were lower in the low plus high Ranch Hand category than in the Comparison group.

In the adjusted analysis of coagulation, the percentage of abnormal RBC morphology measurements was significantly lower in the background Ranch Hand category than in the Comparison group.

Models 4, 5, and 6: Current Dioxin Analyses

Current dioxin analyses of platelet count, similar to the other exposure analyses, led to significant results. Unadjusted for covariates, platelet counts in both discrete and continuous forms were positively associated with each of the current dioxin measurements. However, with the exception of significant and marginally significant associations between discrete platelet counts and current dioxin in Models 4 and 5, the adjusted results became nonsignificant. Adjusted relative risks of abnormally high WBC counts were significantly less than 1.00 in the adjusted analyses of Models 4 and 6. The adjusted relative risk was marginally significant in Model 5. Marginally significant and significant positive associations between RBC counts and current dioxin were found in the unadjusted analyses of Models 4 and 5. Adjusted results of RBC counts became nonsignificant in Model 4 and marginally significant in Model 5.

Marginally significant positive associations between the proportion of zero measurements of absolute eosinophils and current dioxin were found in the unadjusted analysis of Model 5 and the adjusted analyses of Models 4 and 5. Current dioxin analyses on the remaining absolute blood count variables were nonsignificant. Dioxin-by-covariate interactions retained in the adjusted analyses primarily involved either race or lifetime cigarette smoking history.

Among the remaining hematology variables, RBC morphology was significantly related to whole-weight current dioxin adjusted for total lipids in the adjusted analysis of Model 6. Positive relationships of marginal significance also were observed in the lipid-adjusted and whole-weight current dioxin analyses of RBC morphology.

CONCLUSION

The thirteen endpoints analyzed in the hematology assessment provide a comprehensive evaluation of the three peripheral blood lines (erythrocytes, leukocytes, and platelets) and their relation to dioxin exposure. In the analyses of these variables, only platelet count exhibited significant associations with the herbicide exposure indices. Ranch Hands in the enlisted flyer and enlisted groundcrew categories possessed statistically significant higher mean platelet counts than Comparisons, although the result cannot be considered significant from a clinical point of view. Analyses employing extrapolated levels of initial dioxin showed that Ranch Hands with high dioxin levels had significantly greater mean platelet count measurements than Comparisons. Platelet counts also were positively associated with current serum dioxin measurements, although the association became nonsignificant when adjusted for covariates. These results support the results found in both the 1987 followup study and in the serum dioxin analysis of the 1987 followup study, but the biologic significance is uncertain.

Results from the 1987 followup study generated questions regarding the possibility of a subclinical inflammatory response associated with prior dioxin exposure. This was due to elevated WBC counts, platelet counts, and erythrocyte sedimentation rates in Ranch Hands. However, the current study did not produce significant results to support this possibility. Therefore, in conclusion, there is no evidence from the present study that suggests an association between hematopoietic toxicity and prior dioxin exposure.

CHAPTER 16
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