AD-A237 518

Air Force Health Study

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

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In conjunction with

SCRIPPS CLINIC & RESEARCH FOUNDATION, LA JOLLA, CA

NATIONAL OPINION RESEARCH CENTER, CHICAGO, IL

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JUL 0 1 1991
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March 1991

Volume III

20030204076

SERUM DIOXIN ANALYSIS OF 1987 EXAMINATION RESULTS

Contract Number F41689-85-D-0010
SAIC Project Number 1-813-X4-.95, 254/437, 011/942, 943

(Distribution Unlimited)

DISTRIBUTION STATEMENT A
Approved for public release;
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AIR FORCE HEALTH STUDY

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TABLE OF CONTENTS

VOLUME III

PAGE

8. NEUROLOGICAL ASSESSMENT 8-1

INTRODUCTION 8-1

Background 8-1
Summary of Previous Analyses of the 1987 Examination Data 8-3
Parameters of the Neurological Assessment 8-3
Statistical Methods 8-5

RESULTS 8-13

Exposure Analysis 8-13
Longitudinal Analysis 8-135

DISCUSSION 8-141
SUMMARY 8-148

Questionnaire Variables 8-148
Physical Examination Variables 8-160

CONCLUSION 8-162

REFERENCES 8-163

9. PSYCHOLOGICAL ASSESSMENT 9-1

INTRODUCTION 9-1

Background 9-1
Summary of Previous Analyses of the 1987 Examination Data 9-4
Parameters of the Psychological Assessment 9-4

RESULTS 9-16

Exposure Analysis 9-16

DISCUSSION 9-229
SUMMARY 9-232

Questionnaire: Verified 9-232
Questionnaire: Sleep Disorders 9-248
Physical Examination: SCL-90-R Variables 9-252
Physical Examination: MCMI Variables 9-255

CONCLUSION 9-259

REFERENCES 9-260

TABLE OF CONTENTS - REPORT

VOLUME I

EXECUTIVE SUMMARY
ACKNOWLEDGMENTS
CHAPTER 1 - Introduction
CHAPTER 2 - Dioxin Assay
CHAPTER 3 - The Relationship Between the Exposure Index and Dioxin Body Burdens in Ranch Hands
CHAPTER 4 - Statistical Methods Models and Assumptions
CHAPTER 5 - Covariate Associations
CHAPTER 6 - General Health Assessment

VOLUME II

CHAPTER 7 - Malignancy Assessment

VOLUME III

CHAPTER 8 - Neurological Assessment
CHAPTER 9 - Psychological Assessment

VOLUME IV

CHAPTER 10 - Gastrointestinal Assessment
CHAPTER 11 - Dermatologic Assessment

VOLUME V

CHAPTER 12 - Cardiovascular Assessment
CHAPTER 13 - Hematologic Assessment

VOLUME VI

CHAPTER 14 - Renal Assessment
CHAPTER 15 - Endocrine Assessment
CHAPTER 16 - Immunologic Assessment

VOLUME VII

CHAPTER 17 - Pulmonary Assessment
CHAPTER 18 - Conclusions
CHAPTER 19 - Future Directions

VOLUME VIII

APPENDIX A through J

VOLUME IX

APPENDIX K through R

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AL/AOEP, Brooks AFB, TX. 78235

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CHAPTER 8

NEUROLOGICAL ASSESSMENT

INTRODUCTION

Background

The frequent association of subjective neurological symptoms subsequent to herbicide exposure has driven a great deal of the research into the potential neurotoxicity of dioxin. Studies of industrial accidents have demonstrated that the mixed sensorimotor neuropathy associated with extreme chlorophenol toxicity is reversible and there is no scientific evidence to date for any chronic central or peripheral neurological disease associated with low level 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) exposure. Neurobehavioral endpoints in humans, the subject of intensive investigation in this and other studies of Vietnam veterans, are considered separately in Chapter 9, Psychological Assessment.

Earlier research (1, 2) into the effects of perinatal exposure to 2,4-D and 2,4,5-T on neurobehavioral function in weanling rats has been pursued in more recent studies from the same laboratory (3, 4). These and other studies in mice (5) and rabbits (6) have documented changes in the concentrations of several CNS neurotransmitters in association with 2,4-D-induced neurobehavioral dysfunction. In another series of experiments, the neurobehavioral effects of exposure to an ester of 2,4-D were found to be rapidly reversible and the authors proposed a cellular rather than biochemical basis for the tolerance that developed with repeated injections (7, 8, 9).

To date, there has been very little animal research into neurotoxic effects specific to TCDD. One report documented that the intracerebroventricular administration of TCDD in rats was far more toxic than the subcutaneous route, though specific neurological indices were not examined (10). Another study of endpoints associated with acute lethal doses of TCDD in rats concluded that the neuromuscular effects associated with the "wasting syndrome" were primarily on muscle tissue rather than peripheral nerves (11).

The early literature related to 2,4-D-induced neurotoxicity in humans has been summarized in the most recent report of the Air Force Health Study (AFHS) and will not be reviewed in detail here. In association with TCDD exposure, as with 2,4-D, a host of subjective neurological symptoms has been reported and grouped generically under the diagnosis of "neurasthenia." Numerous studies have been published describing populations exposed to TCDD by occupation (12-17), environmental contamination (18-22), and industrial accidents (23-29).

A recent report on the 1976 explosion in Seveso, Italy (24), described the results of examinations conducted in 1982 to 1983 and included objective data derived from a detailed neurological examination and electrophysiological testing. One hundred fifty-two subjects with chloracne, a reliable marker for high-level dioxin exposure, were compared with controls. An abnormality was detected in only 1 of 13 neurophysiological parameters and none of the exposed subjects was found to have a peripheral neuropathy by World Health Organization criteria. These findings were confirmed in another report as well (28). Similar results were

reported in a study conducted 30 years after a runaway reaction that occurred in a trichlorophenol plant in Nitro, West Virginia, in 1949 (15). By neurological examination and nerve conduction velocity studies, no differences were found in 204 exposed subjects (55% had chloracne) compared with 163 controls.

Point source environmental exposure to TCDD has been the focus of numerous epidemiologic studies some of which have included neurological indices in their protocols (18-22). In 1971, waste byproducts contaminated with TCDD from a chlorophenol manufacturing plant were mixed with oils and widely sprayed for dust control in residential areas of eastern Missouri near St. Louis. Soil concentrations in some areas reached 2,200 parts per billion. Comprehensive medical evaluations of exposed and unexposed cohorts have included detailed neurological examinations and in one report (21), quantitative studies of tactile, vibratory, and thermal sensations. A recent review article summarizes the results of these Missouri dioxin studies (30). To date there has been no clinical evidence for any central or peripheral neurological disease associated with these TCDD exposures. The first study (20) to report tissue levels of dioxin in relation to neurological findings found no correlation between the body burden of dioxin and abnormalities in the peripheral indices of pain and vibratory sensation and deep tendon reflexes.

Several studies of Vietnam veterans have included objective neurological data. In the Baseline examination of the AFHS (31), an increased incidence of abnormal Babinski reflexes was noted in Ranch Hand personnel relative to Comparisons, a finding that was not seen at the 1985 examination (32). In a study of 15 veterans who reported subjective symptoms in association with herbicide exposure, one subject was found to have a bilateral peripheral neuropathy related to alcohol abuse. In all others, nerve conduction velocity studies at five peripheral sites were normal (33).

One large-scale study (34) of American Legion veterans who served in Vietnam found an increased incidence of reported neurobehavioral disorders that suggested an association with herbicide exposure. However, the significance is limited by self-reporting bias, the lack of confirmation by clinical examination or medical record review, and the use of unvalidated exposure assumptions.

In contrast to the American Legion study, the Vietnam experience study conducted by the U.S. Centers for Disease Control (CDC) (35) compared 2,490 Vietnam veterans with 1,972 non-Vietnam veterans. Included in the study protocol were comprehensive neurological examinations, nerve conduction velocity studies, and neurophysiological indices of vibratory, thermal, and auditory sensation. Aside from an increased incidence of combat-related high-frequency hearing loss in a pattern typical of a noise etiology, no neurological abnormalities were noted in association with service in Southeast Asia (SEA).

In summary, animal research and studies of humans exposed to high levels of dioxin leave no doubt that the peripheral nervous system is a target organ for acute TCDD toxicity. Longitudinal studies would seem to indicate that the neurological signs and symptoms attributable to acute exposure resolve over time and are not associated with any long-term sequelae.

More detailed summaries of the pertinent scientific literature for the neurological assessment can be found in the report of the previous analyses of the 1987 examination data (36).

Summary of Previous Analyses of the 1987 Examination Data

The neurological health of the Ranch Hand group was not substantially different from the Comparison group. Of the six questionnaire variables relating to neurological disease, the only significant finding was that Ranch Hands had a higher incidence of hereditary and degenerative neurological disease, such as benign essential tremor. The statistical results of the group contrasts for 30 physical examination variables relating to cranial nerve function, peripheral nerve status, and CNS coordination processes were generally not significant. Unadjusted analyses disclosed marginally more balance/Romberg sign and coordination abnormalities for Ranch Hands than for Comparisons. Conversely, Ranch Hands had significantly fewer biceps reflex abnormalities than Comparisons. The adjusted analyses revealed a significant group-by-insecticide exposure interaction for the cranial nerve index (excluding neck range of motion). Stratified results showed a relative risk significantly greater than 1 for participants who had never been exposed to insecticides, and a relative risk marginally less than 1 for participants who had been exposed to insecticides. The adjusted analysis for coordination detected differences in the relative risks with occupation and insecticide exposure. Stratified analyses found a significant group difference for enlisted groundcrew who had never been exposed to insecticides. There were no significant differences for the other strata. Further investigation found a significant group difference for enlisted groundcrew after excluding the insecticide interaction, and a significant adjusted group difference overall after excluding both interactions. Ranch Hands had significantly more coordination abnormalities than Comparisons for each analysis. The longitudinal analyses for the cranial nerve index and the CNS index were not significant.

Parameters of the Neurological Assessment

Dependent Variables

The neurological assessment was primarily based on extensive physical examination data on cranial nerve function, peripheral nerve status, and CNS coordination processes. This information was supplemented by verified histories of neurological diseases.

Questionnaire Data

Data on all major health conditions since the date of the last health interview were collected during the 1987 health interview. All affirmative histories were subjected to medical records verification. The verified information was used to update the health status of each study participant. The neurological diseases and disorders were classified into eight International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) categories: inflammatory diseases (ICD codes 32000-32600), hereditary and degenerative diseases (ICD codes 33000-33700), peripheral disorders (ICD codes 35000-35900), disorders of the eye (ICD codes 37800-37956), external otitis (ICD codes 38010-38081), tympanic membrane disorder (ICD codes 38420-38500), hearing loss (ICD codes 38900-38999), and other neurological disorders (ICD codes 34000-34900). There were 389 cases in the ICD-9-CM category of other neurological disorders based on all assayed participants. The disorders in this category included multiple sclerosis (3 Ranch Hands and 1 Comparison), other demyelinating diseases of the central nervous system (2 Ranch Hands

and 1 Comparison), hemiplegia (4 Ranch Hands and 1 Comparison), other paralytic syndromes (9 Ranch Hands and 4 Comparisons), epilepsy (7 Ranch Hands and 1 Comparison), migraine (20 Ranch Hands and 14 Comparisons), catalepsy or narcolepsy (0 Ranch Hands and 1 Comparison), unspecified encephalopathy (157 Ranch Hands and 152 Comparisons), other conditions of the brain (1 Ranch Hand and 4 Comparisons), and other unspecified disorders of the nervous system (5 Ranch Hands and 2 Comparisons). Some participants had conditions in more than one category. The analyses of questionnaire information in the neurological assessment were based on verified data only. Each of the eight variables was coded as yes/no.

Participants with positive serological tests for syphilis and participants with a verified pre-SEA history of these disorders were excluded from all analyses of these neurological variables.

Physical Examination Data

During the physical examination, assessments were made of cranial nerve function, peripheral nerve status, and CNS coordination processes.

The evaluation of cranial nerve function was based on the following 17 variables: smell, visual fields, light reaction, ocular movement, facial sensation, corneal reflex, jaw clench, smile, palpebral fissure, balance, gag reflex, speech, tongue position relative to midline, palate and uvula movement, neck range of motion, cranial nerve index, and the index excluding neck range of motion. All of these variables were scored as normal/abnormal except jaw clench, which was scored as symmetric/deviated. Left and right determinations were combined to produce a single normal/abnormal result, where normal indicates that both left and right determinations were normal. The cranial nerve index was created by combining responses for the 15 cranial nerve parameters into a single index, which was classified as normal if all parameters were normal. An index was also created excluding the hypoglossal nerve (neck range of motion). No participants had an abnormal corneal reflex. No assayed participants had an abnormal jaw clench, gag reflex, or tongue position relative to midline. One assayed Comparison, but no Ranch Hands, had a palate and uvula movement abnormality.

Peripheral nerve status was assessed by light pin prick, light touch (cotton sticks), visual inspection of muscle mass (and palpation, if indicated), vibratory sensation as measured at the ankle with a tuning fork of 128 Hz, three deep tendon reflexes (patellar, Achilles, and biceps), and the Babinski reflex. Muscle status was a constructed variable using data on bulk, tone of upper and lower extremities and the strength of distal wrist extensors, ankle/toe flexors, proximal deltoids, and hip flexors. Muscle status was classified as normal if all of the components were normal. The reflexes were coded as normal if they were sluggish, active, or very active; reflexes classified as absent, transient clonus, or sustained clonus were coded as abnormal for the analyses.

The evaluation of CNS coordination processes was based on the analysis of the following variables: tremor, coordination, Romberg sign, gait, and CNS index. For these variables, multiple determinations were combined to form a single result, which was normal if all determinations were normal. Coordination was an index defined as normal if the Romberg

sign, finger-nose-finger and heel-knee-shin coordination processes, rapidly alternating movements of pronation/supination of hands, and rapid patting were normal. The CNS index was based on tremor, coordination, and gait; this index was coded as normal if all three of the components were normal.

Participants with positive serological tests for syphilis were excluded from all analyses of these neurological variables. Participants with contact lenses in place were excluded from the analysis of the corneal reflex (n=19 based on all participants). Participants with peripheral edema were excluded from the analyses of pin prick, light touch, and ankle vibration.

Covariates

The neurological assessment analyzed the effects of age, race, lifetime alcohol history, diabetic class, and insecticide exposure in the adjusted statistical analyses. Occupation was included as a covariate for the analyses of other neurological disorders because of a strong association. The lifetime alcohol history covariate was based on self-reported information from the questionnaire. 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 exposure to insecticides covariate represents lifetime exposure based on self-reported questionnaire data.

Age and lifetime alcohol history were treated as continuous variables for all adjusted analyses, but they were categorized to explore interactions. Appendix Table G-1 presents the interaction summaries. Insecticide exposure was categorized (yes/no) for all analyses.

Relation to Baseline, 1985, and 1987 Studies

With the exception of the ICD-9-CM category of other neurological disorders, otitis, hearing loss, and the neurological summary indices, the variables analyzed for this study were also analyzed in the Baseline and 1985 studies. Other neurological disorders, the cranial nerve indices with and without neck range of motion, and the CNS index were variables added to the analysis of the 1985 examination. Analyses of otitis and hearing loss were included in the previous report of the 1987 examination.

The neurological longitudinal analyses were based on the cranial nerve index and the CNS index from the 1985 and 1987 neurological examinations conducted at the Scripps Clinic and Research Foundation (SCRF). To enhance the comparability, the longitudinal assessment contrasted differences between the 1985 and 1987 examinations.

Statistical Methods

The basic statistical analysis methods used in the neurological assessment are described in Chapter 4, Statistical Methods.

Table 8-1 summarizes the statistical analyses performed for the 1987 neurological assessment. The modeling strategy for the adjusted analyses was modified to always include age in the model, regardless of the statistical significance. In general, no covariates other than age were examined in the adjusted analyses of the questionnaire variables

TABLE 8-1.

Statistical Analysis for the Neurological Assessment

Dependent Variables

Variable	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analyses
Inflammatory Diseases	Q/PE-V	D	Yes No	--	U:LR,CS,FT
Hereditary and Degenerative Diseases	Q/PE-V	D	Yes No	AGE	U:LR A:LR
Peripheral Disorders	Q/PE-V	D	Yes No	AGE	U:LR A:LR
Disorders of the Eye	Q/PE-V	D	Yes No	AGE	U:LR A:LR
Otitis	Q/PE-V	D	Yes No	AGE	U:LR A:LR
Tympanic Membrane Disorders	Q/PE-V	D	Yes No	AGE	U:LR A:LR
Hearing Loss	Q/PE-V	D	Yes No	AGE	U:LR A:LR
Other Neurological Disorders	Q/PE-V	D	Yes No	AGE, OCC	U:LR A:LR
Smell	PE	D	Abnormal Normal	AGE	U:LR,CS,FT A:LR
Visual Fields	PE	D	Abnormal Normal	--	U:CS,FT
Light Reaction	PE	D	Abnormal Normal	AGE	U:LR,CS,FT A:LR
Ocular Movement	PE	D	Abnormal Normal	AGE	U:LR,CS,FT A:LR
Facial Sensation	PE	D	Abnormal Normal	AGE	U:LR,CS,FT A:LR
Corneal Reflex	PE	D	Abnormal Normal	--	--

TABLE 8-1. (Continued)

Statistical Analysis for the Neurological Assessment

Dependent Variables

Variable	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analyses
Jaw Clench	PE	D	Deviated Symmetric	--	--
Smile	PE	D	Abnormal Normal	AGE	U:LR A:LR
Palpebral Fissure	PE	D	Abnormal Normal	AGE,RACE, DRKYR,INS, DIAB	U:LR A:LR
Balance	PE	D	Abnormal Normal	--	U:LR,CS,FT
Gag Reflex	PE	D	Abnormal Normal	--	--
Speech	PE	D	Abnormal Normal	--	U:CS,FT
Tongue Position Relative to Midline	PE	D	Abnormal Normal	--	--
Palate and Uvula Movement	PE	D	Abnormal Normal	--	--
Neck Range of Motion	PE	D	Abnormal Normal	AGE,RACE, DRKYR,INS, DIAB	U:LR A:LR
Cranial Nerve Index	PE	D	Abnormal Normal	AGE,RACE, DRKYR,INS, DIAB	U:LR A:LR L:LR
Cranial Nerve Index Without Range of Motion	PE	D	Abnormal Normal	AGE,RACE, DRKYR,INS, DIAB	U:LR A:LR
Pin Prick	PE	D	Abnormal Normal	AGE,RACE, DRKYR,INS, DIAB	U:LR A:LR

TABLE 8-1. (Continued)

Statistical Analysis for the Neurological Assessment

Dependent Variables

Variable	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analyses
Light Touch	PE	D	Abnormal Normal	AGE,RACE, DRKYR,INS, DIAB	U:LR A:LR
Muscle Status	PE	D	Abnormal Normal	AGE,RACE, DRKYR,INS, DIAB	U:LR A:LR
Vibration	PE	D	Abnormal Normal	AGE,RACE, DRKYR,INS, DIAB	U:LR A:LR
Patellar Reflex	PE	D	Abnormal Normal	AGE,RACE, DRKYR,INS, DIAB	U:LR A:LR
Achilles Reflex	PE	D	Abnormal Normal	AGE,RACE, DRKYR,INS, DIAB	U:LR A:LR
Biceps Reflex	PE	D	Abnormal Normal	--	U:CS,FT
Babinski Reflex	PE	D	Abnormal Normal	--	U:LR,CS,FT
Tremor	PE	D	Abnormal Normal	AGE,RACE, DRKYR,INS, DIAB	U:LR A:LR
Coordination	PE	D	Abnormal Normal	AGE,RACE, DRKYR,INS, DIAB	U:LR A:LR
Romberg Sign	PE	D	Abnormal Normal	--	U:LR,CS,FT
Gait	PE	D	Abnormal Normal	AGE,RACE, DRKYR,INS, DIAB	U:LR A:LR

TABLE 8-1. (Continued)

Statistical Analysis for the Neurological Assessment

Dependent Variables

Variable	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analyses
Central Nervous System (CNS) Index	PE	D	Abnormal Normal	AGE,RACE, DRKYR,INS, DIAB	U:LR A:LR L:LR

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 Alcohol History (DRKYR) (Drink-Years)	Q-SR	D/C	≤40 >40
Insecticide Exposure (INS)	Q-SR	D	Yes No
Diabetic Class (DIAB)	LAB/Q/PE-V	D	Diabetic: past history or ≥200 mg/dl glucose Impaired: ≥140-200 mg/dl glucose Normal: <140 mg/dl glucose

TABLE 8-1. (Continued)

Statistical Analysis for the Neurological Assessment

Abbreviations

Data Source:	LAB--1987 SCRF laboratory results MIL--Air Force military records PE--1987 SCRF physical examination Q-SR--NORC questionnaire (self-reported) Q/PE-V--1987 Questionnaire and physical examination (verified)
Data Form:	D--Discrete analysis only D/C--Appropriate form of analysis (either discrete or continuous)
Statistical Analyses:	U--Unadjusted analyses A--Adjusted analyses L--Longitudinal analyses
Statistical Methods:	CS--Chi-square contingency table test FT--Fisher's exact test LR--Logistic regression analysis

(occupation was also included for the analyses of other neurological disorders). The first part of this table lists the dependent variables analyzed, data source, data form, cutpoints, candidate covariates, and statistical analysis methods. The second part of this table provides a description of candidate covariates examined. Abbreviations are used extensively in the body of the table and are defined in the footnotes. Diabetes exhibited a significant positive association with dioxin (see Chapter 15, Endocrine Assessment). Consequently, clinical endpoints in the neurological assessment may be related to dioxin due to the association between dioxin and diabetes. To investigate this possibility, the dioxin effect was evaluated in the context of two models whenever diabetic class was retained in the final model. The results of the analysis adjusting for diabetic class are discussed and tabled in the body of the chapter. Appendix Table G-2 shows additional results for the final model excluding diabetic class. These followup analyses are only discussed if a meaningful change in the results occurred.

Some participants had missing dependent variable or covariate data. Consequently, these individuals could not be included in all analyses. Table 8-2 summarizes the number of participants with missing data, and the number who were excluded from analyses for medical reasons.

Appendix G-1 contains graphic displays of the neurological variables versus initial dioxin for the minimal and maximal cohorts, and the neurological variables versus current dioxin for Ranch Hands and Comparisons. Appendix G-2 presents graphics for dioxin-by-covariate interactions as determined by various statistical models. A guide to assist in interpreting the graphics is found in Chapter 4.

Three statistical models were used to examine the association between a neurological dependent variable and serum dioxin levels. One model related a dependent variable to each Ranch Hand's initial dioxin value (extrapolated from current dioxin values using a first-order pharmacokinetic model). A second model related a dependent variable to each Ranch Hand's current serum dioxin value and each Ranch Hand's time since tour. The phrase "time since tour" is often referred to as "time" in discussions of these results. Both of these models were implemented under the minimal and maximal assumptions (i.e., Ranch Hands with current dioxin above 10 ppt and above 5 ppt, respectively). The third model compared the neurological dependent variable for Ranch Hands having current dioxin values categorized as unknown, low, and high with Comparisons having background levels. The contrast of the entire Ranch Hand group with the complete Comparison group can be found in the previous report of analyses of the 1987 examination (36). All three models were implemented with and without covariate adjustment. Chapter 4 provides a more detailed discussion of the models.

TABLE 8-2.

Number of Participants Excluded and With Missing Data for the Neurological Assessment

Variable	Variable Use	Assumption (Ranch Hands Only) Minimal	Assumption (Ranch Hands Only) Maximal	Categorized Current Dioxin Ranch Hand	Categorized Current Dioxin Comparison
Visual Fields	DEP	0	0	0	2
Light Reaction	DEP	0	0	0	2
Ocular Movement	DEP	0	0	0	1
Facial Sensation	DEP	0	0	0	1
Corneal Reflex	DEP	7	8	7	6
Balance	DEP	0	0	0	1
Speech	DEP	0	0	0	1
Cranial Nerve Index	DEP	8	9	8	11
Cranial Nerve Index Without Range of Motion	DEP	8	9	8	11
Muscle Status	DEP	0	1	1	1
Patellar Reflex	DEP	0	0	0	1
Achilles Reflex	DEP	1	2	2	0
Coordination	DEP	0	1	1	1
Romberg Sign	DEP	0	0	0	1
Gait	DEP	0	1	1	1
CNS Index	DEP	0	1	1	1
Lifetime Alcohol History	COV	6	9	9	2
Diabetic Class	COV	2	2	3	2
Pre-SEA Inflammatory Diseases	EXC	0	0	0	5
Pre-SEA Hereditary and Degenerative Diseases	EXC	0	1	1	0
Pre-SEA Peripheral Disorders	EXC	0	1	2	3
Pre-SEA Disorders of the Eye	EXC	1	2	2	1
Pre-SEA Tympanic Membrane Disorder	EXC	5	5	6	5
Pre-SEA Otitis	EXC	0	0	0	1
Pre-SEA Hearing Loss	EXC	2	3	4	8
Pre-SEA Other Neurological Diseases	EXC	1	2	2	3
Syphilis	EXC	0	1	2	2
Pitting or Nonpitting Edema	EXC	9	12	10	14

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

RESULTS

Exposure Analysis

Questionnaire Variables

Inflammatory Diseases

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

The unadjusted initial dioxin analyses of inflammatory diseases were not significant under both the minimal (Table 8-3 [a]: p=0.761) and maximal (Table [illegible] [b]: p=0.409) assumptions. Under both assumptions, there were only two cases of inflammatory disease. One was in the medium initial dioxin category, the other was in the high category. No adjusted analyses were done because of the sparse number of abnormalities.

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

The interaction between current dioxin and time since tour was not evaluated because only two Ranch Hands had a post-SEA history of inflammatory neurological disease. There was only one case within each time stratum.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The incidence of inflammatory diseases did not differ significantly among current dioxin categories in the unadjusted analysis (Table 8-3 [e]: p=0.616). No adjusted analysis was done because there were only three cases of inflammatory disease (one in each of the background, unknown, and high current dioxin categories, and none in the low category).

Hereditary and Degenerative Diseases

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Under both the minimal and maximal assumptions, initial dioxin was not significantly associated with the incidence of hereditary and degenerative diseases (Table 8-4 [a-d]: p>0.55 for the unadjusted and adjusted analyses). The relative risk was less than 1 in each analysis.

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

The interaction between current dioxin and time since tour was not significant for the minimal and maximal analyses of hereditary and degenerative diseases (Table 8-4 [e-h]: p>0.45 for the unadjusted and adjusted analyses).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The incidence of hereditary and degenerative diseases did not differ significantly among the current dioxin categories in the unadjusted analysis (Table 8-4 [i]: 4.0%, 5.6%, 3.6%, and 3.2% for the background, unknown, low, and high current dioxin categories, p=0.524). The overall contrast was also not significant after adjusting for age (Table 8-4 [j]: p=0.612).

TABLE 8-3.

Analysis of Inflammatory Diseases

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=521)	Low	130	0.0	1.18 (0.41,3.43)	0.761
	Medium	260	0.4		
	High	131	0.8		
b) Maximal (n=741)	Low	184	0.0	1.46 (0.62,3.46)	0.409
	Medium	371	0.3		
	High	186	0.5		

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

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 8-3. (Continued)

Analysis of Inflammatory Diseases

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)	p-Value
c) Minimal						--
(n=521)	≤18.6	0.0 (72)	0.0 (128)	1.9 (54)	--	--
	>18.6	1.7 (58)	0.0 (132)	0.0 (77)	--	--
d) Maximal						--
(n=741)	≤18.6	0.0 (106)	0.0 (191)	1.2 (83)	--	--
	>18.6	0.0 (78)	0.6 (179)	0.0 (104)	--	--

--: Relative risk, confidence interval, and p-value not given due to the sparse number of abnormalities.
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 8-3. (Continued)

Analysis of Inflammatory Diseases

e) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	779	0.1	All Categories		0.616
Unknown	343	0.3	Unknown vs. Background	2.27 (0.14,36.48)	0.999
Low	196	0.0	Low vs. Background	--	0.999
High	187	0.5	High vs. Background	4.18 (0.26,67.18)	0.700
Total	1,505				

--: Relative risk, confidence interval, and p-value not given due to the absence of abnormalities.

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 8-4.

Analysis of Hereditary and Degenerative Diseases

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=521)	Low	130	6.9	0.90 (0.62,1.31)	0.565
	Medium	260	3.1		
	High	131	3.8		
b) Maximal (n=740)	Low	183	4.4	0.94 (0.72,1.24)	0.684
	Medium	371	4.3		
	High	186	3.2		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=521)	0.91 (0.62,1.33)	0.614	AGE (p=0.826)
d) Maximal (n=740)	0.96 (0.73,1.27)	0.781	AGE (p=0.517)

[a]Relative risk for a twofold increase in dioxin.
Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 8-4. (Continued)

Analysis of Hereditary and Degenerative Diseases

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.482[b]
(n=521)	≤18.6	6.9 (72)	3.9 (128)	3.7 (54)	0.81 (0.45,1.48)	0.495[c]
	>18.6	6.9 (58)	1.5 (132)	5.2 (77)	1.07 (0.66,1.73)	0.790[c]
f) Maximal						0.936[b]
(n=740)	≤18.6	2.9 (105)	5.8 (191)	2.4 (83)	0.98 (0.65,1.47)	0.907[c]
	>18.6	5.1 (78)	3.4 (179)	3.9 (104)	1.00 (0.69,1.45)	0.991[c]

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal			0.492[b]	AGE (p=0.727)
(n=521)	≤18.6	0.83 (0.45,1.54)	0.561[c]	
	>18.6	1.09 (0.66,1.78)	0.736[c]	
h) Maximal			0.943[b]	AGE (p=0.442)
(n=740)	≤18.6	1.01 (0.66,1.54)	0.972[c]	
	>18.6	1.03 (0.70,1.51)	0.887[c]	

[a]Relative risk for a twofold increase in dioxin.
[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).
[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 8-4. (Continued)

Analysis of Hereditary and Degenerative Diseases

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	784	4.0	All Categories		0.524
Unknown	342	5.6	Unknown vs. Background	1.43 (0.80,2.57)	0.232
Low	196	3.6	Low vs. Background	0.90 (0.39,2.07)	0.804
High	187	3.2	High vs. Background	0.81 (0.33,1.96)	0.633
Total	1,509				

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	784	All Categories		0.612	AGE (p=0.169)
Unknown	342	Unknown vs. Background	1.41 (0.78,2.53)	0.254	
Low	196	Low vs. Background	0.90 (0.39,2.09)	0.813	
High	187	High vs. Background	0.88 (0.36,2.16)	0.777	
Total	1,509				

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

Peripheral Disorders

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

In both the unadjusted and adjusted initial dioxin analyses, the relative risk of peripheral disorders was not significant under both the minimal and maximal assumptions (Table 8-5 [a-d]: $p>0.55$ for all analyses).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

The current dioxin-by-time since tour interaction was not significant for either the minimal or maximal analyses of peripheral disorders (Table 8-5 [e-h]: $p>0.15$ in each unadjusted and adjusted analysis).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The unadjusted categorized current dioxin analysis of peripheral disorders was not significant, but the highest incidence of peripheral disorders was in the high current dioxin category (Table 8-5 [i]: 14.7%, 12.3%, 12.8%, and 16.0% for the background, unknown, low, and high current dioxin categories, $p>0.25$ for each contrast). The overall contrast, as well as the three Ranch Hand versus background contrasts, remained nonsignificant after adjustment for age (Table 8-5 [j]: $p>0.20$ for each contrast).

Disorders of the Eye

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Under both the minimal and maximal assumptions, the initial dioxin analyses did not show a significant association with the incidence of eye disorders (Table 8-6 [a-d]: $p>0.35$ for the unadjusted and adjusted analyses).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

The current dioxin and time since tour analyses of eye disorders did not find a significant interaction between current dioxin and time under both the minimal and maximal assumptions (Table 8-6 [e-h]: $p>0.80$ in each unadjusted and adjusted analysis).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The incidence of eye disorders did not differ significantly among the four current dioxin categories in the unadjusted analysis (Table 8-6 [i]: 15.8%, 16.7%, 16.9%, and 17.6% for the background, unknown, low, and high current dioxin categories, $p=0.930$). The overall contrast remained nonsignificant (Table 8-6 [j]: $p=0.801$) after adjustment for age.

Tympanic Membrane Disorders

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Under both the minimal and maximal assumptions, initial dioxin was not significantly associated with the incidence of tympanic membrane disorders (Table 8-7 [a-d]: $p>0.60$ for the unadjusted and adjusted analyses).

TABLE 8-5.

Analysis of Peripheral Disorders

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=521)	Low	130	14.6	1.01 (0.83,1.24)	0.900
	Medium	260	14.2		
	High	131	13.7		
b) Maximal (n=740)	Low	183	14.8	1.00 (0.86,1.16)	0.999
	Medium	371	13.7		
	High	186	15.6		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=521)	1.04 (0.85,1.28)	0.703	AGE (p=0.294)
d) Maximal (n=740)	1.05 (0.90,1.22)	0.564	AGE (p=0.003)

[a]Relative risk for a twofold increase in dioxin.
Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 8-5. (Continued)

Analysis of Peripheral Disorders

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.184[b]
(n=521)	≤18.6	12.5 (72)	16.4 (128)	7.4 (54)	0.82 (0.57,1.19)	0.302[c]
	>18.6	13.8 (58)	12.1 (132)	20.8 (77)	1.11 (0.86,1.44)	0.418[c]
f) Maximal						0.255[b]
(n=740)	≤18.6	15.1 (106)	13.6 (191)	13.3 (83)	0.89 (0.70,1.14)	0.371[c]
	>18.6	13.0 (77)	14.0 (179)	18.3 (104)	1.07 (0.88,1.31)	0.488[c]

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal			0.199[b]	AGE (p=0.363)
(n=521)	≤18.6	0.86 (0.59,1.25)	0.421[c]	
	>18.6	1.14 (0.88,1.49)	0.315[c]	
h) Maximal			0.263[b]	AGE (p=0.003)
(n=740)	≤18.6	0.96 (0.74,1.23)	0.732[c]	
	>18.6	1.15 (0.94,1.41)	0.186[c]	

[a]Relative risk for a twofold increase in dioxin.
[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).
[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 8-5. (Continued)

Analysis of Peripheral Disorders

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	781	14.7	All Categories		0.564
Unknown	341	12.3	Unknown vs. Background	0.81 (0.56,1.19)	0.285
Low	196	12.8	Low vs. Background	0.85 (0.53,1.35)	0.482
High	187	16.0	High vs. Background	1.11 (0.71,1.71)	0.650
Total	1,505				

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	781	All Categories		0.236	AGE (p<0.001)
Unknown	341	Unknown vs. Background	0.79 (0.54,1.16)	0.226	
Low	196	Low vs. Background	0.85 (0.53,1.36)	0.506	
High	187	High vs. Background	1.33 (0.85,2.08)	0.215	
Total	1,505				

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 8-6.

Analysis of Disorders of the Eye

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=520)	Low	130	18.5	1.05 (0.87,1.26)	0.602
	Medium	259	17.4		
	High	131	18.3		
b) Maximal (n=739)	Low	183	15.3	1.05 (0.92,1.21)	0.475
	Medium	370	17.6		
	High	186	18.3		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=520)	1.07 (0.89,1.29)	0.486	AGE (p=0.419)
d) Maximal (n=739)	1.07 (0.93,1.23)	0.365	AGE (p=0.306)

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

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 8-6. (Continued)

Analysis of Disorders of the Eye

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.920[b]
(n=520)	≤18.6	20.8 (72)	16.4 (128)	22.2 (54)	1.05 (0.79,1.41)	0.720[c]
	>18.6	15.5 (58)	18.3 (131)	15.6 (77)	1.08 (0.84,1.38)	0.563[c]
f) Maximal						0.832[b]
(n=739)	≤18.6	16.0 (106)	18.9 (191)	20.5 (83)	1.06 (0.87,1.31)	0.557[c]
	>18.6	13.0 (77)	17.4 (178)	15.4 (104)	1.10 (0.90,1.33)	0.346[c]

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal			0.956[b]	AGE (p=0.301)
(n=520)	≤18.6	1.10 (0.81,1.48)	0.546[c]	
	>18.6	1.11 (0.86,1.43)	0.423[c]	
h) Maximal			0.844[b]	AGE (p=0.165)
(n=739)	≤18.6	1.10 (0.89,1.36)	0.391[c]	
	>18.6	1.13 (0.93,1.37)	0.225[c]	

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

[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).

[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 8-6. (Continued)

Analysis of Disorders of the Eye

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	783	15.8	All Categories		0.930
Unknown	342	16.7	Unknown vs. Background	1.06 (0.75,1.50)	0.727
Low	195	16.9	Low vs. Background	1.08 (0.71,1.65)	0.712
High	187	17.6	High vs. Background	1.14 (0.75,1.74)	0.546
Total	1,507				

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	783	All Categories		0.801	AGE (p=0.011)
Unknown	342	Unknown vs. Background	1.05 (0.74,1.48)	0.798	
Low	195	Low vs. Background	1.09 (0.71,1.66)	0.699	
High	187	High vs. Background	1.24 (0.81,1.91)	0.321	
Total	1,507				

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 8-7.

Analysis of Tympanic Membrane Disorder

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=516)	Low	129	5.4	0.94 (0.68,1.29)	0.684
	Medium	257	5.8		
	High	130	6.2		
b) Maximal (n=736)	Low	184	3.8	1.01 (0.80,1.27)	0.959
	Medium	368	6.3		
	High	184	5.4		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=516)	0.99 (0.72,1.37)	0.950	AGE (p=0.153)
d) Maximal (n=736)	1.06 (0.84,1.35)	0.618	AGE (p=0.023)

[a]Relative risk for a twofold increase in dioxin.
Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 8-7. (Continued)

Analysis of Tympanic Membrane Disorder

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal (n=516)						0.435[b]
	≤18.6	2.8 (72)	4.0 (125)	3.7 (54)	1.07 (0.58,1.97)	0.821[c]
	>18.6	8.6 (58)	8.4 (131)	6.6 (76)	0.80 (0.54,1.19)	0.270[c]
f) Maximal (n=736)						0.844[b]
	≤18.6	3.8 (106)	3.7 (189)	3.7 (82)	0.98 (0.63,1.51)	0.922[c]
	>18.6	6.4 (78)	8.4 (178)	5.8 (103)	0.93 (0.69,1.24)	0.616[c]

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal (n=516)			0.419[b]	AGE (p=0.347)
	≤18.6	1.14 (0.61,2.11)	0.681[c]	
	>18.6	0.84 (0.56,1.26)	0.406[c]	
h) Maximal (n=736)			0.817[b]	AGE (p=0.066)
	≤18.6	1.05 (0.67,1.65)	0.830[c]	
	>18.6	0.99 (0.73,1.33)	0.929[c]	

[a]Relative risk for a twofold increase in dioxin.
[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).
[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 8-7. (Continued)

Analysis of Tympanic Membrane Disorder

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	779	4.1	All Categories		0.375
Unknown	342	3.5	Unknown vs. Background	0.85 (0.43,1.67)	0.635
Low	193	6.7	Low vs. Background	1.69 (0.87,3.28)	0.124
High	185	4.9	High vs. Background	1.19 (0.56,2.55)	0.647
Total	1,499				

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	779	All Categories		0.315	AGE (p=0.087)
Unknown	342	Unknown vs. Background	0.83 (0.42,1.64)	0.600	
Low	193	Low vs. Background	1.70 (0.87,3.31)	0.116	
High	185	High vs. Background	1.33 (0.62,2.87)	0.470	
Total	1,499				

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

The unadjusted and adjusted current dioxin and time since tour analyses of tympanic membrane disorders did not find a significant current dioxin-by-time interaction under either the minimal or maximal assumption (Table 8-7 [e-h]: $p>0.40$ in each analysis).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The overall contrast was not significant in both the unadjusted and adjusted categorized current dioxin analysis of tympanic membrane disorders (Table 8-7 [i] and [j]: $p=0.375$ and $p=0.315$, respectively). The highest incidence was in the low current dioxin category (4.1%, 3.5%, 6.7%, and 4.9% for the background, unknown, low, and high current dioxin categories).

Otitis

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Under both the minimal and maximal assumptions, the initial dioxin analyses did not find a significant risk of otitis (Table 8-8 [a-d]: $p>0.20$ for the unadjusted and adjusted analyses).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

Under the minimal assumption, the unadjusted current dioxin and time since tour analysis of otitis did not show a significant current dioxin-by-time interaction (Table 8-8 [e]: $p=0.791$), but a significant interaction was found under the maximal assumption (Table 8-8 [f]: $p=0.032$). In the maximal cohort, the estimated relative risk of otitis was significantly less than 1 for Ranch Hands with a later tour (time$\leq$18.6: Est. RR=0.62, $p=0.012$). In this stratum, the incidence of otitis decreased with current levels of dioxin (14.2%, 7.3%, and 3.6% for the low, medium, and high current dioxin categories). The estimated relative risk was less than 1, but not significant, for Ranch Hands in the maximal cohort with an early tour (time>18.6: Est. RR=0.97, $p=0.760$).

Similar results were noted after adjusting for age. The current dioxin-by-time interaction was not significant under the minimal assumption (Table 8-8 [g]: $p=0.352$), and it remained significant under the maximal assumption (Table 8-8 [h]: $p=0.031$). The adjusted relative risk was significantly less than 1 for Ranch Hands with a later tour (time$\leq$18.6: Adj. RR=0.64, $p=0.020$).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The incidence of otitis did not differ significantly among the current dioxin categories in the unadjusted analysis (Table 8-8 [i]: 12.4%, 14.0%, 12.8%, and 8.6% for the background, unknown, low, and high current dioxin categories, $p=0.308$). The overall contrast remained nonsignificant after adjusting for age (Table 8-8 [j]: $p=0.633$).

Hearing Loss

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Neither the unadjusted minimal nor maximal analyses of hearing loss showed a significant association with initial dioxin (Table 8-9 [a] and [b]: $p=0.504$ for the minimal

TABLE 8-8.

Analysis of Otitis

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=521)	Low	130	8.5	1.04 (0.82,1.31)	0.761
	Medium	260	10.4		
	High	131	10.7		
b) Maximal (n=741)	Low	184	15.2	0.90 (0.76,1.08)	0.246
	Medium	371	10.8		
	High	186	8.6		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=521)	1.13 (0.89,1.43)	0.331	AGE (p=0.004)
d) Maximal (n=741)	0.93 (0.78,1.12)	0.451	AGE (p=0.038)

[a]Relative risk for a twofold increase in dioxin.
Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 8-8. (Continued)

Analysis of Otitis

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.791[b]
(n=521)	≤18.6	2.8 (72)	7.0 (128)	3.7 (54)	0.86 (0.49,1.51)	0.601[c]
	>18.6	13.8 (58)	15.9 (132)	13.0 (77)	0.94 (0.71,1.23)	0.642[c]
f) Maximal						0.032[b]
(n=741)	≤18.6	14.2 (106)	7.3 (191)	3.6 (83)	0.62 (0.42,0.90)	0.012[c]
	>18.6	14.1 (78)	15.6 (179)	12.5 (104)	0.97 (0.79,1.19)	0.760[c]

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal			0.852[b]	AGE (p=0.032)
(n=521)	≤18.6	0.96 (0.54,1.69)	0.886[c]	
	>18.6	1.02 (0.76,1.35)	0.905[c]	
h) Maximal			0.031[b]	AGE (p=0.140)
(n=741)	≤18.6	0.64 (0.43,0.93)	0.020[c]	
	>18.6	1.00 (0.81,1.24)	0.973[c]	

[a]Relative risk for a twofold increase in dioxin.
[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).
[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 8-8. (Continued)

Analysis of Otitis

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	783	12.4	All Categories		0.308
Unknown	343	14.0	Unknown vs. Background	1.15 (0.79,1.67)	0.459
Low	196	12.8	Low vs. Background	1.03 (0.65,1.66)	0.889
High	187	8.6	High vs. Background	0.66 (0.38,1.15)	0.145
Total	1,509				

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	783	All Categories		0.633	AGE ($p<0.001$)
Unknown	343	Unknown vs. Background	1.13 (0.78,1.64)	0.532	
Low	196	Low vs. Background	1.04 (0.65,1.67)	0.863	
High	187	High vs. Background	0.76 (0.43,1.34)	0.343	
Total	1,509				

Note: Background (Comparisons): Current Dioxin $\leq$10 ppt.
Unknown (Ranch Hands): Current Dioxin $\leq$10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin $\leq$33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 8-9.

Analysis of Hearing Loss

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=519)	Low	130	73.9	0.95 (0.81,1.11)	0.504
	Medium	259	71.4		
	High	130	70.0		
b) Maximal (n=738)	Low	183	73.8	0.94 (0.84,1.06)	0.344
	Medium	370	74.6		
	High	185	68.1		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=519)	1.16 (0.97,1.39)	0.100	AGE (p<0.001)
d) Maximal (n=738)	1.08 (0.95,1.22)	0.257	AGE (p<0.001)

[a]Relative risk for a twofold increase in dioxin.
Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 8-9. (Continued)

Analysis of Hearing Loss

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.555[b]
(n=519)	≤18.6	70.8 (72)	70.3 (128)	64.2 (53)	0.84 (0.66,1.08)	0.182[c]
	>18.6	79.3 (58)	72.5 (131)	72.7 (77)	0.93 (0.75,1.15)	0.517[c]
f) Maximal						0.674[b]
(n=738)	≤18.6	68.9 (106)	72.6 (190)	62.2 (82)	0.91 (0.77,1.09)	0.319[c]
	>18.6	84.6 (78)	76.4 (178)	70.2 (104)	0.87 (0.74,1.02)	0.095[c]

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal			0.748[b]	AGE (p<0.001)
(n=519)	≤18.6	1.14 (0.87,1.51)	0.347[c]	
	>18.6	1.21 (0.95,1.55)	0.125[c]	
h) Maximal			0.690[b]	AGE (p<0.001)
(n=738)	≤18.6	1.09 (0.91,1.32)	0.345[c]	
	>18.6	1.04 (0.87,1.24)	0.674[c]	

[a]Relative risk for a twofold increase in dioxin.
[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).
[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 8-9. (Continued)

Analysis of Hearing Loss

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	776	76.0	All Categories		0.082
Unknown	341	75.1	Unknown vs. Background	0.95 (0.71,1.28)	0.731
Low	195	74.9	Low vs. Background	0.94 (0.65,1.35)	0.736
High	186	66.7	High vs. Background	0.63 (0.45,0.89)	0.009
Total	1,498				

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	776	All Categories		0.660	AGE (p<0.001)
Unknown	341	Unknown vs. Background	0.82 (0.60,1.12)	0.211	
Low	195	Low vs. Background	0.95 (0.54,1.40)	0.787	
High	186	High vs. Background	0.91 (0.63,1.31)	0.600	
Total	1,498				

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

analysis and p=0.344 for the maximal analysis). After adjustment for age, the relative risk under the minimal assumption became marginally more than 1 (Table 8-9 [c]: Adj. RR=1.16, p=0.100), although the unadjusted incidence of hearing loss decreased with levels of initial dioxin (73.9%, 71.4%, and 70.0% for the low, medium, and high initial dioxin categories in the minimal cohort). Ranch Hands in the high initial dioxin category were on the average 4.8 years younger than those in the low category. The adjusted maximal analysis did not find a significant increased risk of hearing loss (Table 8-9 [d]: p=0.257).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

Under both the minimal and maximal assumptions, the interaction between current dioxin and time since tour was not significant for the analyses of hearing loss (Table 8-9 [e-h]: p>0.55 in each of the unadjusted and adjusted analysis).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The incidence of hearing loss differed marginally among the current dioxin categories in the unadjusted analysis (Table 8-9 [i]: 76.0%, 75.1%, 74.9%, and 66.7% for the background, unknown, low, and high current dioxin categories, p=0.082). Relative to the background category, there was a significant decreased risk of hearing loss for Ranch Hands in the high current dioxin category (Est. RR=0.63, 95% C.I.: [0.45,0.89], p=0.009). However, this occurred because Ranch Hands in the high current dioxin category were on the average younger than Comparisons in the background category (63% of of Ranch Hands in the high category were born in or after 1942 versus 41% of Comparisons in the background category). For this reason, the overall contrast and the high versus background contrast became nonsignificant after adjustment for age (Table 8-9 [j]: p=0.660 and p=0.600, respectively).

Other Neurological Disorders

Preliminary screening analyses showed that occupation was highly associated with other neurological disorders. The incidence was much higher in enlisted flyers and enlisted groundcrew than in officers. This finding was independent of group membership. The percentages of Ranch Hands in the maximal cohort with other neurological disorders were 7.4 percent for officers, 32.6 percent for enlisted flyers, and 26.2 percent for enlisted groundcrew. For Comparisons with background levels of current dioxin, the incidences were 7.8 percent for officers, 33.6 percent for enlisted flyers, and 28.1 percent for enlisted groundcrew. Occupation is also highly associated with current levels of dioxin. Enlisted groundcrew have the highest current levels followed by enlisted flyers and officers (see Chapter 2, Dioxin Assay). Consequently, an additional model that included occupation was examined in each analysis. Appendix Table G-3 presents the results of these analyses.

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

The unadjusted analyses did not find a significant association between initial dioxin and conditions in the other neurological disorders category under the minimal assumption (Table 8-10 [a]: p=0.392), but under the maximal assumption, the relative risk was significantly more than 1 (Table 8-10 [b]: Est. RR=1.24, p<0.001). The percentage of Ranch Hands in the maximal cohort with a post-SEA history of other neurological disorders increased with levels of initial dioxin (11.5%, 23.5%, and 25.8% for the low, medium, and high initial dioxin categories).

TABLE 8-10.

Analysis of Other Neurological Disorders

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=520)	Low	130	16.2	1.07 (0.91,1.26)	0.392
	Medium	259	29.0		
	High	131	24.4		
b) Maximal (n=739)	Low	183	11.5	1.24 (1.09,1.40)	<0.001
	Medium	370	23.5		
	High	186	25.8		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=520)	1.20 (1.01,1.43)	0.037	AGE (p<0.001)
d) Maximal (n=739)	1.35 (1.18,1.54)	<0.001	AGE (p<0.001)

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

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 8-10. (Continued)

Analysis of Other Neurological Disorders

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.619[b]
(n=520)	≤18.6	16.7 (72)	28.4 (127)	18.5 (54)	1.11 (0.85,1.46)	0.437[c]
	>18.6	19.0 (58)	28.8 (132)	27.3 (77)	1 02 (0.82,1.26)	0.858[c]
f) Maximal						0.114[b]
(n=739)	≤18.6	7.6 (105)	21.1 (190)	25.3 (83)	1.37 (1.12,1.68)	0.002[c]
	>18.6	15.4 (78)	25.7 (179)	27.9 (104)	1.11 (0.94,1.31)	0.204[c]

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal			0.453[b]	AGE (p<0.001)
(n=520)	≤18.6	1.35 (1.01,1.79)	0.041[c]	
	>18.6	1.18 (0.94,1.47)	0.156[c]	
h) Maximal			0.082[b]	AGE (p<0.001)
(n=739)	≤18.6	1.58 (1.27,1.96)	<0.001[c]	
	>18.6	1.24 (1.05,1.48)	0.014[c]	

[a]Relative risk for a twofold increase in dioxin.
[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).
[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5 9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 8-10. (Continued)

Analysis of Other Neurological Disorders

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	781	21.6	All Categories		0.014
Unknown	342	17.0	Unknown vs. Background	0.74 (0.53,1.03)	0.073
Low	195	27.2	Low vs. Background	1.35 (0.94,1.93)	0.100
High	187	26.7	High vs. Background	1.32 (0.92,1.91)	0.135
Total	1,505				

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	781	All Categories		<0.001	AGE (p<0.001)
Unknown	342	Unknown vs. Background	0.71 (0.50,0.99)	0.041	
Low	195	Low vs. Background	1.39 (0.96,2.01)	0.078	
High	187	High vs. Background	1.72 (1.17,2.51)	0.005	
Total	1,505				

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

Adjusting for age, the relative risk was significantly more than 1 under both the minimal (Table 8-10 [c]: Adj. RR=1.20, p=0.037) and maximal (Table 8-10 [d]: Adj. RR=1.35, p<0.001) assumptions. However, the relative risk became nonsignificant under both assumptions, after also including occupation in the model (Appendix Table G-3: Adj. RR=0.97, p=0.740 under the minimal assumption; Adj. RR=1.04, p=0.567 under the maximal assumption).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

Under the minimal assumption, the unadjusted current dioxin and time since tour analysis of the other neurological disorders category did not find a significant current dioxin-by-time interaction (Table 8-10 [e]: p=0.619). The interaction between current dioxin and time was also not significant under the maximal assumption (Table 8-10 [f]: p=0.114), but there was a significant association between current dioxin and other neurological disorders for Ranch Hands with a later tour (time≤18.6: Est. RR=1.37, p=0.002; % yes: 7.6%, 21.1%, and 25.3% for the low, medium, and high current dioxin categories).

After adjusting for age, the current dioxin-by-time interaction remained nonsignificant under the minimal assumption (Table 8-10 [g]: p=0.453), but the relative risk became significantly more than 1 for Ranch Hands with a later tour (time≤18.6: Adj. RR=1.35, p=0.041). Under the maximal assumption, the association between current dioxin and other neurological disorders differed marginally between time strata (Table 8-10 [h]: p=0.082) after adjusting for age. In each time stratum, the relative risk was significantly more than 1. The relative risk was 1.58 (p<0.001) for Ranch Hands in the maximal cohort with a later tour and 1.24 (p=0.014) for those with an earlier tour. However, adjusting for age and occupation, the current dioxin-by-time interaction and all within time stratum results were not significant under both assumptions (Appendix Table G-3: p>0.10 for all analyses).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The incidence of conditions in the other neurological disorders category differed significantly among current dioxin categories in the unadjusted analysis (Table 8-10 [i]: 21.6%, 17.0%, 27.2%, and 26.7% for the background, unknown, low, and high current dioxin categories, p=0.014). The relative risk for the unknown versus background contrast was marginally less than 1 (Est. RR=0.74, 95% C.I.: [0.53,1.03], p=0.073) and marginally more than 1 for the low versus background contrast (Est. RR=1.35, 95% C.I.: [0.94,1.93], p=0.100).

The overall contrast was highly significant after adjusting for age (Table 8-10 [j]: p<0.001). Each Ranch Hand versus background contrast was significant or marginally significant. There was a significant increased risk of other neurological disorders for the high current dioxin category (Adj. RR=1.72, 95% C.I.: [1.17,2.51], p=0.005) and a marginally significant increased risk in the low category (Adj. RR=1.39, 95% C.I.: [0.96,2.01], p=0.078) The relative risk was significantly less than 1 for the unknown category (Adj. RR=0.71, 95% C.I.: [0.50,0.99], p=0.041).

The results of the analyses adjusting for age and occupation were all nonsignificant (Appendix Table G-3: p>0.50 for each contrast). The relative risk for the unknown versus background contrast, which had been significantly less than 1, became more than 1 (Adj.

RR=1.12) and was larger than the relative risk for both the low versus background contrast (Adj. RR=1.09) and the high versus background contrast (Adj. RR=1.06).

Physical Examination Variables

Smell

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Both the minimal and maximal initial dioxin analyses of smell found a relative risk that was less than 1, but not significant (Table 8-11 [a-d]: p>0.30 for the unadjusted and adjusted analyses). There were only four Ranch Hands in the minimal cohort and five Ranch Hands in the maximal cohort with an abnormal sense of smell.

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

Under both the minimal and maximal assumptions, the current dioxin-by-time since tour interaction was not investigated because only one Ranch Hand with more than 18.6 years since tour had an abnormal sense of smell. The association between current dioxin and smell was not significant for Ranch Hands with 18.6 years or less since tour in the unadjusted analyses (Table 8-11 [e] and [f]: p=0.375 for the minimal analysis and p=0.727 for the maximal analysis). No adjusted analyses were done because there were so few abnormalities.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The overall contrast was not significant in both the unadjusted and adjusted categorized current dioxin analyses of smell (Table 8-11 [g] and [h]: p=0.227 and p=0.193, respectively).

Visual Fields

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Under both the minimal and maximal assumptions, there was only one Ranch Hand with a visual field abnormality. Table 8-12 [a] shows that he was in the low initial dioxin category under the minimal assumption. No analyses were performed because of the sparse number of abnormalities.

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

No current dioxin and time since tour analyses were done because there was only one visual field abnormality.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The only two cases with an abnormal visual field were one Comparison in the background category and one Ranch Hand in the unknown current dioxin category. Neither the overall contrast (Table 8-12 [e]: p=0.313) nor the unknown versus background contrast

TABLE 8-11.

Analysis of Smell

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=521)	Low	130	0.8	0.61 (0.21,1.79)	0.324
	Medium	260	1.2		
	High	131	0.0		
b) Maximal (n=741)	Low	184	0.5	0.88 (0.44,1.75)	0.708
	Medium	371	0.8		
	High	186	0.5		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=521)	0.67 (0.22,2.00)	0.432	AGE (p=0.421)
d) Maximal (n=741)	0.93 (0.45,1.89)	0.830	AGE (p=0.378)

[a]Relative risk for a twofold increase in dioxin.
Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 8-11. (Continued)

Analysis of Smell

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						--
(n=521)	≤18.6	1.4	1.6	0.0	0.50 (0.11,2.31)	0.375[b]
		(72)	(128)	(54)		
	>18.6	0.0	0.8	0.0	--	--
		(58)	(132)	(77)		
f) Maximal						--
(n=741)	≤18.6	0.9	1.6	0.0	0.86 (0.36,2.03)	0.727[b]
		(106)	(191)	(83)		
	>18.6	0.0	0.6	0.0	--	--
		(78)	(179)	(104)		

[a]Relative risk for a twofold increase in dioxin.
[b]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).
--: Relative risk, confidence interval, and p-value not given due to the sparse number of abnormalities.
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 8-11. (Continued)

Analysis of Smell

g) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	784	0.8	All Categories		0.227
Unknown	343	0.3	Unknown vs. Background	0.38 (0.05,3.16)	0.640
Low	196	1.5	Low vs. Background	2.02 (0.50,8.13)	0.522
High	187	0.0	High vs. Background	--	0.552
Total	1,510				

h) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	784	All Categories		0.193	AGE (p=0.176)
Unknown	343	Unknown vs. Background	0.37 (0.04,3.09)	0.359	
Low	196	Low vs. Background	2.05 (0.51,8.28)	0.317	
High	187	High vs. Background	--	--	
Total	1,510				

--: Relative risk/confidence interval/p-value not given due to the absence of abnormalities.

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 8-12.

Analysis of Visual Fields

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.)	p-Value
a) Minimal (n=521)	Low	130	0.8	--	--
	Medium	260	0.0		
	High	131	0.0		
b) Maximal (n=741)	Low	184	0.0	--	--
	Medium	371	0.3		
	High	186	0.0		

--: Relative risk, confidence interval, and p-value not given due to the sparse number of abnormalities.
Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 8-12. (Continued)

Analysis of Visual Fields

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)	p-Value
c) Minimal (n=521)						--
	≤18.6	0.0 (72)	0.0 (128)	0.0 (54)	--	--
	>18.6	1.7 (58)	0.0 (132)	0.0 (77)	--	--
d) Maximal (n=741)						--
	≤18.6	0.0 (106)	0.0 (191)	0.0 (83)	--	--
	>18.6	0.0 (78)	0.6 (179)	0.0 (104)	--	--

--: Relative risk, confidence interval, and p-value not given due to the sparse number of abnormalities.
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 8-12. (Continued)

Analysis of Visual Fields

e) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	782	0.8	All Categories		0.313
Unknown	343	0.3	Unknown vs. Background	0.38 (0.05,3.15)	0.636
Low	196	0.0	Low vs. Background	--	0.520
High	187	0.0	High vs. Background	--	0.550
Total	1,508				

--: Relative risk and confidence interval not given due to the absence of abnormalities.

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

was significant (p=0.636) in the unadjusted analysis. No adjusted analysis was done due to sparse data.

Light Reaction

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Initial dioxin was not associated significantly with the prevalence of light reaction abnormalities under both the minimal and maximal assumptions (Table 8-13 [a-d]: p>0.30 for the unadjusted and adjusted analyses).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

The interaction between current dioxin and time since tour was not evaluated under the minimal assumption because only one Ranch Hand with an early tour had an abnormal light reaction. He was in the high current dioxin category. The unadjusted minimal analysis did not find a significant association between current dioxin and light reaction for Ranch Hands with a later tour (Table 8-13 [e]: p=0.943). The current dioxin-by-time interaction was not significant in the unadjusted maximal analysis of light reaction (Table 8-13 [f]: p=0.432). No adjusted analysis was done because of the sparse number of abnormalities.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The prevalence of light reaction abnormalities did not differ significantly among the four current dioxin categories in the unadjusted analysis (Table 8-13 [g]: p=0.565). The overall contrast remained nonsignificant after adjustment for age (Table 8-13 [h]: p=0.287).

Ocular Movement

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Under both the minimal and maximal assumptions there were only three ocular movement abnormalities. For the minimal cohort, they were all in the medium initial dioxin category; for the maximal cohort, three were in the medium initial dioxin category and one was in the low category. The association with initial dioxin was not significant in either cohort (Table 8-14 [a-d]: p>0.90 for the unadjusted and adjusted analyses).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

The interaction between current dioxin and time since tour could not be analyzed because no Ranch Hands with a later tour had an abnormal ocular movement. The association between current dioxin and ocular movement was not significant for Ranch Hands with an early tour in the unadjusted analyses (Table 8-14 [e]: p=0.783 for the minimal analysis; Table 8-14 [f]: p=0.818 for the maximal analysis). Adjusted analyses were not done due to the sparseness of the data.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The prevalence of abnormal ocular movement did not differ significantly among the current dioxin categories in either the unadjusted (Table 8-14 [g]: p=0.1[illegible]) or adjusted (Table 8-14 [h]: p=0.170) analysis.

TABLE 8-13.

Analysis of Light Reaction

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=521)	Low	130	0.8	1.49 (0.67,3.30)	0.346
	Medium	260	0.0		
	High	131	1.5		
b) Maximal (n=741)	Low	184	1.6	0.98 (0.54,1.77)	0.950
	Medium	371	0.3		
	High	186	1.1		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=521)	1.42 (0.61,3.29)	0.435	AGE (p=0.541)
d) Maximal (n=741)	0.99 (0.54,1.82)	0.990	AGE (p=0.815)

[a]Relative risk for a twofold increase in dioxin.
Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 8-13. (Continued)

Analysis of Light Reaction

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						--
(n=521)	≤18.6	1.4 (72)	0.0 (128)	1.9 (54)	0.95 (0.25,3.64)	0.943[b]
	>18.6	0.0 (58)	0.0 (132)	1.3 (77)	--	--
f) Maximal						0.432[†]
(n=741)	≤18.6	1.9 (106)	0.5 (191)	1.2 (83)	0.83 (0.34,1.99)	0.671[b]
	>18.6	1.3 (78)	0.0 (179)	1.0 (104)	1.35 (0.57,3.17)	0.494[b]

[a]Relative risk for a twofold increase in dioxin.
[b]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).
--: Relative risk, confidence interval, and p-value not given due to the sparse number of abnormalities.
[†]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 8-13. (Continued)

Analysis of Light Reaction

g) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	782	1.0	All Categories		0.565
Unknown	343	0.9	Unknown vs. Background	0.85 (0.23,3.24)	0.999
Low	196	0.0	Low vs. Background	--	0.332
High	187	1.1	High vs. Background	1.05 (0.22,4.97)	0.999
Total	1,508				

h) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	782	All Categories		0.287	AGE (p=0.309)
Unknown	343	Unknown vs. Background	0.84 (0.22,3.18)	0.794	
Low	196	Low vs. Background	--	--	
High	187	High vs. Background	1.20 (0.25,5.87)	0.819	
Total	1,508				

--: Relative risk, confidence interval, and p-value not given due to the absence of abnormalities.
Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 8-14.

Analysis of Ocular Movement

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=521)	Low	130	0.0	0.97 (0.37,2.53)	0.958
	Medium	260	1.2		
	High	131	0.0		
b) Maximal (n=741)	Low	184	0.5	1.02 (0.51,2.08)	0.944
	Medium	371	0.8		
	High	186	0.0		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=521)	1.01 (0.38,2.68)	0.988	AGE (p=0.781)
d) Maximal (n=741)	1.00 (0.49,2.07)	0.988	AGE (p=0.779)

[a]Relative risk for a twofold increase in dioxin.
Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 8-14. (Continued)

Analysis of Ocular Movement

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal (n=521)	≤18.6	0.0 (72)	0.0 (128)	0.0 (54)	--	-- --
	>18.6	0.0 (58)	2.3 (132)	0.0 (77)	0.82 (0.20,3.41)	0.783[b]
f) Maximal (n=741)	≤18.6	0.0 (106)	0.0 (191)	0.0 (83)	--	-- --
	>18.6	1.3 (78)	1.7 (179)	0.0 (104)	0.88 (0.31,2.52)	0.818[b]

[a]Relative risk for a twofold increase in dioxin.
[b]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).
--: Relative risk, confidence interval, and p-value not given due to the sparse number of abnormalities.
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 8-14. (Continued)

Analysis of Ocular Movement

g) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	783	0.5	All Categories		0.165
Unknown	343	0.3	Unknown vs. Background	0.57 (0.06,5.11)	0.999
Low	196	1.5	Low vs. Background	3.03 (0.67,13.63)	0.296
High	187	0.0	High vs. Background	--	0.848
Total	1,509				

h) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	783	All Categories		0.170	AGE (p=0.455)
Unknown	343	Unknown vs. Background	0.59 (0.07,5.31)	0.636	
Low	196	Low vs. Background	3.01 (0.67,13.56)	0.150	
High	187	High vs. Background	--	--	
Total	1,509				

--: Relative risk/confidence interval/p-value not given due to the absence of abnormalities.
Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

Facial Sensation

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Under both the minimal and maximal assumptions, initial dioxin was not associated significantly with the prevalence of facial sensation abnormalities in either the unadjusted or adjusted analyses (Table 8-15 [a-d]: $p>0.60$ for all analyses). There were only three assayed Ranch Hands with an abnormal facial sensation.

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

The interaction between current dioxin and time since tour was not investigated because there was only one Ranch Hand with an early tour who had a facial sensation abnormality. Under both the minimal and maximal assumptions, current dioxin was not associated significantly with facial sensation for Ranch Hands with a later tour (Table 8-15 [e] and [f]: $p=0.454$ and $p=0.203$, in the unadjusted analyses, respectively). No adjusted analysis was done because of sparse data.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The prevalence of facial sensation abnormalities did not differ significantly among the current dioxin categories in both the unadjusted and adjusted categorized current dioxin analyses (Table 8-15 [g] and [h]: $p=0.543$ and $p=0.313$, respectively).

Smile

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Initial dioxin was not significantly associated with the prevalence of smile abnormalities under both the minimal and maximal assumptions (Table 8-16 [a-d]: $p>0.10$ for the unadjusted and adjusted analyses). Only three Ranch Hands in the minimal cohort and five Ranch Hands in the maximal cohort had an abnormal smile.

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

The current dioxin-by-time since tour interaction was not analyzed because only one Ranch Hand with a later tour had a smile abnormality. For Ranch Hands with an early tour, current dioxin was marginally associated with smile in the unadjusted minimal analysis (Table 8-16 [e]: Est. RR=2.53, $p=0.059$), but there was no significant association in the unadjusted maximal analysis (Table 8-16 [f]: $p=0.668$). For the minimal analysis, both Ranch Hands with a later tour who had a smile abnormality were in the high current dioxin category. No adjusted analyses were done because of sparse data.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The categorized current dioxin analyses of smile did not reveal a significant contrast in either the unadjusted or adjusted analysis (Table 8-16 [g] and [h]: $p>0.35$ for all contrasts).

TABLE 8-15.

Analysis of Facial Sensation

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=521)	Low	130	0.8	0.87 (0.31,2.40)	0.779
	Medium	260	0.4		
	High	131	0.8		
b) Maximal (n=741)	Low	184	0.0	1.21 (0.57,2.58)	0.628
	Medium	371	0.5		
	High	186	0.5		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=521)	0.77 (0.26,2.25)	0.619	AGE (p=0.365)
d) Maximal (n=741)	1.12 (0.51,2.44)	0.776	AGE (p=0.394)

[a]Relative risk for a twofold increase in dioxin.
Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 8-15. (Continued)

Analysis of Facial Sensation

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						--
(n=521)	≤18.6	0.0 (72)	0.8 (128)	1.9 (54)	1.55 (0.49,4.88)	0.454[b]
	>18.6	1.7 (58)	0.0 (132)	0.0 (77)	--	--
f) Maximal						--
(n=741)	≤18.6	0.0 (106)	0.5 (191)	1.2 (83)	1.88 (0.71,4.97)	0.203[b]
	>18.6	0.0 (78)	0.6 (179)	0.0 (104)	--	--

[a]Relative risk for a twofold increase in dioxin.
[b]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).
--: Relative risk, confidence interval, and p-value not given due to the sparse number of abnormalities.
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 8-15. (Continued)

Analysis of Facial Sensation

g) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	783	0.6	All Categories		0.543
Unknown	343	0.0	Unknown vs. Background	--	0.334
Low	196	0.5	Low vs. Background	0.80 (0.09,6.87)	0.999
High	187	0.5	High vs. Background	0.84 (0.10,7.20)	0.999
Total	1,509				

h) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	783	All Categories		0.313	AGE (p=0.809)
Unknown	343	Unknown vs. Background	--	--	
Low	196	Low vs. Background	0.80 (0.09,6.87)	0.836	
High	187	High vs. Background	0.80 (0.09,7.10)	0.842	
Total	1,509				

--: Relative risk/confidence interval/p-value not given due to the absence of abnormalities.
Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 8-16.

Analysis of Smile

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=521)	Low	130	0.0	1.87 (0.88,3.98)	0.124
	Medium	260	0.4		
	High	131	1.5		
b) Maximal (n=741)	Low	184	1.1	1.24 (0.69,2.21)	0.485
	Medium	371	0.3		
	High	186	1.1		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=521)	1.88 (0.88,4.02)	0.124	AGE (p=0.889)
d) Maximal (n=741)	1.18 (0.65,2.15)	0.588	AGE (p=0.518)

[a]Relative risk for a twofold increase in dioxin.
Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 8-16. (Continued)

Analysis of Smile

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal (n=521)						--
	≤18.6	0.0 (72)	0.8 (128)	0.0 (54)	--	--
	>18.6	0.0 (58)	0.0 (132)	2.6 (77)	2.53 (0.96,6.66)	0.059[b]
f) Maximal (n=741)						--
	≤18.6	0.0 (106)	0.5 (191)	0.0 (83)	--	--
	>18.6	2.6 (78)	0.0 (179)	1.9 (104)	1.15 (0.60,2.19)	0.668[b]

[a]Relative risk for a twofold increase in dioxin.
[b]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).
--: Relative risk, confidence interval, and p-value not given due to the sparse number of abnormalities.
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 8-16. (Continued)

Analysis of Smile

g) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	784	1.2	All Categories		0.711
Unknown	343	0.6	Unknown vs. Background	0.51 (0.11,2.35)	0.384
Low	196	0.5	Low vs. Background	0.44 (0.06,3.51)	0.439
High	187	1.1	High vs. Background	0.93 (0.20,4.34)	0.927
Total	1,510				

h) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	784	All Categories		0.671	AGE (p=0.190)
Unknown	343	Unknown vs. Background	0.49 (0.11,2.30)	0.369	
Low	196	Low vs. Background	0.45 (0.06,3.55)	0.445	
High	187	High vs. Background	1.11 (0.23,5.30)	0.898	
Total	1,510				

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

Palpebral Fissure

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Under both the minimal and maximal assumptions, the initial dioxin analyses did not find a significant association with palpebral fissure (Table 8-17 [a-d]: $p>0.35$ in the unadjusted and adjusted analyses).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

The interaction between current dioxin and time since tour was not significant for the minimal and maximal analyses of palpebral fissure (Table 8-17 [e-h]: $p>0.20$ in the unadjusted and adjusted analyses).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The percentages of participants with an abnormal palpebral fissure did not differ significantly among the current dioxin categories in the unadjusted analysis (Table 8-17 [i]: 1.3%, 1.2%, 2.0%, and 1.6% for the background, unknown, low, and high current dioxin categories, $p=0.850$). After adjustment for age, the overall contrast remained nonsignificant (Table 8-17 [j]: $p=0.803$).

Balance

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Under both the minimal and maximal assumptions, initial dioxin was not significantly associated with balance in the unadjusted analyses (Table 8-18 [a] and [b]: $p=0.871$ and $p=0.479$). No adjusted analyses were done because only two assayed Ranch Hands had an abnormal balance (one in the medium initial dioxin category and one in the high category under both assumptions).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

The current dioxin-by-time since tour interaction could not be evaluated because no Ranch Hands with a later tour had an abnormal balance. Under both the minimal and maximal assumptions, current dioxin was not significantly associated with balance in the unadjusted analyses for Ranch Hands with an early tour (Table 8-18 [c] and [d]: $p=0.921$ and $p=0.770$, respectively). No adjusted analyses were done because of sparse data.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The unadjusted categorized current dioxin analysis of balance did not show a significant overall contrast (Table 8-18 [e]: $p=0.117$). There were no abnormalities in the background or unknown current dioxin categories and there was one abnormality in both the low and high current dioxin categories.

TABLE 8-17.

Analysis of Palpebral Fissure

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=521)	Low	130	0.8	1.27 (0.76,2.14)	0.376
	Medium	260	1.5		
	High	131	2.3		
b) Maximal (n=741)	Low	184	1.6	1.13 (0.75,1.70)	0.564
	Medium	371	1.1		
	High	186	2.2		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=519)	1.22 (0.71,2.08)	0.483	AGE (p=0.582) DIAB*INS (p=0.040)
d) Maximal (n=741)	1.12 (0.74,1.71)	0.598	AGE (p=0.857)

[a]Relative risk for a twofold increase in dioxin.
Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 8-17. (Continued)

Analysis of Palpebral Fissure

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.552[b]
(n=521)	≤18.6	0.0 (72)	1.6 (128)	0.0 (54)	0.79 (0.18,3.43)	0.758[c]
	>18.6	1.7 (58)	1.5 (132)	3.9 (77)	1.25 (0.70,2.23)	0.451[c]
f) Maximal						0.228[b]
(n=741)	≤18.6	1.9 (106)	1.1 (191)	0.0 (83)	0.67 (0.25,1.81)	0.427[c]
	>18.6	1.3 (78)	1.7 (179)	2.9 (104)	1.26 (0.78,2.02)	0.347[c]

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal			0.453[b]	AGE (p=0.744)
(n=519)	≤18.6	0.74 (0.18,3.08)	0.681[c]	DIAB*INS (p=0.038)
	>18.6	1.27 (0.71,2.26)	0.423[c]	
h) Maximal			0.229[b]	AGE (p=0.700)
(n=741)	≤18.6	0.66 (0.24,1.76)	0.403[c]	
	>18.6	1.22 (0.75,2.00)	0.420[c]	

[a]Relative risk for a twofold increase in dioxin.
[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).
[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 8-17. (Continued)

Analysis of Palpebral Fissure

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	784	1.3	All Categories		0.850
Unknown	343	1.2	Unknown vs. Background	0.91 (0.28,2.93)	0.879
Low	196	2.0	Low vs. Background	1.61 (0.50,5.20)	0.424
High	187	1.6	High vs. Background	1.26 (0.34,4.63)	0.726
Total	1,510				

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	784	All Categories		0.803	AGE (p=0.211)
Unknown	343	Unknown vs. Background	0.90 (0.28,2.88)	0.853	
Low	196	Low vs. Background	1.63 (0.50,5.25)	0.416	
High	187	High vs. Background	1.45 (0.39,5.42)	0.584	
Total	1,510				

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 8-18.

Analysis of Balance

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=521)	Low	130	0.0	1.10 (0.36,3.30)	0.871
	Medium	260	0.4		
	High	131	0.8		
b) Maximal (n=741)	Low	184	0.0	1.39 (0.58,3.34)	0.479
	Medium	371	0.3		
	High	186	0.5		

[a]Relative risk for a twofold increase in dioxin.
Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 8-18. (Continued)

Analysis of Balance

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
c) Minimal (n=521)	≤18.6	0.0 (72)	0.0 (128)	0.0 (54)	--	-- --
	>18.6	0.0 (58)	0.8 (132)	1.3 (77)	0.92 (0.18,4.70)	0.921[b]
d) Maximal (n=741)	≤18.6	0.0 (106)	0.0 (191)	0.0 (83)	--	-- --
	>18.6	0.0 (78)	0.6 (179)	1.0 (104)	1.21 (0.34,4.24)	0.770[b]

[a]Relative risk for a twofold increase in dioxin.
[b]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).
--: Relative risk, confidence interval, and p-value not given due to the sparse number of abnormalities.
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 8-18. (Continued)

Analysis of Balance

e) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	783	0.0	All Categories		0.117
Unknown	343	0.0	Unknown vs. Background	--	--
Low	196	0.5	Low vs. Background	--	0.400
High	187	0.5	High vs. Background	--	0.386
Total	1,509				

--: Relative risk/confidence interval/p-value not given due to the absence of abnormalities.
Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

Speech

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

No initial dioxin analyses were done for speech because only one Ranch Hand had a speech abnormality under both the minimal and maximal assumptions. Table 8-19 shows that he was in the medium initial dioxin category.

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

No current dioxin and time since tour analyses were done because there was only one speech abnormality.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

For the categorized current dioxin analyses, there was one speech abnormality in the background category and one in the low current dioxin category. Neither the overall contrast nor the low versus background contrast was significant in the unadjusted analysis (Table 8-19 [e]: p=0.421 and p=0.720, respectively). No adjusted analysis was done due to sparse data.

Neck Range of Motion

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

The unadjusted initial dioxin analyses of neck range of motion did not find a significant association under both the minimal (Table 8-20 [a]: p=0.748) and maximal (Table 8-20 [b]: p=0.356) assumptions. The adjusted minimal analysis revealed two significant initial dioxin-by-covariate interactions—initial dioxin-by-race (Table 8-20 [c]: p=0.001) and initial dioxin-by-diabetic class (p=0.008). Separate analyses were done for Blacks and non-Blacks to explore the interactions. The analyses for Blacks found that only one Black Ranch Hand had an abnormal range of motion and he was in the low initial dioxin category.

The initial dioxin-by-diabetic class interaction was significant for non-Blacks. Further stratification by diabetic class showed a significant association between initial dioxin and range of motion for non-Black diabetics (Appendix Table G-1: Adj. RR=2.20, p=0.002; % abnormal: 7.7%, 17.2%, and 21.1% for the low, medium, and high initial dioxin categories). Initial dioxin was not associated significantly with range of motion for either diabetically impaired non-Blacks (Adj. RR=0.52, p=0.221) or for normal non-Blacks (Adj. RR=1.20, p=0.267). After excluding the initial dioxin-by-covariate interactions, the relative risk was marginally more than 1 in the adjusted minimal analysis (Table 8-20 [c]: Adj. RR=1.24, p=0.087).

The initial dioxin-by-diabetic class interaction was also significant in the adjusted maximal analysis (Table 8-20 [d]: p=0.004). Stratified findings were consistent with the results of the adjusted minimal analysis for non-Blacks. For diabetic Ranch Hands, initial dioxin was associated significantly with range of motion (Appendix Table G-1: Adj. RR=1.85, p=0.004; % abnormal: 10.0%, 12.2%, and 19.4% for the low, medium, and high initial dioxin categories), but the association was not significant for either diabetically impaired (Adj. RR=0.61, p=0.122) or normal Ranch Hands (Adj. RR=1.01, p=0.956). After excluding

TABLE 8-19.

Analysis of Speech

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.)	p-Value
a) Minimal (n=521)	Low	130	0.0	--	--
	Medium	260	0.4		
	High	131	0.0		
b) Maximal (n=741)	Low	184	0.0	--	--
	Medium	371	0.3		
	High	186	0.0		

--: Relative risk, confidence interval, and p-value not given due to the sparse number of abnormalities.
Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 8-19. (Continued)

Analysis of Speech

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)	p-Value
c) Minimal						--
(n=521)	≤18.6	0.0 (72)	0.0 (128)	0.0 (54)	--	--
	>18.6	0.0 (58)	0.8 (132)	0.0 (77)	--	--
d) Maximal						--
(n=741)	≤18.6	0.0 (106)	0.0 (191)	0.0 (83)	--	--
	>18.6	0.0 (78)	0.6 (179)	0.0 (104)	--	--

--: Relative risk, confidence interval, and p-value not given due to the sparse number of abnormalities.
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 8-19. (Continued)

Analysis of Speech

e) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	783	0.1	All Categories		0.421
Unknown	343	0.0	Unknown vs. Background	--	0.999
Low	196	0.5	Low vs. Background	4.01 (0.25,64.40)	0.720
High	187	0.0	High vs. Background	--	0.999
Total	1,509				

--: Relative risk and confidence interval not given due to the absence of abnormalities.

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 8-20.

Analysis of Neck Range of Motion

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=521)	Low	130	9.2	1.04 (0.82,1.31)	0.748
	Medium	260	11.2		
	High	131	9.2		
b) Maximal (n=741)	Low	184	14.1	0.92 (0.78,1.10)	0.356
	Medium	371	11.3		
	High	186	8.6		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=519)	1.24 (0.97,1.59)***	0.087***	INIT*RACE (p=0.001) INIT*DIAB (p=0.008) AGE (p<0.001)
d) Maximal (n=739)	1.05 (0.87,1.27)***	0.597***	INIT*DIAB (p=0.004) AGE*RACE (p=0.003)

[a]Relative risk for a twofold increase in dioxin.
***Log_2 (initial dioxin)-by-covariate interaction ($p \leq 0.01$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction.
Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.
INIT: Log_2 (initial dioxin).

TABLE 8-20. (Continued)

Analysis of Neck Range of Motion

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.110[b]
(n=521)	≤18.6	8.3 (72)	12.5 (128)	1.9 (54)	0.74 (0.47,1.18)	0.207[c]
	>18.6	6.9 (58)	12.1 (132)	13.0 (77)	1.14 (0.86,1.52)	0.359[c]
f) Maximal						0.024[b]
(n=741)	≤18.6	16.0 (106)	11.0 (191)	6.0 (83)	0.71 (0.52,0.96)	0.024[c]
	>18.6	11.5 (78)	11.2 (179)	11.5 (104)	1.08 (0.86,1.34)	0 516[c]

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal			0.257[b]	AGE*RACE (p=0.003)
(n=521)	≤18.6	1.06 (0.65,1.71)	0.824[c]	
	>18.6	1.45 (1.07,1.96)	0.017[c]	
h) Maximal			0.026[b]	AGE*RACE (p=0.004)
(n=741)	≤18.6	0.83 (0.59,1.16)	0.270[c]	
	>18.6	1.30 (1.03,1.65)	0.029[c]	

[a]Relative risk for a twofold increase in dioxin.
[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).
[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 8-20. (Continued)

Analysis of Neck Range of Motion

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	784	11.7	All Categories		0.692
Unknown	343	12.2	Unknown vs. Background	1.05 (0.71,1.55)	0.808
Low	196	12.2	Low vs. Background	1.05 (0.65,1.69)	0.843
High	187	9.1	High vs. Background	0.75 (0.44,1.30)	0.305
Total	1,510				

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	782	All Categories		0.830**	DXCAT*DIAB (p=0.039)
					AGE (p<0.001)
Unknown	342	Unknown vs. Background	0.97 (0.63,1.47)**	0.867**	RACE (p=0.004)
Low	194	Low vs. Background	1.11 (0.66,1.86)**	0.703**	DIAB*INS (p=0.025)
High	187	High vs. Background	1.28 (0.71,2.32)**	0.413**	
Total	1,505				

**Categorized current dioxin-by-covariate interaction ($0.01<p\leq0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction.

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.
DXCAT: Categorized current dioxin.

the interaction, the adjusted maximal analysis did not find a significant association (Table 8-20 [d]: p=0.597).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

The unadjusted current dioxin and time since tour analyses of range of motion did not find a significant current dioxin-by-time interaction under the minimal assumption (Table 8-20 [e]: p=0.110), but under the maximal assumption, the interaction was significant (Table 8-20 [f]: p=0.024). The relative risk was significantly less than 1 for Ranch Hands in the maximal cohort with a later tour (time≤18.6: Est. RR=0.71, p=0.024; % abnormal: 16.0%, 11.0%, and 6.0% for the low, medium, and high current dioxin categories). The relative risk was more than 1, but not significant, for Ranch Hands in the maximal cohort with an early tour (time>18.6: Est. RR=1.08, p=0.516; % abnormal: 11.5%, 11.2%, and 11.5% for the low, medium, and high current dioxin categories).

In the adjusted minimal analysis, the current dioxin-by-time interaction remained nonsignificant (Table 8-20 [g]: p=0.257), but the relative risk for Ranch Hands with an early tour became significant (time>18.6: Adj. RR=1.45, p=0.017) after adjustment for the age-by-race interaction. The interaction between current dioxin and time remained significant in the adjusted maximal analysis (Table 8-20 [g]: p=0.026), but the significance of the within time strata results changed. After adjustment for the age-by-race interaction, the relative risk became nonsignificant for Ranch Hands with a later tour (time≤18.6: Adj. RR=0.83, p=0.270), and it became significantly more than 1 for Ranch Hands with an early tour (time>18.6: Adj. RR=1.30, p=0.029).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The prevalence of range of motion abnormalities did not differ significantly among current dioxin categories in the unadjusted analysis (Table 8-20 [i]: 11.7%, 12.2%, 12.2%, and 9.1% for the background, unknown, low, and high current dioxin categories, p=0.692). The adjusted analysis found a significant interaction between categorized current dioxin and diabetic class (Table 8-20 [j]: p=0.039). Appendix Table G-1 presents stratified results that show a marginally significant difference among the percentages of abnormalities within the diabetic stratum (15.2%, 10.5%, 5.9%, and 22.6% for the background, unknown, low, and high current dioxin categories, p=0.094). However, none of the three Ranch Hand versus background contrasts was significant (p>0.10 for each contrast). The overall contrast was not significant in either the diabetically impaired stratum (p=0.240) or in the normal stratum (p=0.631). After excluding the interaction, the adjusted analysis was not significant (Table 8-20 [j]: p>0.40 for all contrasts).

Cranial Nerve Index

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

The unadjusted initial dioxin analyses of the cranial nerve index were not significant under both the minimal (Table 8-21 [a]: p=0.812) and maximal (Table 8-21 [b]: p=0.467) assumptions. However, after adjustment for the age-by-race interaction, the relative risk became marginally more than 1 under the minimal assumption (Table 8-21 [c]: Adj. RR=1.21, p=0.090). The percentages of participants in the minimal cohort with an abnormal

TABLE 8-21.

Analysis of Cranial Nerve Index

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=513)	Low	128	12.5	1.03 (0.83,1.26)	0.812
	Medium	256	15.2		
	High	129	12.4		
b) Maximal (n=732)	Low	183	17.5	0.95 (0.81,1.10)	0.467
	Medium	367	15.0		
	High	182	11.5		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=513)	1.21 (0.97,1.50)	0.090	AGE*RACE (p=0.010)
d) Maximal (n=730)	1.05 (0.89,1.23)**	0.591**	INIT*DIAB (p=0.034) AGE*RACE (p=0.033)

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

**Log_2 (initial dioxin)-by-covariate interaction ($0.01<p\leq0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 8-21. (Continued)

Analysis of Cranial Nerve Index

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.114[b]
(n=513)	≤18.6	10.0 (70)	16.8 (125)	3.8 (53)	0.76 (0.51,1.14)	0.186[c]
	>18.6	12.1 (58)	16.0 (131)	17.1 (76)	1.11 (0.86,1.43)	0.424[c]
f) Maximal						0.021[b]
(n=732)	≤18.6	20.0 (105)	14.4 (187)	7.4 (81)	0.74 (0.57,0.97)	0.027[c]
	>18.6	14.1 (78)	15.6 (179)	14.7 (102)	1.09 (0.89,1.32)	0.411[c]

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal			0.225[b]	AGE*RACE (p=0.012)
(n=513)	≤18.6	1.00 (0.65,1.52)	0.986[c]	
	>18.6	1.34 (1.02,1.74)	0.033[c]	
h) Maximal			0.023[b]	AGE*RACE (p=0.029)
(n=732)	≤18.6	0.84 (0.63,1.12)	0.236[c]	
	>18.6	1.25 (1.02,1.54)	0.034[c]	

[a]Relative risk for a twofold increase in dioxin.
[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).
[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 8-21. (Continued)

Analysis of Cranial Nerve Index

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	773	16.0	All Categories		0.338
Unknown	341	14.7	Unknown vs. Background	0.90 (0.63,1.28)	0.559
Low	194	17.5	Low vs. Background	1.11 (0.73,1.69)	0.617
High	183	11.5	High vs. Background	0.68 (0.41,1.11)	0.123
Total	1,491				

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	773	All Categories		0.665	AGE (p<0.001) RACE (p=0.063)
Unknown	341	Unknown vs. Background	0.84 (0.58,1.22)	0.356	
Low	194	Low vs. Background	1.14 (0.73,1.77)	0.558	
High	183	High vs. Background	0.98 (0.58,1.64)	0.931	
Total	1,491				

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

cranial nerve index were 12.5, 15.2, and 12.4 percent for the low, medium, and high initial dioxin categories.

The initial dioxin-by-diabetic class interaction was significant in the adjusted maximal analysis (Table 8-21 [d]: p=0.034). Stratified results parallel the findings for range of motion. Appendix Table G-1 shows that there was a significant increased risk of cranial nerve index abnormalities associated with initial dioxin for diabetic Ranch Hands (Adj. RR=1.69, p=0.009; % abnormal: 10.0%, 12.2%, and 22.6% for the low, medium, and high initial dioxin categories). The relative risk was not significant for both diabetically impaired (Adj. RR=0.89, p=0.603) and normal Ranch Hands (Adj. RR=0.99, p=0.916). After excluding the interaction the adjusted maximal analysis was not significant (Table 8-21 [d]: Adj. RR=1.05, p=0.591).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

The current dioxin and time since tour analyses for the cranial nerve index displayed findings similar to the corresponding analyses for range of motion. In the unadjusted analyses, the current dioxin-by-time interaction was not significant under the minimal assumption (Table 8-21 [e]: p=0.114), but it was significant under the maximal assumption (Table 8-21 [f]: p=0.021). There was a significant decreased risk of cranial nerve index abnormalities for Ranch Hands in the maximal cohort with a later tour (time>18.6: Est. RR=0.74, p=0.027; % abnormal: 20.0%, 14.4%, and 7.4% for the low, medium, and high current dioxin categories) that contrasted with a nonsignificant increased risk for Ranch Hands in the maximal cohort with an early tour (time≤18.6: Est. RR=1.09, p=0.411).

After adjusting for the age-by-race interaction, the relative risk became significantly more than 1 for Ranch Hands in the minimal cohort with an early tour (Table 8-21 [g]: Adj. RR=1.34, p=0.033), although the current dioxin-by-time interaction remained nonsignificant (p=0.225). In the adjusted maximal analysis, the current dioxin-by-time interaction remained significant (Table 8-21 [h]: p=0.023). As in the adjusted minimal analysis, the adjusted maximal analysis found a relative risk significantly more than 1 for Ranch Hands with an early tour (time>18.6: Adj. RR=1.25, p=0.034). After adjustment, the relative risk became nonsignificant for Ranch Hands in the maximal cohort with a later tour (time≤18.6: Adj. RR=0.84, p=0.236).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The unadjusted categorized current dioxin analysis did not find a significant difference in the prevalence of cranial nerve index abnormalities among the four categories (Table 8-21 [i]: 16.0%, 14.7%, 17.5%, and 11.5% for the background, unknown, low, and high current dioxin categories, p=0.338). The overall contrast remained nonsignificant (Table 8-21 [j]: p=0.665) after adjustment for age and race.

Cranial Nerve Index Without Range of Motion

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Under both the minimal and maximal assumptions, the cranial nerve index without range of motion was not associated significantly with initial dioxin (Table 8-22 [a-d]: p>0.65 for all unadjusted and adjusted analyses).

TABLE 8-22.

Analysis of Cranial Nerve Index Without Range of Motion

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=513)	Low	128	3.9	1.05 (0.75,1.48)	0.760
	Medium	256	4.3		
	High	129	5.4		
b) Maximal (n=732)	Low	183	4.4	1.06 (0.82,1.37)	0.653
	Medium	367	3.8		
	High	182	5.0		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=513)	1.04 (0.73,1.48)	0.829	AGE (p=0.826) INS (p=0.085)
d) Maximal (n=732)	1.05 (0.81,1.37)	0.692	AGE (p=0.833)

[a]Relative risk for a twofold increase in dioxin.
Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 8-22. (Continued)

Analysis of Cranial Nerve Index Without Range of Motion

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.620[b]
(n=513)	≤18.6	2.9 (70)	4.0 (125)	3.8 (53)	0.89 (0.46,1.72)	0.725[c]
	>18.6	5.2 (58)	4.6 (131)	6.6 (76)	1.08 (0.72,1.63)	0.716[c]
f) Maximal						0.509[b]
(n=732)	≤18.6	4.8 (105)	3.7 (187)	2.5 (81)	0.93 (0.59,1.46)	0.750[c]
	>18.6	3.9 (78)	5.0 (179)	4.9 (102)	1.12 (0.81,1.55)	0.499[c]

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal			0.612[b]	AGE (p=0.978)
(n=513)	≤18.6	0.87 (0.44,1.71)	0.687[c]	INS (p=0.087)
	>18.6	1.06 (0.69,1.63)	0.783[c]	
h) Maximal			0.509[b]	AGE (p=0.736)
(n=732)	≤18.6	0.92 (0.58,1.44)	0.710[c]	
	>18.6	1.10 (0.79,1.54)	0.562[c]	

[a]Relative risk for a twofold increase in dioxin.
[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).
[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 8-22. (Continued)

Analysis of Cranial Nerve Index Without Range of Motion

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	773	5.1	All Categories		0.320
Unknown	341	2.9	Unknown vs. Background	0.57 (0.28,1.15)	0.117
Low	194	5.7	Low vs. Background	1.13 (0.57,2.25)	0.725
High	183	3.8	High vs. Background	0.75 (0.33,1.70)	0.489
Total	1,491				

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	773	All Categories		0.277**	DXCAT*INS (p=0.018) AGE (p=0.018)
Unknown	341	Unknown vs. Background	0.53 (0.26,1.09)**	0.084**	
Low	194	Low vs. Background	1.09 (0.54,2.19)**	0.807**	
High	183	High vs. Background	0.84 (0.36,1.93)**	0.674**	
Total	1,491				

**Categorized current dioxin-by-covariate interaction ($0.01<p\leq0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction.

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

The association between current dioxin and the cranial nerve index without range of motion did not differ significantly between time since tour strata under both the minimal and maximal assumptions (Table 8-22 [e-h]: p>0.50 for each unadjusted and adjusted analysis).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The prevalence of cranial nerve index abnormalities, excluding range of motion abnormalities, did not differ significantly among current dioxin categories in the unadjusted categorized current dioxin analysis (Table 8-22 [i]: 5.1%, 2.9%, 5.7%, and 3.8% for the background, unknown, low, and high current dioxin categories, p=0.320).

The adjusted analysis detected a significant categorized current dioxin-by-insecticide exposure interaction (Table 8-22 [j]: p=0.018). Stratified results showed a marginally significant overall contrast for participants who had never been exposed to insecticides (Appendix Table G-1: p=0.056). The percentages of abnormalities were 2.7, 2.0, 9.8, and 7.5 percent for the background, unknown, low, and high current dioxin categories in this stratum. Relative to the background category, there was a significant increased risk of an abnormality for Ranch Hands in the low current dioxin category (Adj. RR=3.76, 95% C.I.: [1.20,11.76], p=0.023) and a marginally significant increased risk for Ranch Hands in the high current dioxin category (Adj. RR=3.34, 95% C.I.: [0.98,11.34], p=0.053). The overall contrast was not significant for Ranch Hands who had been exposed to insecticides (p=0.113), although the adjusted relative risk was marginally less than 1 for the unknown versus background contrast (Adj. RR=0.46, 95% C.I.: [0.21,1.02], p=0.056). In this stratum, the prevalences for the background, unknown, low, and high current dioxin categories were 6.8, 3.3, 4.2, and 2.3 percent.

After excluding the interaction, the overall contrast was not significant in the adjusted analysis (Table 8-22 [j]: p=0.277), although there was a marginally significant decreased risk for Ranch Hands in the unknown category relative to the background category (Adj. RR=0.53, 95% C.I.: [0.26,1.09], p=0.084).

Pin Prick

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

The unadjusted initial dioxin analyses did not find a significant association with pin prick under both the minimal (Table 8-23 [a]: p=0.941) and maximal (Table 8-23 [b]: p=0.632) assumptions. Under both assumptions, the adjusted analyses detected a significant initial dioxin-by-diabetic class interaction (Table 8-23 [c] and [d]: p=0.032 in the minimal analysis and p=0.042 in the maximal analysis). Stratified results under the minimal assumption showed a marginally significant increased risk of pin prick abnormalities for diabetic Ranch Hands (Appendix Table G-1: Adj. RR=1.58, p=0.069). In this stratum, the percentages of abnormalities were 7.7, 6.9, and 21.1 percent for the low, medium, and high initial dioxin categories. The relative risk was less than 1, but not significant in both the diabetically impaired (Adj. RR=0.20, p=0.175) and normal strata (Adj. RR=0.92, p=0.682). Stratified results under the maximal assumption showed that initial dioxin was marginally associated with a decreased risk of a pin prick abnormality for diabetically impaired Ranch Hands (Adj.

TABLE 8-23.

Analysis of Pin Prick

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=512)	Low	128	9.4	1.01 (0.76,1.34)	0.941
	Medium	255	5.9		
	High	129	6.2		
b) Maximal (n=729)	Low	183	6.0	1.05 (0.85,1.30)	0.632
	Medium	363	6.6		
	High	183	7.1		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=510)	1.07 (0.80,1.44)**	0.633**	INIT*DIAB (p=0.032) AGE*RACE (p=0.036)
d) Maximal (n=727)	1.10 (0.89,1.37)**	0.390**	INIT*DIAB (p=0.042) AGE*RACE (p=0.022)

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

**Log_2 (initial dioxin)-by-covariate interaction ($0.01<p\leq0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 8-23. (Continued)

Analysis of Pin Prick

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.123[b]
(n=512)	≤18.6	12.7 (71)	6.4 (125)	5.6 (54)	0.80 (0.50,1.29)	0.363[c]
	>18.6	7.0 (57)	3.9 (130)	8.0 (75)	1.28 (0.88,1.87)	0.194[c]
f) Maximal						0.971[b]
(n=729)	≤18.6	3.8 (105)	8.5 (189)	6.2 (81)	1.06 (0.77,1.45)	0.743[c]
	>18.6	7.7 (78)	5.8 (174)	6.9 (102)	1.06 (0.80,1.42)	0.676[c]

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal			0.184**[b]	CURR*TIME*DRKYR (p=0.019)
(n=506)	≤18.6	0.89 (0.55,1.46)**	0.649**[c]	AGE*RACE (p=0.039)
	>18.6	1.33 (0.91,1.95)**	0.137**[c]	
h) Maximal			0.970**[b]	CURR*TIME*DRKYR (p=0.029)
(n=720)	≤18.6	1.12 (0.80,1.57)**	0.500**[c]	AGE*RACE (p=0.030)
	>18.6	1.13 (0.84,1.52)**	0.406**[c]	

[a]Relative risk for a twofold increase in dioxin.
[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).
[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).
**Log_2 (current dioxin)-by-time-by-covariate interaction ($0.01<p\leq0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction.
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.
CURR: Log_2 (current dioxin).
TIME: Time since tour.

TABLE 8-23. (Continued)

Analysis of Pin Prick

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	771	5.8	All Categories		0.925
Unknown	339	5.3	Unknown vs. Background	0.90 (0.52,1.59)	0.727
Low	194	5.2	Low vs. Background	0.88 (0.43,1.77)	0.714
High	183	6.6	High vs. Background	1.13 (0.59,2.19)	0.712
Total	1,487				

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	759	All Categories		0.878	DIAB (p=0.010) AGE*INS (p=0.035)
Unknown	338	Unknown vs. Background	0.97 (0.54,1.71)	0.902	
Low	192	Low vs. Background	0.84 (0.40,1.77)	0.643	
High	183	High vs. Background	1.22 (0.61,2.42)	0.571	
Total	1,482				

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

RR=0.44, p=0.093) that contrasted with nonsignificant increased risks for diabetic (Adj. RR=1.40, p=0.111) and normal (Adj. RR=1.06, p=0.678) Ranch Hands.

Under both assumptions, the adjusted initial dioxin analyses were not significant after excluding the interaction with diabetic class (Table 8-23 [c] and [d]: p=0.633 in the minimal analysis and p=0.390 in the maximal analysis).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

In the unadjusted analyses of pin prick, the interaction between current dioxin and time since tour was not significant under both the minimal (Table 8-23 [e]: p=0.123) and maximal (Table 8-23 [f]: p=0.971) assumptions. Under both assumptions, the adjusted analyses detected a significant current dioxin-by-time-by-lifetime alcohol history interaction (Table 8-23 [g] and [h]: p=0.019 in the minimal analysis and p=0.029 in the maximal analysis). Lifetime alcohol history was dichotomized to explore the interaction. Appendix Table G-1 shows that the current dioxin-by-time interaction was significant for Ranch Hands in the minimal cohort who had 40 drink-years or less (p=0.013). In this stratum, pin prick was associated significantly with current dioxin for Ranch Hands with an early tour (≤40 drink-years, time>18.6: Adj. RR=1.81, p=0.011; % abnormal: 2.6%, 4.3%, and 10.7% for the low, medium, and high current dioxin categories). By contrast, the relative risk was less than 1, but not significant for Ranch Hands with a later tour (≤40 drink-years, time≤18.6: Adj. RR=0.73, p=0.337). The current dioxin-by-time interaction was not significant for Ranch Hands in the minimal cohort who had more than 40 drink-years (p=0.108).

Stratified results under the maximal assumption found that the interaction between current dioxin and time was not significant for Ranch Hands who had 40 drink-years or less (p=0.203), but it was significant for Ranch Hands who had more than 40 drink-years (p=0.022). In both lifetime alcohol history strata, current dioxin was marginally associated with pin prick for Ranch Hands with an early tour, but the direction of the results differed. The relative risk was marginally more than 1 for those who had 40 drink-years or less (Adj. RR=1.39, p=0.055; % abnormal: 6.3%, 4.1%, and 9.2% for the low, medium, and high current dioxin categories), while it was marginally less than 1 for those who had more than 40 drink-years (Adj. RR=0.42, p=0.089; % abnormal: 15.4%, 10.0%, and 0.0% for the low, medium, and high current dioxin categories). For Ranch Hands with a later tour, the relative risk was not significant in either lifetime alcohol history stratum.

After excluding the interaction with lifetime alcohol history, the adjusted analyses did not find a significant current dioxin-by-time interaction under both the minimal (Table 8-23 [g]: p=0.184) and maximal (Table 8-23 [h]: p=0.970) assumptions.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

Both the unadjusted and adjusted categorized current dioxin analyses of pin prick did not find a significant contrast (Table 8-23 [i] and [j]: p>[illegible] for all contrasts).

Light Touch

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

The unadjusted initial dioxin analyses did not find a significant association with light touch under both the minimal (Table 8-24 [a]: p=0.928) and maximal (Table 8-24 [b]: p=0.940) assumptions. The adjusted analyses were also not significant (Table 8-24 [c] and [d]: p=0.951 for the minimal analysis and p=0.938 for the maximal analysis).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

Under the minimal assumption, the association between current dioxin and light touch differed significantly between time since tour strata in the unadjusted analysis (Table 8-24 [e]: p=0.023), although the association was not significant within both time strata. The relative risk was more than 1 for Ranch Hands with an early tour (time>18.6: Est. RR=1.43, p=0.111) and it was less than 1 for Ranch Hands with a later tour (time≤18.6: Est. RR=0.59, p=0.129). The current dioxin-by-time interaction was not significant under the maximal assumption in the unadjusted analysis (Table 8-24 [f]: p=0.401).

The adjusted analyses supported the unadjusted findings. The interaction between current dioxin and time was significant under the minimal assumption (Table 8-24 [g]: p=0.048), although neither within time stratum result was significant (time>18.6: Adj. RR=1.39, p=0.182; time≤18.6: Adj. RR=0.62, p=0.207). Under the maximal assumption, the adjusted analysis did not find a significant current dioxin-by-time interaction (Table 8-24 [h]: p=0.397).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The prevalence of light touch abnormalities did not differ significantly among current dioxin categories in the unadjusted analysis (Table 8-24 [i]: p=0.994). The adjusted analysis was also not significant (Table 8-24 [j]: p=0.989).

Muscle Status

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Under both the minimal and maximal assumptions, the initial dioxin analyses of muscle status did not find a significant association (Table 8-25 [a-d]: p>0.35 for all unadjusted and adjusted analyses).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

The association between current dioxin and muscle status did not differ significantly between time since tour strata in the unadjusted analyses (Table 8-25 [e] and [f]: p=0.869 for the minimal analysis and p=0.629 for the maximal analysis). The current dioxin-by-time interaction remained nonsignificant after covariate adjustment (Table 8-25 [g] and [h]: p=0.710 for the minimal analysis and p=0.422 for the maximal analysis).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The unadjusted categorized current dioxin analysis did not find a significant difference in the prevalence of muscle status abnormalities among the four categories (Table 8-25 [i]: p=0.974). The adjusted analysis detected a significant categorized current dioxin-by-diabetic

TABLE 8-24.

Analysis of Light Touch

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=512)	Low	128	6.3	0.99 (0.69,1.40)	0.928
	Medium	255	3.9		
	High	129	3.9		
b) Maximal (n=729)	Low	183	4.4	1.01 (0.78,1.30)	0.940
	Medium	363	4.7		
	High	183	4.4		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=504)	1.01 (0.69,1.50)	0.951	DIAB (p=0.039) AGE*RACE (p=0.017) AGE*DRKYR (p=0.043)
d) Maximal (n=727)	0.99 (0.75,1.30)	0.938	DIAB (p=0.116) AGE*RACE (p=0.019)

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

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 8-24. (Continued)

Analysis of Light Touch

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.023[b]
(n=512)	≤18.6	8.5 (71)	4.8 (125)	1.9 (54)	0.59 (0.30,1.17)	0.129[c]
	>18.6	3.5 (57)	2.1 (130)	5.3 (75)	1.43 (0.92,2.22)	0.111[c]
f) Maximal						0.401[b]
(n=729)	≤18.6	2.9 (105)	6.4 (189)	2.5 (81)	0.89 (0.59,1.35)	0.583[c]
	>18.6	5.1 (78)	4.0 (174)	4.9 (102)	1.12 (0.80,1.56)	0.517[c]

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal			0.048[b]	DIAB (p=0.060)
(n=504)	≤18.6	0.62 (0.30,1.30)	0.207[c]	AGE*RACE (p=0.029)
	>18.6	1.39 (0.86,2.24)	0.182[c]	AGE*DRKYR (p=0.035)
h) Maximal			0.397[b]	DIAB (p=0.135)
(n=727)	≤18.6	0.85 (0.54,1.36)	0.504[c]	AGE*RACE (p=0.020)
	>18.6	1.08 (0.77,1.53)	0.648[c]	

[a]Relative risk for a twofold increase in dioxin.
[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).
[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 8-24. (Continued)

Analysis of Light Touch

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	771	4.3	All Categories		0.994
Unknown	339	4.1	Unknown vs. Background	0.96 (0.51,1.82)	0.909
Low	194	4.1	Low vs. Background	0.96 (0.44,2.12)	0.923
High	183	3.8	High vs. Background	0.89 (0.39,2.04)	0.733
Total	1,487				

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	769	All Categories		0.989	AGE (p=0.377) DIAB*INS (p=0.044)
Unknown	338	Unknown vs. Background	1.09 (0.57,2.09)	0.797	
Low	192	Low vs. Background	0.97 (0.42,2.27)	0.943	
High	183	High vs. Background	0.93 (0.39,2.22)	0.876	
Total	1,482				

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 8-25.

Analysis of Muscle Status

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=521)	Low	130	0.8	1.03 (0.61,1.71)	0.922
	Medium	260	2.3		
	High	131	2.3		
b) Maximal (n=740)	Low	183	1.1	1.17 (0.79,1.72)	0.439
	Medium	371	1.9		
	High	186	1.6		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=519)	1.09 (0.65,1.83)	0.747	AGE (p=0.175) DIAB (p=0.126)
d) Maximal (n=729)	1.21 (0.80,1.83)	0.381	AGE (p=0.064) DIAB*DRKYR (p=0.005)

[a]Relative risk for a twofold increase in dioxin.
Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 8-25. (Continued)

Analysis of Muscle Status

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.869[b]
(n=521)	≤18.6	0.0 (72)	3.9 (128)	1.9 (54)	1.07 (0.51,2.25)	0.859[c]
	>18.6	3.5 (58)	0.0 (132)	2.6 (77)	0.98 (0.44,2.15)	0.953[c]
f) Maximal						0.629[b]
(n=740)	≤18.6	1.0 (105)	2.1 (191)	2.4 (83)	1.30 (0.75,2.25)	0.348[c]
	>18.6	1.3 (78)	1.1 (179)	1.9 (104)	1.07 (0.59,1.94)	0.835[c]

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal			0.710[b]	AGE (p=0.127)
(n=519)	≤18.6	1.28 (0.59,2.79)	0.533[c]	DIAB (p=0.141)
	>18.6	1.05 (0.48,2.31)	0.908[c]	
h) Maximal			0.422[b]	AGE (p=0.041)
(n=729)	≤18.6	1.55 (0.83,2.90)	0.167[c]	DIAB*DRKYR (p=0.005)
	>18.6	1.10 (0.59,2.03)	0.766[c]	

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

[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).

[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 8-25. (Continued)

Analysis of Muscle Status

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	783	2.2	All Categories		0.974
Unknown	342	1.8	Unknown vs. Background	0.80 (0.31,2.06)	0.650
Low	196	2.0	Low vs. Background	0.94 (0.31,2.82)	0.910
High	187	2.1	High vs. Background	0.98 (0.33,2.96)	0.978
Total	1,508				

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	779	All Categories		0.945**	DXCAT*DIAB (p=0.019) AGE (p=0.014)
Unknown	338	Unknown vs. Background	0.77 (0.30,1.99)**	0.586**	DIAB*DRKYR (p=0.011)
Low	192	Low vs. Background	0.92 (0.30,2.81)**	0.884**	
High	183	High vs. Background	1.08 (0.34,3.45)**	0.893**	
Total	1,492				

**Categorized current dioxin-by-covariate interaction ($0.01<p\leq0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction.

Note: Background (Comparisons): Current Dioxin $\leq$10 ppt.
Unknown (Ranch Hands): Current Dioxin $\leq$10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin $\leq$33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

class interaction (Table 8-25 [j]: p=0.019). Stratified results did not reveal a significant contrast for either diabetic (Appendix Table G-1: p>0.30 for all contrasts) or normal participants (p>0.20 for all contrasts). The percentages of muscle status abnormalities differed significantly among categories for diabetically impaired participants (0.0%, 6.4%, 0.0%, and 0.0% for the background, unknown, low, and high current dioxin categories, p=0.022), but this finding was affected by the sparse number of abnormalities (three in the unknown category and none in the other categories). The interaction occurred partly because the high and background categories contained the highest percentage of abnormalities in the normal strata, the unknown category had the most abnormalities in the impaired strata, and the low current dioxin category had the highest percentage of abnormalities in the diabetic stratum.

After excluding the interaction, the adjusted analysis was not significant (Table 8-25 [j]: p>0.55 for all contrasts).

Vibration

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Under both the minimal and maximal assumptions the initial dioxin analyses did not find a significant association with vibration (Table 8-26 [a-d]: p>0.60 for all unadjusted and adjusted analyses).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

The current dioxin-by-time since tour interaction was not significant in the analyses of vibration under both the minimal and maximal assumptions (Table 8-26 [e-h]: p>0.80 in each unadjusted and adjusted analysis).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The prevalence of vibration abnormalities did not differ significantly among the current dioxin categories in the unadjusted analysis (Table 8-26 [i]: 1.4%, 0.9%, 1.6%, and 1.6% for the background, unknown, low, and high current dioxin categories, p=0.844). The overall contrast remained nonsignificant after covariate adjustment (Table 8-26 [j]: p=0.584).

Patellar Reflex

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

The unadjusted initial dioxin analyses of the patellar reflex were not significant under both the minimal (Table 8-27 [a]: p=0.661) and maximal (Table 8-27 [b]: p=0.304) assumptions. The adjusted analyses were also not significant (Table 8-27 [c] and [d]: p=0.686 for the minimal analysis and p=0.182 for the maximal analysis).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

Under both the minimal and maximal assumptions, the association between current dioxin and patellar reflex did not differ significantly between time since tour strata (Table 8-27 [e-h]: p>0.50 in each analysis).

TABLE 8-26.

Analysis of Vibration

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=512)	Low	128	2.3	0.87 (0.50,1.52)	0.620
	Medium	255	2.4		
	High	129	0.8		
b) Maximal (n=729)	Low	183	1.1	1.07 (0.72,1.60)	0.737
	Medium	363	1.9		
	High	183	1.6		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=512)	0.87 (0.48,1.59)	0.644	AGE*INS (p=0.005)
d) Maximal (n=729)	1.11 (0.73,1.70)	0.619	AGE*INS (p=0.005)

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

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 8-26. (Continued)

Analysis of Vibration

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal (n=512)						0.847[b]
	≤18.6	1.4 (71)	1.6 (125)	0.0 (54)	0.87 (0.28,2.72)	0.806[c]
	>18.6	5.3 (57)	2.3 (130)	1.3 (75)	0.76 (0.38,1.53)	0.438[c]
f) Maximal (n=729)						0.885[b]
	≤18.6	1.0 (105)	1.1 (189)	1.2 (81)	1.06 (0.49,2.30)	0.879[c]
	>18.6	1.3 (78)	2.9 (174)	2.0 (102)	0.99 (0.61,1.63)	0.974[c]

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal (n=512)			0.897[b]	AGE*INS (p=0.004)
	≤18.6	0.82 (0.25,2.71)	0.751[c]	
	>18.6	0.75 (0.36,1.59)	0.457[c]	
h) Maximal (n=727)			0.900[b]	AGE*INS (p=0.006)
	≤18.6	1.11 (0.50,2.48)	0.794[c]	DIAB (p=0.131)
	>18.6	1.05 (0.62,1.77)	0.862[c]	

[a]Relative risk for a twofold increase in dioxin.
[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).
[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 8-26. (Continued)

Analysis of Vibration

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	771	1.4	All Categories		0.844
Unknown	339	0.9	Unknown vs. Background	0.62 (0.17,2.22)	0.460
Low	194	1.6	Low vs. Background	1.09 (0.30,3.93)	0.901
High	183	1.6	High vs. Background	1.15 (0.32,4.17)	0.830
Total	1,487				

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	771	All Categories		0.584	AGE*RACE (p=0.017)
Unknown	339	Unknown vs. Background	0.63 (0.17,2.29)	0.478	
Low	194	Low vs. Background	1.21 (0.33,4.46)	0.774	
High	183	High vs. Background	1.99 (0.52,7.57)	0.312	
Total	1,487				

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 8-27.

Analysis of Patellar Reflex

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=521)	Low	130	0.0	1.12 (0.68,1.83)	0.661
	Medium	260	3.1		
	High	131	1.5		
b) Maximal (n=741)	Low	184	1.1	1.23 (0.84,1.79)	0.304
	Medium	371	1.6		
	High	186	2.2		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=519)	1.11 (0.67,1.85)	0.686	AGE (p=0.641) DIAB (p=0.107)
d) Maximal (n=739)	1.33 (0.89,2.00)	0.182	AGE*DIAB (p=0.021)

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

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 8-27. (Continued)

Analysis of Patellar Reflex

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal (n=521)						0.820[b]
	≤18.6	0.0 (72)	3.1 (128)	0.0 (54)	1.16 (0.48,2.80)	0.740[c]
	>18.6	1.7 (58)	2.3 (132)	2.6 (77)	1.02 (0.54,1.93)	0.945[c]
f) Maximal (n=741)						0.786[b]
	≤18.6	0.9 (106)	1.1 (191)	2.4 (83)	1.27 (0.66,2.44)	0.470[c]
	>18.6	1.3 (78)	1.7 (179)	2.9 (104)	1.13 (0.69,1.86)	0.615[c]

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal (n=519)			0.738[b]	AGE (p=0.718)
	≤18.6	1.19 (0.49,2.93)	0.700[c]	DIAB (p=0.099)
	>18.6	0.99 (0.52,1.91)	0.983[c]	
h) Maximal (n=739)			0.535[b]	AGE*DIAB (p=0.014)
	≤18.6	1.52 (0.75,3.11)	0.248[c]	
	>18.6	1.18 (0.72,1.96)	0.510[c]	

[a]Relative risk for a twofold increase in dioxin.
[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).
[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 8-27. (Continued)

Analysis of Patellar Reflex

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	783	1.2	All Categories		0.434
Unknown	343	1.2	Unknown vs. Background	1.01 (0.31,3.32)	0.981
Low	196	2.0	Low vs. Background	1.79 (0.55,5.88)	0.336
High	187	2.7	High vs. Background	2.36 (0.78,7.13)	0.127
Total	1,509				

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	783	All Categories		0.343	AGE (p=0.241) RACE (p=0.112)
Unknown	343	Unknown vs. Background	1.05 (0.32,3.45)	0.935	
Low	196	Low vs. Background	1.80 (0.55,5.94)	0.332	
High	187	High vs. Background	2.75 (0.89,8.50)	0.078	
Total	1,509				

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The prevalence of patellar reflex abnormalities did not differ significantly among current dioxin categories in the unadjusted analysis, although the high current dioxin category had relatively more abnormalities than the other categories (Table 8-27 [i]: 1.2%, 1.2%, 2.0%, and 2.7% for the background, unknown, low, and high current dioxin categories, p=0.45[illegible]). The overall contrast remained nonsignificant after adjustment for age and race (Table 8-27 [j]: p=0.343), but the high versus background contrast became marginally significant (Adj. RR=2.75, 95% C.I.: [0.89.8.50], p=0.078).

Achilles Reflex

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

In the unadjusted analyses, initial dioxin was not significantly associated with the Achilles reflex under either the minimal (Table 8-28 [a]: p=0.718) or maximal (Table 8-28 [b]: p=0.273) assumption. Adjusting for age, race, and the diabetic class-by-lifetime alcohol history interaction, the association remained nonsignificant under both assumptions (Table 8-28 [c] and [d]: p=0.698 for the minimal analysis and p=0.224 for the maximal analysis). However, because of the association between dioxin and diabetes (see Chapter 15 for a discussion of diabetes), an additional model was examined that did not adjust for diabetic class. Adjusting for age and race only (lifetime alcohol history stepped out of the model), the relative risk was marginally more than 1 under the maximal assumption (Appendix Table G-2: Adj. RR=1.26, p=0.063). The percentages of Ranch Hands in the maximal cohort with an abnormal Achilles reflex were 2.7, 6.2, and 5.4 percent for the low, medium, and high initial dioxin categories. The results under the minimal assumption remained nonsignificant after excluding diabetic class (p=0.771).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

Under the minimal assumption, the association between current dioxin and the Achilles reflex differed significantly between time since tour strata in the unadjusted analysis (Table 8-28 [e]: p=0.049). The relative risk was marginally less than 1 for Ranch Hands in the minimal cohort with a later tour (time≤18.6: Est. RR=0.59, p=0.098) in contrast to a nonsignificant relative risk that was more than 1 for Ranch Hands in the minimal cohort with an early tour (time>18.6: Est. RR=1.17, p=0.387). The current dioxin-by-time interaction was not significant in the unadjusted maximal analysis, nor was there a significant relative risk within either time stratum.

After adjustment for age, race, and the diabetic class-by-lifetime alcohol history interaction, the interaction between current dioxin and time became marginally significant under the minimal assumption (Table 8-28 [g]: p=0.064), with neither of the within time stratum results significant. Adjusting for the same covariates, the current dioxin-by-time interaction was not significant under the maximal assumption, although the relative risk became marginally more than 1 for Ranch Hands with an early tour (time>18.6: Adj. RR=1.33, p=0.073). Adjusting for age and race only, the relative risk was significantly more than 1 in this stratum (Appendix Table G-2: Adj. RR=1.42, p=0.022).

TABLE 8-28.

Analysis of Achilles Reflex

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=520)	Low	130	6.2	0.95 (0.70,1.28)	0.718
	Medium	259	7.3		
	High	131	3.8		
b) Maximal (n=739)	Low	183	2.7	1.14 (0.91,1.42)	0.273
	Medium	370	6.2		
	High	186	5.4		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=512)	0.94 (0.68,1.29)	0.698	AGE (p=0.033) RACE (p=0.040) DIAB*DRKYR (p=0.002)
d) Maximal (n=728)	1.17 (0.91,1.49)	0.224	AGE (p=0.002) RACE (p=0.052) DIAB*DRKYR (p=0.020)

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

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 8-23. (Continued)

Analysis of Achilles Reflex

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal (n=520)						0.049[b]
	≤18.6	5.6 (72)	8.7 (127)	0.0 (54)	0.59 (0.31,1.10)	0.098[c]
	>18.6	1.7 (58)	8.3 (132)	6.5 (77)	1.17 (0.82,1.69)	0.387[c]
f) Maximal (n=739)						0.305[b]
	≤18.6	2.9 (105)	6.8 (190)	2.4 (83)	0.97 (0.65,1.43)	0.861[c]
	>18.6	3.9 (78)	5.0 (179)	7.7 (104)	1.24 (0.93,1.66)	0.143[c]

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal (n=512)			0.064[b]	AGE (p=0.039)
	≤18.6	0.61 (0.33,1.15)	0.126[c]	RACE (p=0.034)
	>18.6	1.17 (0.79,1.74)	0.425[c]	DIAB*DRKYR (p=0.002)
h) Maximal (n=728)			0.243[b]	AGE (p=0.001)
	≤18.6	0.99 (0.65,1.50)	0.950[c]	RACE (p=0.052)
	>18.6	1.33 (0.97,1.81)	0.073[c]	DIAB*DRKYR (p=0.020)

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

[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).

[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 8-28. (Continued)

Analysis of Achilles Reflex

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	784	5.6	All Categories		0.290
Unknown	342	3.8	Unknown vs. Background	0.66 (0.35,1.25)	0.205
Low	195	7.7	Low vs. Background	1.40 (0.76,2.57)	0.277
High	187	5.4	High vs. Background	0.95 (0.47,1.92)	0.887
Total	1,508				

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	782	All Categories		0.313**	DXCAT*RACE (p=0.045)
					AGE (p<0.001)
Unknown	341	Unknown vs. Background	0.66 (0.35,1.26)**	0.211**	DIAB (p=0.002)
Low	193	Low vs. Background	1.39 (0.74,2.60)**	0.303**	
High	187	High vs. Background	1.06 (0.51,2.23)**	0.871**	
Total	1,503				

**Categorized current dioxin-by-covariate interaction ($0.01<p\leq0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction.

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The unadjusted categorized current dioxin analysis of the Achilles reflex did not find a significant difference in the prevalences among the four categories (Table 8-28 [i]: 5.6%, 3.8%, 7.7%, and 5.4% for the background, unknown, low, and high current dioxin categories, p=0.290). The adjusted analysis detected a significant interaction between categorized current dioxin and race (Table 8-28 [j]: p=0.045). Stratified results show a marginally significant overall contrast for Blacks (Appendix Table G-1: p=0.078), but this finding may be affected by sparse data. Only two Black Ranch Hands (unknown current dioxin category) and three Black Comparisons in the background category had an abnormal Achilles reflex. None of the contrasts was significant for non-Blacks (p>0.10 for each contrast). After excluding the interaction, the overall contrast was not significant in the adjusted analysis (Table 8-28 [j]: p=0.313).

Biceps Reflex

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Under the minimal assumption, no Ranch Hands had an abnormal biceps reflex. One Ranch Hand had an abnormal biceps reflex under the maximal assumption. Table 8-29 [b] shows that he was in the low initial dioxin category. No analyses were done due to sparse data.

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

No current dioxin and time since tour analyses were done for the biceps reflex because there was only one Ranch Hand abnormality. Table 8-29 [d] shows that he was in the low current dioxin category with a time since tour 18.6 years or less.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The unadjusted categorized current dioxin analysis found that 10 Comparisons in the background current dioxin category had an abnormal biceps reflex (1.3%) versus 1 Ranch Hand in the unknown category (0.6%). Neither the overall contrast (Table 8-29 [e]: p=0.135) nor the unknown versus background contrast (p=0.482) was significant.

Babinski Reflex

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Under both the minimal and maximal assumptions there were only two Ranch Hands with an abnormal Babinski reflex. For each cohort, one was in the medium initial dioxin category and the other was in the high initial dioxin category. In the unadjusted analyses, initial dioxin was not associated with the Babinski reflex under both assumptions (Table 8-30 [a] and [b]: p=0.552 under the minimal assumption and p=0.285 under the maximal assumption). No adjusted analyses were done because of the sparse number of abnormalities.

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

The current dioxin-by-time interaction could not be investigated because no Ranch Hands with a time since tour 18.6 years or less had an abnormal Babinski reflex. The

TABLE 8-29.

Analysis of Biceps Reflex

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.)	p-Value
a) Minimal (n=521)	Low	130	0.0	--	--
	Medium	260	0.0		
	High	131	0.0		
b) Maximal (n=741)	Low	184	0.5	--	--
	Medium	371	0.0		
	High	186	0.0		

--: Relative risk, confidence interval, and p-value not given due to the sparse number of abnormalities.
Note. Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 8-29. (Continued)

Analysis of Biceps Reflex

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)	p-Value
c) Minimal						--
(n=521)	≤18.6	0.0 (72)	0.0 (128)	0.0 (54)	--	--
	>18.6	0.0 (58)	0.0 (132)	0.0 (77)	--	--
d) Maximal						--
(n=741)	≤18.6	0.9 (106)	0.0 (191)	0.0 (83)	--	--
	>18.6	0.0 (78)	0.0 (179)	0.0 (104)	--	--

--: Relative risk, confidence interval, and p-value not given due to the sparse number of abnormalities.
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 8-29. (Continued)

Analysis of Biceps Reflex

e) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	784	1.3	All Categories		0.135
Unknown	343	0.6	Unknown vs. Background	0.45 (0.10,2.08)	0.482
Low	196	0.0	Low vs. Background	--	0.212
High	187	0.0	High vs. Background	--	0.232
Total	1,510				

--: Relative risk and confidence interval not given due to the absence of abnormalities.

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 8-30.

Analysis of Babinski Reflex

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=521)	Low	130	0.0	1.37 (0.51,3.73)	0.552
	Medium	260	0.4		
	High	131	0.8		
b) Maximal (n=741)	Low	184	0.0	1.62 (0.70,3.75)	0.285
	Medium	371	0.3		
	High	186	0.5		

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

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 8-30. (Continued)

Analysis of Babinski Reflex

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
c) Minimal						--
(n=521)	≤18.6	0.0 (72)	0.0 (128)	0.0 (54)	--	--
	>18.6	1.7 (58)	0.0 (132)	1.3 (77)	0.96 (0.20,4.72)	0.964[b]
d) Maximal						--
(n=741)	≤18.6	0.0 (106)	0.0 (191)	0.0 (83)	--	--
	>18.6	0.0 (78)	0.6 (179)	1.0 (104)	1.24 (0.36,4.30)	0.734[b]

[a]Relative risk for a twofold increase in dioxin.
[b]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).
--: Relative risk, confidence interval, and p-value not given due to the sparse number of abnormalities.
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 8-30. (Continued)

Analysis of Babinski Reflex

e) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	784	0.3	All Categories		0.641
Unknown	343	0.6	Unknown vs. Background	2.29 (0.32,16.35)	0.712
Low	196	0.0	Low vs. Background	--	0.999
High	187	0.5	High vs. Background	2.10 (0.19,23.31)	0.948
Total	1,510				

--: Relative risk and confidence interval not given due to the absence of abnormalities.

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

association between current dioxin and the Babinski reflex was not significant for Ranch Hands with a time since tour more than 18.6 years under both the minimal (Table 8-30 [c]: p=0.964) and maximal (Table 8-30 [d]: p=0.734) assumptions. No adjusted analyses were done due to sparse data.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The overall contrast was not significant in the unadjusted categorized current dioxin analysis of the Babinski reflex (Table 8-30 [e]: p=0.641). No adjusted analysis was done because there were only five participants with an abnormal Babinski reflex (two in the background category, two in the unknown current dioxin category, and one in the high current dioxin category).

Tremor

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Under both the minimal and maximal assumptions, initial dioxin was not associated significantly with tremor (Table 8-31 [a-d]: p>0.60 for all unadjusted and adjusted analyses).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

The unadjusted current dioxin and time since tour analyses of tremor did not find a significant interaction between current dioxin and time under either the minimal (Table 8-31 [e]: p=0.402) or maximal (Table 8-31 [f]: p=0.101) assumption.

The current dioxin-by-time interaction remained nonsignificant in the adjusted minimal analysis (Table 8-31 [g]: p=0.409), but the adjusted maximal analysis detected a significant interaction among current dioxin, time, and age (Table 8-31 [h]: p=0.044). Age was categorized to explore the interaction. Stratified results revealed a significant current dioxin-by-time interaction for older Ranch Hands, those born before 1942 (Appendix Table G-1: p=0.008). The within time stratum findings showed that there was a significant increased risk of tremor associated with initial dioxin for older Ranch Hands with a later tour (time≤18.6: Adj. RR=2.96, p=0.005; % abnormal: 0.0%, 0.9%, and 11.5% for the low, medium, and high initial dioxin categories). The relative risk was less than 1, but not significant for older Ranch Hands with an early tour (time>18.6: Adj. RR=0.70, p=0.432). For younger Ranch Hands, those born in or after 1942, the current dioxin-by-time interaction was not significant (p=0.954), nor were either of the within time stratum results significant (p=0.670 for time≤18.6 and p=0.440 for time>18.6).

After excluding the interaction, the current dioxin-by-time interaction was not significant for the adjusted maximal analysis (Table 8-31 [h]: p=0.102).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The prevalence of tremor abnormalities did not differ significantly among current dioxin categories in the unadjusted analysis, although the high category had the highest percentage of abnormalities (Table 8-31 [i]: 2.7%, 2.6%, 2.0%, and 3.7% for the background, unknown,

TABLE 8-31.

Analysis of Tremor

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=521)	Low	130	2.3	1.08 (0.69,1.67)	0.744
	Medium	260	2.3		
	High	131	3.1		
b) Maximal (n=741)	Low	184	2.7	1.08 (0.78,1.50)	0.643
	Medium	371	1.9		
	High	186	3.2		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=521)	1.05 (0.66,1.66)	0.850	AGE (p=0.598)
d) Maximal (n=741)	1.08 (0.77,1.51)	0.675	AGE (p=0.861)

[a]Relative risk for a twofold increase in dioxin.
Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 8-31. (Continued)

Analysis of Tremor

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.402[b]
(n=521)	≤18.6	1.4 (72)	2.3 (128)	3.7 (54)	1.41 (0.71,2.79)	0.326[c]
	>18.6	1.7 (58)	2.3 (132)	3.9 (77)	0.95 (0.52,1.75)	0.877[c]
f) Maximal						0.101[b]
(n=741)	≤18.6	0.0 (106)	2.1 (191)	3.6 (83)	1.56 (0.92,2.65)	0.102[c]
	>18.6	5.1 (78)	1.7 (179)	3.9 (104)	0.87 (0.55,1.37)	0.548[c]

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal			0.409[b]	AGE (p=0.631)
(n=521)	≤18.6	1.35 (0.67,2.75)	0.404[c]	
	>18.6	0.92 (0.49,1.73)	0.789[c]	
h) Maximal			0.102**[b]	CURR*TIME*AGE (p=0.044)
(n=741)	≤18.6	1.53 (0.89,2.63)**	0.126**[c]	
	>18.6	0.85 (0.54,1.37)**	0.512**[c]	

[a]Relative risk for a twofold increase in dioxin.
[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).
[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).
**Log_2 (current dioxin)-by-time-by-covariate interaction ($0.01<p\leq0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction.
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 8-31. (Continued)

Analysis of Tremor

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	784	2.7	All Categories		0.788
Unknown	343	2.6	Unknown vs. Background	0.98 (0.44,2.16)	0.958
Low	196	2.0	Low vs. Background	0.76 (0.26,2.23)	0.614
High	187	3.7	High vs. Background	1.41 (0.59,3.37)	0.436
Total	1,510				

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	784	All Categories		0.657	AGE (p=0.089) INS (p=0.126)
Unknown	343	Unknown vs. Background	0.90 (0.40,1.99)	0.789	
Low	196	Low vs. Background	0.71 (0.24,2.10)	0.532	
High	187	High vs. Background	1.51 (0.62,3.70)	0.364	
Total	1,510				

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

low, and high current dioxin categories, p>0.40 for each contrast). All contrasts remained nonsignificant after covariate adjustment (Table 8-31 [j]: p>0.35 for each contrast).

Coordination

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

The unadjusted initial dioxin analyses of coordination did not detect a significant association (Table 8-32 [a] and [b]: p=0.414 under the minimal assumption and p=0.178 under the maximal assumption), although the percentages of abnormalities increased with initial dioxin (0.0%, 1.9%, and 2.3% for the low, medium, and high initial dioxin categories of the minimal cohort; 0.5%, 1.1%, and 2.2% for the corresponding categories of the maximal cohort).

The relative risk remained nonsignificant after adjustment for age and the diabetic class-by-lifetime alcohol history interaction (Table 8-32 [c] and [d]: p=0.296 under the minimal assumption and p=0.101 under the maximal assumption). However, because of the association between dioxin and diabetes, an additional model was examined that excluded the diabetic class-by-lifetime alcohol history interaction under both assumptions. Adjusting for age only, initial dioxin was marginally associated with coordination under the maximal assumption (Table G-2: Adj. RR=1.49, p=0.085), but the association remained nonsignificant under the minimal assumption (Adj. RR=1.41, p=0.220).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

The interaction between current dioxin and time since tour was not significant in the unadjusted analyses of coordination (Table 8-32 [e] and [f]: p=0.312 under the minimal assumption and p=0.128 under the maximal assumption). The relative risk was marginally more than 1 for Ranch Hands in the maximal cohort with a later tour (time≤18.6: Est. RR=2.00, p=0.051; % abnormal: 0.0%, 0.5%, and 3.6% for the low, medium, and high current dioxin categories).

Adjusting for age, the minimal analysis did not find a significant current dioxin-by-time interaction (Table 8-32 [g]: p=0.257), although the relative risk was marginally more than 1 for Ranch Hands with a later tour (time>18.6: Adj. RR=2.14, p=0.071). Under the maximal assumption, adjusting for age and the diabetic class-by-lifetime alcohol history interaction, the current dioxin-by-time interaction was marginally significant (Table 8-32 [h]: p=0.086) and the relative risk was significantly more than 1 for Ranch Hands with a later tour (time≤18.6: Adj. RR=2.53, p=0.019). The adjusted relative risk was more than 1, but not significant for Ranch Hands in the maximal cohort with an early tour (time>18.6: Adj. RR=1.11, p=0.753).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The prevalence of coordination abnormalities differed marginally among current dioxin categories in the unadjusted analysis (Table 8-32 [i]: 0.4%, 1.2%, 1.0%, and 2.7% for the background, unknown, low, and high current dioxin categories, p=0.056). There was a significant increased risk for the high category relative to the background category (Est. RR=7.14, 95% C.I.: [1.69,30.16], p=0.007).

TABLE 8-32.

Analysis of Coordination

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=521)	Low	130	0.0	1.25 (0.74,2.11)	0.414
	Medium	260	1.9		
	High	131	2.3		
b) Maximal (n=740)	Low	183	0.5	1.35 (0.89,2.06)	0.178
	Medium	371	1.1		
	High	186	2.2		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=513)	1.35 (0.78,2.36)	0.296	AGE (p=0.050) DIAB*DRKYR (p=0.046)
d) Maximal (n=729)	1.48 (0.94,2.32)	0.101	AGE (p=0.041) DIAB*DRKYR (p=0.047)

[a]Relative risk for a twofold increase in dioxin.
Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 8-32. (Continued)

Analysis of Coordination

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.312[b]
(n=521)	≤18.6	0.0 (72)	1.6 (128)	3.7 (54)	1.69 (0.75,3.79)	0.206[c]
	>18.6	1.7 (58)	0.8 (132)	2.6 (77)	0.94 (0.42,2.11)	0.885[c]
f) Maximal						0.128[b]
(n=740)	≤18.6	0.0 (105)	0.5 (191)	3.6 (83)	2.00 (1.00,4.03)	0.051[c]
	>18.6	1.3 (78)	1.1 (179)	1.9 (104)	0.99 (0.53,1.84)	0.962[c]

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal			0.257[b]	AGE (p=0.032)
(n=521)	≤18.6	2.14 (0.94,4.91)	0.071[c]	
	>18.6	1.14 (0.52,2.51)	0.748[c]	
h) Maximal			0.086[b]	AGE (p=0.025)
(n=729)	≤18.6	2.53 (1.16,5.48)	0.019[c]	DIAB*DRKYR (p=0.049)
	>18.6	1.11 (0.58,2.11)	0.758[c]	

[a]Relative risk for a twofold increase in dioxin.
[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).
[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 8-32. (Continued)

Analysis of Coordination

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	783	0.4	All Categories		0.056
Unknown	342	1.2	Unknown vs. Background	3.08 (0.68,13.82)	0.143
Low	196	1.0	Low vs. Background	2.68 (0.44,16.15)	0.282
High	187	2.7	High vs. Background	7.14 (1.69,30.16)	0.007
Total	1,508				

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	781	All Categories		0.006**	DXCAT*AGE (p=0.049) RACE (p=0.093)
Unknown	341	Unknown vs. Background	4.68 (0.84,25.97)**	0.077**	DIAB*INS (p=0.038)
Low	194	Low vs. Background	3.89 (0.53,28.40)**	0.180**	
High	187	High vs. Background	18.30 (3.26,102.7)**	0.001**	
Total	1,503				

**Categorized current dioxin-by-covariate interaction ($0.01<p\leq0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction.

Note: Background (Comparisons): Current Dioxin $\leq$10 ppt.
Unknown (Ranch Hands): Current Dioxin $\leq$10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin $\leq$33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

The adjusted analysis detected a significant categorized current dioxin-by-age interaction (Table 8-32 [j]: p=0.049). Age was dichotomized to explore the interaction. There was a significant overall difference in the prevalences of coordination abnormalities among categories for older Ranch Hands, those born before 1942 (Appendix Table G-1: 0.2%, 1.3%, 0.0%, and 5.7% for the background, unknown, low, and high current dioxin categories, p=0.003). The relative risk was significantly more than 1 for the high versus background contrast (Adj. RR=32.71, 95% C.I.: [3.50,306.0], p=0.002). No contrasts were significant in the younger Ranch Hand stratum, but the background category had the fewest percentage of abnormalities (0.3%, 0.9%, 2.5%, and 0.9% for the background, unknown, low, and high current dioxin categories, p>0.10 for each contrast).

After excluding the interaction, the adjusted analysis displayed a significant overall contrast (Table 8-32 [j]: p=0.006). The high versus background contrast was significant (Adj. RR=18.30, 95% C.I.: [3.26,102.7], p=0.001) and the unknown versus background contrast was marginally significant (Adj. RR=4.68, 95% C.I.: [0.84,25.97], p=0.077).

Romberg Sign

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Under both the minimal and maximal assumptions, there were only two assayed Ranch Hands with an abnormal Romberg sign. The association with initial dioxin was not significant (Table 8-33 [a] and [b]: p=0.871 in the unadjusted minimal analysis and p=0.479 in the unadjusted maximal analysis). No adjusted analyses were done because of the sparse number of abnormalities.

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

The current dioxin and time since tour analyses of Romberg sign could not investigate the interaction between current dioxin and time because no Ranch Hands with a later tour had an abnormal Romberg sign. For Ranch Hands with an early tour, the association between current dioxin and Romberg sign was not significant (Table 8-33 [c] and [d]: p=0.921 for the unadjusted minimal analysis and p=0.770 for the unadjusted maximal analysis). No adjusted analyses were done due to sparse data.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The overall contrast among current dioxin categories was not significant in the unadjusted analysis of Romberg sign (Table 8-33 [e]: p=0.117). The low and high current dioxin categories each had one abnormality; there were no abnormalities in the background and unknown categories. No adjusted analysis was done because of the sparse number of abnormalities.

Gait

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Although the percentages of gait abnormalities increased with initial dioxin, the relative risk was not significant in the unadjusted analyses under both the minimal (Table 8-34 [a]: Est. RR=1.27, p=0.236; % abnormal: 0.8%, 3.5%, and 3.8% for the low, medium, and high initial dioxin categories) and maximal (Table 8-34 [b]: Est RR=1.25, p=0.154; % abnormal:

TABLE 8-33.

Analysis of Romberg Sign

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=521)	Low	130	0.0	1.10 (0.36,3.30)	0.871
	Medium	260	0.4		
	High	131	0.8		
b) Maximal (n=741)	Low	184	0.0	1.39 (0.58,3.34)	0.479
	Medium	371	0.3		
	High	186	0.5		

[a]Relative risk for a twofold increase in dioxin.
Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 8-33. (Continued)

Analysis of Romberg Sign

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
c) Minimal (n=521)						--
	≤18.6	0.0 (72)	0.0 (128)	0.0 (54)	--	--
	>18.6	0.0 (58)	0.8 (132)	1.3 (77)	0.92 (0.18,4.70)	0.921[b]
d) Maximal (n=741)						--
	≤18.6	0.0 (106)	0.0 (191)	0.0 (83)	--	--
	>18.6	0.0 (78)	0.6 (179)	1.0 (104)	1.21 (0.34,4.24)	0.770[b]

[a]Relative risk for a twofold increase in dioxin.
[b]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).
--: Relative risk, confidence interval, and p-value not given due to the sparse number of abnormalities.
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 8-33. (Continued)

Analysis of Romberg Sign

e) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	783	0.0	All Categories		0.117
Unknown	343	0.0	Unknown vs. Background	--	--
Low	196	0.5	Low vs. Background	--	0.400
High	187	0.5	High vs. Background	--	0.386
Total	1,509				

--: Relative risk/confidence interval/p-value not given due to the absence of abnormalities.
Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 8-34.

Analysis of Gait

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=521)	Low	130	0.8	1.27 (0.87,1.87)	0.236
	Medium	260	3.5		
	High	131	3.8		
b) Maximal (n=740)	Low	183	1.6	1.25 (0.93,1.69)	0.154
	Medium	371	2.7		
	High	186	3.2		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=513)	1.24 (0.82,1.87)	0.323	AGE (p=0.514) DIAB (p=0.051) DRKYR (p=0.132) INS (p=0.062)
d) Maximal (n=729)	1.30 (0.94,1.80)	0.123	AGE (p=0.696) DIAB (p=0.042) DRKYR (p=0.034)

[a]Relative risk for a twofold increase in dioxin.
Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 8-34. (Continued)

Analysis of Gait

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.880[b]
(n=521)	≤18.6	1.4 (72)	1.6 (128)	1.9 (54)	1.18 (0.49,2.84)	0.705[c]
	>18.6	1.7 (58)	4.6 (132)	5.2 (77)	1.10 (0.69,1.73)	0.692[c]
f) Maximal						0.824[b]
(n=740)	≤18.6	1.0 (105)	1.6 (191)	2.4 (83)	1.08 (0.58,2.04)	0.806[c]
	>18.6	1.3 (78)	3.9 (179)	4.8 (104)	1.17 (0.82,1.68)	0.382[c]

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal			0.901[b]	AGE (p=0.720)
(n=513)	≤18.6	1.14 (0.47,2.75)	0.768[c]	DIAB (p=0.036)
	>18.6	1.07 (0.67,1.73)	0.771[c]	DRKYR (p=0.137) INS (p=0.053)
h) Maximal			0.949[b]	AGE (p=0.917)
(n=729)	≤18.6	1.21 (0.61,2.40)	0.577[c]	DIAB (p=0.032)
	>18.6	1.18 (0.81,1.73)	0.379[c]	DRKYR (p=0.037)

[a]Relative risk for a twofold increase in dioxin.
[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).
[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 8-34. (Continued)

Analysis of Gait

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	783	2.2	All Categories		0.657
Unknown	342	2.6	Unknown vs. Background	1.22 (0.54,2.76)	0.637
Low	196	3.1	Low vs. Background	1.42 (0.55,3.66)	0.464
High	187	3.7	High vs. Background	1.75 (0.72,4.29)	0.219
Total	1,508				

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	779	All Categories		0.482**	DXCAT*DIAB (p=0.047) AGE (p=0.135)
Unknown	338	Unknown vs. Background	1.06 (0.45,2.50)**	0.889**	DRKYR (p=0.044)
Low	192	Low vs. Background	1.50 (0.58,3.88)**	0.399**	
High	183	High vs. Background	2.03 (0.81,5.08)**	0.131**	
Total	1,492				

**Categorized current dioxin-by-covariate interaction ($0.01<p\leq0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction.

Note: Background (Comparisons): Current Dioxin $\leq$10 ppt.
Unknown (Ranch Hands): Current Dioxin $\leq$10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin $\leq$33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

1.6%, 2.7%, and 3.2% for the low, medium, and high initial dioxin categories) assumptions. The adjusted analyses displayed essentially the same findings as the unadjusted analyses (Table 8-34 [c] and [d]: Adj. RR=1.24, p=0.323 for the minimal analysis and Adj. RR=1.30, p=0.123 for the maximal analysis).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

Under both the minimal and maximal assumptions, the interaction between current dioxin and time since tour was not significant in the analyses of gait (Table 8-34 [e-h]: p>0.80 in each analysis).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The unadjusted categorized current dioxin analysis of gait did not find a significant overall contrast (Table 8-34 [i]: p=0.657), but the high current dioxin category had the highest percentage of abnormalities (2.2%, 2.6%, 3.1%, and 3.7% for the background, unknown, low, and high current dioxin categories). Each Ranch Hand versus background contrast was also not significant (p>0.20 for each contrast).

The adjusted analysis detected a significant categorized current dioxin-by-diabetic class interaction (Table 8-34 [j]: p=0.047). Stratified results showed a marginally significant overall contrast among categories for normal participants (Appendix Table G-1: p=0.095; 2.3%, 0.7%, 2.7%, and 4.0% for the background, unknown, low, and high current dioxin categories), although none of the Ranch Hand versus background contrasts was significant (p>0.10 for each contrast). There was also a marginally significant overall contrast for diabetically impaired individuals (p=0.052), but the only abnormalities were in the unknown (8.5%, n=47) and background (1.9%, n=107) categories; the unknown versus background contrast was marginally significant (Adj. RR=5.27, 95% C.I.: [0.92,30.11], p=0.062). The overall contrast was not significant for diabetic individuals (p=0.630), but the percentages of gait abnormalities increased with current dioxin (1.5%, 5.3%, 5.9%, and 6.5% for the background, unknown, low, and high current dioxin categories). None of the Ranch Hand versus background contrasts was significant in this stratum (p>0.25 for each contrast).

After excluding the interaction, the adjusted analysis did not reveal any significant findings (Table 8-34 [j]: p>0.10 for each contrast).

CNS Index

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

In the unadjusted analyses, initial dioxin was not significantly associated with the CNS index under the minimal assumption (Table 8-35 [a]: p=0.171), but the estimated relative risk was marginally more than 1 under the maximal assumption (Table 8-35 [b]: Est. RR=1.24, p=0.064). In the maximal cohort, the percentages of CNS abnormalities were 3.8, 4.6, and 7.0 percent for the low, medium, and high initial dioxin categories.

Under both assumptions, the adjusted analyses detected a significant initial dioxin-by-age interaction (Table 8-35 [c] and [d]: p=0.019 in the adjusted minimal analysis and p=0.044 in the adjusted maximal analysis). Age was categorized to explore the interactions. Both analyses found a significant increased risk of CNS abnormalities for older Ranch Hands,

TABLE 8-35.

Analysis of CNS Index

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=521)	Low	130	3.1	1.23 (0.92,1.64)	0.171
	Medium	260	5.8		
	High	131	7.6		
b) Maximal (n=740)	Low	183	3.8	1.24 (0.99,1.55)	0.064
	Medium	371	4.6		
	High	186	7.0		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=521)	1.25 (0.93,1.68)**	0.145**	INIT*AGE (p=0.019)
d) Maximal (n=731)	1.26 (1.00,1.59)**	0.050**	INIT*AGE (p=0.044) DRKYR (p=0.077)

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

**Log_2 (initial dioxin)-by-covariate interaction ($0.01<p\leq0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 8-35. (Continued)

Analysis of CNS Index

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.383[b]
(n=521)	≤18.6	2.8 (72)	4.7 (128)	7.4 (54)	1.43 (0.87,2.34)	0.159[c]
	>18.6	3.5 (58)	6.1 (132)	9.1 (77)	1.08 (0.74,1.57)	0.686[c]
f) Maximal						0.256[b]
(n=740)	≤18.6	1.0 (105)	3.7 (191)	8.4 (83)	1.44 (0.99,2.10)	0.056[c]
	>18.6	5.1 (78)	5.0 (179)	8.7 (104)	1.09 (0.82,1.46)	0.541[c]

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal			0.372[b]	AGE (p=0.628)
(n=521)	≤18.6	1.47 (0.88,2.43)	0.137[c]	
	>18.6	1.11 (0.75,1.63)	0.607[c]	
h) Maximal			0.165[b]	AGE (p=0.768)
(n=731)	≤18.6	1.55 (1.05,2.31)	0.029[c]	DRKYR (p=0.074)
	>18.6	1.10 (0.82,1.48)	0.511[c]	

[a]Relative risk for a twofold increase in dioxin.
[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).
[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 8-35. (Continued)

Analysis of CNS Index

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	783	4.9	All Categories		0.276
Unknown	342	5.3	Unknown vs. Background	1.09 (0.61,1.94)	0.771
Low	196	4.6	Low vs. Background	0.94 (0.45,1.99)	0.878
High	187	8.6	High vs. Background	1.83 (1.00,3.37)	0.050
Total	1,508				

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	783	All Categories		0.137**	DXCAT*AGE (p=0.018) RACE*INS (p=0.023)
Unknown	342	Unknown vs. Background	1.01 (0.56,1.81)**	0.973**	
Low	196	Low vs. Background	0.91 (0.43,1.92)**	0.798**	
High	187	High vs. Background	2.08 (1.11,3.89)**	0.023**	
Total	1,508				

**Categorized current dioxin-by-covariate interaction ($0.01<p\leq0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction.

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

those born before 1942 (Appendix Table G-2: Adj. RR=1.66, p=0.010 in the minimal analysis and Adj. RR=1.53, p=0.009 in the maximal analysis). In both cohorts, the prevalence of abnormalities increased with initial dioxin for older Ranch Hands (2.3%, 4.0%, and 12.5% for the low, medium, and high initial dioxin categories in the minimal cohort; 2.7%, 3.3%, and 10.3% for the corresponding categories in the maximal cohort). For younger Ranch Hands, the relative risk was not significant (Adj. RR=0.87, p=0.523 in the minimal cohort; Adj. RR=1.00, p=0.976 in the maximal cohort).

After excluding the interaction, the adjusted minimal analysis was not significant (Table 8-35 [c]: p=0.145), but the adjusted maximal analysis displayed a significant increased risk (Table 8-35 [d]: Adj. RR=1.26, p=0.050).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

The unadjusted current dioxin and time since tour analyses of the CNS index did not find a significant interaction between current dioxin and time (Table 8-35 [e] and [f]: p=0.383 under the minimal assumption and p=0.256 under the maximal assumption). There was a marginally significant association between current dioxin and the CNS index for Ranch Hands with a later tour under the maximal assumption (time≤18.6: Est. RR=1.44, p=0.056; % abnormal: 1.0%, 3.7%, and 8.4% for the low, medium, and high current dioxin categories). None of the other within time stratum results was significant in the unadjusted analyses.

The adjusted analyses displayed similar findings. The current dioxin-by-time interaction was not significant under either assumption (Table 8-35 [g] and [h]: p=0.372 under the minimal assumption and p=0.165 under the maximal assumption). Under the maximal assumption, the relative risk of an abnormal CNS index was significant for Ranch Hands with a later tour (Adj. RR=1.55, p=0.029).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The overall contrast was not significant in the unadjusted categorized current dioxin analysis of the CNS index (Table 8-35 [i]: p=0.276), although there were relatively more abnormalities in the high current dioxin category than in the background category (8.6% versus 4.9%; Est. RR=1.83, 95% C.I.: [1.00,3.37], p=0.050). The percentages of abnormalities in the low (4.6%) and unknown (5.3%) current dioxin categories were not significantly different from the background percentage (p>0.75 for both contrasts).

The adjusted analysis detected a significant categorized current dioxin-by-age interaction (Table 8-35 [j]: p=0.018). Stratified results showed that the prevalence of CNS abnormalities differed significantly among current dioxin categories for older participants (Appendix Table G-1: 5.9%, 5.3%, 1.7%, and 12.9% for the background, unknown, low, and high current dioxin categories, p=0.017). For older individuals, the relative risk was significantly more than 1 for the high versus background contrast (Adj. RR=2.39, 95% C.I.: [1.07,5.34], p=0.034) and it was marginally less than 1 for the low versus background contrast (Adj. RR=0.27, 95% C.I.: [0.06,1.16], p=0.079). The overall contrast was not significant for younger men (p=0.401) although the low versus background relative risk was marginally more than 1 (Adj. RR=2.50, 95% C.I.: [0.93,6.72], p=0.069). In this stratum, the prevalences for the background, unknown, low, and high current dioxin categories were 3.4, 5.1, 8.6, and 6.0 percent. The interaction occurred partly because the low category had the

fewest percentage of abnormalities in the older age stratum, but it had the highest percentage of abnormalities in the younger age stratum.

After deleting the interaction, the adjusted analysis supported the unadjusted findings. The overall contrast was not significant (Table 8-35 [j]: p=0.137), but the high current dioxin category had a significant increased risk of CNS abnormalities (Adj. RR=2.08, 95% C.I.: [1.11,3.89], p=0.023).

Longitudinal Analysis

Physical Examination Variables

The neurological assessment conducted longitudinal analyses for the cranial nerve index and the CNS index. These analyses only included participants who were normal at the 1985 examination to determine whether the incidence between 1985 and 1987 for these two variables was associated with dioxin. The longitudinal analyses investigated the change between 1985 and 1987 because SCRF conducted both of these neurological examinations.

Cranial Nerve Index

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Under the minimal assumption, the longitudinal analysis found that initial dioxin was not significantly associated with the percentage of Ranch Hands who developed a cranial nerve index abnormality between the 1985 and 1987 examinations (Table 8-36 [a]: p=0.288). However, under the maximal assumption, there was a marginally significant decreased risk (Table 8-36 [b]: Est. RR= 0.83, p=0.055). The percentages of Ranch Hands in the maximal cohort with an abnormal index in 1987 (based on those who were normal in 1985) were 15.3, 12.7, and 7.3 percent for the low, medium, and high initial dioxin categories.

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

Under the minimal assumption. the longitudinal analysis of the cranial nerve index did not detect a significant current dioxin-by-time since tour interaction (Table 8-36 [c]: p=0.756). Thus, the association with current dioxin did not differ between time strata.

However, under the maximal assumption, there was a marginally significant interaction between current dioxin and time (Table 8-36 [d]: p=0.086). For Ranch Hands in the maximal cohort with a later tour, the relative risk of developing a cranial nerve index abnormality between 1985 and 1987 was significantly less than 1 (time≤18.6: Est. RR=0.68, p=0.017; % abnormal: 19.8%, 11.7%, and 6.6% for the low, medium, and high current dioxin categories).

The relative risk was less than 1, but not significant for Ranch Hands in the maximal cohort with an early tour (time>18.6: Est. RR=0.97, p=0.816).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The percentage of participants who developed a cranial nerve index abnormality between the 1985 and 1987 examinations did not differ significantly among the four current

TABLE 8-36.

Longitudinal Analysis of Cranial Nerve Index

Ranch Hands - Log_2 (Initial Dioxin)

Assumption	Initial Dioxin	Percent Abnormal/(n) Examination 1982	1985	1987
a) Minimal	Low	51.8 (114)	6.6 (121)	12.4 (121)
	Medium	52.8 (231)	7.2 (251)	15.5 (251)
	High	58.3 (115)	8.0 (125)	12.8 (125)

Initial Dioxin	Normal in 1985: n in 1987	Normal in 1985: Percent Abnormal in 1987	Est. Relative Risk (95% C.I.)[a]	p-Value
Low	113	10.6	0.87 (0.67,1.13)	0.288
Medium	233	12.5		
High	115	7.8		

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

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Summary statistics for 1982 are provided for reference purposes for participants who attended the Baseline, 1985, and 1987 examinations. P-values given are in reference to a contrast of 1985 and 1987 results. Statistical analyses are based only on participants who were normal in 1985 (see Chapter 4, Statistical Methods).

TABLE 8-36. (Continued)

Longitudinal Analysis of Cranial Nerve Index

Ranch Hands - Log_2 (Initial Dioxin)

Assumption	Initial Dioxin	Percent Abnormal/(n) Examination 1982	1985	1987
b) Maximal	Low	52.3 (155)	12.8 (172)	18.6 (172)
	Medium	52.5 (326)	6.8 (355)	15.2 (355)
	High	56.4 (163)	7.3 (177)	11.9 (177)

Initial Dioxin	Normal in 1985: n in 1987	Normal in 1985: Percent Abnormal in 1987	Est. Relative Risk (95% C.I.)[a]	p-Value
Low	150	15.3	0.83 (0.69,1.01)	0.055
Medium	331	12.7		
High	164	7.3		

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

Note: Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.
Summary statistics for 1982 are provided for reference purposes for participants who attended the Baseline, 1985, and 1987 examinations. P-values given are in reference to a contrast of 1985 and 1987 results. Statistical analyses are based only on participants who were normal in 1985 (see Chapter 4, Statistical Methods).

TABLE 8-36. (Continued)

Longitudinal Analysis of Cranial Nerve Index

Ranch Hands - Log_2 (Current Dioxin) and Time

Assumption	Time (Yrs.)	Examination	Percent Abnormal/(n) Current Dioxin Low	Medium	High
c) Minimal	≤18.6	1982	54.7 (64)	52.2 (113)	52.2 (46)
		1985	7.6 (66)	8.3 (121)	0.0 (50)
		1987	10.6 (66)	16.5 (121)	4.0 (50)
	>18.6	1982	49.0 (49)	55.5 (119)	58.0 (69)
		1985	5.4 (56)	6.2 (129)	13.3 (75)
		1987	12.5 (56)	16.3 (129)	17.3 (75)

Time (Yrs.)	Normal in 1985: Percent Abnormal/(n) in 1987 Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
					0.756[b]
≤18.6	9.8 (61)	11.7 (111)	4.0 (50)	0.77 (0.48,1.23)	0.278[c]
>18.6	11.3 (53)	14.1 (121)	9.2 (65)	0.84 (0.60,1.19)	0.338[c]

[a]Relative risk for a twofold increase in dioxin.
[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).
[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Summary statistics for 1982 are provided for reference purposes for participants who attended the Baseline, 1985, and 1987 examinations. P-values given are in reference to a contrast of 1985 and 1987 results. Statistical analyses are based only on participants who were normal in 1985 (see Chapter 4, Statistical Methods).

TABLE 8-36. (Continued)

Longitudinal Analysis of Cranial Nerve Index

Ranch Hands - Log_2 (Current Dioxin) and Time

Assumption	Time (Yrs.)	Examination	Percent Abnormal/(n) Current Dioxin Low	Medium	High
d) Maximal	≤18.6	1982	46.0 (87)	54.4 (169)	51.4 (72)
		1985	11.3 (97)	7.9 (177)	2.6 (78)
		1987	21.7 (97)	14.7 (177)	7.7 (78)
	>18.6	1982	56.1 (66)	52.5 (158)	59.8 (92)
		1985	14.5 (76)	5.7 (176)	11.0 (100)
		1987	14.5 (76)	15.9 (176)	15.0 (100)

Time (Yrs.)	Normal in 1985: Percent Abnormal/(n) in 1987 Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
≤18.6	19.8 (86)	11.7 (163)	6.6 (76)	0.68 (0.50,0.93)	0.086[b] 0.017[c]
>18.6	7.7 (65)	14.5 (166)	7.9 (89)	0.97 (0.75,1.25)	0.816[c]

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

[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).

[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).

Note: Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.
Summary statistics for 1982 are provided for reference purposes for participants who attended the Baseline, 1985, and 1987 examinations. P-values given are in reference to a contrast of 1985 and 1987 results. Statistical analyses are based only on participants who were normal in 1985 (see Chapter 4, Statistical Methods).

TABLE 8-36. (Continued)

Longitudinal Analysis of Cranial Nerve Index

e) Ranch Hands and Comparisons by Current Dioxin Category

Current Dioxin Category	Percent Abnormal/(n) Examination 1982	1985	1987
Background	52.0 (641)	9.0 (733)	16.1 (733)
Unknown	50.0 (286)	10.6 (320)	15.6 (320)
Low	52.8 (176)	7.4 (190)	17.9 (190)
High	56.1 (164)	7.3 (178)	11.8 (178)

Current Dioxin Category	Normal in 1985: n in 1987	Normal in 1985: Percent Abnormal in 1987	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	667	12.7	All Categories		0.125
Unknown	286	13.3	Unknown vs. Background	1.05 (0.70,1.58)	0.818
Low	176	14.8	Low vs. Background	1.19 (0.74,1.91)	0.479
High	165	7.3	High vs. Background	0.54 (0.29,1.01)	0.053

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.
Summary statistics for 1982 are provided for reference purposes for participants who attended the Baseline, 1985, and 1987 examinations. P-values given are in reference to a contrast of 1985 and 1987 results. Statistical analyses are based only on participants who were normal in 1985 (see Chapter 4, Statistical Methods).

dioxin categories in the longitudinal analysis (Table 8-36 [e]: 12.7%, 13.3%, 14.8%, and 7.3% for the background, unknown, low, and high current dioxin categories, p=0.125). However, the relative risk of developing an abnormal cranial nerve index for the high versus background contrast was marginally less than 1 (Est. RR=0.54; 95% C.I.: [0.29,1.01], p=0.053).

CNS Index

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Under the minimal assumption, the longitudinal analysis of the CNS index did not find a significant risk associated with initial dioxin (Table 8-37 [a]: Est. RR=1.25, p=0.207), but the relative risk was marginally significant under the maximal assumption (Table 8-37 [b]: Est. RR=1.27, p=0.087). The percentages of Ranch Hands in the maximal cohort with an abnormal CNS index at the 1987 examination (based on those who were normal at the 1985 examination) were 2.4, 3.5, and 5.2 percent for the low, medium, and high initial dioxin categories.

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

The current dioxin-by-time since tour interaction was not significant for the longitudinal analysis of the CNS index under either the minimal or the maximal assumption (Table 8-37 [c] and [d]: p=0.654 and p=0.409, respectively). However, under the maximal assumption, the relative risk was marginally more than 1 for Ranch Hands with a later tour (time$\leq$18.6: Est. RR=1.45, p=0.080). For these Ranch Hands, the percentages with an abnormal CNS index (based on those who were normal in 1985) were 1.0, 2.9, and 7.8 percent for the low, medium, and high current dioxin categories.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The longitudinal analysis did not find a significant difference in the percentages of participants with an abnormal CNS index at the 1987 examination (based on those who were normal in 1985) among the current dioxin categories (Table 8-37 [e]: 4.4%, 3.8%, 3.2%, and 6.8% for the background, unknown, low, and high current dioxin categories, p=0.382). The three Ranch Hand versus background contrasts were also not significant (p>0.15 for each contrast).

DISCUSSION

Although definitive diagnosis usually requires laboratory testing beyond the scope of the current study, the data analyzed in this chapter can be relied upon to detect the presence, if not the cause, of neurologic disease, including disorders of the peripheral nervous system. In clinical practice, the neurological assessment can be divided into examinations of the peripheral and the cranial nerves. The central, cranial, and peripheral nerve variables examined can provide specific clues in the anatomic site of neurological lesions and clarify the need for additional diagnostic studies.

As indices of CNS function, tremor and coordination are less specific and more subject to individual variation in the absence of underlying neurological disease. Tremor, for example, may occur as a benign familial trait, may be reflective of alcohol withdrawal, or may be a marker of extrapyramidal motor system disease as in Parkinson's syndrome. The Romberg sign may signal a lesion in the cerebellum but is more often indicative of impaired position

TABLE 8-37.

Longitudinal Analysis of CNS Index

Ranch Hands - Log_2 (Initial Dioxin)

Assumption	Initial Dioxin	Percent Abnormal/(n) Examination 1982	1985	1987
a) Minimal	Low	30.6 (121)	5.6 (125)	3.2 (125)
	Medium	27.8 (245)	3.5 (255)	5.9 (255)
	High	24.0 (121)	3.9 (128)	7.8 (128)

Initial Dioxin	Normal in 1985: n in 1987	Percent Abnormal in 1987	Est. Relative Risk (95% C.I.)[a]	p-Value
Low	118	2.5	1.25 (0.89,1.75)	0.207
Medium	246	4.1		
High	123	5.7		

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

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Summary statistics for 1982 are provided for reference purposes for participants who attended the Baseline, 1985, and 1987 examinations. P-values given are in reference to a contrast of 1985 and 1987 results. Statistical analyses are based only on participants who were normal in 1985 (see Chapter 4, Statistical Methods).

TABLE 8-37. (Continued)

Longitudinal Analysis of CNS Index

Ranch Hands - Log_2 (Initial Dioxin)

Assumption	Initial Dioxin	Percent Abnormal/(n) Examination 1982	1985	1987
b) Maximal	Low	22.3 (166)	2.9 (175)	4.0 (175)
	Medium	28.1 349)	3.6 (361)	4.7 (361)
	High	25.7 (171)	4.4 (182)	7.1 (182)

Initial Dioxin	Normal in 1985: n in 1987	Normal in 1985: Percent Abnormal in 1987	Est. Relative Risk (95% C.I.)[a]	p-Value
Low	170	2.4	1.27 (0.97,1.65)	0.087
Medium	348	3.5		
High	174	5.2		

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

Note: Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.
Summary statistics for 1982 are provided for reference purposes for participants who attended the Baseline, 1985, and 1987 examinations. P-values given are in reference to a contrast of 1985 and 1987 results. Statistical analyses are based only on participants who were normal in 1985 (see Chapter 4, Statistical Methods).

TABLE 8-37. (Continued)

Longitudinal Analysis of CNS Index

Ranch Hands - Log_2 (Current Dioxin) and Time

Assumption	Time (Yrs.)	Examination	Percent Abnormal/(n) Current Dioxin Low	Medium	High
c) Minimal	≤18.6	1982	23.9 (67)	27.7 (119)	20.4 (49)
		1985	5.9 (68)	3.2 (125)	3.9 (51)
		1987	2.9 (68)	4.8 (125)	7.8 (51)
	>18.6	1982	37.0 (54)	27.6 (127)	28.2 (71)
		1985	5.3 (57)	3.1 (130)	5.2 (77)
		1987	3.5 (57)	6.2 (130)	9.1 (77)

Time (Yrs.)	Normal in 1985: Percent Abnormal/(n) in 1987 Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
					0.654[b]
≤18.6	3.1 (64)	4.1 (121)	6.1 (49)	1.39 (0.81,2.39)	0.230[c]
>18.6	0.0 (54)	4.8 (126)	5.5 (73)	1.18 (0.75,1.87)	0.473[c]

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

[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).

[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).

Note: Minimal–Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Summary statistics for 1982 are provided for reference purposes for participants who attended the Baseline, 1985, and 1987 examinations. P-values given are in reference to a contrast of 1985 and 1987 results. Statistical analyses are based only on participants who were normal in 1985 (see Chapter 4, Statistical Methods).

TABLE 8-37. (Continued)

Longitudinal Analysis of CNS Index

Ranch Hands - Log_2 (Current Dioxin) and Time

Assumption	Time (Yrs.)	Examination	Percent Abnormal/(n) Current Dioxin Low	Medium	High
d) Maximal	≤18.6	1982	18.7 (91)	25.7 (179)	24.0 (75)
		1985	2.0 (99)	4.4 (183)	3.8 (80)
		1987	1.0 (99)	3.8 (183)	8.8 (80)
	>18.6	1982	25.7 (74)	30.4 (171)	28.1 (96)
		1985	2.6 (76)	4.0 (177)	3.9 (103)
		1987	5.3 (76)	5.1 (177)	8.7 (103)

Time (Yrs.)	Normal in 1985: Percent Abnormal/(n) in 1987 Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
					0.409[b]
≤18.6	1.0 (97)	2.9 (175)	7.8 (77)	1.45 (0.96,2.21)	0.080[c]
>18.6	2.7 (74)	2.9 (170)	6.1 (99)	1.15 (0.80,1.66)	0.448[c]

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

[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).

[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).

Note: Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.
Summary statistics for 1982 are provided for reference purposes for participants who attended the Baseline, 1985, and 1987 examinations. P-values given are in reference to a contrast of 1985 and 1987 results. Statistical analyses are based only on participants who were normal in 1985 (see Chapter 4, Statistical Methods).

TABLE 8-37. (Continued)

Longitudinal Analysis of CNS Index

e) Ranch Hands and Comparisons by Current Dioxin Category

Current Dioxin Category	Percent Abnormal/(n) Examination 1982	1985	1987
Background	26.4 (666)	3.1 (748)	5.0 (748)
Unknown	23.7 (304)	3.4 (327)	5.5 (327)
Low	27.1 (188)	3.6 (193)	4.7 (193)
High	26.3 (171)	3.8 (183)	8.7 (183)

Current Dioxin Category	Normal in 1985: n in 1987	Normal in 1985: Percent Abnormal in 1987	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	725	4.4	All Categories		0.382
Unknown	316	3.8	Unknown vs. Background	0.85 (0.43,1.68)	0.649
Low	186	3.2	Low vs. Background	0.72 (0.30,1.75)	0.472
High	176	6.8	High vs. Background	1.58 (0.80,3.14)	0.187

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.
Summary statistics for 1982 are provided for reference purposes for participants who attended the Baseline, 1985, and 1987 examinations. P-values given are in reference to a contrast of 1985 and 1987 results. Statistical analyses are based only on participants who were normal in 1985 (see Chapter 4, Statistical Methods).

sense in the lower extremities or of inner ear disease. Finally, the mental status examination is important in the CNS assessment. Extensive psychometric studies were conducted, as in previous examination cycles, and are reported in Chapter 9.

Of the eight historical variables analyzed, only the ICD-9-CM category of "other neurologic disorders" was found to have a significant positive association with the body burden of dioxin. In the maximal cohort, a statistically significant increase in the diseases included in this category was noted in association with the extrapolated initial level of serum dioxin. Also, for Ranch Hands with less than 18.6 years since service in Vietnam, there was a significant association with current levels of serum dioxin. These positive findings were no longer present after adjustment for age and military occupation. There was no apparent increase in the historical incidence of peripheral neuropathy in association with serum dioxin levels or in Ranch Hand participants relative to Comparisons. The serum dioxin analyses did not find a significant association with an increased risk of hereditary and degenerative diseases. This finding contrasted with the results from the previous report (36), which found that the incidence of hereditary and degenerative diseases differed significantly between the Ranch Hand and Comparison groups (5.5% versus 3.5%).

Related to the extrapolated initial level of serum dioxin, there were no significant associations noted in any of the directly measured physical examination variables. Several indices (neck range of motion and cranial nerve index) were found to have statistically significant but inconsistent associations with the current level of serum dioxin without evidence for a dose-response effect. Participants more removed from their tour of duty in Vietnam were at slightly greater risk. Significant differences between current dioxin categories were not noted in either index.

Of the neurological disorders considered, only peripheral neuropathy has been clearly shown to be associated with TCDD exposure in other studies. Of the eight peripheral motor and sensory indices examined, no significant associations were found with the initial, current serum dioxin levels, or categorical dioxin levels.

In the adjusted analysis of the current serum dioxin, participants less removed from active duty in Vietnam were more likely to show abnormalities in coordination and in the CNS index in a pattern consistent with a dose-response effect. Further, for both indices, Ranch Hands with higher levels of serum dioxin were at increased risk relative to Comparisons, particularly with respect to coordination (Adj. RR=18.30; p=0.001). In the longitudinal analysis of the CNS index under the maximal assumption, there was a marginally significant positive association with initial dioxin. Ranch Hands with the highest levels of initial dioxin had a higher incidence of abnormalities (5.2%) than those in the medium (3.5%) or low (2.4%) initial dioxin categories. Though it would be difficult to explain these results on the basis of cause and effect, they are consistent with those described in the 1987 report and will be evaluated in future examination cycles.

In summary, data analyzed in this chapter revealed no consistent evidence for clinically significant neurological disease associated with the current body burden of dioxin. Statistically significant associations were noted but not in patterns consistent with a dose-response effect.

SUMMARY

The neurological assessment focused on extensive physical examination data for cranial nerve function, peripheral nerve status, and CNS coordination processes. Verified histories of neurological diseases were also examined. Three sets of analyses were performed to assess the association between dioxin and the neurological variables. Table 8-38 summarizes the results of the initial dioxin analyses. Table 8-39 presents the results of the current dioxin and time since tour analyses, and Table 8-40 summarizes the categorized current dioxin analyses. Table 8-41 lists the dioxin-by-covariate interactions found in the adjusted analyses.

Questionnaire Variables

Information from the questionnaire was verified and grouped into eight categories of neurological diseases: inflammatory diseases, hereditary and degenerative diseases, peripheral disorders, disorders of the eye, external otitis, tympanic membrane disorders, hearing loss, and other neurological diseases.

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Under both the minimal and maximal assumptions, initial dioxin was not significantly associated with inflammatory diseases, hereditary and degenerative diseases, peripheral disorders, eye disorders, tympanic membrane disorder, and otitis. There was a marginally significant increased risk of hearing loss under the minimal assumption after adjustment for age, but the relative risk was not significant under the maximal assumption.

Under both assumptions, initial dioxin was associated with a significant increased risk of conditions in the other neurological disorders category after adjusting for age. However, further investigation indicated that this was related to a significant association between occupation and other neurological disorders. Independent of group membership, officers had a much lower incidence of other neurological disorders than either enlisted flyers or enlisted groundcrew. Ranch Hand officers also had the lowest levels of dioxin in general. After adjusting for age and occupation, the association between initial dioxin and other neurological disorders became nonsignificant under both assumptions.

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

The current dioxin and time since tour analyses were generally not significant for the questionnaire variables. Under the maximal assumption, the association between current dioxin and otitis differed significantly between time strata, but this was due to a significant decreased risk of otitis for Ranch Hands with a later tour. Adjusting for age, current dioxin was significantly associated with other neurological disorders in both time strata under the maximal assumption, but these associations became nonsignificant when occupation was included in the model.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The categorized current dioxin analyses of the questionnaire variables displayed few significant results. The unadjusted analyses found a marginally significant difference in the prevalence of hearing loss among the four current dioxin categories, with a significant decreased risk in the high category relative to the background category. Ranch Hands in the

TABLE 8-38.

Summary of Initial Dioxin Analyses for Neurological Variables Based on Minimal and Maximal Assumptions (Ranch Hands Only)

	Unadjusted		Adjusted	
Variable	Minimal	Maximal	Minimal	Maximal
Questionnaire				
Inflammatory Diseases	NS	NS	--	--
Hereditary and Degenerative Diseases	ns	ns	ns	ns
Peripheral Disorders	NS	NS	NS	NS
Disorders of the Eye	NS	NS	NS	NS
Tympanic Membrane Disorder	ns	NS	ns	NS
Otitis	NS	ns	NS	ns
Hearing Loss	ns	ns	NS*	NS
Other Neurological Disorders	NS	+<0.001	+0.037[a]	+<0.001[a]
Other Neurological Disorders	--	--	ns[b]	NS[b]
Physical Examination				
Cranial Nerve Function				
Smell	ns	ns	ns	ns
Visual Fields	--	--	--	--
Light Reaction	NS	ns	NS	ns
Ocular Movement	ns	NS	NS	NS
Facial Sensation	ns	NS	ns	NS
Smile	NS	NS	NS	NS
Palpebral Fissure	NS	NS	NS	NS
Balance[c]	NS	NS	--	--
Speech	--	--	--	--
Neck Range of Motion	NS	ns	*** (NS*)	*** (NS)
Cranial Nerve Index	NS	ns	NS*	** (NS)
Cranial Nerve Index Without Range of Motion	NS	NS	NS	NS
Peripheral Nerve Status				
Pin Prick	NS	NS	** (NS)	** (NS)
Light Touch	ns	NS	NS	ns
Muscle Status	NS	NS	NS	NS
Vibration	ns	NS	ns	NS
Patellar Reflex	NS	NS	NS	NS
Achilles Reflex	ns	NS	ns	NS

TABLE 8-38. (Continued)

Summary of Initial Dioxin Analyses for Neurological Variables Based on Minimal and Maximal Assumptions (Ranch Hands Only)

	Unadjusted		Adjusted	
Variable	Minimal	Maximal	Minimal	Maximal
Peripheral Nerve Status (continued)				
Achilles Reflex[d]	--	--	NS	NS*
Biceps Reflex	--	--	--	--
Babinski Reflex	NS	NS	--	--
Central Nervous System Coordination Processes				
Tremor	NS	NS	NS	NS
Coordination	NS	NS	NS	NS
Coordination[d]	--	--	NS	NS*
Romberg Sign[c]	NS	NS	--	--
Gait	NS	NS	NS	NS
CNS Index	NS	NS*	** (NS)	** (+0.050)

[a]Adjusted for age.

[b]Adjusted for age and occupation. Appendix Table G-3 presents a detailed description of these analyses.

[c]Balance same as Romberg sign.

[d]Adjusted results presented for model without diabetic class. Appendix Table G-2 presents a detailed description of this analysis.

+: Relative risk 1.00 or greater.

--: Analysis not applicable or not performed due to the sparse number of abnormalities.

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

NS*/ns*: Marginally significant ($0.05<p\leq0.10$).

** (NS)/** (ns): Log_2 (initial dioxin)-by-covariate interaction ($0.01<p\leq0.05$); not significant when interaction is deleted; refer to Appendix Table G-1 for a detailed description of this interaction.

** (0.050): Log_2 (initial dioxin)-by-covariate interaction ($0.01<p\leq0.05$); significant ($p=0.050$) when interaction is deleted; refer to Appendix Table G-1 for a detailed description of this interaction.

*** (NS): Log_2 (initial-dioxin)-by-covariate interaction ($p\leq0.01$); not significant when interaction is deleted; refer to Appendix Table G-1 for a detailed description of this interaction.

*** (NS*): Log_2 (initial dioxin)-by-covariate interaction ($p\leq0.01$); marginally significant when interaction is deleted; refer to Appendix Table G-1 for a detailed description of this interaction.

Note: P-value given if $p\leq0.05$.
A capital "NS" denotes relative risk 1.00 or greater; a lowercase "ns" denotes relative risk less than 1.00.

TABLE 8-39.

Summary of Current Dioxin and Time Analyses for Neurological Variables Based on Minimal and Maximal Assumptions (Ranch Hands Only)

	Unadjusted					
	Minimal			Maximal		
Variable	C*T	≤18.6	>18.6	C*T	≤18.6	>18.6
Questionnaire						
Inflammatory Diseases	--	--	--	--	--	--
Hereditary and Degenerative Diseases	NS	ns	NS	NS	ns	NS
Peripheral Disorders	NS	ns	NS	NS	ns	NS
Disorders of the Eye	NS	NS	NS	NS	NS	NS
Tympanic Membrane Disorder	ns	NS	ns	ns	ns	ns
Otitis	NS	ns	ns	+0.032	-0.012	ns
Hearing Loss	NS	ns	ns	ns	ns	ns*
Other Neurological Disorders	ns	NS	NS	ns	+0.002	NS
Physical Examination						
Cranial Nerve Function						
Smell	--	ns	--	--	ns	--
Visual Fields	--	--	--	--	--	--
Light Reaction	--	ns	--	NS	ns	NS
Ocular Movement	--	--	ns	--	--	ns
Facial Sensation	--	NS	--	--	NS	--
Smile	--	--	NS*	--	--	NS
Palpebral Fissure	NS	ns	NS	NS	ns	NS
Balance[a]	--	--	ns	--	--	NS
Speech	--	--	--	--	--	--
Neck Range of Motion	NS	ns	NS	+0.024	-0.024	NS
Cranial Nerve Index	NS	ns	NS	+0.021	-0.027	NS
Cranial Nerve Index Without Range of Motion	NS	ns	NS	NS	ns	NS
Peripheral Nerve Status						
Pin Prick	NS	ns	NS	NS	NS	NS
Light Touch	+0.023	ns	NS	NS	ns	NS
Muscle Status	ns	NS	ns	ns	NS	NS
Vibration	ns	ns	ns	ns	NS	ns
Patellar Reflex	ns	NS	NS	ns	NS	NS

TABLE 8-39. (Continued)

Summary of Current Dioxin and Time Analyses for Neurological Variables Based on Minimal and Maximal Assumptions (Ranch Hands Only)

	Unadjusted					
	Minimal			Maximal		
Variable	C*T	≤18.6	>18.6	C*T	≤18.6	>18.6
Peripheral Nerve Status (continued)						
Achilles Reflex	+0.049	ns*	NS	NS	ns	NS
Biceps Reflex	--	--	--	--	--	--
Babinski Reflex	--	--	ns	--	--	NS
Central Nervous System Coordination Processes						
Tremor	ns	NS	ns	ns	NS	ns
Coordination	ns	NS	ns	ns	NS*	ns
Romberg Sign[a]	--	--	ns	--	--	NS
Gait	ns	NS	NS	NS	NS	NS
CNS Index	ns	NS	NS	ns	NS*	NS

[a]Balance same as Romberg sign.

+: C*T: Relative risk for ≤18.6 category less than relative risk for <18.6 category.
≤18.6: Relative risk 1.00 or greater.

-: ≤18.6: Relative risk less than 1.00.

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

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

NS*/ns*: Marginally significant ($0.05<p\leq0.10$).

Note: P-value given if $p\leq0.05$.
C*T: Log_2 (current dioxin)-by-time interaction hypothesis test.
≤18.6: Log_2 (current dioxin) hypothesis test for Ranch Hands with time since end of tour of 18.6 years or less.
>18.6: Log_2 (current dioxin) hypothesis test for Ranch Hands with time since end of tour greater than 18.6 years.
A capital "NS" denotes relative risk for ≤18.6 category less than relative risk for >18.6 category or relative risk 1.00 or greater; a lowercase "ns" denotes relative risk for <18.6 category greater than relative risk for >18.6 category or relative risk less than 1.00.

TABLE 8-39. (Continued)

Summary of Current Dioxin and Time Analyses for Neurological Variables Based on Minimal and Maximal Assumptions (Ranch Hands Only)

	Adjusted					
	Minimal			Maximal		
Variable	C*T	≤18.6	>18.6	C*T	≤18.6	>18.6
Questionnaire						
Inflammatory Diseases	--	--	--	--	--	--
Hereditary and Degenerative Diseases	NS	ns	NS	NS	NS	NS
Peripheral Disorders	NS	ns	NS	NS	ns	NS
Disorders of the Eye	NS	NS	NS	NS	NS	NS
Tympanic Membrane Disorder	ns	NS	ns	ns	NS	ns
Otitis	NS	ns	NS	+0.031	-0.020	NS
Hearing Loss	NS	NS	NS	ns	NS	NS
Other Neurological Disorders[b]	ns	+0.041	NS	ns*	+<0.001	+0.014
Other Neurological Disorders[c]	ns	NS	ns	ns	NS	ns
Physical Examination						
Cranial Nerve Function						
Smell	--	--	--	--	--	--
Visual Fields	--	--	--	--	--	--
Light Reaction	--	--	--	--	--	--
Ocular Movement	--	--	--	--	--	--
Facial Sensation	--	--	--	--	--	--
Smile	--	--	--	--	--	--
Palpebral Fissure	NS	ns	NS	NS	ns	NS
Balance[a]	--	--	--	--	--	--
Speech	--	--	--	--	--	--
Neck Range of Motion	NS	NS	+0.017	+0.026	ns	+0.029
Cranial Nerve Index	NS	NS	+0.033	+0.023	ns	+0.034
Cranial Nerve Index Without Range of Motion	NS	ns	NS	NS	ns	NS
Peripheral Nerve Status						
Pin Prick	** (NS)	** (ns)	** (NS)	** (NS)	** (NS)	** (NS)
Light Touch	+0.048	ns	NS	NS	ns	NS
Muscle Status	ns	NS	NS	ns	NS	NS
Vibration	ns	ns	ns	ns	NS	NS

TABLE 8-39. (Continued)

Summary of Current Dioxin and Time Analyses for Neurological Variables Based on Minimal and Maximal Assumptions (Ranch Hands Only)

	Adjusted					
	Minimal			Maximal		
Variable	C*T	≤18.6	>18.6	C*T	≤18.6	>18.6
Peripheral Nerve Status (continued)						
Patellar Reflex	ns	NS	ns	ns	NS	NS
Achilles Reflex	NS*	ns	NS	NS	ns	NS*
Biceps Reflex	--	--	--	--	--	--
Babinski Reflex	--	--	--	--	--	--
Central Nervous System Coordination Processes						
Tremor	ns	NS	ns	** (ns)	** (NS)	** (ns)
Coordination	ns	NS*	NS	ns*	+0.019	NS
Romberg Sign[a]	--	--	--	--	--	--
Gait	ns	NS	NS	ns	NS	NS
CNS Index	ns	NS	NS	ns	+0.029	NS

[a]Balance same as Romberg sign.
[b]Adjusted for age.
[c]Adjusted for age and occupation. Appendix Table G-3 presents a detailed description of these analyses.
+: C*T: Relative risk for ≤18.6 category less than relative risk for >18.6 category.
≤18.6 or >18.6: Relative risk 1.00 or greater.
-: ≤18.6: Relative risk less than 1.00.
--: Analysis not performed due to the sparse number of abnormalities.
NS/ns: Not significant ($p>0.10$).
NS*/ns*: Marginally significant ($0.05<p\leq0.10$).
** (NS)/** (ns): Log_2 (current dioxin)-by-time-by-covariate interaction ($0.01<p\leq0.05$); not significant when interaction is deleted; refer to Appendix Table G-1 for a detailed description of this interaction.
Note: P-value given if $p\leq0.05$.
C*T: Log_2 (current dioxin)-by-time interaction hypothesis test.
≤18.6: Log_2 (current dioxin) hypothesis test for Ranch Hands with time since end of tour of 18.6 years or less.
>18.6: Log_2 (current) hypothesis test for Ranch Hands with time since end of tour greater than 18.6 years.
A capital "NS" denotes relative risk for ≤18.6 category less than relative risk for >18.6 category or relative risk 1.00 or greater; a lowercase "ns" denotes relative risk for ≤18.6 category greater than relative risk for >18.6 category or relative risk less than 1.00.

TABLE 8-40.

Summary of Categorized Current Dioxin Analyses for Neurological Variables (Ranch Hands and Comparisons)

		Unadjusted		
Variable	All	Unknown versus Background	Low versus Background	High versus Background
Questionnaire				
Inflammatory Diseases	NS	NS	ns	NS
Hereditary and Degenerative Diseases	NS	NS	ns	ns
Peripheral Disorders	NS	ns	ns	NS
Disorders of the Eye	NS	NS	NS	NS
Tympanic Membrane Disorder	NS	ns	NS	NS
Otitis	NS	NS	NS	ns
Hearing Loss	NS*	ns	ns	-0.009
Other Neurological Disorders	0.014	ns*	NS*	NS
Physical Examination				
Cranial Nerve Function				
Smell	NS	ns	NS	ns
Visual Fields	NS	ns	ns	ns
Light Reaction	NS	ns	ns	NS
Ocular Movement	NS	ns	NS	ns
Facial Sensation	NS	ns	ns	ns
Smile	NS	ns	ns	ns
Palpebral Fissure	NS	ns	NS	NS
Balance[a]	NS	--	NS	NS
Speech	NS	ns	NS	ns
Neck Range of Motion	NS	NS	NS	ns
Cranial Nerve Index	NS	ns	NS	ns
Cranial Nerve Index Without Range of Motion	NS	ns	NS	ns
Peripheral Nerve Status				
Pin Prick	NS	ns	ns	NS
Light Touch	NS	ns	ns	ns
Muscle Status	NS	ns	ns	ns
Vibration	NS	ns	NS	NS
Patellar Reflex	NS	NS	NS	NS

TABLE 8-40. (Continued)

Summary of Categorized Current Dioxin Analyses for Neurological Variables (Ranch Hands and Comparisons)

	Unadjusted			
Variable	All	Unknown versus Background	Low versus Background	High versus Background
Peripheral Nerve Status (continued)				
Achilles Reflex	NS	ns	NS	ns
Biceps Reflex	NS	ns	ns	ns
Babinski Reflex	NS	NS	ns	NS
Central Nervous System Coordination Processes				
Tremor	NS	ns	ns	NS
Coordination	NS*	NS	NS	+0.007
Romberg Sign[a]	NS	--	NS	NS
Gait	NS	NS	NS	NS
CNS Index	NS	NS	ns	+0.050

[a]Balance same as Romberg sign.
+: Relative risk 1.00 or greater.
-: Relative risk less than 1.00.
--: Analysis not performed due to the absence of abnormalities.
NS/ns: Not significant ($p>0.10$).
NS*/ns*: Marginally significant ($0.05<p\leq0.10$).
Note: P-value given if $p\leq0.05$.
A capital "NS" denotes relative risk 1.00 or greater; a lowercase "ns" denotes relative risk less than 1.00; a capital "NS" in the first column does not imply directionality.

TABLE 8-40. (Continued)

Summary of Categorized Current Dioxin Analyses
for Neurological Variables
(Ranch Hands and Comparisons)

Variable	All	Adjusted Unknown versus Background	Adjusted Low versus Background	Adjusted High versus Background
Questionnaire				
Inflammatory Diseases	--	--	--	--
Hereditary and Degenerative Diseases	NS	NS	ns	ns
Peripheral Disorders	NS	ns	ns	NS
Disorders of the Eye	NS	NS	NS	NS
Tympanic Membrane Disorder	NS	ns	NS	NS
Otitis	NS	NS	NS	ns
Hearing Loss	NS	ns	ns	ns
Other Neurological Disorders[b]	<0.001	-0.041	NS*	+0.005
Other Neurological Disorders[c]	NS	NS	NS	NS
Physical Examination				
Cranial Nerve Function				
Smell	NS	ns	NS	--
Visual Fields	--	--	--	--
Light Reaction	NS	ns	--	NS
Ocular Movement	NS	ns	NS	--
Facial Sensation	NS	--	ns	ns
Smile	NS	ns	ns	NS
Palpebral Fissure	NS	ns	NS	NS
Balance[a]	--	--	--	--
Speech	--	--	--	--
Neck Range of Motion	** (NS)	** (ns)	** (NS)	** (NS)
Cranial Nerve Index	NS	ns	NS	ns
Cranial Nerve Index Without Range of Motion	** (NS)	** (ns*)	** (NS)	** (ns)
Peripheral Nerve Status				
Pin Prick	NS	ns	ns	NS
Light Touch	NS	NS	ns	ns
Muscle Status	** (NS)	** (ns)	** (ns)	** (NS)
Vibration	NS	ns	NS	NS

TABLE 8-40. (Continued)

Summary of Categorized Current Dioxin Analyses for Neurological Variables (Ranch Hands and Comparisons)

Variable	All	Adjusted: Unknown versus Background	Adjusted: Low versus Background	Adjusted: High versus Background
Peripheral Nerve Status (continued)				
Patellar Reflex	NS	NS	NS	NS*
Achilles Reflex	** (NS)	** (ns)	** (NS)	** (NS)
Biceps Reflex	--	--	--	--
Babinski Reflex	--	--	--	--
Central Nervous System Coordination Processes				
Tremor	NS	ns	ns	NS
Coordination	** (0.006)	** (NS*)	** (NS)	** (+0.001)
Romberg Sign[a]	--	--	--	--
Gait	** (NS)	** (NS)	** (NS)	** (NS)
CNS Index	** (NS)	** (NS)	** (ns)	** (+0.023)

[a]Balance same as Romberg sign.
[b]Adjusted for age.
[c]Adjusted for age and occupation. Appendix Table G-3 presents a detailed description of this analysis.
+: Relative risk 1.00 or greater.
-: Relative risk less than 1.00.
--: Analysis not performed due to the absence of abnormalities.
NS/ns: Not significant ($p>0.10$).
NS*: Marginally significant ($0.05<p\leq0.10$).
** (NS)/** (ns): Categorized current dioxin-by-covariate interaction ($0.01<p\leq0.05$); not significant when interaction is deleted; refer to Appendix Table G-1 for a detailed description of this interaction.
** (NS*)/** (ns*): Categorized current dioxin-by-covariate interaction ($0.01<p\leq0.05$); marginally significant when interaction is deleted; refer to Appendix Table G-1 for a detailed description of this interaction.
**(...): Categorized current dioxin-by-covariate interaction ($0.01<p\leq0.05$); significant when interaction is deleted and p-value is given in parentheses; refer to Appendix Table G-1 for a detailed description of this interaction.
Note: P-value given if $p\leq0.05$.
A capital "NS" denotes relative risk 1.00 or greater; a lowercase "ns" denotes relative risk less than 1.00; a capital "NS" in the first column does not imply directionality.

TABLE 8-41.

Summary of Dioxin-by-Covariate Interactions from Adjusted Analysis of Neurology Variables

Variable	Assumption	Covariate
Model 1: Log_2 (Initial Dioxin)		
Neck Range of Motion	Minimal	RACE, DIAB
Neck Range of Motion	Maximal	DIAB
Cranial Nerve Index	Maximal	DIAB
Pin Prick	Minimal	DIAB
Pin Prick	Maximal	DIAB
CNS Index	Minimal	AGE
CNS Index	Maximal	AGE
Model 2: Log_2 (Current Dioxin) and Time		
Pin Prick	Minimal	DRKYR
Pin Prick	Maximal	DRKYR
Tremor	Maximal	AGE
Model 3: Ranch Hands and Comparisons by Current Dioxin Category		
Neck Range of Motion	--	DIAB
Cranial Nerve Index Without Range of Motion	--	INS
Muscle Status	--	DIAB
Achilles Reflex	--	RACE
Coordination	--	AGE
Gait	--	DIAB
CNS Index	--	AGE

high current dioxin category had the lowest incidence of hearing loss. However, after adjustment for age, these contrasts became nonsignificant because Ranch Hands in the high current dioxin category were younger on average than men in the other categories. The incidence of conditions in the category of other neurological disorders differed significantly among categories whether unadjusted or adjusted for age, but when occupation was included in the model all contrasts were not significant.

Physical Examination Variables

The neurological assessment analyzed 12 variables to examine the association between dioxin and cranial nerve function (smell, visual fields, light reaction, ocular movement, facial sensation, smile, palpebral fissure, balance, speech, neck range of motion, a cranial nerve index, and the index without range of motion). Pin prick, light touch, muscle status, vibration, patellar reflex, Achilles reflex, biceps reflex, and the Babinski reflex were analyzed to assess peripheral nerve status. The CNS coordination processes were based on tremor, coordination, Romberg sign (balance), gait and a CNS summary index. There were few abnormalities for many of these variables, limiting the statistical power to detect a significant difference.

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Under both the minimal and maximal assumptions, the unadjusted initial dioxin analyses were not significant for all neurological examination variables, although the relative risk was marginally more than 1 for the CNS index under the maximal assumption. The adjusted minimal analyses found that there was a marginally significant increased risk for range of motion. Under the maximal assumption, the adjusted analyses of the Achilles reflex and coordination displayed a relative risk that was marginally more than 1 when diabetic class was excluded from the model. The risks were not significant when diabetic class was in the model. After adjusting for age and lifetime alcohol history, the adjusted relative risk of an abnormal CNS index was significantly more than 1 under the maximal assumption.

Under one or both assumptions, the adjusted analyses detected significant initial dioxin-by-diabetic class interactions for range of motion, the cranial nerve index, and pin prick. Stratified results revealed significant or marginally significant positive associations between initial dioxin and these variables for diabetic Ranch Hands. By contrast, the relative risks were less than 1, although not significant (marginally significant for pin prick under the maximal assumption), for diabetically impaired individuals.

Under both the minimal and maximal assumptions, the adjusted analyses for the CNS index found a significant interaction between initial dioxin and age. Categorizing age to explore the interaction revealed a significant positive association between initial dioxin and the CNS index for Ranch Hands born before 1942. The relative risk was not significant for younger Ranch Hands.

Under the maximal assumption, the longitudinal analyses found that initial dioxin was associated with a marginally significant decreased risk of developing a cranial nerve index abnormality between 1985 and 1987, and a marginally significant increased risk of developing a CNS index abnormality. The initial dioxin longitudinal analyses under the minimal assumption were not significant.

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

The current dioxin and time since tour analyses were generally not significant for the neurological examination variables. Under the minimal assumption, the adjusted current dioxin and time analyses displayed a significant current dioxin-by-time interaction for light touch and a marginally significant interaction for the Achilles reflex, but the within time stratum results were not significant. For Ranch Hands in the minimal cohort with an early tour, there was a marginally significant positive association between current dioxin and smile in the unadjusted analysis and a significant increased risk of range of motion abnormalities and an abnormal cranial nerve index in the adjusted analyses.

The adjusted maximal analyses found a significant current dioxin-by-time interaction for range of motion and for the cranial nerve index. Consistent with the adjusted minimal analysis, the relative risk for both these variables was significantly more than 1 for Ranch Hands with an early tour. The adjusted maximal analyses also detected a significant increased risk for coordination and the CNS index for Ranch Hands with a later tour. The adjusted relative risk of an abnormal Achilles reflex was marginally more than 1 for Ranch Hands in the maximal cohort with an early tour.

Other adjusted analyses were not significant except for a significant current dioxin-by-time-by-lifetime alcohol history interaction for pin prick and a significant current dioxin-by-time-by-age interaction for tremor.

Under the maximal assumption, the longitudinal analyses of the cranial nerve index found a marginally significant current dioxin-by-time interaction that was due to a significant decreased risk of developing an abnormality between 1985 and 1987 for Ranch Hands with a later tour. The current dioxin and time longitudinal analyses of the cranial nerve index were not significant under the minimal assumption. Under both assumptions, the interaction between current dioxin and time was not significant in the longitudinal analyses of the CNS index, but the relative risk of developing an abnormality was marginally more than 1 for Ranch Hands in the maximal cohort with a later tour.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The unadjusted analyses found a marginally significant difference in the prevalence of coordination abnormalities among current dioxin categories, but otherwise the overall contrast was not significant for the other examination variables. In the unadjusted analyses, the high versus background contrast exhibited a significant increased risk for both coordination and the CNS index. The results for coordination are consistent with previous results from the 1987 study, which found a significant group difference. No other contrasts were significant in the unadjusted analyses.

The adjusted analyses displayed comparable findings. The overall contrast was significant in the adjusted analysis of coordination, but not for the other variables. In the adjusted analyses of coordination and the CNS index, the relative risk for the high versus background contrast was significantly more than 1. Several contrasts became marginally significant after covariate adjustment. Relative to the background category, there was a marginally significant increased risk of patellar reflex abnormalities in the high current dioxin category, a marginally significant increased risk of coordination abnormalities in the unknown

category, and a marginally significant decreased risk of cranial nerve index abnormalities without range of motion in the unknown category.

The adjusted analyses encountered several categorized current dioxin-by-covariate interactions, which are listed in Table 8-41. The interaction between categorized current dioxin and age was significant for the CNS index. For older Ranch Hands, the relative risk was significantly more than 1 for the high versus background contrast. This is consistent with the results for the CNS index from the initial dioxin analyses. Stratified results to explore the other interactions disclosed no consistent pattern indicative of a dioxin effect. The longitudinal analysis of the cranial nerve index displayed a marginally significant decreased risk of developing an abnormality for the high current dioxin category relative to the background category. The longitudinal analysis of the CNS index showed no significant results, but the high current dioxin category had the highest incidence.

CONCLUSION

Overall, the neurological assessment did not indicate that dioxin was associated with neurological disease, although some analyses revealed a significant association with the CNS index and coordination. The adjusted analyses for the historical questionnaire variables were not significant and few statistically significant results were noted for the physical examination variables. The previous report found that Ranch Hands had a significantly higher incidence of hereditary and degenerative diseases (mostly benign essential tremor) than Comparisons, but the serum dioxin analyses provided no support that dioxin levels were associated significantly with an increased risk. The adjusted categorized current dioxin analyses for coordination found that the relative risk was significantly greater than 1 for Ranch Hands in the high current dioxin category. This is consistent with the previous report's finding that the Ranch Hand group had significantly more coordination abnormalities than the Comparison group (1.5% versus 0.6%). The serum dioxin analyses showed significant associations with the CNS index, including a marginally significant association with initial dioxin under the maximal assumption in the longitudinal analyses.

CHAPTER 8

REFERENCES

1. Mohammad, F.K., and V.E.V. St. Omer. 1985. Developing rat brain monoamine levels following in utero exposure to a mixture of 2,4-dicholorophenoxyacetic and 2,4,5-trichlorophenoxyacetic acids. *Toxicol. Lett.* 29:215-23.

2. Mohammad, F.K., and V.E.V. St. Omer. 1986. Behavioral and developmental effects in rats following in utero exposure to 2,4-D/2,4,5-T mixture. *Neurobehav. Toxicol. Teratol.* 8:551-60.

3. Mohammad, F.K., and V.E.V. St. Omer. 1988. Effects of prenatal exposure to 2,4-D/2,4,5-T mixture on postnatal changes in rat brain glutamate, GABA, protein, and nucleic acid levels. *Bull. Environ. Contam. Toxicol.* 40:294-300.

4. Mohammad, F.K., and V.E.V. St. Omer. 1988. Behavioral and neurochemical alterations in rats prenatally exposed to 2,4-dichlorophenoxyacetate (2,4-D) and 2,4,5-trichlorophenoxyacetate (2,4,5-D) mixture. *Teratology* 37:515.

5. St. Omer, V.E.V., and F.K. Mohammad. 1987. Ontogeny of swimming behavior and brain catecholamine turnover in rats prenatally exposed to a mixture of 2,4-D and 2,4,5-T. *Neuropharmacology* 26:1351-58.

6. Kim, C.S., R.F. Keizer, and J.B. Pritchard. 1988. 2,4-dichlorophenoxyacetic acid intoxication increases its accumulation within the brain. *Brain Res.* 440:216-26.

7. Schulze, G.E. 1988. 2,4-D-n-butyl ester (2,4-D ester) induced ataxia in rats: Role for n-butanol formation. *Neurotoxicol. Teratol.* 10:81-84.

8. Schulze, G.E., and J.A. Dougherty. 1988. Neurobehavioral toxicity of 2,4-D-n-butyl ester (2,4-D ester): Tolerance and lack of cross-tolerance. *Neurotoxicol. Teratol.* 10:75-79.

9. Schulze, G.E., and J.A. Dougherty. 1988. Neurobehavioral toxicity and tolerance to the herbicide 2,4-dichlorophenoxyacetic and acid-n-butyl ester (2,4-D ester). *Fund. Appl. Toxicol.* 10:413-24.

10. Pohjanvirta, R., L. Tuomisto, and J. Tuomisto. 1989. The central nervous system may be involved in TCDD toxicity. *Toxicology* 58:167-74.

11. Silbergeld, E.K., and S.R. Max. 1986. Neuromuscular targets for the action of 2,3,7,8-TCDD. Abstract of a paper presented at the 6th International Symposium on Chlorinated Dioxins and Related Compounds, 16-19 September, at Fukuoka, Japan.

12. Klawans, H.L., R.S. Wilson, and D.G. Garron. 1987. Neurologic problems following exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD, dioxin). In *Neurotoxins and their pharmacological implications*, ed. P. Jenner. New York: Raven Press.

13. Oliver, R.M. 1975. Toxic effects of 2,3,7,8-tetrachlorodibenzo-1,4-dioxin in laboratory workers. *Br. J. Ind. Med.* 32:49-53.

14. Singer, R., M. Moses, J. Valciukas, R. Lilis, and I.J. Selikoff. 1982. Nerve conduction velocity studies of workers employed in the manufacture of phenoxy herbicides. *Environ. Res.* 29:297-311.

15. Moses, M., R. Lilis, K.D. Crow, J. Thornton, A. Fischbein, H.A. Anderson, and I.J. Selikoff. 1984. Health status of workers with past exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin in the manufacture of 2,4,5-trichlorophenoxyacetic acid: Comparison of findings with and without chloracne. *Am. J. Ind. Med.* 5:161-82.

16. Filippini, G., B. Bordo, P. Crenna, N. Massetto, M. Musicco, and R. Boeri. 1981. Relationship between clinical and electrophysiological findings and indicators of heavy exposure to 2,3,7,8-tetrachlorodibenzo-dioxin. *Scand. J. Work Environ. Health* 7:257-62.

17. Pazderova-Vejlupkova, J., M. Nemcova, J. Pickova, L. Jirasek, and E. Lukas. 1981. The development and prognosis of chronic intoxication by tetrachlorodibenzo-p-dioxin in men. *Arch. Environ. Health* 36:5-11.

18. Webb, K.B., S.M. Ayres, J. Mikes, and R.G. Evans. 1986. The diagnosis of dioxin-associated illness. *Am. J. Prev. Med.* 2:103-108.

19. Webb, K.B., R.G. Evans, P.A. Stehr, and S.M. Ayres. 1987. Pilot study on health effects of environmental 2,3,7,8-TCDD in Missouri. *Am. J. of Ind. Med.* 11:685-91.

20. Webb, K.B., R.G. Evans, A.P. Knutsen, S.T. Roodman, D.W. Roberts, W.F. Schramm, B.B. Gibson, J.S. Andrews, Jr., L.L. Needham, and D.G. Patterson. 1989. Medical evaluation of subjects with known body levels of 2,3,7,8-tetrachlorodibenzo-p-dioxin. *J. of Toxicol. and Environ. Health* 8:183-93.

21. Hoffman, R.E., P.A. Stehr-Green, K.B. Webb, R.G. Evans, A.P. Knutsen, W.F. Schramm, B.B. Gibson, and K.K. Steinberg. 1986. Health effects of long-term exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *JAMA* 225:2031-38.

22. Stehr, P.A., G. Stein, H. Falk, E. Sampson, S.J. Smith, K. Steinberg, K. Webb, S. Ayres, W. Schramm, H.D. Donnell, W.B. Gedney. 1986. A pilot epidemiologic study of possible health effects associated with 2,3,7,8-tetrachlorodibenzo-p-dioxin contaminations in Missouri. *Arch. of Environ. Health* 41:16-22.

23. Boeri, R., B. Bordo, P. Crenna, G. Filippini, M. Massetto, and A. Zecchini. 1978. Preliminary results of a neurological investigation of the population exposed to TCDD in the Seveso region. *Riv. Pat. Nerv. Ment.* 99:111-28.

24. Barbieri, S., C. Pirovano, and G. Scarlato. 1986. 2,3,7,8-tetrachlorodibenzo-para-dioxin and peripheral nervous-system involvement—A clinical and neurophysiological controlled-study on subjects with chloracne from the Seveso area. *Muscle and Nerve* 9:134.

25. Barbieri, S., C. Pirovano, G. Scarlato, P. Tarchini, A. Zappa, and M. Maranzana. 1988. Long-term effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin on the peripheral nervous system. Clinical and neurophysiological controlled study on subjects with chloracne from the Seveso area. *Neuroepidemiology* 7:29-37.

26. Pocchiari, F., S. Vittorio, and Z. Alfredo. 1978. Human health effects from accidental release of tetrachlorodibenzo-p-dioxin (TCDD) at Seveso, Italy. Paper presented at the Academy of Sciences Health Effects of Halogenated Aromatic Hydrocarbon Conference, 24-27 June, at New York.

27. Suskind, R.R., and V.S. Hertzberg. 1984. Human health effects of 2,4,5-T and its toxic contaminants. *JAMA* 251:2372-80.

28. Assennato, G., D. Cervino, P.F. Ciccarelli, G. Longo, and F. Merlo. 1988. Follow-up of subjects who developed chloracne following TCDD exposure at Seveso. Abstract of a paper presented at the 8th International Symposium on Chlorinated Dioxins and Related Compounds, 21-26 August, at Umeá, Sweden.

29. Assennato, G., P. Cannatelli, E. Emmett, I. Ghezzi, and F. Merlo. 1989. Medical monitoring of dioxin clean-up workers. *Am. Ind. Hyg. Assoc. J.* (United States) 50:586-92.

30. Stehr-Green, P.A., J.S. Andrews, Jr., R.E. Hoffman, K.B. Webb, and W.F. Schramm. 1988. An overview of the Missouri dioxin studies. *Arch. Environ. Health* 43:174-77.

31. Lathrop, G.D., W.H. Wolfe, R.A. Albanese, and P.M. Moynahan. 1984. Epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Baseline morbidity study results, NTIS: AD A 138 340. USAF School of Medicine, Brooks Air Force Base, Texas.

32. Lathrop, G.D., S.G. Machado, T.G. Karrison, W.D. Grubbs, M.S. Thomas, W.H. Wolfe, J.E. Michalek, J.C. Miner, and M.R. Peterson. 1987. Epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: First followup examination results, NTIS: AD A 188 262. USAF School of Aerospace Medicine, Brooks Air Force Base, Texas.

33. Dyro, F.M. 1985. Conduction velocities and Agent Orange exposure. *Electroencephalogr. Clin. Neurophysiol.* 60:112.

34. Stellman, S.D., J.M. Stellman, and J.F. Sommer, Jr. 1988. Health and reproductive outcomes among American Legionnaires in relation to combat and herbicide exposure in Vietnam. *Environ. Res.* 47:150-74.

35. U.S. Centers for Disease Control. 1988. Health status of Vietnam veterans. In Part 2, Physical health. The Centers for Disease Control Vietnam experience study. *JAMA* 259:2708-14.

36. Thomas, W.F., W.D. Grubbs, T.G. Karrison, M.B. Lustik, R.H. Roegner, D.E. Williams, W.H. Wolfe, J.E. Michalek, and J.C. Miner. 1990. Epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: 1987 followup examination results, NTIS: AD A 222 573. USAF School of Aerospace Medicine, Brooks Air Force Base, Texas.

CHAPTER 9

PSYCHOLOGICAL ASSESSMENT

INTRODUCTION

Background

Chronic psychological disorders rarely are recognized as primary clinical endpoints following exposure to chlorophenols, phenoxy herbicides, and dioxin. Experimental animal studies provide little insight into potential psychological consequences of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) exposure in humans. Signs of toxicity in animals (lethargy, stupor, poor coordination, lack of feeding, and agitation) have been observed in multiple studies involving many species and have been attributed to the "wasting syndrome" of multiorgan toxicity rather than to primary central nervous system (CNS) toxicity (1).

A recent study of monkeys perinatally exposed to TCDD (2) is much more relevant to human research. Though the results were not uniform, subtle and selective deficits were noted in learning with TCDD-exposed monkeys that exhibited retarded learning of shape but not of spatial or color reversals.

Studies attempting to define human psychological/behavioral disorders related to TCDD exposure often are flawed by a number of limitations including the bias of self-reporting, the lack of confirmation by psychological testing, and the unreliable indices of exposure. Using chloracne as a reliable marker for high-level exposure, early studies of industrial chemical workers provided the first suggestion of psychological effects. Studies shortly after a Nitro, West Virginia, accident in 1949 documented nervousness, fatigue, irritability, cold intolerance, and decreased libido in many of the workers with chloracne. Most of these symptoms resolved over a 4-year period (3, 4). Two followup studies of expanded plant cohorts in 1979 noted a strong association between chloracne and reported symptoms of diminished libido, sexual dysfunction, and insomnia (5, 6). None of these studies included validation by neurobehavioral testing.

Other industrially based studies reported a wide range of acute and subacute subjective symptoms including fatigue, decreased libido, impotence, sleep disturbances, reduced emotional responses, sensory deficits, reading difficulties, memory loss, and emotional disorders (7-13). One study found a relationship between chloracne and hypomania as reflected in the Minnesota Multiphasic Personality Inventory (MMPI) (14). Another study noted that two of three chemists involved in the synthesis of TCDD developed marked personality changes (15). Although data interpretation problems exist, a Czechoslovakian 10-year followup study cited eight cases of severe dementia in exposed workers and reported that symptoms of anxiety and depression decreased over the followup period (13).

A contemporary cross-sectional morbidity study of a mobile-home park en ironmentally contaminated with dioxin documented psychological changes in exposed residents (16). Significant abnormalities were recorded in the exposed group for the tension/anxiety and anger/hostility scales of the Profile of Mood States Inventory as well as the vocabulary

subtest of the Wechsler Adult Intelligence Scale. However, cerebral function, as assessed by the Halstead-Reitan Battery (HRB), revealed no significant group differences.

Many epidemiologic studies have confirmed that the Vietnam War exacted an emotional toll of its veterans, particularly those who served in heavy combat. The possibility of occult disease consequent to herbicide exposure has introduced an additional element of uncertainty with its own set of adverse psychological implications. Relevant to this is a recent study of the psychological characteristics of 153 Vietnam veterans with comparable combat experience. Fifty-eight of these veterans reported moderate to high herbicide exposure in contrast to 95 veterans with minimal or no exposure. The perceived exposed cohort scored significantly higher on MMPI scales F, hypochondriasis, depression, paranoia, psychasthenia, schizophrenia, mania, and social introversion (17).

In addition to unreliable exposure estimates, this study of psychopathology in veterans was further complicated by the confounding effects of combat stress and the post-traumatic stress disorder (PTSD). In 1980, the American Psychiatric Association established the term *post-traumatic stress disorder* to define a condition caused by extreme psychic trauma; e.g., natural disaster, war, imprisonment, or torture (18). PTSD comprises symptoms of anxiety, "powder-keg" anger, depression, irritability, restlessness, recurrent intrusive dreams, flashbacks, and sleeplessness. Quiescent PTSD may be reactivated acutely in some individuals by a specific triggering event (19). Although a concise definition of PTSD exists, the best means of diagnosing it is controversial. Some investigators prefer a full and thorough clinical interview (20) while others favor empiric symptom scales (15). Each method serves a different, but highly related, purpose: clinical diagnosis in individuals versus an epidemiologic and statistical contrast of groups.

The prevalence of PTSD in Vietnam veterans is unknown; even the qualitative assessments of "common" or "rare" are debatable (20, 21). Eighteen percent of the nearly 100,000 Vietnam veterans registered in the Veterans Administration's Agent Orange Registry in 1983 complained of nervousness and 10 percent cited personality disorders (22). In a group of 132 veterans included in the Registry (most of whom were selected for inclusion in the study based on referral for psychotherapy), 53 percent met criteria for PTSD, based on symptoms of sleep disorders (53%), mood depression (36%), suicidal thoughts (35%), and irritability (31%) (23).

In another large study conducted by the Veterans Administration that focused on the association between Vietnam service and combat experience, eight PTSD indices (24) found a high incidence (16%) of PTSD in veterans of the Vietnam era. Though the study was recently published, the data were collected in 1979 before the public controversy surrounding the potential health consequences of exposure to Agent Orange. After adjustment for the potential confounding effects of military service and demographic factors, the level of combat exposure was significantly associated with all eight symptoms of PTSD in a dose-response pattern.

Many studies have attempted to investigate the relationship between PTSD and herbicide exposure in Vietnam veterans. The methods employed to determine exposure include self-reporting, use of chloracne symptoms (both self-reported and medically

diagnosed), and various attempts to link the geographic location of a veteran during service in Vietnam to areas of herbicide use. All of these methods have questionable validity. Self-reporting has been shown to be highly inaccurate for most applications (25). One study in which chloracne was used as an index of exposure examined 6 Vietnam veterans and 25 control subjects selected from the same sample group. Evidence was found for significant psychological disorders in the exposed subjects based on the results of a neuropsychological battery (26). Principal limitations of the study included the small sample size and lack of histologic confirmation of chloracne diagnosis.

The probabilistic approach is a more recent method used to determine herbicide exposure in Vietnam veterans. To develop probabilities for exposure, one study used data based on self-reported locations of service in Vietnam and Department of Defense records on locations where herbicides were employed (25). Based on the resulting probability distribution, 100 randomly selected Vietnam veterans were assessed for psychological problems and for self-reporting bias in symptoms. A similar incidence of psychological disorders was noted in the two groups using the probabilistic approach. In contrast, by self-reported exposure estimates, significant group differences were found. The authors concluded that self-reported indices of exposure were unreliable and that psychological symptomatology was significantly influenced by individual perception of exposure.

A larger study using the probabilistic approach selected 6,810 American Legionnaires who served during the Vietnam War (27). The group was divided into those who served in Southeast Asia (SEA) and those who served elsewhere at the same time. Those who served in SEA were considered the "possibly exposed" group (including 102 known handlers of herbicides); those who served elsewhere were considered unexposed. The probability of exposure was based on the time and location of service of each veteran and the time(s) of herbicide use in each area as identified from data released by the Army Joint Services Environmental Support Group. The level of combat experience was evaluated along with a number of social and behavioral effects. The results of the study showed that though herbicide exposure independently could not predict reported psycho-social outcomes, it could anticipate the outcomes when used as a cross-product with combat, indicating that a synergistic effect may be occurring (28). Reported outcomes were not verified by medical records review or psychological testing and exposure was not verified.

Though not specifically designed to investigate endpoints from Agent Orange exposure, the Vietnam Experience Study (VES) by the U.S. Centers for Disease Control included comprehensive psychological testing in Vietnam and non-Vietnam veterans (29). Results revealed an increased incidence of psychological dysfunction related to service in Vietnam including depression (4.5% of Vietnam veterans versus 3.2% in non-Vietnam veterans), anxiety (4.9% versus 3.2%), and alcohol abuse or dependence (13.7% versus 9.2%).

Lacking a valid index of herbicide exposure, research efforts to date can be summarized as contributing a great deal to our understanding of the psychological consequences associated with military service in Vietnam but very little to resolving the question of behavioral endpoints to TCDD toxicity. Further insight in this regard must await additional studies based on more accurate methods of determining the body burden of dioxin.

More detailed summaries of the pertinent scientific literature for the psychological assessment can be found in the report of the previous analyses of the 1987 examination data (30).

Summary of Previous Analyses of the 1987 Examination Data

The psychological assessment was based on verified psychological disorders; reported sleep disorders; and two clinical psychological tests, the Symptom Check List-90-Revised (SCL-90-R) and the Millon Clinical Multiaxial Inventory (MCMI). The verified data on lifetime psychological disorders showed no group differences for psychoses, drug dependence, and anxiety. However, marginally more Ranch Hands than Comparisons had a verified history of alcohol dependence and "other neuroses" based on unadjusted analyses. The Ranch Hands reported experiencing great or disabling fatigue during the day and talking in their sleep more frequently than the Comparisons. No group differences were detected in the other 13 sleep disorder variables in the unadjusted analyses. Although no significant differences between the Ranch Hands and Comparisons were found in the unadjusted analyses of the 12 SCL-90-R variables, the Ranch Hands had marginally more abnormalities than the Comparisons for depression, somatization, and an index of the general severity of symptoms. The results of the unadjusted analyses of the MCMI scores revealed that the Ranch Hands had significantly higher mean antisocial and paranoid scores than the Comparisons. Marginally significant differences were identified on the narcissistic and psychotic delusion scores, where the mean score of the Ranch Hands exceeded that of the Comparisons. After adjustment for the covariates, a significant difference remained on the narcissistic score. The Comparisons had a significantly higher mean dependent score than the Ranch Hands. Significant group-by-covariate interactions were frequently noted in the adjusted analyses, which made direct contrast of the two groups difficult.

Parameters of the Psychological Assessment

Dependent Variables

Questionnaire and physical examination data were used in the psychological assessment.

Questionnaire Data

At the face-to-face interview of the 1987 examination, each participant was asked whether he had a mental or emotional disorder since the date of his last interview. Reported disorders for which treatment was obtained were subsequently verified by reviews of medical records. Information on verified psychological disorders from the 1987 examination was combined with verified disorders from the Baseline and 1985 examinations, and a series of dependent variables regarding verified history of psychological disorders was created. In particular, the verified histories of psychoses, alcohol dependence, drug dependence, anxiety, and an International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) diagnostic code-based category of "other neuroses" (ICD codes 300-302, 305-309, and 311) were studied. Participants with a verified pre-SEA history of a psychological disorder were excluded from the analyses pertaining to that disorder.

Each participant was also asked a series of questions regarding sleep problems (31). Each participant was asked whether he had a current or past problem with the following 12

sleep disorders: (1) trouble falling asleep, (2) waking up during the night, (3) waking up too early and can't go back to sleep, (4) waking up unrefreshed, (5) involuntarily falling asleep during the day, (6) great or disabling fatigue during the day, (7) frightening dreams, (8) talking in sleep, (9) sleepwalking, (10) abnormal movement or activity during the night, (11) sleep problems requiring medication, and (12) snoring loudly in all sleeping positions. Each of these conditions was considered to be a problem if the participant responded yes to having either a current or past problem. In addition, a participant was considered as having insomnia currently or in the past if he responded yes to any of the first three conditions (31). Also, an overall sleep disorder index was constructed, where a sleep disorder was defined as yes if a participant responded affirmatively to any of these conditions, either currently or in the past. Each of the 12 conditions, along with insomnia and the sleep disorder index, was dichotomized and analyzed.

Each participant was asked the average number of hours he slept per night. This dependent variable was analyzed in its continuous form.

The presence of PTSD, based on a subset of 49 questions (32) from the MMPI administered at the 1985 examination, was used as an exclusionary criterion for all verified psychological disorders and all sleep disorder variables. This covariate was dichotomized as yes/no using greater than 30 affirmative responses as a positive indicator of PTSD. Of the participants at the 1987 examination with a dioxin assay, 12 were classified as having PTSD (9 Ranch Hands and 3 Comparisons) by this criteria.

Physical Examination Data

Two instruments new to the 1987 examination, the SCL-90-R and the MCMI, were used in the psychological assessment. Participants with PTSD were excluded from the analysis of the variables from the SCL-90-R and the MCMI.

SCL-90-R

The SCL-90-R is a multidimensional self-reported symptom inventory designed to measure symptomatic psychological distress in terms of nine primary symptom dimensions and three global indices of distress (33). Each participant was asked to respond to 90 questions in terms of a 5-point scale: not at all (0), a little bit (1), moderately (2), quite a bit (3), and extremely (4). Responses were grouped into the nine primary symptom categories, and a raw score for a participant for a category was determined by adding the scores of the answered questions in that category and dividing by the number of answered questions in that category. The raw scores were then converted to T-scores (reference scores for a given population norm) for analysis. These nine categories were anxiety, depression, hostility, interpersonal sensitivity, obsessive-compulsive behavior, paranoid ideation, phobic anxiety, psychoticism, and somatization.

Three global indices also were analyzed: the global severity index (GSI), the positive symptom total (PST), and the positive symptom distress index (PSDI). The GSI was defined as the sum of the scores of all answered questions divided by the number of answered questions on the entire test. This index combines information on the number of symptoms and the intensity of distress. The PST was the number of questions to which the

participant responded positively (i.e., 1, 2, 3, or 4). The PSDI was determined by adding the scores of all answered questions and dividing by the PST. This index describes the intensity of the positive symptoms. Each of these indices was also converted to a T-score.

The T-scores from the nine primary symptom categories were classified as normal or abnormal, with abnormal being defined as a T-score of a least 63. Less than 10 percent of the scores for each category were judged to be abnormal, based on this criterion. These symptom categories and indices are described more fully in Appendix H, pages H-1 to H-4.

MCMI

The MCMI (34) is a self-administered test consisting of 175 items and divided into 20 scales. Each of its 20 scales was constructed as an operational measure of a syndrome derived from a theory of personality and psychopathology. The MCMI was not designed to be a general personality instrument to be used for "normal" populations or for purposes other than diagnostic screening or clinical assessment. The 20 scales are organized into three broad categories to reflect distinctions between basic personality patterns, pathological personality disorders, and clinical symptom syndromes. Many of these scales are directly or indirectly correlated. The MCMI scales are described more fully in Appendix H, pages H-5 to H-11.

Basic Personality Patterns. Eight scales from the MCMI focus on everyday ways of functioning that characterize patients even when they are not suffering acute symptom states. These scales reflect relatively enduring and pervasive traits that typify styles of behaving, perceiving, thinking, feeling, and relating to others. These eight scales are schizoid (asocial), avoidant, dependent (submissive), histrionic (gregarious), narcissistic, antisocial (aggressive), compulsive (conforming), and passive-aggressive (negativistic).

Pathological Personality Disorders. Three MCMI scales describe patients who clearly evidence chronic or periodically severe pathology in the overall structure of personality. These scales are schizotypal (schizoid), borderline (cycloid), and paranoid.

Clinical Symptom Syndromes. Nine scales from the MCMI measure reactive disorders, often precipitated by external events, that are of substantially briefer duration than the personality disorders. Six scales—anxiety, somatoform, hypomanic, dysthymic, alcohol abuse, and drug abuse—represent disorders of moderate severity. The other three scales—psychotic thinking, psychotic depression, and psychotic delusions—reflect disorders of marked severity.

Raw scores were derived for each of these scales and were converted to base rate (BR) scores based on known personality and syndrome prevalence data. The BR scores for each of these 20 scales were analyzed as continuous variables. High scores indicated greater emotional illness or psychological abnormality than low scores. Unlike the SCL-90-R, scores were not classified as "normal" for these scales.

Transformations were applied to certain MCMI variables. In particular, a natural logarithm transformation was applied to the schizoid and avoidant scores. This

transformation was performed after adding 1.0 to the avoidant scores because some participants had a score of 0. A square root transformation was used with the dependent, passive-aggressive, and hypomania scores, and a square transformation was applied to the histrionic and compulsive scores. All statistics were converted back to the original units for presentation.

Covariates

Covariates examined in the adjusted statistical analyses of the psychological assessment included age, race, education level (high school, college), current alcohol use (drinks/day), and lifetime alcohol history (drink-years). Age, lifetime alcohol history, and current alcohol use were used in the continuous form for modeling purposes for general linear models and logistic regression analyses. These variables were discretized for presentation of covariate interactions with dioxin.

The lifetime alcohol history and current alcohol use covariates were based on self-reported information from the questionnaire. For lifetime alcohol history, the respondent's average daily alcoholic consumption was determined for various drinking stages throughout his lifetime, and an estimate of the corresponding total number of drink-years (1 drink-year=365 drinks) was derived. The current alcohol use covariate was based on the average drinks per day for the month prior to completing the questionnaire.

Relation to Baseline, 1985, and 1987 Studies

The dependent variables dealing with a history of mental or emotional disorders were analyzed for the Baseline and 1985 studies. However, the variables concerned with sleep disorders, the SCL-90-R, and the MCMI were new to the 1987 study and the serum dioxin analyses. PTSD was an exclusionary criterion for analyses of the 1987 examination data. For the 1985 examination report, PTSD was used as a covariate.

Statistical Methods

Three statistical analysis approaches were used to examine the association between a health endpoint dependent variable and serum dioxin levels. One model related a dependent variable to each Rand Hand's initial dioxin value (extrapolated from current dioxin values using a first-order pharmacokinetic model). A second model related a dependent variable to each Ranch Hand's current serum dioxin value and each Ranch Hand's time since tour. The phrase "time since tour" is often referred to as "time" in discussions of these results. Both of these models were implemented under the minimal and maximal assumptions (i.e., Ranch Hands with current dioxin above 10 ppt and above 5 ppt, respectively). The third model compared the health endpoint dependent variable for Ranch Hands having current dioxin values categorized as unknown, low, and high with Comparisons having background levels. The contrast of the entire Ranch Hand group with the complete Comparison group can be found in the previous report of analyses of the 1987 examination (30). All three models were implemented with and without covariate adjustment. Chapter 4, Statistical Methods, provides a more detailed discussion of the models. Table 9-1 summarizes the statistical analyses performed for the serum dioxin analyses of the psychological assessment. The first part of this table describes the dependent variables; the second part provides a further

TABLE 9-1.

Statistical Analysis for the Psychological Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analyses
Psychoses	Q/PE-V	D	Yes No	AGE,RACE, ALC,DRKYR, EDUC	U:LR A:LR
Alcohol Dependence	Q/PE-V	D	Yes No	AGE,RACE, EDUC	U:LR A:LR
Drug Dependence	Q/PE-V	D	Yes No	--	--
Anxiety	Q/PE-V	D	Yes No	AGE,RACE, ALC,DRKYR, EDUC	U:LR A:LR
Other Neuroses	Q/PE-V	D	Yes No	AGE,RACE, ALC,DRKYR, EDUC	U:LR A:LR
Trouble Falling Asleep	Q-SR	D	Yes No	AGE,RACE, ALC,DRKYR, EDUC	U:LR A:LR
Waking Up During the Night	Q-SR	D	Yes No	AGE,RACE, ALC,DRKYR, EDUC	U:LR A:LR
Waking Up Too Early and Can't Go Back to Sleep	Q-SR	D	Yes No	AGE,RACE, ALC,DRKYR, EDUC	U:LR A:LR
Waking Up Unrefreshed	Q-SR	D	Yes No	AGE,RACE, ALC,DRKYR, EDUC	U:LR A:LR

TABLE 9-1. (Continued)

Statistical Analysis for the Psychological Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analyses
Involuntarily Falling Asleep During the Day	Q-SR	D	Yes No	AGE,RACE, ALC,DRKYR, EDUC	U:LR A:LR
Great or Disabling Fatigue During the Day	Q-SR	D	Yes No	AGE,RACE, ALC,DRKYR, EDUC	U:LR A:LR
Frightening Dreams	Q-SR	D	Yes No	AGE,RACE, ALC,DRKYR, EDUC	U:LR A:LR
Talking in Sleep	Q-SR	D	Yes No	AGE,RACE, ALC,DRKYR, EDUC	U:LR A:LR
Sleepwalking	Q-SR	D	Yes No	AGE,RACE, ALC,DRKYR, EDUC	U:LR A:LR
Abnormal Movement/Activity During the Night	Q-SR	D	Yes No	AGE,RACE, ALC,DRKYR, EDUC	U:LR A:LR
Sleep Problems Requiring Medication	Q-SR	D	Yes No	AGE,RACE, ALC,DRKYR, EDUC	U:LR A:LR
Snore Loudly in All Sleeping Positions	Q-SR	D	Yes No	AGE,RACE, ALC,DRKYR, EDUC	U:LR A:LR

TABLE 9-1. (Continued)

Statistical Analysis for the Psychological Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analyses
Insomnia	Q-SR	D	Yes No	AGE,RACE, ALC,DRKYR, EDUC	U:LR A:LR
Overall Sleep Disorder Index	Q-SR	D	Abnormal Normal	AGE,RACE, ALC,DRKYR, EDUC	U:LR A:LR
Average Sleep Each Night (hours)	Q-SR	C	--	AGE,RACE, ALC,DRKYR, EDUC	U:GLM A:GLM
Symptom Check List-90-Revised (SCL-90-R) Anxiety	PE	D	Abnormal Normal	AGE,RACE, ALC,DRKYR, EDUC	U:LR A:LR
SCL-90-R Depression	PE	D	Abnormal Normal	AGE,RACE, ALC,DRKYR, EDUC	U:LR A:LR
SCL-90-R Hostility	PE	D	Abnormal Normal	AGE,RACE, ALC,DRKYR, EDUC	U:LR A:LR
SCL-90-R Interpersonal Sensitivity	PE	D	Abnormal Normal	AGE,RACE, ALC,DRKYR, EDUC	U:LR A:LR
SCL-90-R Obsessive-Compulsive Behavior	PE	D	Abnormal Normal	AGE,RACE, ALC,DRKYR, EDUC	U:LR A:LR

TABLE 9-1. (Continued)

Statistical Analysis for the Psychological Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analyses
SCL-90-R Paranoid Ideation	PE	D	Abnormal Normal	AGE,RACE, ALC,DRKYR, EDUC	U:LR A:LR
SCL-90-R Phobic Anxiety	PE	D	Abnormal Normal	AGE,RACE, ALC,DRKYR, EDUC	U:LR A:LR
SCL-90-R Psychoticism	PE	D	Abnormal Normal	AGE,RACE, ALC,DRKYR, EDUC	U:LR A:LR
SCL-90-R Somatization	PE	D	Abnormal Normal	AGE,RACE, ALC,DRKYR EDUC	U:LR A:LR
SCL-90-R Global Severity Index (GSI)	PE	D	Abnormal Normal	AGE,RACE, ALC,DRKYR, EDUC	U:LR A:LR
SCL-90-R Positive Symptom Total (PST)	PE	D	Abnormal Normal	AGE,RACE, ALC,DRKYR, EDUC	U:LR A:LR
SCL-90-R Positive Symptom Distress Index (PSDI)	PE	D	Abnormal Normal	AGE,RACE, ALC,DRKYR, EDUC	U:LR A:LR

TABLE 9-1. (Continued)

Statistical Analysis for the Psychological Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analyses
Millon Clinical Multiaxial Inventory					
Basic Personality Patterns					
Schizoid Score	PE	C	–	AGE,RACE, ALC,DRKYR, EDUC	U:GLM A:GLM
Avoidant Score	PE	C	–	AGE,RACE, ALC,DRKYR, EDUC	U:GLM A:GLM
Dependent Score	PE	C	–	AGE,RACE, ALC,DRKYR, EDUC	U:GLM A:GLM
Histrionic Score	PE	C	–	AGE,RACE, ALC,DRKYR, EDUC	U:GLM A:GLM
Narcissistic Score	PE	C	–	AGE,RACE, ALC,DRKYR, EDUC	U:GLM A:GLM
Antisocial Score	PE	C	–	AGE,RACE, ALC,DRKYR, EDUC	U:GLM A:GLM
Compulsive Score	PE	C	–	AGE,RACE, ALC,DRKYR, EDUC	U:GLM A:GLM
Passive-Aggressive Score	PE	C	–	AGE,RACE, ALC,DRKYR, EDUC	U:GLM A:GLM

TABLE 9-1. (Continued)

Statistical Analysis for the Psychological Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analyses
Pathological Personality Disorders					
Schizotypal Score	PE	C	- -	AGE,RACE, ALC,DRKYR, EDUC	U:GLM A:GLM
Borderline Score	PE	C	- -	AGE,RACE, ALC,DRKYR, EDUC	U:GLM A:GLM
Paranoid Score	PE	C	- -	AGE,RACE, ALC,DRKYR, EDUC	U:GLM A:GLM
Clinical Symptom Syndromes					
Anxiety Score	PE	C	- -	AGE,RACE, ALC,DRKYR, EDUC	U:GLM A:GLM
Somatoform Score	PE	C	- -	AGE,RACE, ALC,DRKYR, EDUC	U:GLM A:GLM
Hypomania Score	PE	C	- -	AGE,RACE, ALC,DRKYR, EDUC	U:GLM A:GLM
Dysthymia Score	PE	C	- -	AGE,RACE, ALC,DRKYR, EDUC	U:GLM A:GLM
Alcohol Abuse Score	PE	C	- -	AGE,RACE, EDUC	U:GLM A:GLM

TABLE 9-1. (Continued)

Statistical Analysis for the Psychological Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analyses
Clinical Symptom Syndromes (Continued)					
Drug Abuse Score	PE	C	- -	AGE,RACE, ALC,DRKYR, EDUC	U:GLM A:GLM
Psychotic Thinking Score	PE	C	- -	AGE,RACE, ALC,DRKYR, EDUC	U:GLM A:GLM
Psychotic Depression Score	PE	C	- -	AGE,RACE, ALC,DRKYR, EDUC	U:GLM A:GLM
Psychotic Delusion Score	PE	C	- -	AGE,RACE, ALC,DRKYR, EDUC	U:GLM A:GLM

Covariates

Variable (Abbreviation)	Data Source	Data Form	Cutpoints
Age (AGE)	MIL	D/C	Born ≥1942 Born <1942
Race (RACE)	MIL	D	Black Non-Black
Current Alcohol Use (ALC) (drinks/day)	Q-SR	D/C	0-1 >1

TABLE 9-1. (Continued)

Statistical Analysis for the Psychological Assessment

Covariates

Variable (Abbreviation)	Data Source	Data Form	Cutpoints
Lifetime Alcohol History (DRKYR) (drink-years)	Q-SR	D/C	0 >0-40 >40
Education (EDUC)	Q-SR	D	College High School

Abbreviations

Data Source:
MIL--Air Force military records
PE--1987 SCRF psychological examination
Q-SR--1987 NORC questionnaire (self-reported)
Q/PE-V--1987 Questionnaire and physical examination (verified)

Data Form:
D--Discrete analysis only
C--Continuous analysis only
D/C--Appropriate form for analysis (either discrete or continuous)

Statistical Analyses:
U--Unadjusted analyses
A--Adjusted analyses

Statistical Methods:
GLM--General linear models analysis
LR--Logistic regression analysis

description of the candidate covariates. Abbreviations are used extensively in the body of the table and are defined in footnotes.

Appendix H contains graphic displays of individual health endpoint dependent variables versus initial dioxin for the minimal and maximal Ranch Hand cohorts, and individual health endpoint variables versus current dioxin for Ranch Hands and Comparisons. Graphics for dioxin-by-covariate interactions determined by various statistical models are also presented in Appendix H. A guide to assist in interpreting the graphics is found in Chapter 4.

In addition to the participants who were excluded from the psychological assessment due to medical reasons, dependent variable and covariate data were missing for several variables. Table 9-2 provides the number of participants excluded as well as the number of participants with missing data.

RESULTS

Exposure Analysis

Questionnaire Variables

Psychoses (Verified)

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

The unadjusted analysis of the frequency of Ranch Hands with a verified history of psychoses detected a marginally significant negative association with initial dioxin under the minimal assumption (Table 9-3 [a]: Est. RR=0.64, p=0.099). The percentage of Ranch Hands having verified cases of psychoses for the low, medium, and high initial dioxin categories were 4.6, 1.6, and 2.3 percent. Based on the maximal assumption, there was not a significant association between initial dioxin and Ranch Hands with a verified incidence of psychoses (Table 9-3 [b]: p=0.841).

After incorporating race and education in the model based on the minimal assumption, the negative association between initial dioxin and psychoses was significant (Table 9-3 [c]: Adj. RR=0.57, p=0.042). The maximal adjusted analysis of initial dioxin and psychoses remained nonsignificant (Table 9-3 [d]: p=0.647).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

In the unadjusted analysis based on psychoses with current dioxin and time since tour, there was not a significant current dioxin-by-time interaction under either the minimal or the maximal assumption (Table 9-3 [e] and [f]: p=0.351 and p=0.361). Thus, under each assumption, the estimated relative risks of the two time strata did not differ significantly from one another. Similarly, the adjusted analysis exhibited a nonsignificant interaction between current dioxin and time since tour for both the minimal and the maximal assumptions (Table 9-3 [g] and [h]: p=0.332 and p=0.403).

TABLE 9-2.

Number of Participants Excluded and With Missing Data for the Psychological Assessment

Variable	Variable Use	Assumption (Ranch Hands Only) Minimal	Assumption (Ranch Hands Only) Maximal	Categorized Current Dioxin Ranch Hand	Categorized Current Dioxin Comparison
Frightening Dreams	DEP	2	2	3	3
Talking in Sleep	DEP	1	1	1	1
Overall Sleep Disorder Index	DEP	2	2	3	3
12 SCL-90-R Variables	DEP	52	82	88	93
20 MCMI Variables	DEP	2	2	2	2
Current Alcohol Use	COV	3	5	5	0
Lifetime Alcohol History	COV	6	9	9	2
Education	COV	4	5	5	5
Presence of PTSD (1985)	EXC	5	8	8	3
Pre-SEA Anxiety	EXC	1	1	1	2
Pre-SEA Other Neuroses	EXC	4	8	8	6

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

TABLE 9-3.

Analysis of Psychoses (Verified)

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=516)	Low	130	4.6	0.64 (0.36,1.14)	0.099
	Medium	256	1.6		
	High	130	2.3		
b) Maximal (n=734)	Low	182	0.0	1.04 (0.70,1.54)	0.841
	Medium	369	2.7		
	High	183	1.6		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=512)	0.57 (0.31,1.04)	0.042	RACE (p=0.145) EDUC (p=0.033)
d) Maximal (n=729)	0.91 (0.59,1.39)	0.647	EDUC (p=0.014)

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

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 9-3. (Continued)

Analysis of Psychoses (Verified)

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.351[b]
(n=516)	≤18.6	2.8 (72)	3.1 (128)	5.6 (54)	0.81 (0.41,1.62)	0.552[c]
	>18.6	3.5 (57)	1.6 (129)	0.0 (76)	0.42 (0.11,1.57)	0.197[c]
f) Maximal						0.361[b]
(n=734)	≤18.6	0.0 (105)	3.2 (190)	3.6 (83)	1.27 (0.78,2.08)	0.334[c]
	>18.6	0.0 (78)	2.3 (176)	0.0 (102)	0.85 (0.40,1.81)	0.669[c]

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal			0.332[b]	EDUC (p=0.038)
(n=512)	≤18.6	0.75 (0.37,1.53)	0.425[c]	
	>18.6	0.37 (0.10,1.41)	0.146[c]	
h) Maximal			0.403[b]	EDUC (p=0.016)
(n=729)	≤18.6	1.11 (0.65,1.89)	0.710[c]	
	>18.6	0.75 (0.34,1.65)	0.470[c]	

[a]Relative risk for a twofold increase in dioxin.
[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).
[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 9-3. (Continued)

Analysis of Psychoses (Verified)

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	783	2.7	All Categories		0.377
Unknown	341	1.2	Unknown vs. Background	0.43 (0.15,1.26)	0.125
Low	194	2.1	Low vs. Background	0.76 (0.26,2.25)	0.625
High	185	1.6	High vs. Background	0.60 (0.18,2.03)	0.409
Total	1,503				

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	776	All Categories		0.385	AGE (p=0.148) DRKYR (p=0.070) EDUC (p=0.086)
Unknown	336	Unknown vs. Background	0.50 (0.17,1.47)	0.207	
Low	190	Low vs. Background	0.73 (0.25,2.18)	0.578	
High	180	High vs. Background	0.46 (0.13,1.60)	0.223	
Total	1,482				

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In the unadjusted analysis of the percentage of participants with a confirmed incidence of psychoses, the contrast of the four current dioxin categories was nonsignificant (Table 9-3 [i]: p=0.377). The adjusted analysis also failed to detect a significant difference among the percentages of verified psychoses of the four current dioxin categories (Table 9-3 [j]: p=0.385).

Alcohol Dependence (Verified)

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Under both the minimal and maximal assumptions, the unadjusted and adjusted analyses displayed a nonsignificant association between initial dioxin and alcohol dependence in Ranch Hands (Table 9-4 [a-d]: p>0.40 for all analyses).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

In the unadjusted analysis of alcohol dependence in Ranch Hands, there was not a significant current dioxin-by-time since tour interaction for either the minimal or maximal cohort (Table 9-4 [e] and [f]: p=0.393 and p=0.163). In the adjusted analysis of alcohol dependence in Ranch Hands with current dioxin and time since tour, the current dioxin-by-time interaction was again nonsignificant under both the minimal and the maximal assumptions (Table 9-4 [g] and [h]: p=0.375 and p=0.199). Thus, under both assumptions of the unadjusted and the adjusted analyses, the relative risks of the time strata did not differ significantly from one another.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In both the unadjusted and the adjusted analyses of the frequency of alcohol dependence in Ranch Hands and Comparisons, the simultaneous contrast of the four current dioxin categories was not significant (Table 9-4 [i] and [j]: p=0.563 and p=0.444, respectively).

Drug Dependence (Verified)

Analyses of drug dependence with initial dioxin, current dioxin and time since tour, and Ranch Hands and Comparisons by current dioxin category are not presented due to the sparse number of participants with a confirmed history of drug dependence since the end of their tour. There were no Ranch Hands and only two Comparisons having a verified history of drug dependence (Table 9-5).

Anxiety (Verified)

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Based on the minimal assumption, the unadjusted analysis of verified anxiety displayed a nonsignificant association between initial dioxin and the percentage of Ranch Hands with a verified history of anxiety since the end of their tour (Table 9-6 [a]: p=0.159). However, the maximal unadjusted analysis found a significant positive association between initial dioxin and Ranch Hands with a confirmed history of anxiety (Table 9-6 [b]: Est. RR=1.16,

TABLE 9-4.

Analysis of Alcohol Dependence (Verified)

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=516)	Low	130	10.8	1.00 (0.76,1.30)	0.999
	Medium	256	5.9		
	High	130	8.5		
b) Maximal (n=734)	Low	182	3.9	1.09 (0.89,1.32)	0.413
	Medium	369	8.9		
	High	183	7.1		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=512)	0.94 (0.71,1.24)	0.666	EDUC (p=0.003)
d) Maximal (n=729)	1.03 (0.83,1.27)	0.821	AGE (p=0.091) EDUC (p=0.002)

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

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 9-4. (Continued)

Analysis of Alcohol Dependence (Verified)

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal (n=516)						0.393[b]
	≤18.6	8.3 (72)	5.5 (128)	7.4 (54)	1.14 (0.73,1.78)	0.551[c]
	>18.6	15.8 (57)	5.4 (129)	9.2 (76)	0.89 (0.62,1.27)	0.529[c]
f) Maximal (n=734)						0.163[b]
	≤18.6	3.8 (105)	5.3 (190)	8.4 (83)	1.27 (0.92,1.77)	0.151[c]
	>18.6	7.7 (78)	10.2 (176)	7.8 (102)	0.94 (0.73,1.22)	0.657[c]

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal (n=512)			0.375[b]	EDUC (p=0.003)
	≤18.6	1.09 (0.69,1.71)	0.726[c]	
	>18.6	0.83 (0.57,1.21)	0.329[c]	
h) Maximal (n=729)			0.199[b]	EDUC (p=0.002)
	≤18.6	1.16 (0.82,1.64)	0.403[c]	
	>18.6	0.87 (0.66,1.14)	0.320[c]	

[a]Relative risk for a twofold increase in dioxin.
[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).
[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 9-4. (Continued)

Analysis of Alcohol Dependence (Verified)

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	783	6.0	All Categories		0.563
Unknown	341	7.3	Unknown vs. Background	1.24 (0.75,2.05)	0.404
Low	194	5.2	Low vs. Background	0.85 (0.42,1.72)	0.652
High	185	8.1	High vs. Background	1.38 (0.75,2.53)	0.295
Total	1,503				

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	778	All Categories		0.444	AGE (p=0.044) EDUC (p=0.010)
Unknown	339	Unknown vs. Background	1.32 (0.79,2.19)	0.286	
Low	192	Low vs. Background	0.81 (0.40,1.64)	0.557	
High	184	High vs. Background	1.37 (0.74,2.54)	0.323	
Total	1,493				

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 9-5.

Analysis of Drug Dependence (Verified)

Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes
Background	783	0.3
Unknown	341	0.0
Low	194	0.0
High	185	0.0
Total	1,503	

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 9-6.

Analysis of Anxiety (Verified)

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=515)	Low	129	13.2	1.14 (0.95,1.37)	0.159
	Medium	256	17.6		
	High	130	20.0		
b) Maximal (n=733)	Low	182	14.8	1.16 (1.01,1.34)	0.034
	Medium	368	14.4		
	High	183	19.7		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=511)	1.09 (0.90,1.31)	0.393	EDUC (p=0.019)
d) Maximal (n=728)	1.09 (0.94,1.26)	0.256	EDUC (p=0.009)

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

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 9-6. (Continued)

Analysis of Anxiety (Verified)

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.700[b]
(n=515)	≤18.6	15.3 (72)	19.5 (128)	22.2 (54)	1.14 (0.85,1.52)	0.381[c]
	>18.6	8.9 (56)	16.3 (129)	18.4 (76)	1.23 (0.95,1.58)	0.111[c]
f) Maximal						0.418[b]
(n=733)	≤18.6	11.4 (105)	17.4 (190)	19.3 (83)	1.26 (1.02,1.55)	0.034[c]
	>18.6	15.4 (78)	14.9 (175)	16.7 (102)	1.12 (0.92,1.35)	0.263[c]

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal			0.809[b]	EDUC (p=0.022)
(n=511)	≤18.6	1.10 (0.82,1.48)	0.522[c]	
	>18.6	1.15 (0.89,1.50)	0.279[c]	
h) Maximal			0.399[b]	EDUC (p=0.010)
(n=728)	≤18.6	1.18 (0.95,1.48)	0.131[c]	
	>18.6	1.04 (0.85,1.28)	0.679[c]	

[a]Relative risk for a twofold increase in dioxin.
[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).
[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 9-6. (Continued)

Analysis of Anxiety (Verified)

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	781	15.1	All Categories		0.372
Unknown	340	13.2	Unknown vs. Background	0.86 (0.59,1.24)	0.414
Low	194	18.0	Low vs. Background	1.24 (0.82,1.87)	0.316
High	185	17.8	High vs. Background	1.22 (0.80,1.86)	0.359
Total	1,500				

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	774	All Categories		0.778	DRKYR (p=0.013) EDUC (p=0.030)
Unknown	335	Unknown vs. Background	0.90 (0.61,1.31)	0.567	
Low	190	Low vs. Background	1.15 (0.75,1.76)	0.518	
High	180	High vs. Background	1.08 (0.70,1.68)	0.727	
Total	1,479				

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

p=0.034). Under the maximal assumption, the corresponding frequencies of Ranch Hands with a verified history of anxiety for the low, medium, and high initial dioxin categories were 14.8, 14.4, and 19.7 percent.

After adjusting for education, neither the minimal nor the maximal analysis displayed a significant association between initial dioxin and the frequency of Ranch Hands with a confirmed history of anxiety since the end of their tour (Table 9-6 [c] and [d]: p=0.393 and p=0.256, respectively).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

In the unadjusted analysis of the verified incidence of anxiety in Ranch Hands since the end of their tour, the interaction between current dioxin and time since tour was not significant for either the minimal or the maximal assumption (Table 9-6 [e] and [f]: p=0.700 and p=0.418). However, under the maximal assumption, there was a significant positive association between current dioxin and verified cases of anxiety for Ranch Hands with 18.6 years or less since the end of their tour (Table 9-6 [f]: Est. RR=1.26, p=0.034). The percentages of Ranch Hands with a confirmed history of anxiety within this time stratum were 11.4, 17.4, and 19.3 percent for the low, medium, and high current dioxin categories.

After an adjustment for education, the analysis of verified anxiety with current dioxin and time since tour did not find a significant current dioxin-by-time interaction under either the minimal or the maximal assumption (Table 9-6 [g] and [h]: p=0.809 and p=0.399).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In both the unadjusted and the adjusted analysis of participants with a history of verified anxiety subsequent to the end of their tour, the simultaneous contrast of the four current dioxin categories was not significant (Table 9-6 [i] and [j]: p=0.372 and p=0.778, respectively).

Other Neuroses (Verified)

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Based on the minimal assumption, the unadjusted analysis did not find a significant association between initial dioxin and the frequency of Ranch Hands with a history of conditions in the "other neuroses" category since the end of their tour (Table 9-7 [a]: p=0.268). In contrast, the maximal unadjusted analysis did detect a significant positive association between initial dioxin and Ranch Hands with a history of other neuroses (Table 9-7 [b]: Est. RR=1.17, p=0.004). The percentage of Ranch Hands with documented cases of other neuroses since the end of their tour became larger with increasing initial dioxin (low, 31.5%; medium, 43.7%; high, 46.2%).

After the inclusion of lifetime alcohol history and education in the model, the adjusted analysis did not find a significant association between initial dioxin and Ranch Hands with a history of other confirmed neuroses for either the minimal or the maximal cohort (Table 9-7 [c] and [d]: p=0.673 and p=0.331).

TABLE 9-7.

Analysis of Other Neuroses (Verified)

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I)[a]	p-Value
a) Minimal (n=512)	Low	128	39.1	1.08 (0.94,1.25)	0.268
	Medium	255	45.9		
	High	129	46.5		
b) Maximal (n=726)	Low	178	31.5	1.17 (1.05,1.30)	0.004
	Medium	366	43.7		
	High	182	46.2		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=502)	1.03 (0.89,1.20)	0.673	DRKYR (p=0.003) EDUC (p=0.001)
d) Maximal (n=712)	1.06 (0.94,1.19)	0.331	DRKYR (p<0.001) EDUC (p<0.001)

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

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 9-7. (Continued)

Analysis of Other Neuroses (Verified)

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.294[b]
(n=512)	≤18.6	36.1 (72)	46.1 (128)	53.7 (54)	1.20 (0.95,1.51)	0.136[c]
	>18.6	38.2 (55)	45.3 (128)	45.3 (75)	1.02 (0.84,1.23)	0.874[c]
f) Maximal						0.082[b]
(n=726)	≤18.6	30.8 (104)	42.6 (190)	47.0 (83)	1.30 (1.09,1.53)	0.003[c]
	>18.6	33.3 (75)	47.4 (173)	40.6 (101)	1.06 (0.92,1.23)	0.420[c]

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal			0.282[b]	DRKYR (p=0.002)
(n=502)	≤18.6	1.15 (0.90,1.47)	0.252[c]	EDUC (p=0.002)
	>18.6	0.97 (0.79,1.19)	0.765[c]	
h) Maximal			0.112[b]	DRKYR (p<0.001)
(n=712)	≤18.6	1.18 (0.98,1.41)	0.075[c]	EDUC (p<0.001)
	>18.6	0.97 (0.83,1.14)	0.731[c]	

[a]Relative risk for a twofold increase in dioxin.
[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).
[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 9-7. (Continued)

Analysis of Other Neuroses (Verified)

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	777	37.1	All Categories		0.008
Unknown	335	35.5	Unknown vs. Background	0.94 (0.72,1.22)	0.624
Low	193	48.7	Low vs. Background	1.61 (1.17,2.21)	0.003
High	184	43.5	High vs. Background	1.31 (0.94,1.81)	0.108
Total	1,489				

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	770	All Categories		0.024	DRKYR ($p<0.001$) EDUC ($p<0.001$)
Unknown	330	Unknown vs. Background	1.06 (0.81,1.40)	0.661	
Low	189	Low vs. Background	1.65 (1.19,2.30)	0.003	
High	179	High vs. Background	1.22 (0.87,1.72)	0.251	
Total	1,468				

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

The unadjusted analysis of other neuroses with current dioxin and time since tour did not detect a significant current dioxin-by-time interaction under the minimal assumption (Table 9-7 [e]: p=0.294). Based on the maximal assumption, the interaction between current dioxin and time since tour was marginally significant (Table 9-7 [f]: p=0.082). Under this assumption, there was a significant positive association between current dioxin and the prevalence of conditions in the "other neuroses" category in Ranch Hands with 18.6 years or less since tour (Est. RR=1.30, p=0.003). In contrast, there was a nonsignificant positive association between current dioxin and other neuroses for Ranch Hands with more than 18.6 years since tour (Est. RR=1.06, p=0.420). The relative frequency of Ranch Hands with other confirmed neuroses for the time greater than 18.6 years stratum under the maximal assumption were 30.8, 42.6, and 47.0 for percent low, medium, and high current dioxin.

After adjusting for lifetime alcohol history and education, both the minimal and the maximal analyses of other neuroses displayed a nonsignificant current dioxin-by-time interaction (Table 9-7 [g] and [h]: p=0.282 and p=0.112, respectively). However, under the maximal assumption, there was a marginally significant positive association between current dioxin and the percentage of Ranch Hands with a history of other neuroses since the end of their tour (Table 9-7 [h]: Adj. RR=1.18, p=0.075).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In the unadjusted analysis of "other neuroses," the simultaneous contrast of the four current dioxin categories was significant (Table 9-7 [i]: p=0.008). The relative frequencies of other neuroses for the background, unknown, low, and high current dioxin categories were 37.1, 35.5, 48.7, and 43.5 percent. Specifically, the percentage of Ranch Hands in the low current dioxin category having confirmed cases of other neuroses was significantly higher than the corresponding percentage of Comparisons in the background category (Est. RR=1.61, 95% C.I.: [1.17,2.21], p=0.003).

After adjusting for lifetime alcohol history and education, the analysis detected a significant difference in the frequencies of other neuroses among the four current dioxin categories (Table 9-7 [j]: p=0.024). Similar to the unadjusted analysis, the contrast of the low and background current dioxin categories was significant (Adj. RR=1.65, 95% C.I.: [1.19,2.30], p=0.003).

Trouble Falling Asleep

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

The unadjusted analysis of the frequency of Ranch Hands reporting trouble falling asleep was not significant for either the minimal or the maximal assumption (Table 9-8 [a] and [b]: p=0.779 and p=0.875).

In the adjusted analysis, the minimal cohort exhibited a marginally significant negative association between trouble falling asleep and initial dioxin (Table 9-8 [c]: Est. RR=0.80, p=0.100). However, under the maximal assumption, the adjusted analysis displayed a

TABLE 9-8.

Analysis of Trouble Falling Asleep

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=516)	Low	130	13.9	0.97 (0.75,1.24)	0.779
	Medium	256	7.0		
	High	130	10.0		
b) Maximal (n=734)	Low	182	9.9	1.01 (0.84,1.22)	0.875
	Medium	369	8.4		
	High	183	9.3		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=506)	0.80 (0.60,1.05)	0.100	AGE (p<0.001) DRKYR (p=0.018) EDUC*ALC (p=0.030)
d) Maximal (n=720)	0.88 (0.71,1.07)	0.192	AGE (p<0.001) DRKYR (p=0.017) EDUC*ALC (p=0.050)

[a]Relative risk for a twofold increase in dioxin.
Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 9-8. (Continued)

Analysis of Trouble Falling Asleep

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.683[b]
(n=516)	≤18.6	12.5 (72)	10.2 (128)	11.1 (54)	0.94 (0.64,1.37)	0.747[c]
	>18.6	10.5 (57)	6.2 (129)	9.2 (76)	1.05 (0.74,1.48)	0.802[c]
f) Maximal						0.537[b]
(n=734)	≤18.6	6.7 (105)	10.5 (190)	10.8 (83)	1.10 (0.84,1.44)	0.488[c]
	>18.6	9.0 (78)	8.5 (176)	7.8 (102)	0.98 (0.75,1.27)	0.863[c]

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal			0.674[b]	AGE (p<0.001)
(n=506)	≤18.6	0.74 (0.49,1.11)	0.148[c]	DRKYR (p=0.025)
	>18.6	0.83 (0.56,1.23)	0.352[c]	EDUC (p=0.087)
h) Maximal			0.359[b]	AGE (p<0.001)
(n=720)	≤18.6	0.95 (0.71,1.27)	0.743[c]	DRKYR (p=0.020)
	>18.6	0.79 (0.59,1.07)	0.123[c]	EDUC*ALC (p=0.049)

[a]Relative risk for a twofold increase in dioxin.
[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).
[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 9-8. (Continued)

Analysis of Trouble Falling Asleep

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	783	12.1	All Categories		0.144
Unknown	341	9.4	Unknown vs. Background	0.75 (0.49,1.14)	0.182
Low	194	7.2	Low vs. Background	0.56 (0.31,1.01)	0.054
High	185	9.2	High vs. Background	0.73 (0.43,1.26)	0.262
Total	1,503				

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	776	All Categories		0.084	AGE (p=0.003) DRKYR (p=0.004)
Unknown	336	Unknown vs. Background	0.82 (0.53,1.26)	0.360	EDUC (p=0.064)
Low	190	Low vs. Background	0.56 (0.31,1.02)	0.057	
High	180	High vs. Background	0.58 (0.33,1.03)	0.062	
Total	1,482				

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

nonsignificant relationship between trouble falling asleep and initial dioxin (Table 9-8 [d]: p=0.192).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

In the unadjusted analysis of trouble falling asleep based on current dioxin and time since tour, the interaction between current dioxin and time was not significant for either the minimal or the maximal cohort (Table 9-8 [e] and [f]: p=0.683 and p=0.537); thus the relationship between trouble falling asleep and current dioxin was not statistically different between time strata for either cohort. The association between trouble falling asleep and current dioxin within each time stratum was also nonsignificant for both the minimal and maximal analyses.

After adjusting for covariate information, the interaction between current dioxin and time remained nonsignificant under both the minimal and maximal assumptions (Table 9-8 [g] and [h]: p=0.674 and p=0.359). The association between current dioxin and trouble falling asleep within the time strata also remained nonsignificant under both assumptions.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In the unadjusted analysis of trouble falling asleep, the simultaneous contrast of the four current dioxin categories was not significant (Table 9-8 [i]: p=0.144). However, the contrast of the Ranch Hands in the low category versus the Comparisons in the background category was marginally significant (Est. RR=0.56, 95% C.I.: [0.31,1.01], p=0.054) with the percentage of Ranch Hands who reported trouble falling asleep lower than the corresponding percentage of the Comparisons. The frequencies of reported trouble falling asleep for Comparisons in the background category and Ranch Hands in the unknown, low, and high current dioxin categories were 12.1, 9.4, 7.2, and 9.2 percent.

After adjusting for age, lifetime alcohol history, and education, there was a marginally significant difference in the frequency of trouble falling asleep for participants in the four current dioxin categories (Table 9-8 [j]: p=0.084). Similar to the unadjusted analysis, there was a marginally significant difference in the percentage of Ranch Hands in the low category who had trouble falling asleep and the percentage of Comparisons in the background category who also reported trouble falling asleep (Adj. RR=0.56, 95% C.I.: [0.31,1.02], p=0.057). In addition, the contrast of the Ranch Hands in the high category versus the Comparisons in the background category was of borderline significance (Adj. RR=0.58, 95% C.I.: [0.33,1.03], p=0.062) with the Ranch Hands having a lower risk of trouble falling asleep than the Comparisons.

Waking Up During the Night

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

The unadjusted analysis of reports of waking up during the night under both the minimal and the maximal assumptions displayed a nonsignificant association with initial dioxin (Table 9-9 [a] and [b]: p=0.411 and p=0.632, respectively).

TABLE 9-9.

Analysis of Waking Up During the Night

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I)[a]	p-Value
a) Minimal (n=516)	Low	130	19.2	0.92 (0.74,1.13)	0.411
	Medium	256	12.1		
	High	130	12.3		
b) Maximal (n=734)	Low	182	14.8	0.96 (0.82,1.12)	0.632
	Medium	369	14.4		
	High	183	12.0		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=506)	0.87 (0.69,1.09)	0.212	EDUC*DRKYR (p=0.046)
d) Maximal (n=720)	0.91 (0.77,1.08)	0.270	DRKYR (p=0.063) EDUC (p=0.104)

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

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 9-9. (Continued)

Analysis of Waking Up During the Night

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.772[b]
(n=516)	≤18.6	19.4 (72)	12.5 (128)	16.7 (54)	0.97 (0.70,1.34)	0.838[c]
	>18.6	17.5 (57)	10.9 (129)	11.8 (76)	0.91 (0.67,1.22)	0.517[c]
f) Maximal						0.356[b]
(n=734)	≤18.6	13.3 (105)	14.2 (190)	16.9 (83)	1.04 (0.83,1.31)	0.745[c]
	>18.6	15.4 (78)	14.2 (176)	9.8 (102)	0.89 (0.71,1.12)	0.325[c]

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
g) Minimal			****	CURR*TIME*AGE (p=0.002)
(n=510)	≤18.6	****	****	DRKYR (p=0.003)
	>18.6	****	****	
h) Maximal			****	CURR*TIME*ALC (p=0.009)
(n=720)	≤18.6	****	****	DRKYR (p=0.088)
	>18.6	****	****	EDUC (p=0.128)

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

[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).

[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).

****Log_2 (current dioxin)-by-time-by-covariate interaction ($p \leq 0.01$); adjusted relative risk, confidence interval, and p-value not presented.

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.
CURR: Log_2(current dioxin)
TIME: Time since tour.

TABLE 9-9. (Continued)

Analysis of Waking Up During the Night

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	783	14.1	All Categories		0.842
Unknown	341	12.3	Unknown vs. Background	0.86 (0.59,1.26)	0.435
Low	194	12.4	Low vs. Background	0.86 (0.54,1.39)	0.543
High	185	13.0	High vs. Background	0.91 (0.57,1.46)	0.703
Total	1,503				

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	781	All Categories		0.803**	DXCAT*RACE (p=0.046) AGE (p=0.061)
Unknown	338	Unknown vs. Background	0.84 (0.57,1.24)**	0.370**	DRKYR (p<0.001)
Low	192	Low vs. Background	0.87 (0.53,1.41)**	0.562**	
High	181	High vs. Background	0.98 (0.60,1.60)**	0.928**	
Total	1,492				

**Categorized current dioxin-by-covariate interaction ($0.01<p\leq0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction.

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.
DXCAT: Categorized current dioxin.

Based on both the minimal and the maximal assumptions, the association between waking up during the night and initial dioxin was also nonsignificant after adjustment for covariate information (Table 9-9 [c] and [d]: p=0.212 and p=0.270, respectively).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

The current dioxin-by-time since tour interaction was not significant in either the unadjusted minimal or maximal analysis of waking up during the night (Table 9-9 [e] and [f]: p=0.772 and p=0.356), and the association between waking up during the night and current dioxin within each time stratum was also nonsignificant under both assumptions.

In the adjusted analysis under the minimal assumption, there was a significant interaction among current dioxin, time, and age (Table 9-9 [g]: p=0.002). To examine this interaction, associations between the frequency of Ranch Hands who reported waking up during the night and current dioxin are presented separately for each time and age stratum (Appendix Table H-1). For the Ranch Hands born in or after 1942, the current dioxin-by-time interaction was not significant (p=0.136). There was a nonsignificant negative association between current dioxin and waking up during the night for Ranch Hands with 18.6 years or less since tour (Adj. RR=0.76, p=0.258) and a nonsignificant positive association for the time greater than 18.6 years stratum (Adj. RR=1.24, p=0.336).

For the older Ranch Hands, there was a significant current dioxin-by-time interaction (Appendix Table H-1: p=0.033). For this group of Ranch Hands, there was a marginally significant negative association between waking up during the night and current dioxin for the time greater than 18.6 years stratum (Adj. RR=0.61, p=0.082) and a nonsignificant positive association with current dioxin for the time less than 18.6 years time stratum (Adj. RR=1.34, p=0.253).

The adjusted analysis of the maximal cohort displayed a significant current dioxin-by-time-by-current alcohol use interaction (Table 9-9 [h]: p=0.009). Associations between the percentage of Ranch Hands who reported waking up during the night and current dioxin were examined separately for each time and current alcohol use stratum (Appendix Table H-1). For those Ranch Hands who drank one or fewer drinks per day, the current dioxin-by-time interaction was nonsignificant (p=0.909). For those who drank more than one drink per day, there was a highly significant current dioxin-by-time since tour interaction (p=0.007) indicating a difference in the effect of current dioxin for the two time strata. Also, for the time greater than 18.6 years stratum, there was a marginally significant negative association between current dioxin and reports of waking up during the night (Adj. RR=0.42, p=0.058) and a nonsignificant positive association for the time less than or equal to 18.6 years stratum (Adj. RR=1.39, p=0.181).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In the unadjusted analysis of waking up during the night, the contrast of the four current dioxin categories was not significant (Table 9-9 [i]: p=0.842).

The adjusted analysis of waking up during the night by current dioxin category detected a significant interaction between categorized current dioxin and race (Table 9-9 [j]: p=0.046). To examine this interaction, separate analyses are presented for Blacks and non-Blacks in Appendix Table H-1. For the Black stratum, the percentages of participants who reported waking up during the night for the background, unknown, low, and high current dioxin categories were 2.1, 16.7, 0.0, and 25.0 percent. The overall contrast of the four current dioxin categories was significant (Appendix Table H-1: p=0.041). Similarly, the contrasts of the Comparisons in the background category and the Ranch Hands in the unknown and high categories were marginally significant (Adj. RR=19.01, 95% C.I.: [0.91,396.6], p=0.057 and Adj. RR=15.38, 95% C.I.: [0.90,263.8], p=0.059, respectively).

In the analysis of waking up during the night for the non-Black stratum, the contrast of the four current dioxin categories was not significant (Appendix Table H-1: p=0.632). The percentages of participants who reported waking up during the night for the background, unknown, low, and high current dioxin categories were 14.7, 12.0, 12.7, and 12.7 percent.

After deletion of the categorized current dioxin-by-race interaction from the model, the adjusted analysis did not detect a significant difference in the frequency of reports of trouble falling asleep among the four current dioxin categories (Table 9-9 [j]: p=0.803).

Waking Up Too Early and Can't Go Back to Sleep

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Neither the unadjusted minimal analysis nor the unadjusted maximal analysis detected a significant association between the frequency of Ranch Hands who reported waking up too early and not being able to fall back to sleep and initial dioxin (Table 9-10 [a] and [b]: p=0.576 and p=0.874, respectively).

Based on the minimal assumption, a significant interaction between initial dioxin and age was detected for the adjusted analysis (Table 9-10 [c]: p=0.041). To examine this interaction, the association between the sleep disorder of waking up too early with an inability to go back to sleep and initial dioxin was analyzed separately for Ranch Hands born in or after 1942 and for Ranch Hands born before 1942. For the younger group of Ranch Hands, there was a marginally significant negative association between the aforementioned sleep disorder and initial dioxin (Appendix Table H-1: Adj. RR=0.75, p=0.094). However, for the older group of Ranch Hands, there was a nonsignificant positive association (Adj. RR=1.11, p=0.526). Without the interaction of initial dioxin and age in the model, the adjusted relative risk was nonsignificant (Table 9-10 [c]: p=0.432).

No significant association between the frequency of Ranch Hands reporting waking up too early and not being able to fall back asleep and initial dioxin was detected for the adjusted maximal analysis (Table 9-10 [d]: p=0.668).

TABLE 9-10.

Analysis of Waking Up Too Early and Can't Go Back to Sleep

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=516)	Low	130	13.1	0.94 (0.74,1.18)	0.576
	Medium	256	10.6		
	High	130	10.0		
b) Maximal (n=734)	Low	182	10.4	1.01 (0.85,1.21)	0.874
	Medium	369	10.8		
	High	183	9.3		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=510)	0.91 (0.71,1.16)**	0.432**	INIT*AGE (p=0.041) DRKYR (p=0.015)
d) Maximal (n=720)	0.96 (0.79,1.16)	0.668	DRKYR (p=0.072) EDUC*ALC (p=0.035)

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

**Log_2 (initial dioxin)-by-covariate interaction ($0.01<p\leq0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.
INIT: Log_2 (initial dioxin).

TABLE 9-10. (Continued)

Analysis of Waking Up Too Early and Can't Go Back to Sleep

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.286[b]
(n=516)	≤18.6	8.3 (72)	12.5 (128)	13.0 (54)	1.07 (0.75,1.53)	0.705[c]
	>18.6	17.5 (57)	8.5 (129)	9.2 (76)	0.82 (0.58,1.15)	0.252[c]
f) Maximal						0.566[b]
(n=734)	≤18.6	10.5 (105)	11.1 (190)	12.1 (83)	1.09 (0.85,1.40)	0.509[c]
	>18.6	7.7 (78)	11.4 (176)	7.8 (102)	0.98 (0.77,1.26)	0.884[c]

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal			0.336[b]	DRKYR (p=0.013)
(n=510)	≤18.6	1.08 (0.75,1.54)	0.688[c]	
	>18.6	0.85 (0.61,1.18)	0.327[c]	
h) Maximal			0.406[b]	DRKYR (p=0.057)
(n=720)	≤18.6	1.07 (0.82,1.40)	0.617[c]	EDUC*ALC (p=0.033)
	>18.6	0.91 (0.70,1.20)	0.518[c]	

[a]Relative risk for a twofold increase in dioxin.
[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).
[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 9-10. (Continued)

Analysis of Waking Up Too Early and Can't Go Back to Sleep

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	783	11.8	All Categories		0.849
Unknown	341	10.6	Unknown vs. Background	0.89 (0.59,1.33)	0.563
Low	194	11.3	Low vs. Background	0.96 (0.59,1.57)	0.874
High	185	9.7	High vs. Background	0.81 (0.48,1.38)	0.437
Total	1,503				

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	781	All Categories		0.830	DRKYR ($p<0.001$)
Unknown	338	Unknown vs. Background	0.87 (0.58,1.33)	0.528	
Low	192	Low vs. Background	0.94 (0.57,1.56)	0.823	
High	181	High vs. Background	0.80 (0.47,1.38)	0.422	
Total	1,492				

Note: Background (Comparisons): Current Dioxin $\leq$10 ppt.
Unknown (Ranch Hands): Current Dioxin $\leq$10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin $\leq$33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

Neither the unadjusted nor the adjusted analysis of nonrestorative sleep detected a significant interaction between current dioxin and time since tour under either the minimal or the maximal assumption (Table 9-10 [e-h]: p>0.25 for each analysis).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In both the unadjusted and the adjusted analyses of waking up too early and can't go back to sleep, the contrast of the four current dioxin categories was not significant (Table 9-10 [i] and [j]: p=0.849 and p=0.830, respectively).

Waking Up Unrefreshed

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

In the unadjusted analysis performed under the minimal assumption, no significant association was found between the frequency of Ranch Hands who reported waking up unrefreshed and initial dioxin (Table 9-11 [a]: p=0.213). For the maximal cohort, the estimated relative risk was significant (Table 9-11 [b]: Est. RR=1.21, p=0.027), indicating a positive relationship between the sleep disorder and initial dioxin. The associated relative frequencies of Ranch Hands who reported waking up unrefreshed for low, medium, and high levels of initial dioxin were 8.2, 8.9, and 13.1 percent for the maximal cohort.

After adjusting for covariate information, the analysis of the minimal cohort remained nonsignificant (Table 9-11 [c]: p=0.613). For the maximal cohort, after adjusting for education, age, and lifetime alcohol history, the association between Ranch Hands who reported waking up unrefreshed and initial dioxin was no longer significant (Table 9-11 [d]: p=0.336).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

In the unadjusted analysis of the frequency of reports of waking up unrefreshed, the interaction of current dioxin and time since tour was not significant under the minimal assumption (Table 9-11 [e]: p=0.509), nor was it significant under the maximal assumption (Table 9-11 [f]: p=0.361). Thus, the estimated relative risks for the two time strata under each assumption did not differ significantly from one another. For the maximal cohort, the positive association between waking up unrefreshed and current dioxin was significant within the time greater than 18.6 years stratum (Est. RR=1.27, p=0.030). The relative frequencies of Ranch Hands who reported waking up unrefreshed strongly increased with current dioxin (low, 6.4%; medium, 10.2%; high, 16.7%) for this time stratum.

In the minimal adjusted analysis of waking up unrefreshed, there was a significant current dioxin-by-time-by-age interaction (Table 9-11 [g]: p=0.032). In order to examine this interaction, separate analyses are presented for Ranch Hands born in or after 1942 and for those born before 1942 (Appendix Table H-1). The current dioxin-by-time interaction

TABLE 9-11.

Analysis of Waking Up Unrefreshed

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I)[a]	p-Value
a) Minimal (n=516)	Low	130	10.8	1.15 (0.93,1.43)	0.213
	Medium	256	10.2		
	High	130	13.9		
b) Maximal (n=734)	Low	182	8.2	1.21 (1.03,1.43)	0.027
	Medium	369	8.9		
	High	183	13.1		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=510)	1.06 (0.85,1.33)	0.613	AGE (p=0.009) DRKYR (p=0.006)
d) Maximal (n=720)	1.09 (0.91,1.31)	0.336	AGE (p=0.010) DRKYR (p=0.021) EDUC (p=0.126)

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

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 9-11. (Continued)

Analysis of Waking Up Unrefreshed

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.509[b]
(n=516)	≤18.6	8.3 (72)	9.4 (128)	9.3 (54)	0.99 (0.66,1.48)	0.950[c]
	>18.6	12.3 (57)	10.9 (129)	18.4 (76)	1.16 (0.89,1.52)	0.272[c]
f) Maximal						0.361[b]
(n=734)	≤18.6	6.7 (105)	9.5 (190)	8.4 (83)	1.07 (0.81,1.43)	0.620[c]
	>18.6	6.4 (78)	10.2 (176)	16.7 (102)	1.27 (1.02,1.57)	0.030[c]

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal			0.413**[b]	CURR*TIME*AGE (p=0.032)
(n=510)	≤18.6	0.86 (0.56,1.32)**	0.484**[c]	DRKYR (p=0.008)
	>18.6	1.06 (0.80,1.39)**	0.705**[c]	
h) Maximal			0.428[b]	AGE (p=0.006)
(n=720)	≤18.6	0.96 (0.71,1.30)	0.783[c]	DRKYR (p=0.026)
	>18.6	1.11 (0.88,1.40)	0.364[c]	EDUC (p=0.112)

[a]Relative risk for a twofold increase in dioxin.
[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).
[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).
**Log_2 (current dioxin)-by-time-by-covariate interaction ($0.01<p\leq0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction.
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 9-11. (Continued)

Analysis of Waking Up Unrefreshed

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	783	9.3	All Categories		0.071
Unknown	341	6.2	Unknown vs. Background	0.64 (0.39,1.06)	0.030
Low	194	9.3	Low vs. Background	0.99 (0.58,1.71)	0.985
High	185	13.0	High vs. Background	1.45 (0.89,2.37)	0.139
Total	1,503				

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	776	All Categories		0.230	DRKYR (p=0.018) RACE*EDUC (p=0.038)
Unknown	336	Unknown vs. Background	0.63 (0.37,1.06)	0.083	EDUC*ALC (p=0.012)
Low	190	Low vs. Background	0.94 (0.54,1.65)	0.833	AGE*ALC (p=0.019)
High	180	High vs. Background	1.19 (0.71,1.99)	0.519	
Total	1,482				

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

was not significant for either the younger or the older group of Ranch Hands (p=0.227 and p=0.393). For the younger Ranch Hands, there was a nonsignificant negative association between current dioxin and waking up unrefreshed (Adj. RR=0.70, p=0.163) within the less than or equal to 18.6 years time stratum and a nonsignificant positive association within the greater than 18.6 years time stratum (Adj. RR=1.02, p=0.902). In contrast, for the older Ranch Hands, there was a nonsignificant positive association between current dioxin and reports of waking up unrefreshed for both time strata (≤18.6: Adj. RR=1.55, p=0.257; >18.6: Adj. RR=1.05, p=0.832).

After excluding the current dioxin-by-time-by-age interaction from the model and adjusting for only age and lifetime alcohol history, the association of current dioxin and time since tour with the sleep disorder of waking up unrefreshed was still nonsignificant (Table 9-11 [g]: p=0.413).

The adjusted analysis for the maximal assumption did not display a significant current dioxin-by-time since tour interaction (Table 9-11 [h]: p=0.428) and also did not exhibit a significant association within either time stratum.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The unadjusted analysis of waking up unrefreshed detected a marginally significant difference among the percentages of participants who reported waking up unrefreshed in the four current dioxin categories (Table 9-11 [i]: p=0.071). The percentages for the background, unknown, low, and high current dioxin categories were 9.3, 5.2, 9.3, and 13.0 percent. The contrast of Ranch Hands in the unknown category versus Comparisons in the background category was of borderline significance (Est. RR=0.64, 95% C.I.: [0.39,1.06], p=0.080) with the percentage of Ranch Hands who reported waking up unrefreshed lower than the corresponding percentage of Comparisons.

In the adjusted analysis of waking up unrefreshed, the overall contrast of the four current dioxin categories was not significant (Table 9-11 [j]: p=0.230). However, the specific contrast of Ranch Hands in the unknown category versus Comparisons in the background category was of borderline significance (Adj. RR=0.63, 95% C.I.: [0.37,1.06], p=0.083).

Involuntarily Falling Asleep During the Day

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

For both minimal and maximal assumptions, no significant association was found between the percentage of Ranch Hands who reported involuntarily falling asleep during the day and initial dioxin in the unadjusted analyses (Table 9-12 [a] and [b]: p=0.399 and p=0.871, respectively).

After adjusting for covariate information, both the minimal and maximal analyses displayed an interaction between initial dioxin and race (Table 9-12 [c] and [d]: p=0.024 and p=0.043, respectively). To investigate these interactions, the association between involuntarily falling asleep during the day and initial dioxin was analyzed separately for Blacks and non-Blacks (Appendix Table H-1). For the Black stratum of both the minimal and

TABLE 9-12.

Analysis of Involuntarily Falling Asleep During the Day

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=516)	Low	130	4.6	0.85 (0.59,1.24)	0.399
	Medium	256	4.3		
	High	130	4.6		
b) Maximal (n=734)	Low	182	3.9	1.02 (0.79,1.33)	0.871
	Medium	369	3.8		
	High	183	4.9		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=510)	0.84 (0.58,1.22)**	0.349**	INIT*RACE (p=0.024) DRKYR (p=0.056)
d) Maximal (n=725)	1.01 (0.77,1.32)**	0.940**	INIT*RACE (p=0.043) DRKYR (p=0.049) ALC (p=0.071)

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

**Log_2 (initial dioxin)-by-covariate interaction ($0.01<p\leq0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 9-12. (Continued)

Analysis of Involuntarily Falling Asleep During the Day

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.135[b]
(n=516)	≤18.6	4.2 (72)	3.9 (128)	7.4 (54)	1.13 (0.67,1.91)	0.638[c]
	>18.6	7.0 (57)	3.9 (129)	2.6 (76)	0.61 (0.33,1.16)	0.132[c]
f) Maximal						0.075[b]
(n=734)	≤18.6	1.0 (105)	4.2 (190)	7.2 (83)	1.28 (0.88,1.88)	0.201[c]
	>18.6	3.9 (78)	5.1 (176)	2.9 (102)	0.77 (0.51,1.18)	0.229[c]

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal			0.152[b]	DRKYR (p=0.081)
(n=510)	≤18.6	1.14 (0.67,1.92)	0.627[c]	
	>18.6	0.64 (0.35,1.18)	0.153[c]	
h) Maximal			0.084[b]	ALC (p=0.056)
(n=725)	≤18.6	1.28 (0.87,1.89)	0.208[c]	DRKYR (p=0.061)
	>18.6	0.78 (0.51,1.19)	0.248[c]	

[a]Relative risk for a twofold increase in dioxin.
[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).
[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 9-12. (Continued)

Analysis of Involuntarily Falling Asleep During the Day

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	783	3.5	All Categories		0.693
Unknown	341	3.5	Unknown vs. Background	1.02 (0.51,2.04)	0.952
Low	194	2.6	Low vs. Background	0.74 (0.28,1.95)	0.543
High	185	4.9	High vs. Background	1.43 (0.66,3.10)	0.362
Total	1,503				

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	776	All Categories		0.736	RACE*EDUC (p=0.005) DRKYR*ALC (p=0.003)
Unknown	336	Unknown vs. Background	1.08 (0.53,2.20)	0.837	
Low	190	Low vs. Background	0.77 (0.29,2.06)	0.604	
High	180	High vs. Background	1.43 (0.64,3.17)	0.382	
Total	1,482				

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

maximal cohort, there was only a single report of a Ranch Hand involuntarily falling asleep during the day, and under both assumptions the report occurred in the high initial dioxin category. Thus, due to the occurrence of a single abnormality, the relative risk, confidence interval, and p-value are not presented for the Black stratum of either the minimal or maximal analysis.

For the non-Black Ranch Hands, there was a nonsignificant negative association between initial dioxin and reports of involuntarily falling asleep during the day for both the minimal and the maximal analyses (Appendix Table H-1: p=0.220 and p=0.852).

After deletion of the initial dioxin-by-race interaction from the minimal and the maximal analyses, there was not a significant association between initial dioxin and involuntarily falling asleep during the day (Table 9-12 [c] and [d]: p>0.30 for each analysis).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

The minimal unadjusted analysis of reports of involuntarily falling asleep during the day with current dioxin and time since tour displayed a nonsignificant current dioxin-by-time interaction (Table 9-12 [e]: p=0.135). Under the maximal assumption, the unadjusted analysis detected a marginally significant current dioxin-by-time since tour interaction (Table 9-12 [f]: p=0.075), indicating that the relationship between involuntarily falling asleep during the day and current dioxin differed marginally between time strata. For Ranch Hands with 18.6 years or less since tour, there was a nonsignificant positive association between the sleep disorder and current dioxin (Est. RR=1.28, p=0.201), and within the greater than 18.6 years time stratum, there was a nonsignificant negative association (Est. RR=0.77, p=0.229).

The results of the adjusted analyses were concurrent with those of the unadjusted analyses. Under the minimal assumption, the current dioxin-by-time since tour interaction was nonsignificant (Table 9-12 [g]: p=0.152), and the association between current dioxin and involuntarily falling asleep during the day was also nonsignificant within each time stratum. The adjusted analysis based on the maximal assumption still displayed a marginally significant current dioxin-by-time since tour interaction (Table 9-12 [h]: p=0.084). Within the less than or equal to 18.6 years time stratum, there was a nonsignificant positive association between current dioxin and reports of involuntarily falling asleep during the day (Adj. RR=1.28, p=0.208). Also, for the time greater than 18.6 years stratum, there was a nonsignificant negative association (Adj. RR=0.78, p=0.248).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In both the unadjusted and the adjusted analyses of involuntarily falling asleep during the day, the simultaneous contrast of the four current dioxin categories was nonsignificant (Table 9-12 [i] and [j]: p=0.693 and p=0.736, respectively).

Great or Disabling Fatigue During the Day

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Neither the unadjusted minimal nor the unadjusted maximal analysis detected a significant association between initial dioxin and the frequency of Ranch Hands who reported having great or disabling fatigue during the day (Table 9-13 [a] and [b]: p=0.653 and p=0.372, respectively).

These results did not change after adjusting for education, age, and lifetime alcohol history (Table 9-13 [c] and [d]: p=0.111 and p=0.421, respectively).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

Under both the minimal and maximal assumptions, the unadjusted analysis of great or disabling fatigue during the day displayed a nonsignificant current dioxin-by-time since tour interaction (Table 9-13 [e] and [f]: p=0.943 and p=0.386, respectively) as well as nonsignificant associations between current dioxin and great or disabling fatigue during the day within each time stratum.

The adjusted analysis of the minimal cohort exhibited a significant current dioxin-by-time-by-age interaction (Table 9-13 [g]: p=0.003). After stratifying the Ranch Hands by age, there was a nonsignificant current dioxin-by-time since tour interaction for Ranch Hands born in or after 1942 (Appendix Table H-1: p=0.526). A nonsignificant negative association between current dioxin and great or disabling fatigue during the day was detected for both time strata (≤18.6: p=0.197; >18.6: p=0.566). For the older Ranch Hands there was significant current dioxin-by-time interaction (p=0.008), but the positive association between current dioxin and the sleep disorder was nonsignificant for the time less than or equal to 18.6 years stratum (p=0.805). For the time greater than 18.6 years stratum, only three Ranch Hands (all in the low current dioxin category) reported the sleep disorder; therefore, the relative risk, confidence interval, and p-value are not presented.

The adjusted analysis under the maximal assumption displayed a nonsignificant current dioxin-by-time since tour interaction (Table 9-13 [h]: p=0.320) as well as a nonsignificant association between current dioxin and great or disabling fatigue during the day within each time stratum.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

Both the unadjusted and the adjusted analysis of great or disabling fatigue during the day and categorized current dioxin were nonsignificant (Table 9-13 [i] and [j]: p=0.226 and p=0.475, respectively).

Frightening Dreams

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

The unadjusted analysis of the frequency of Ranch Hands reporting frightening dreams was not significantly associated with initial dioxin under the minimal assumption (Table 9-14

TABLE 9-13.

Analysis of Great or Disabling Fatigue During the Day

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=516)	Low	130	6.2	0.92 (0.65,1.31)	0.653
	Medium	256	5.5		
	High	130	2.3		
b) Maximal (n=734)	Low	182	2.8	1.13 (0.87,1.46)	0.372
	Medium	369	4.1		
	High	183	4.9		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=506)	0.74 (0.50,1.09)	0.111	AGE (p=0.085) DRKYR (p=0.012) EDUC (p=0.039)
d) Maximal (n=720)	0.89 (0.66,1.19)	0.421	AGE (p=0.141) DRKYR (p=0.018) EDUC (p<0.001)

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

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 9-13. (Continued)

Analysis of Great or Disabling Fatigue During the Day

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.943[b]
(n=516)	≤18.6	4.2 (72)	6.3 (128)	3.7 (54)	0.88 (0.50,1.53)	0.644[c]
	>18.6	7.0 (57)	4.7 (129)	2.6 (76)	0.90 (0.56,1.46)	0.671[c]
f) Maximal						0.386[b]
(n=734)	≤18.6	1.0 (105)	4.7 (190)	4.8 (83)	1.25 (0.84,1.87)	0.265[c]
	>18.6	3.9 (78)	5.1 (176)	2.9 (102)	0.99 (0.69,1.42)	0.948[c]

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal			****	CURR*TIME*AGE
(n=506)	≤18.6	****	****	(p=0.003)
	>18.6	****	****	DRKYR (p=0.013)
				EDUC (p=0.038)
h) Maximal			0.320[b]	AGE (p=0.131)
(n=720)	≤18.6	1.02 (0.66,1.57)	0.945[c]	DRKYR (p=0.022)
	>18.6	0.75 (0.49,1.16)	0.193[c]	EDUC (p<0.001)

[a]Relative risk for a twofold increase in dioxin.
[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).
[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).
****Log_2 (current dioxin)-by-time-by-covariate interaction ($p \leq 0.01$); adjusted relative risk, confidence interval, and p-value not presented.
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 9-13. (Continued)

Analysis of Great or Disabling Fatigue During the Day

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	783	2.6	All Categories		0.226
Unknown	341	1.8	Unknown vs. Background	0.68 (0.27,1.72)	0.418
Low	194	4.6	Low vs. Background	1.86 (0.83,4.14)	0.131
High	185	3.8	High vs. Background	1.50 (0.62,3.60)	0.364
Total	1,503				

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	776	All Categories		0.475	AGE (p=0.023) DRKYR (p=0.015)
Unknown	336	Unknown vs. Background	0.90 (0.35,2.29)	0.819	EDUC (p=0.004)
Low	190	Low vs. Background	1.85 (0.82,4.21)	0.141	
High	180	High vs. Background	0.95 (0.36,2.47)	0.909	
Total	1,482				

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 9-14.

Analysis of Frightening Dreams

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=514)	Low	130	3.9	1.19 (0.88,1.61)	0.270
	Medium	255	4.3		
	High	129	7.8		
b) Maximal (n=732)	Low	182	1.7	1.33 (1.04,1.68)	0.025
	Medium	369	4.1		
	High	181	6.6		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=504)	1.13 (0.81,1.57)**	0.486**	INIT*EDUC (p=0.046) DRKYR (p=0.004) AGE*ALC (p=0.003)
d) Maximal (n=723)	1.27 (0.98,1.65)	0.072	DRKYR (p=0.009) AGE*ALC (p=0.023)

[a]Relative risk for a twofold increase in dioxin.
**Log_2 (initial dioxin)-by-covariate interaction ($0.01<p\leq0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction.
Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 9-14. (Continued)

Analysis of Frightening Dreams

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.744[b]
(n=514)	≤18.6	2.8 (72)	7.0 (128)	9.6 (52)	1.35 (0.87,2.09)	0.179[c]
	>18.6	5.3 (57)	1.6 (129)	6.6 (76)	1.21 (0.77,1.92)	0.406[c]
f) Maximal						0.379[b]
(n=732)	≤18.6	1.0 (105)	4.2 (190)	11.1 (81)	1.56 (1.11,2.19)	0.011[c]
	>18.6	2.6 (78)	2.3 (176)	5.9 (102)	1.24 (0.86,1.79)	0.241[c]

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal			****	CURR*TIME*RACE (p=0.004)
(n=508)	≤18.6	****	****	DRKYR (p<0.001)
	>18.6	****	****	AGE*ALC (p<0.001)
h) Maximal			0.528**[b]	CURR*TIME*RACE (p=0.046)
(n=723)	≤18.6	1.50 (1.03,2.17)**	0.033**[c]	DRKYR (p=0.004)
	>18.6	1.26 (0.85,1.88)**	0.247**[c]	AGE*ALC (p=0.020)

[a]Relative risk for a twofold increase in dioxin.
[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).
[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).
**Log_2 (current dioxin)-by-time-by-covariate interaction ($0.01<p\leq0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction.
****Log_2 (current dioxin)-by-time-by-covariate interaction ($p\leq0.01$); adjusted relative risk, confidence interval, and p-value not presented.
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 9-14. (Continued)

Analysis of Frightening Dreams

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	780	3.1	All Categories		0.010
Unknown	341	2.4	Unknown vs. Background	0.76 (0.34,1.70)	0.500
Low	194	2.6	Low vs. Background	0.83 (0.31,2.21)	0.714
High	183	8.2	High vs. Background	2.81 (1.44,5.48)	0.002
Total	1,498				

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dixoin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	778	All Categories		0.035	AGE (p=0.100) DRKYR (p=0.089)
Unknown	338	Unknown vs. Background	0.80 (0.35,1.80)	0.584	
Low	192	Low vs. Background	0.85 (0.32,2.26)	0.745	
High	179	High vs. Background	2.54 (1.28,5.02)	0.007	
Total	1,487				

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

[a]: p=0.270). Based on the maximal assumption, the estimated relative risk was significant (Table 9-14 [b]: Est. RR=1.33, p=0.025) indicating a positive association between initial dioxin and frightening dreams. The associated relative frequencies of Ranch Hands who experienced frightening dreams for the low, medium, and high initial dioxin categories of the maximal cohort were 1.7, 4.1, and 6.6 percent.

Based upon the minimal assumption, the adjusted analysis detected a significant initial dioxin-by-education interaction (Table 9-14 [c]: p=0.046). After stratifying by education level, a nonsignificant negative association was found between initial dioxin and reports of frightening dreams for Ranch Hands with a high school education (Appendix Table H-1: Adj. RR=0.78, p=0.321). A marginally significant positive association between initial dioxin and frightening dreams was found for Ranch Hands with a college level education (Adj. RR=1.59, p=0.083). The relative frequencies of reported frightening dreams for this stratum of Ranch Hands were 1.5, 4.7, and 9.5 percent. After the deletion of the initial dioxin-by-education interaction, the adjusted minimal analysis showed no significant association between initial dioxin and frightening dreams (Table 9-14 [c]: p=0.486).

In the maximal adjusted analysis, there was a marginally significant positive relationship between initial dioxin and the frequency of Ranch Hands who had experienced frightening dreams (Table 9-14 [d]: Adj. RR=1.27, p=0.072).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

The unadjusted analysis of frightening dreams under the minimal assumption detected a nonsignificant current dioxin-by-time since tour interaction (Table 9-14 [e]: p=0.744) and a nonsignificant association between current dioxin and reports of frightening dreams within each time stratum. Under the maximal assumption, there was also a nonsignificant current dioxin-by-time since tour interaction (Table 9-14 [f]: p=0.379). However, for the time less than or equal to 18.6 years stratum, there was a significant positive association between current dioxin and the frequency of Ranch Hands who reported having frightening dreams (Est. RR=1.56, p=0.011; relative frequencies: low, 1.0%; medium, 4.2%; high, 11.1%).

The adjusted analyses revealed a significant current dioxin-by-time-by-race interaction for both the minimal and maximal cohorts (Table 9-14 [g] and [h]: p=0.004 and p=0.046). Stratified results are presented in Appendix Table H-1. The Black stratum of both the minimal and maximal cohorts contained only two reports of frightening dreams; thus, due to the sparse number of abnormalities, the relative risks, confidence intervals, and p-values are not presented for these strata.

For the non-Black stratum of the minimal analysis, the current dioxin-by-time since tour interaction was not significant (Appendix Table H-1: p=0.630), and the positive association between current dioxin and frightening dreams was also nonsignificant within each time stratum (≤18.6: p=0.694; >18.6: p=0.299). For the non-Black stratum of the maximal analysis, the current dioxin-by-time since tour interaction was also nonsignificant (p=0.723). Within the less than or equal to 18.6 years time stratum, there was a marginally significant positive association between current dioxin and reports of frightening dreams (Adj.

RR=1.41, p=0.071). For Ranch Hands with more than 18.6 years since tour, there was a nonsignificant positive association (p=0.230).

For the maximal adjusted analysis after deletion of the current dioxin-by-time-by-race interaction, the current dioxin-by-time since tour interaction remained nonsignificant (Table 9-14 [h]: p=0.528). For Ranch Hands with 18.6 years or less since tour, there was a significant positive association between current dioxin and the frequency of Ranch Hands who reported frightening dreams (Adj. RR=1.50, p=0.033).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The unadjusted analysis of frightening dreams and categorized current dioxin detected a significant difference among the four current dioxin categories (Table 9-14 [i]: p=0.010). The percentages of participants in the background, unknown, low, and high current dioxin categories who reported having frightening dreams were 3.1, 2.4, 2.6, and 8.2 percent. The contrast of Ranch Hands in the high category and Comparisons in the background category was also significant (Est. RR=2.81, 95% C.I.: [1.44,5.48], p=0.002) with Ranch Hands having a higher risk of frightening dreams than the Comparisons.

The overall contrast of the four current dioxin categories was also significant for the adjusted analysis of frightening dreams (Table 9-14 [j]: p=0.035). Similar to the unadjusted analysis, the percentage of Ranch Hands in the high current dioxin category who had experienced frightening dreams was significantly higher than the corresponding percentage of Comparisons (Adj. RR=2.54, 95% C.I.: [1.28,5.02], p=0.007).

Talking in Sleep

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

In the unadjusted analysis of the frequency of Ranch Hands who reported talking in their sleep, the association with initial dioxin was not significant for either the minimal or maximal assumption (Table 9-15 [a] and [b]: p=0.389 and p=0.112).

Under both the minimal and maximal assumptions, the association between reports of Ranch Hands who talk in their sleep and initial dioxin also was nonsignificant when adjusted for covariate information (Table 9-15 [c] and [d]: p=0.924 and p=0.493, respectively).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

The association between current dioxin and the frequency of Ranch Hands who reported talking in their sleep did not differ significantly between time since tour strata for either the unadjusted minimal or maximal analysis (Table 9-15 [e] and [f]: p=0.728 and p=0.768).

This current dioxin-by-time interaction remained nonsignificant after adjusting for covariate information (Table 9-15 [g] and [h]: p=0.860 and p=0.787, respectively).

TABLE 9-15.

Analysis of Talking in Sleep

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=515)	Low	130	6.2	1.14 (0.85,1.54)	0.389
	Medium	255	4.3		
	High	130	6.9		
b) Maximal (n=733)	Low	182	2.8	1.21 (0.96,1.53)	0.112
	Medium	369	4.6		
	High	182	6.6		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=509)	1.02 (0.74,1.39)	0.924	AGE (p=0.004) DRKYR (p=0.011)
d) Maximal (n=724)	1.09 (0.86,1.38)	0.493	AGE (p=0.001) DRKYR (p=0.014)

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

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 9-15. (Continued)

Analysis of Talking in Sleep

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.728[b]
(n=515)	≤18.6	8.3 (72)	3.9 (128)	9.4 (53)	1.27 (0.82,1.98)	0.286[c]
	>18.6	7.0 (57)	3.1 (129)	5.3 (76)	1.14 (0.74,1.75)	0.550[c]
f) Maximal						0.768[b]
(n=733)	≤18.6	3.8 (105)	4.2 (190)	9.8 (82)	1.31 (0.94,1.83)	0.115[c]
	>18.6	1.3 (78)	4.6 (176)	4.9 (102)	1.22 (0.86,1.71)	0.260[c]

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal			0.860[b]	AGE (p=0.010)
(n=509)	≤18.6	1.09 (0.68,1.74)	0.727[c]	DRKYR (p=0.008)
	>18.6	1.03 (0.66,1.60)	0.904[c]	
h) Maximal			0.787[b]	AGE (p=0.004)
(n=724)	≤18.6	1.16 (0.82,1.63)	0.406[c]	DRKYR (p=0.011)
	>18.6	1.08 (0.76,1.55)	0.662[c]	

[a]Relative risk for a twofold increase in dioxin.
[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).
[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 9-15. (Continued)

Analysis of Talking in Sleep

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	782	3.6	All Categories		0.131
Unknown	341	3.2	Unknown vs. Background	0.90 (0.44,1.82)	0.765
Low	194	2.6	Low vs. Background	0.71 (0.27,1.87)	0.491
High	184	7.1	High vs. Background	2.05 (1.04,4.03)	0.038
Total	1,501				

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	775	All Categories		0.532	AGE (p<0.001)
Unknown	336	Unknown vs. Background	1.03 (0.49,2.15)	0.938	RACE (p=0.140)
Low	190	Low vs. Background	0.67 (0.25,1.78)	0.425	EDUC*DRKYR
High	179	High vs. Background	1.45 (0.72,2.92)	0.303	(p=0.033)
Total	1,480				

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In the unadjusted analysis of talking in sleep, the overall contrast of the four current dioxin categories was not significant (Table 9-15 [i]: p=0.131). However, the percentage of Ranch Hands in the high category who reported talking in their sleep was significantly higher than the percentage of Comparisons in the background category (Est. RR=2.05, 95% C.I.: [1.04,4.03], p=0.038). The percentages of participants who reported talking in their sleep for the background, unknown, low, and high current dioxin categories were 3.6, 3.2, 2.6, and 7.1 percent.

After adjusting for age, race, and an education-by-lifetime alcohol history interaction, the overall contrast remained nonsignificant (Table 9-15 [j]: p=0.532); the high versus background contrast became nonsignificant (p=0.303).

Sleepwalking

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

The unadjusted analysis under both the minimal and the maximal assumptions displayed a nonsignificant association between initial dioxin and sleepwalking (Table 9-16 [a] and [b]: p=0.894 and p=0.462, respectively).

After adjusting for covariate information, the minimal analysis found a significant initial dioxin-by-education interaction (Table 9-16 [c]: p=0.010). To examine this interaction, the Ranch Hands were categorized by their education level. Stratified analyses detected a significant negative association between initial dioxin and sleepwalking for Ranch Hands with a high school education (Appendix Table H-1: Adj. RR=0.38, p=0.049). The relative frequencies of sleepwalking for the low, medium, and high initial dioxin categories were 6.3, 1.8, and 0.0 percent. For Ranch Hands with a college education, there was a nonsignificant positive association between initial dioxin and sleepwalking (Adj. RR=1.57, p=0.190).

The adjusted maximal analysis displayed a nonsignificant association between initial dioxin and sleepwalking (Table 9-16 [d]: p=0.779).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

Neither the unadjusted minimal nor the unadjusted maximal analysis of sleepwalking detected a significant current dioxin-by-time since tour interaction (Table 9-16 [e] and [f]: p=0.166 and p=0.990, respectively). The association between current dioxin and sleepwalking was also nonsignificant within each time stratum.

The adjusted analyses found nonsignificant results consistent with those of the unadjusted analyses (Table 9-16 [g] and [h]: p=0.111 and p=0.941, minimal and maximal, respectively).

TABLE 9-16.

Analysis of Sleepwalking

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=516)	Low	130	4.6	1.03 (0.67,1.59)	0.894
	Medium	256	2.0		
	High	130	2.3		
b) Maximal (n=734)	Low	182	0.6	1.13 (0.82,1.56)	0.452
	Medium	369	3.0		
	High	183	3.3		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=506)	****	****	INIT*EDUC (p=0.010) AGE (p=0.046) DRKYR (p=0.060)
d) Maximal (n=725)	1.05 (0.75,1.48)	0.779	AGE (p=0.065) DRKYR*ALC (p=0.036)

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

****Log_2 (initial dioxin)-by-covariate interaction ($p \leq 0.01$); adjusted relative risk, confidence interval, and p-value not presented.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 9-16. (Continued)

Analysis of Sleepwalking

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.166[b]
(n=516)	≤18.6	6.9 (72)	2.3 (128)	1.9 (54)	0.83 (0.42,1.64)	0.582[c]
	>18.6	1.8 (57)	1.6 (129)	2.6 (76)	1.55 (0.85,2.82)	0.151[c]
f) Maximal						0.990[b]
(n=734)	≤18.6	1.0 (105)	3.2 (190)	3.6 (83)	1.14 (0.70,1.85)	0.592[c]
	>18.6	2.6 (78)	1.1 (176)	3.9 (102)	1.14 (0.72,1.80)	0.581[c]

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal			0.111[b]	AGE (p=0.021)
(n=510)	≤18.6	0.66 (0.31,1.37)	0.260[c]	DRKYR (p=0.046)
	>18.6	1.39 (0.75,2.56)	0.291[c]	
h) Maximal			0.941[b]	AGE (p=0.082)
(n=725)	≤18.6	1.03 (0.63,1.68)	0.915[c]	DRKYR*ALC (p=0.037)
	>18.6	1.05 (0.64,1.73)	0.838[c]	

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

[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).

[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 9-16. (Continued)

Analysis of Sleepwalking

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	783	1.8	All Categories		0.131
Unknown	341	2.1	Unknown vs. Background	1.15 (0.46,2.88)	0.763
Low	194	0.5	Low vs. Background	0.28 (0.04,2.18)	0.226
High	185	3.8	High vs. Background	2.16 (0.86,5.43)	0.102
Total	1,503				

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	776	All Categories		0.416	RACE (p=0.056) AGE*DRKYR (p=0.012) EDUC*DRKYR (p=0.007)
Unknown	336	Unknown vs. Background	1.34 (0.51,3.50)	0.548	
Low	190	Low vs. Background	0.34 (0.04,2.67)	0.308	
High	180	High vs. Background	1.54 (0.52,4.52)	0.436	
Total	1,482				

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In both the unadjusted and the adjusted analyses of sleepwalking, the overall contrast of the four current dioxin categories was not significant (Table 9-16 [i] and [j]: p=0.131 and p=0.416, respectively).

Abnormal Movement/Activity During the Night

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Under both assumptions, the unadjusted analyses investigating the association between the frequency of Ranch Hands who reported abnormal movement/activity during the night and initial dioxin found nonsignificant results (Table 9-17 [a] and [b]: p=0.613 and p=0.126, respectively). After adjusting for covariate information, the association between initial dioxin and the sleep disorder remained nonsignificant for both minimal and maximal cohorts (Table 9-17 [c] and [d]: p=0.718 and p=0.581).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

In the unadjusted analyses of the association of reports of abnormal movement/activity during the night with current dioxin and time since tour, there was a nonsignificant current dioxin-by-time interaction for both the minimal and the maximal cohorts (Table 9-17 [e] and [f]: p=0.706 and p=0.910). The association between current dioxin and the sleep disorder was also nonsignificant within each time stratum.

Consistent with the unadjusted results, the minimal and maximal adjusted analyses also exhibited a nonsignificant current dioxin-by-time interaction (Table 9-17 [g] and [h]: p=0.499 and p=0.793, respectively). Also, the association between abnormal movement/activity during the night and current dioxin was nonsignificant within each time stratum.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In the unadjusted and the adjusted analyses of abnormal movement/activity during the night, there were no significant differences among the percentages of participants who reported abnormal movement/activity during the night of the four current dioxin categories (Table 9-17 [i] and [j]: p=0.118 and p=0.200, respectively).

Sleep Problems Requiring Medication

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Under both the minimal and maximal assumptions, the unadjusted analysis displayed a nonsignificant association between initial dioxin and reports of sleep problems requiring medication (Table 9-18 [a] and [b]: p=0.136 and p=0.193, respectively).

For the minimal cohort, after adjusting for education, age, and lifetime alcohol history, there was a significant negative association between initial dioxin and reports of sleep problems requiring medication (Table 9-18 [c]: Adj. RR=0.47, p=0.023). The unadjusted

TABLE 9-17.

Analysis of Abnormal Movement/Activity During the Night

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=516)	Low	130	3.9	1.09 (0.78,1.52)	0.613
	Medium	256	4.7		
	High	130	4.6		
b) Maximal (n=734)	Low	182	1.7	1.23 (0.95,1.60)	0.126
	Medium	369	3.8		
	High	183	4.9		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=509)	0.99 (0.69,1.42)	0.718	AGE (p=0.079) RACE*EDUC (p=0.002) RACE*ALC (p=0.013)
d) Maximal (n=729)	1.08 (0.82,1.44)	0.581	AGE (p=0.037) EDUC (p=0.033)

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

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 9-17. (Continued)

Analysis of Abnormal Movement/Activity During the Night

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.706[b]
(n=516)	≤18.6	2.8 (72)	6.3 (128)	5.6 (54)	1.19 (0.72,1.95)	0.500[c]
	>18.6	7.0 (57)	2.3 (129)	4.0 (76)	1.04 (0.64,1.69)	0.883[c]
f) Maximal						0.910[b]
(n=734)	≤18.6	2.9 (105)	5.3 (190)	3.6 (83)	1.27 (0.87,1.84)	0.210[c]
	>18.6	0.0 (78)	4.0 (176)	2.9 (102)	1.31 (0.88,1.94)	0.178[c]

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal			0.499[b]	AGE (p=0.087)
(n=509)	≤18.6	1.08 (0.62,1.86)	0.791[c]	RACE*EDUC
	>18.6	0.87 (0.50,1.48)	0.600[c]	(p=0.002)
				RACE*ALC (p=0.012)
h) Maximal			0.793[b]	AGE (p=0.070)
(n=729)	≤18.6	1.07 (0.72,1.60)	0.732[c]	EDUC (p=0.029)
	>18.6	1.16 (0.76,1.76)	0.496[c]	

[a]Relative risk for a twofold increase in dioxin.
[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).
[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 9-17. (Continued)

Analysis of Abnormal Movement/Activity During the Night

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	783	3.3	All Categories		0.118
Unknown	341	1.8	Unknown vs. Background	0.52 (0.21,1.28)	0.155
Low	194	5.7	Low vs. Background	1.75 (0.85,3.61)	0.129
High	185	3.2	High vs. Background	0.98 (0.40,2.41)	0.958
Total	1,503				

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	778	All Categories		0.200	AGE (p=0.0[illegible]) EDUC (p=0.134)
Unknown	339	Unknown vs. Background	0.60 (0.24,1.50)	0.276	
Low	192	Low vs. Background	1.73 (0.83,3.60)	0.143	
High	184	High vs. Background	0.80 (0.32,2.01)	0.635	
Total	1,493				

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 9-18.

Analysis of Sleep Problems Requiring Medication

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=516)	Low	130	3.1	0.63 (0.32,1.22)	0.136
	Medium	256	2.0		
	High	130	0.8		
b) Maximal (n=734)	Low	182	2.8	0.76 (0.49,1.18)	0.193
	Medium	369	2.2		
	High	183	1.1		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=506)	0.47 (0.23,0.97)	0.023	AGE (p=0.005) DRKYR (p=0.082) EDUC (p=0.070)
d) Maximal (n=720)	0.61 (0.38,0.99)	0.032	DRKYR (p=0.075) EDUC*AGE (p=0.050)

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

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 9-18. (Continued)

Analysis of Sleep Problems Requiring Medication

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.655[b]
(n=516)	≤18.6	1.4 (72)	2.3 (128)	0.0 (54)	0.42 (0.10,1.80)	0.244[c]
	>18.6	3.5 (57)	2.3 (129)	1.3 (76)	0.61 (0.26,1.44)	0.261[c]
f) Maximal						0.939[b]
(n=734)	≤18.6	1.0 (105)	2.6 (190)	0.0 (83)	0.72 (0.33,1.56)	0.403[c]
	>18.6	3.9 (78)	2.8 (176)	1.0 (102)	0.69 (0.39,1.24)	0.213[c]

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal			0.681[b]	AGE (p=0.002)
(n=512)	≤18.6	0.26 (0.05,1.26)	0.095[c]	EDUC (p=0.061)
	>18.6	0.38 (0.14,1.04)	0.060[c]	
h) Maximal			0.968[b]	DRKYR (p=0.117)
(n=720)	≤18.6	0.53 (0.23,1.21)	0.132[c]	EDUC*AGE (p=0.048)
	>18.6	0.54 (0.29,1.03)	0.064[c]	

[a]Relative risk for a twofold increase in dioxin.
[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).
[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 9-18. (Continued)

Analysis of Sleep Problems Requiring Medication

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	783	1.5	All Categories		0.368
Unknown	341	2.1	Unknown vs. Background	1.35 (0.53,3.45)	0.535
Low	194	2.6	Low vs. Background	1.70 (0.59,4.88)	0.325
High	185	0.5	High vs. Background	0.35 (0.05,2.70)	0.314
Total	1,503				

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	776	All Categories		0.230	DRKYR (p=0.102) EDUC (p=0.029)
Unknown	336	Unknown vs. Background	1.57 (0.60,4.07)	0.355	
Low	190	Low vs. Background	1.62 (0.56,4.69)	0.376	
High	180	High vs. Background	0.29 (0.04,2.26)	0.237	
Total	1,482				

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

percentages of Ranch Hands who experienced sleep problems that required medication decreased with increasing initial dioxin levels (low, 3.1%; medium, 2.0%; high, 0.8%). Under the maximal assumption, after the adjustment for lifetime alcohol history and an education-by-age interaction, there was also a significant negative relationship between initial dioxin and reports of sleep problems that required medication (Table 9-18 [d]: Adj. RR=0.61, p=0.032). The unadjusted frequencies of Ranch Hands who reported this sleep disorder for the low, medium, and high initial dioxin categories were 2.8, 2.2, and 1.1 percent in the maximal cohort.

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

In the unadjusted analysis of sleep problems requiring medication performed under both minimal and maximal assumptions, the interaction between current dioxin and time since tour was not significant (Table 9-18 [e] and [f]: p=0.655 and p=0.939, respectively), and the association between current dioxin and sleep problems requiring medication was also nonsignificant within each time stratum.

After adjusting for age and education, the minimal analysis of sleep problems requiring medication still displayed a nonsignificant current dioxin-by-time interaction (Table 9-18 [g]: p=0.681). However, both time strata exhibited a marginally significant negative association between current dioxin and the sleep disorder (≤18.6: Adj. RR=0.26, p=0.095; >18.6: Adj. RR=0.38, p=0.060). For Ranch Hands with 18.6 years or less since tour, the unadjusted percentages of reported sleep problems requiring medication for low, medium, and high current dioxin were 1.4, 2.3, and 0.0 percent. The corresponding percentages of Ranch Hands with more than 18.6 years since tour were 3.5, 2.3, and 1.3 percent.

In the maximal analysis of sleep problems requiring medication, the adjustment for lifetime alcohol history and an education-by-age interaction did not change the lack of significance of the current dioxin-by-time since tour interaction (Table 9-18 [h]: p=0.968). Within the time greater than 18.6 years stratum, there was a marginally significant negative association between current dioxin and the frequency of Ranch Hands who experienced sleep problems requiring medication (Adj. RR=0.54, p=0.064). The unadjusted percentages of Ranch Hands who reported this sleep disorder for low, medium, and high current dioxin were 3.9, 2.8, and 1.0 percent.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

Neither the unadjusted nor the adjusted analysis of sleep problems requiring medication detected a significant difference among the four current dioxin categories (Table 9-18 [i] and [j]: p=0.368 and p=0.230, respectively).

Snore Loudly in All Sleeping Positions

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

The unadjusted analysis of the frequency of Ranch Hands who reported that they snore loudly in all sleeping positions showed no significant association with initial dioxin for either the minimal or maximal cohort (Table 9-19 [a] and [b]: p=0.629 and p=0.290).

TABLE 9-19.

Analysis of Snore Loudly in All Sleeping Positions

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I)[a]	p-Value
a) Minimal (n=516)	Low	130	9.2	0.94 (0.73,1.21)	0.629
	Medium	256	9.8		
	High	130	8.5		
b) Maximal (n=734)	Low	182	5.5	1.11 (0.92,1.34)	0.290
	Medium	369	8.7		
	High	183	8.7		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=509)	0.95 (0.72,1.24)**	0.694**	INIT*AGE (p=0.030) EDUC*ALC (p=0.002)
d) Maximal (n=720)	1.16 (0.94,1.42)	0.170	EDUC*DRKYR (p=0.040) EDUC*ALC (p=0.005)

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

**Log_2 (initial dioxin)-by-covariate interaction ($0.01<p\leq0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 9-19. (Continued)

Analysis of Snore Loudly in All Sleeping Positions

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal (n=516)						0.665[b]
	≤18.6	6.9 (72)	8.6 (128)	3.7 (54)	0.96 (0.61,1.52)	0.866[c]
	>18.6	14.0 (57)	10.1 (129)	11.8 (76)	0.85 (0.61,1.17)	0.320[c]
f) Maximal (n=734)						0.891[b]
	≤18.6	3.8 (105)	7.4 (190)	7.2 (83)	1.10 (0.80,1.52)	0.557[c]
	>18.6	3.9 (78)	11.9 (176)	9.8 (102)	1.07 (0.84,1.36)	0.575[c]

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal (n=509)			0.692[b]	EDUC*ALC (p=0.004)
	≤18.6	0.99 (0.61,1.59)	0.960[c]	
	>18.6	0.88 (0.63,1.22)	0.443[c]	
h) Maximal (n=720)			0.653[b]	EDUC*ALC (p=0.005)
	≤18.6	1.20 (0.84,1.71)	0.309[c]	EDUC*DRKYR (p=0.037)
	>18.6	1.09 (0.84,1.40)	0.511[c]	

[a]Relative risk for a twofold increase in dioxin.
[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).
[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 9-19. (Continued)

Analysis of Snore Loudly in All Sleeping Positions

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	783	6.9	All Categories		0.114
Unknown	341	4.7	Unknown vs. Background	0.66 (0.37,1.18)	0.162
Low	194	9.8	Low vs. Background	1.47 (0.85,2.54)	0.172
High	185	8.7	High vs. Background	1.28 (0.71,2.29)	0.409
Total	1,503				

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	776	All Categories		0.049	EDUC*DRKYR ($p<0.001$)
Unknown	336	Unknown vs. Background	0.54 (0.29,1.00)	0.050	
Low	190	Low vs. Background	1.34 (0.76,2.39)	0.316	
High	180	High vs. Background	1.34 (0.74,2.44)	0.330	
Total	1,482				

Note: Background (Comparisons): Current Dioxin ≤ 10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤ 10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤ 33.3 ppt.
High (Ranch Hands): Current Dioxin > 33.3 ppt.

Based on the minimal assumption, the adjusted analysis of snoring loudly in all sleeping positions displayed a significant initial dioxin-by-age interaction (Table 9-19 [c]: p=0.030). This interaction was investigated by dichotomizing the age of the Ranch Hands (Appendix Table H-1). The stratified analyses found a slight negative association between the sleep disorder and initial dioxin for Ranch Hands born in or after 1942 (Adj. RR=0.72) and a slight positive association for those born before 1942 (Adj. RR=1.30); however, these associations were not statistically significant (p=0.106 and p=0.165, respectively). After deleting the interaction from the model, the relationship between initial dioxin and those who snore loudly in all sleeping positions was nonsignificant (Table 9-19 [c]: p=0.694).

A nonsignificant association was found between initial dioxin and those who snore loudly in all sleeping positions for the adjusted analysis of the maximal cohort (Table 9-19 [d]: p=0.170).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

The unadjusted and adjusted current dioxin and time since tour analyses of Ranch Hands who reported snoring loudly in all sleeping positions detected a nonsignificant current dioxin-by-time since tour interaction for both the minimal and maximal cohorts (Table 9-19 [e-h]: p>0.30 for all interaction and time stratum-specific analyses).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In the unadjusted analysis of the frequency of Ranch Hands and Comparisons who reported snoring loudly in all sleeping positions, the contrast of the four current dioxin categories was not significant (Table 9-19 [i]: p=0.114). However, after adjusting for an education-by-lifetime alcohol history interaction, the simultaneous contrast of the four current dioxin categories was significant (Table 9-19 [j]: p=0.049). Specifically, the contrast of Ranch Hands in the unknown category and Comparisons in the background category was significant (Est. RR=0.54, 95% C.I.: [0.29,1.00], p=0.050) with the Ranch Hands having a lower percentage of reports of snoring loudly in all sleeping positions than the Comparisons. The unadjusted relative frequencies of this sleep disorder for the background, unknown, low, and high current dioxin categories were 6.9, 4.7, 9 8, and 8.7 percent.

Insomnia

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

The analysis of the frequency of Ranch Hands who reported having insomnia did not exhibit a significant association with initial dioxin for either the unadjusted minimal or maximal analysis (Table 9-20 [a] and [b]: p=0.338 and p=0.694).

These nonsignificant findings did not change after adjusting for education and lifetime alcohol history (Table 9-20 [c] and [d]: p=0.154 and p=0.253, respectively).

TABLE 9-20.

Analysis of Insomnia

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I)[a]	p-Value
a) Minimal (n=516)	Low	130	30.0	0.92 (0.77,1.09)	0.338
	Medium	256	22.3		
	High	130	20.0		
b) Maximal (n=734)	Low	182	24.7	0.98 (0.86,1.11)	0.694
	Medium	369	24.4		
	High	183	19.7		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=506)	0.88 (0.74,1.05)	0.154	DRKYR (p=0.042) EDUC (p=0.046)
d) Maximal (n=720)	0.93 (0.81,1.06)	0.253	DRKYR (p=0.144) EDUC (p=0.022)

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

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 9-20. (Continued)

Analysis of Insomnia

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.402[b]
(n=516)	≤18.6	25.0 (72)	26.6 (128)	25.9 (54)	1.02 (0.78,1.33)	0.883[c]
	>18.6	29.8 (57)	19.4 (129)	18.4 (76)	0.87 (0.68,1.12)	0.283[c]
f) Maximal						0.077[b]
(n=734)	≤18.6	20.0 (105)	24.7 (190)	27.7 (83)	1.11 (0.92,1.34)	0.283[c]
	>18.6	25.6 (78)	25.0 (176)	15.7 (102)	0.88 (0.73,1.05)	0.156[c]

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal			0.347[b]	DRKYR (p=0.031)
(n=506)	≤18.6	1.00 (0.76,1.30)	0.978[c]	EDUC (p=0.054)
	>18.6	0.84 (0.65,1.08)	0.165[c]	
h) Maximal			0.058[b]	DRKYR (p=0.132)
(n=720)	≤18.6	1.07 (0.88,1.30)	0.502[c]	EDUC (p=0.028)
	>18.6	0.83 (0.68,1.00)	0.051[c]	

[a]Relative risk for a twofold increase in dioxin.
[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).
[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 9-20. (Continued)

Analysis of Insomnia

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	783	23.8	All Categories		0.810
Unknown	341	21.7	Unknown vs. Background	0.89 (0.66,1.21)	0.453
Low	194	23.2	Low vs. Background	0.97 (0.67,1.41)	0.870
High	185	21.1	High vs. Background	0.86 (0.58,1.27)	0.439
Total	1,503				

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	776	All Categories		0.847	DRKYR (p<0.001) EDUC*AGE (p=0.015)
Unknown	336	Unknown vs. Background	0.92 (0.67,1.25)	0.581	
Low	190	Low vs. Background	0.99 (0.68,1.44)	0.944	
High	180	High vs. Background	0.85 (0.57,1.28)	0.435	
Total	1,482				

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

In the unadjusted minimal analysis of insomnia, the current dioxin-by-time since tour interaction was not significant (Table 9-20 [e]: p=0.402) and neither was the association between current dioxin and insomnia within each time stratum. Under the maximal assumption, the unadjusted analysis detected a marginally significant current dioxin-by-time interaction (Table 9-20 [f]: p=0.077). However, for Ranch Hands with 18.6 years or less since tour, there was a nonsignificant positive association between current dioxin and reports of insomnia (Est. RR=1.11, p=0.283), and for Ranch Hands with greater than 18.6 years since tour, there was a nonsignificant negative association (Est. RR=0.88, p=0.156).

After adjusting for education and lifetime alcohol history, the minimal analysis of insomnia remained nonsignificant (Table 9-20 [g]: p=0.347). In the maximal adjusted analysis of insomnia, the current dioxin-by-time interaction was again marginally significant (Table 9-20 [h]: p=0.058). Within the less than or equal to 18.6 years time stratum, there was a nonsignificant positive association between current dioxin and insomnia (Adj. RR=1.07, p=0.502) and a marginally significant negative association between current dioxin and insomnia for the time greater than 18.6 years stratum (Adj. RR=0.83, p=0.051). For Ranch Hands with more than 18.6 years since tour, the percentages of reported insomniacs were about the same for the low and medium current dioxin categories (25.6% and 25.0%) but the percentage was much lower for the high current dioxin category (15.7%).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In both the unadjusted and the adjusted analysis of insomnia, the overall contrast of the four current dioxin categories was not significant (Table 9-20 [i] and [j]: p=0.810 and p=0.847, respectively).

Overall Sleep Disorder Index

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Based on the unadjusted analysis of the overall sleep disorder index, a composite variable of the 12 individual sleep disorders, no significant association with initial dioxin was detected for either the minimal or the maximal cohort (Table 9-21 [a] and [b]: p=0.476 and p=0.662).

In the adjusted analysis of the overall sleep disorder index, there was still no significant relationship with initial dioxin under either assumption (Table 9-21 [c] and [d]: p=0.178 and p=0.528, respectively).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

Under both the minimal and the maximal assumptions, the unadjusted analysis of the overall sleep disorder index exhibited a nonsignificant current dioxin-by-time since tour interaction (Table 9-21 [e] and [f]: p=0.336 and p=0.160, respectively). The association between the overall sleep disorder index and current dioxin was also nonsignificant within each time stratum under both assumptions.

TABLE 9-21.

Analysis of Overall Sleep Disorder Index

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=514)	Low	130	41.5	0.95 (0.82,1.10)	0.476
	Medium	255	37.3		
	High	129	33.3		
b) Maximal (n=732)	Low	182	35.2	1.03 (0.92,1.14)	0.662
	Medium	369	36.0		
	High	181	35.9		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=504)	0.90 (0.76,1.05)	0.178	AGE (p=0.096) ALC (p=0.140) DRKYR (p=0.098) EDUC (p=0.014)
d) Maximal (n=718)	0.96 (0.85,1.08)	0.528	AGE (p=0.050) ALC (p=0.106) DRKYR (p=0.115) EDUC (p=0.011)

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

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 9-21. (Continued)

Analysis of Overall Sleep Disorder Index

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.336[b]
(n=514)	≤18.6	40.3 (72)	38.3 (128)	36.5 (52)	1.05 (0.82,1.33)	0.717[c]
	>18.6	43.9 (57)	35.7 (129)	31.6 (76)	0.90 (0.73,1.10)	0.290[c]
f) Maximal						0.160[b]
(n=732)	≤18.6	30.5 (105)	35.8 (190)	43.2 (81)	1.13 (0.95,1.34)	0.162[c]
	>18.6	32.1 (78)	39.8 (176)	31.4 (102)	0.96 (0.82,1.12)	0.586[c]

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal			0.274[b]	AGE (p=0.105)
(n=504)	≤18.6	0.99 (0.77,1.28)	0.950[c]	ALC (p=0.142)
	>18.6	0.83 (0.67,1.03)	0.091[c]	DRKYR (p=0.109)
				EDUC (p=0.013)
h) Maximal			0.147[b]	AGE (p=0.047)
(n=718)	≤18.6	1.05 (0.88,1.26)	0.562[c]	ALC (p=0.121)
	>18.6	0.89 (0.75,1.04)	0.150[c]	DRKYR (p=0.127)
				EDUC (p=0.013)

[a]Relative risk for a twofold increase in dioxin.
[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).
[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 9-21. (Continued)

Analysis of Overall Sleep Disorder Index

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	780	33.9	All Categories		0.522
Unknown	341	30.5	Unknown vs. Background	0.86 (0.65,1.13)	0.272
Low	194	34.0	Low vs. Background	1.01 (0.72,1.40)	0.963
High	183	36.6	High vs. Background	1.13 (0.81,1.58)	0.478
Total	1,498				

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	773	All Categories		0.751	DRKYR (p<0.001) EDUC*AGE (p=0.017)
Unknown	336	Unknown vs. Background	0.89 (0.67,1.17)	0.394	
Low	190	Low vs. Background	0.99 (0.71,1.39)	0.958	
High	178	High vs. Background	1.09 (0.77,1.55)	0.620	
Total	1,477				

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

After adjusting for education, age, lifetime alcohol history, and current alcohol use, the minimal analysis of the overall sleep disorder index displayed a nonsignificant interaction between current dioxin and time since tour (Table 9-21 [g]: p=0.274). However, there was a marginally significant negative association between current dioxin and the overall sleep disorder index for those Ranch Hands in the time greater than 18.6 years stratum (Adj. RR=0.83, p=0.091). The unadjusted frequencies of the overall sleep disorder index for low, medium, and high current dioxin were 43.9, 35.7, and 31.6 percent for this time stratum.

In the maximal adjusted analysis of the overall sleep disorder index, the current dioxin-by-time since tour interaction was not significant (Table 9-21 [h]: p=0.147).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

Neither the unadjusted nor the adjusted analysis detected a significant difference among the four current dioxin categories in the frequency of participants who reported at least one sleep disorder (Table 9-21 [i] and [j]: p=0.522 and p=0.751, respectively).

Average Sleep Each Night

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

In both the unadjusted and adjusted analyses under the minimal and maximal assumptions, the association between initial dioxin and the average sleep each night of the Ranch Hands was nonsignificant (Table 9-22 [a-d]: p≥0.25 for each analysis).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

The unadjusted analyses of average sleep each night for both the minimal and maximal cohorts displayed a nonsignificant interaction between current dioxin and time since tour (Table 9-22 [e] and [f]: p=0.758 and p=0.444, respectively).

For the adjusted analyses, a significant current dioxin-by-time-by-race interaction was found under both the minimal and maximal assumptions (Table 9-22 [g] and [h]: p=0.006 and p=0.049). To examine this interaction, associations between average sleep each night and current dioxin were investigated separately for each time and race stratum (Appendix Table H-1).

For the Black stratum under the minimal assumption, there was a significant current dioxin-by-time since tour interaction (Appendix Table H-1: p=0.006). The time less than or equal to 18.6 years stratum displayed a marginally significant positive association between average sleep each night and current dioxin (p=0.056), and a significant negative association was found for the time over 18.6 years stratum (p=0.032). The adjusted mean average hours of sleep each night for Black Ranch Hands with time less than or equal to 18.6 years since tour for low and medium current dioxin were 5.90 and 6.92, with no participants in the high category. The corresponding adjusted means for Black Ranch Hands with more than 18.6 years since tour were 6.59, 5.98, and 6.03 hours, respectively. The non-Black stratum exhibited a nonsignificant current dioxin-by-time interaction (p=0.968), and each time

TABLE 9-22.

Analysis of Average Sleep Each Night (Hours)

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Mean	Slope (Std. Error)	p-Value
a) Minimal	Low	130	6.84	-0.025 (0.041)	0.544
(n=516)	Medium	256	6.91		
(R^2=0.001)	High	130	6.79		
b) Maximal	Low	182	6.95	-0.033 (0.029)	0.250
(n=734)	Medium	369	6.91		
(R^2=0.002)	High	183	6.79		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Initial Dioxin	n	Adj. Mean	Adj. Slope (Std. Error)	p-Value	Covariate Remarks
c) Minimal	Low	129	6.53	-0.006 (0.042)	0.890	AGE (p=0.008)
(n=512)	Medium	254	6.53			RACE (p=0.002)
(R^2=0.037)	High	129	6.53			
d) Maximal	Low	181	6.65	-0.018 (0.029)	0.535	AGE (p=0.017)
(n=729)	Medium	366	6.63			RACE (p<0.001)
(R^2=0.028)	High	182	6.55			

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 9-22. (Continued)

Analysis of Average Sleep Each Night (Hours)

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Mean/(n) Current Dioxin Low	Medium	High	Slope (Std. Error)	p-Value
e) Minimal						0.758[b]
(n=516)	≤18.6	6.90	6.75	6.72	-0.031 (0.067)	0.644[c]
(R^2=0.007)		(72)	(128)	(54)		
	>18.6	7.05	6.97	6.80	-0.058 (0.055)	0.295[c]
		(57)	(129)	(76)		
f) Maximal						0.444[b]
(n=734)	≤18.6	7.01	6.83	6.70	-0.069 (0.044)	0.118[c]
(R^2=0.005)		(105)	(190)	(83)		
	>18.6	6.88	7.00	6.83	-0.024 (0.039)	0.544[c]
		(78)	(176)	(102)		

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Mean/(n) Current Dioxin Low	Medium	High	Adj. Slope (Std. Error)	p-Value	Covariate Remarks
g) Minimal						****	CURR*TIME*RACE
(n=516)	≤18.6	****	****	****	****	****	(p=0.006)
(R^2=0.056)		(72)	(128)	(54)			AGE (p=0.032)
	>18.6	****	****	****	****	****	
		(57)	(129)	(76)			
h) Maximal						0.400**[b]	CURR*TIME*RACE
(n=734)	≤18.6	6.71**	6.55**	6.44**	-0.056 (0.045)**	0.212**[c]	(p=0.049)
(R^2=0.038)		(105)	(190)	(83)			AGE (p=0.044)
	>18.6	6.54**	6.70**	6.57**	-0.007 (0.040)**	0.869**[c]	
		(78)	(176)	(102)			

[a]Slope and standard error based on average sleep each night versus log_2 dioxin.

[b]Test of significance for homogeneity of slopes (current dioxin continuous, time categorized).

[c]Test of significance for slope equal to 0 (current dioxin continuous, time categorized).

**Log_2 (current dioxin)-by-covariate interaction ($0.01<p\leq0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of this interaction.

****Log_2 (current dioxin)-by-time-by-covariate interaction ($p\leq0.01$); adjusted mean, adjusted slope, standard error, and p-value not presented.

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 9-22. (Continued)

Analysis of Average Sleep Each Night (Hours)

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Mean	Contrast	Difference of Means (95% C.I.)	p-Value
Background	783	6.89	All Categories		0.403
Unknown	341	6.92	Unknown vs. Background	0.03 (-0.10,0.16)	0.638
Low	194	6.91	Low vs. Background	0.02 (-0.14,0.18)	0.809
High	185	6.77	High vs. Background	-0.12 (-0.28,0.04)	0.149
Total	1,503		(R^2=0.002)		

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Adj. Mean	Contrast	Difference of Adj. Means (95% C.I.)	p-Value	Covariate Remarks
Background	778	6.61	All Categories		0.725	AGE (p=0.030)
Unknown	339	6.61	Unknown vs. Background	0.00 (-0.13,0.12)	0.947	RACE (p<0.001) EDUC (p=0.012)
Low	192	6.66	Low vs. Background	0.05 (-0.11,0.21)	0.539	
High	184	6.54	High vs. Background	-0.07 (-0.23,0.10)	0.410	
Total	1,493		(R^2=0.030)			

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

stratum exhibited a nonsignificant negative association between current dioxin and average sleep each night.

In the maximal analysis of the current dioxin-by-time-by-race interaction, there was a marginally significant interaction between current dioxin and time since tour for the Black stratum (Appendix Table H-1: p=0.068). For the time less than or equal to 18.6 years stratum, there was a nonsignificant positive relationship between current dioxin and average sleep each night (p=0.353), and for the over 18.6 years time stratum, there was a marginally significant negative slope (p=0.070). The adjusted mean average hours of sleep each night for Black Ranch Hands with more than 18.6 years since tour for low, medium, and high current dioxin were 6.00, 6.55, and 5.19. For the non-Black stratum, the current dioxin-by-time since tour interaction was not significant (p=0.261). The time less than or equal to 18.6 years stratum displayed a nonsignificant negative association between current dioxin and average sleep each night (p=0.179), and the time over 18.6 years stratum showed a nonsignificant positive association (p=0.884).

After removal of the current dioxin-by-time-by-race interaction and adjusting for age and race, the maximal analysis exhibited no significant results (Table 9-22 [h]: p>0.20 for all results).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In both the unadjusted and the adjusted analyses of average sleep each night, the simultaneous contrast of the four current dioxin categories was not significant (Table 9-22 [i] and [j]: p=0.403 and p=0.725, respectively).

Physical Examination Variables

Anxiety—SCL-90-R

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Based upon the minimal assumption, the unadjusted analysis detected a nonsignificant association between initial dioxin and the SCL-90-R anxiety variable (Table 9-23 [a]: p=0.149). The maximal unadjusted analysis exhibited a significant positive association (Table 9-23 [b]: Est. RR=1.27, p=0.022) with prevalence rates of abnormal anxiety T-scores for low, medium, and high levels of initial dioxin of 5.1, 5.8, and 12.1 percent.

After adjusting for covariate information, the minimal analysis of the SCL-90-R anxiety variable remained nonsignificant (Table 9-23 [c]: p=0.217). The association between initial dioxin and anxiety under the maximal assumption, however, was nonsignificant after being adjusted for education and a race-by-current alcohol use interaction (Table 9-23 [d]: p=0.122).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

Under the minimal assumption, the unadjusted analysis of the SCL-90-R anxiety variable detected a nonsignificant current dioxin-by-time since tour interaction (Table 9-23

TABLE 9-23.

Analysis of Anxiety (SCL-90-R)

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=464)	Low	116	6.0	1.21 (0.94,1.56)	0.149
	Medium	229	8.7		
	High	119	10.1		
b) Maximal (n=652)	Low	158	5.1	1.27 (1.04,1.55)	0.022
	Medium	328	5.8		
	High	166	12.1		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=459)	1.19 (0.91,1.55)	0.217	RACE*ALC (p=0.002) AGE*DRKYR (p=0.004)
d) Maximal (n=644)	1.18 (0.96,1.46)	0.122	EDUC (p=0.105) RACE*ALC (p=0.006)

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

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 9-23. (Continued)

Analysis of Anxiety
(SCL-90-R)

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.183[b]
(n=464)	≤18.6	7.7 (65)	8.9 (113)	12.5 (48)	1.01 (0.66,1.54)	0.959[c]
	>18.6	3.8 (53)	6.1 (114)	12.7 (71)	1.45 (1.03,2.05)	0.031[c]
f) Maximal						0.868[b]
(n=652)	≤18.6	3.3 (92)	8.2 (171)	9.7 (72)	1.26 (0.92,1.72)	0.153[c]
	>18.6	6.4 (63)	5.0 (159)	11.6 (95)	1.30 (0.99,1.71)	0.057[c]

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal			0.099[b]	RACE*ALC (p=0.001)
(n=459)	≤18.6	0.95 (0.61,1.49)	0.827[c]	AGE*DRKYR
	>18.6	1.51 (1.05,2.19)	0.028[c]	(p=0.006)
h) Maximal			0.851[b]	EDUC (p=0.108)
(n=644)	≤18.6	1.17 (0.85,1.62)	0.335[c]	RACE*ALC (p=0.005)
	>18.6	1.22 (0.92,1.63)	0.172[c]	

[a]Relative risk for a twofold increase in dioxin.
[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).
[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 9-23. (Continued)

Analysis of Anxiety (SCL-90-R)

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	690	5.4	All Categories		0.043
Unknown	294	4.4	Unknown vs. Background	0.82 (0.43,1.56)	0.539
Low	171	7.6	Low vs. Background	1.45 (0.75,2.80)	0.265
High	167	10.8	High vs. Background	2.13 (1.18,3.85)	0.012
Total	1,322				

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	685	All Categories		0.320	AGE (p=0.103) ALC (p=0.003)
Unknown	291	Unknown vs. Background	0.90 (0.46,1.73)	0.746	EDUC (p=0.007)
Low	167	Low vs. Background	1.43 (0.73,2.77)	0.295	
High	166	High vs. Background	1.64 (0.88,3.05)	0.119	
Total	1,309				

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

[e]: p=0.183). For the time greater than 18.6 years stratum, there was a significant positive association between current dioxin and anxiety (Est. RR=1.45, p=0.031). Within this stratum, the frequency of Ranch Hands with an abnormal anxiety T-score increased with increasing current dioxin (low, 3.8%; medium, 6.1%; high, 12.7%). The maximal cohort displayed similar results with a nonsignificant current dioxin-by-time interaction (Table 9-23 [f]: p=0.868) and a marginally significant positive association between current dioxin and anxiety within the time greater than 18.6 years stratum (Est. RR=1.30, p=0.057). For this time stratum, the percentages of Ranch Hands with abnormal anxiety T-scores for low, medium, and high current dioxin were 6.4, 5.0, and 11.6 percent.

After adjusting for two covariate interactions, race-by-current alcohol use and age-by-lifetime alcohol history, the minimal analysis of the SCL-90-R anxiety variable displayed a marginally significant current dioxin-by-time since tour interaction (Table 9-23 [g]: p=0.099). Within the less than or equal to 18.6 years time stratum, there was a nonsignificant negative association between current dioxin and anxiety (Adj. RR=0.95, p=0.827), but for the over 18.6 years time stratum the positive association was significant (Adj. RR=1.51, p=0.028).

In the maximal analysis of the SCL-90-R anxiety variable, the adjustment for education and a race-by-current alcohol use interaction did not alter the lack of significance of the current dioxin-by-time interaction (Table 9-23 [h]: p=0.851), but it did cause the association between current dioxin and anxiety for the time greater than 18.6 years stratum to become nonsignificant (p=0.172).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The unadjusted analysis of the SCL-90-R anxiety variable with categorized current dioxin displayed a significant overall difference among the four current dioxin categories (Table 9-23 [i]: p=0.043). The unadjusted frequencies of abnormal anxiety T-scores for the background, unknown, low, and high current dioxin categories were 5.4, 4.4, 7.6, and 10.8 percent. The only significant contrast was the high category versus the background category (Est. RR=2.13, 95% C.I.: [1.18,3.85], p=0.012) indicating that the percent of abnormal anxiety T-scores was significantly higher for the Ranch Hands in the high group than for the Comparisons in the background group.

After adjusting for education, age, and current alcohol use, the overall analysis of the SCL-90-R anxiety variable with categorized current dioxin was nonsignificant (Table 9-23 [j]: p=0.320); the high versus background contrast became nonsignificant (p=0.119).

Depression—SCL-90-R

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

The unadjusted minimal analysis of the SCL-90-R depression variable detected a marginally significant positive association between initial dioxin and depression (Table 9-24 [a]: Est. RR=1.24, p=0.075). The prevalence rates of Ranch Hands with abnormal depression T-scores increased steadily with increasing levels of initial dioxin (low, 8.6%; medium, 9.2%; high, 12.6%). Based on the maximal assumption, the unadjusted analysis

TABLE 9-24.

Analysis of Depression (SCL-90-R)

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=464)	Low	116	8.6	1.24 (0.98,1.57)	0.075
	Medium	229	9.2		
	High	119	12.6		
b) Maximal (n=652)	Low	158	7.6	1.23 (1.02,1.48)	0.029
	Medium	328	7.0		
	High	166	13.9		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=455)	1.11 (0.86,1.42)	0.438	EDUC (p=0.070) AGE*DRKYR (p=0.003)
d) Maximal (n=640)	1.09 (0.89,1.33)	0.393	AGE (p=0.133) DRKYR (p=0.110) EDUC (p=0.005)

[a]Relative risk for a twofold increase in dioxin.
Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 9-24. (Continued)

Analysis of Depression
(SCL-90-R)

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.222[b]
(n=464)	≤18.6	10.8 (65)	9.7 (113)	14.6 (48)	1.09 (0.74,1.59)	0.668[c]
	>18.6	5.7 (53)	7.0 (114)	14.1 (71)	1.48 (1.07,2.04)	0.017[c]
f) Maximal						0.961[b]
(n=652)	≤18.6	5.4 (92)	9.4 (171)	12.5 (72)	1.27 (0.95,1.69)	0.101[c]
	>18.6	11.1 (63)	5.0 (159)	13.7 (95)	1.26 (0.98,1.62)	0.075[c]

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal			0.284[b]	EDUC (p=0.071)
(n=455)	≤18.6	0.98 (0.65,1.47)	0.918[c]	AGE*DRKYR (p=0.004)
	>18.6	1.30 (0.92,1.85)	0.137[c]	
h) Maximal			0.916[b]	EDUC (p=0.003)
(n=648)	≤18.6	1.17 (0.86,1.57)	0.315[c]	
	>18.6	1.14 (0.87,1.49)	0.333[c]	

[a]Relative risk for a twofold increase in dioxin.
[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).
[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 9-24. (Continued)

Analysis of Depression (SCL-90-R)

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	690	7.3	All Categories		0.081
Unknown	294	6.5	Unknown vs. Background	0.88 (0.51,1.53)	0.660
Low	171	7.6	Low vs. Background	1.05 (0.56,1.99)	0.873
High	167	13.2	High vs. Background	1.94 (1.14,3.31)	0.015
Total	1,322				

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	685	All Categories		0.286	ALC (p=0.021) RACE*EDUC (p=0.029)
Unknown	291	Unknown vs. Background	0.92 (0.53,1.61)	0.780	RACE*AGE (p=0.009)
Low	167	Low vs. Background	1.10 (0.58,2.10)	0.765	
High	166	High vs. Background	1.70 (0.97,2.98)	0.064	
Total	1,309				

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

displayed a significant positive relationship between initial dioxin and depression (Table 9-24 [b]: Est. RR=1.23, p=0.029). The percentages of Ranch Hands with abnormal depression T-scores were nearly the same for Ranch Hands in the low and medium initial dioxin categories, but the percentage was larger for the high initial dioxin category (low, 7.6%; medium, 7.0%; and high, 13.9%).

After adjusting the minimal analysis for education and an age-by-lifetime alcohol history interaction, the association between initial dioxin and depression was nonsignificant (Table 9-24 [c]: p=0.438). Similarly, after adjusting the maximal analysis for age, lifetime alcohol history, and education, the relationship between initial dioxin and depression was also nonsignificant (Table 9-24 [d]: p=0.393).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

Under both minimal and maximal assumptions, the unadjusted analysis of the SCL-90-R depression variable did not detect a significant current dioxin-by-time since tour interaction (Table 9-24 [e] and [f]: p=0.222 and p=0.961, respectively). For the minimal cohort, there was a significant positive association between current dioxin and depression for Ranch Hands in the over 18.6 years time stratum (Table 9-24 [e]: Est. RR=1.48, p=0.017). Similarly, the maximal analysis detected a marginally significant positive association between current dioxin and depression for Ranch Hands with more than 18.6 years since tour (Table 9-24 [f]: Est. RR=1.26, p=0.075).

After adjusting the minimal cohort for education and an age-by-lifetime alcohol history interaction and adjusting the maximal cohort for education alone, the analyses were nonsignificant (Table 9-24 [g] and [h]: p>0.10 for all analyses).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In the unadjusted analysis of the SCL-90-R depression variable the simultaneous contrast of the four current dioxin categories was marginally significant (Table 9-24 [i]: p=0.081). For the background, unknown, low, and high current dioxin categories, the percentages of abnormal depression T-scores were 7.3, 6.5, 7.6, and 13.2 percent. The only significant difference detected was between Ranch Hands in the high category and the Comparisons in the background category (Table 9-24 [i]: Est. RR=1.94, 95% C.I.: [1.14,3.31], p=0.015).

The adjustment for current alcohol use, a race-by-education interaction, and a race-by-age interaction, removed the marginal significance of the overall test for differences in the percentage of abnormal depression T-scores among the four current dioxin categories (Table 9-24 [j]: p=0.286). The contrast between Ranch Hands in the high category and the Comparisons in the background category was marginally significant after the covariate adjustment (Table 9-24 [j]: Est. RR=1.70, 95% C.I.: [0.97,2.98], p=0.064).

Hostility—SCL-90-R

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

The unadjusted analysis of the SCL-90-R hostility variable did not detect a significant association with initial dioxin for either the minimal or maximal cohort (Table 9-25 [a] and [b]: p=0.555 and p=0.140).

These nonsignificant results did not change after adjusting for a race-by-current alcohol use interaction and an education-by-age interaction (Table 9-25 [c] and [d]: p=0.757 and p=0.773, respectively).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

The tests for homogeneity of relative risks and the tests for relative risk equal to one within each time stratum were not significant for either the unadjusted or adjusted minimal and maximal analyses of the SCL-90-R hostility variable (Table 9-25 [e-h]: p>0.15 for each analysis).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In the analysis of the SCL-90-R hostility variable, the overall contrast of the four current dioxin categories was not significant for either the unadjusted or adjusted analysis (Table 9-25 [i] and [j]: p=0.602 and p=0.849).

Interpersonal Sensitivity—SCL-90-R

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

The unadjusted analysis of the minimal cohort did not detect a significant association between initial dioxin and the SCL-90-R interpersonal sensitivity variable (Table 9-26 [a]: p=0.220). The same association was marginally significant under the maximal assumption in the unadjusted analysis (Table 9-26 [b]: Est. RR=1.22, p=0.084), with increasing prevalence rates of abnormal interpersonal sensitivity scores for initial dioxin levels (low, 3.8%; medium, 5.2%; high, 9.0%).

The minimal adjusted analysis exhibited a significant initial dioxin-by-education interaction (Table 9-26 [c]: p=0.040). To investigate this interaction, the analyses were stratified by education level (Appendix Table H-1). For Ranch Hands with a high school education, there was a nonsignificant positive association between initial dioxin and interpersonal sensitivity (Adj. RR=1.32, p=0.124), and for Ranch Hands with a college education, there was a nonsignificant negative association (Adj. RR=0.45, p=0.192). After deletion of the interaction, the relationship between initial dioxin and interpersonal sensitivity was nonsignificant (Table 9-26 [c]: p=0.435). The adjusted maximal analysis displayed a similar nonsignificant association (Table 9-26 [d]: p=0.458) after adjustment for education and lifetime alcohol history.

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

Under the minimal assumption, the unadjusted analysis found that the association between current dioxin and interpersonal sensitivity did not differ significantly between time

TABLE 9-25.

Analysis of Hostility (SCL-90-R)

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=464)	Low	116	4.3	1.10 (0.80,1.52)	0.555
	Medium	229	5.7		
	High	119	5.9		
b) Maximal (n=652)	Low	158	3.2	1.21 (0.95,1.55)	0.140
	Medium	328	4.3		
	High	166	6.6		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=458)	0.95 (0.65,1.38)	0.757	RACE*ALC (p=0.015) EDUC*AGE (p=0.006)
d) Maximal (n=644)	1.04 (0.78,1.37)	0.773	RACE*ALC (p=0.009) EDUC*AGE (p=0.047)

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

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 9-25. (Continued)

Analysis of Hostility (SCL-90-R)

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.988[b]
(n=464)	≤18.6	4.6 (65)	4.4 (113)	8.3 (48)	1.12 (0.66,1.89)	0.685[c]
	>18.6	5.8 (53)	6.1 (114)	5.6 (71)	1.11 (0.73,1.69)	0.630[c]
f) Maximal						0.543[b]
(n=652)	≤18.6	2.2 (92)	4.1 (171)	6.9 (72)	1.33 (0.90,1.98)	0.152[c]
	>18.6	3.2 (63)	5.7 (159)	5.3 (95)	1.14 (0.82,1.58)	0.450[c]

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal			0.803[b]	RACE*ALC (p=0.015)
(n=458)	≤18.6	0.89 (0.50,1.60)	0.700[c]	EDUC*AGE (p=0.006)
	>18.6	0.97 (0.58,1.63)	0.907[c]	
h) Maximal			0.510[b]	AGE (p=0.009)
(n=644)	≤18.6	1.10 (0.73,1.66)	0.658[c]	EDUC (p=0.051)
	>18.6	0.92 (0.62,1.35)	0.654[c]	RACE*ALC (p=0.012)

[a]Relative risk for a twofold increase in dioxin.
[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).
[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 9-25. (Continued)

Analysis of Hostility (SCL-90-R)

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	690	4.4	All Categories		0.602
Unknown	294	3.7	Unknown vs. Background	0.86 (0.42,1.73)	0.663
Low	171	5.9	Low vs. Background	1.37 (0.65,2.85)	0.406
High	167	6.0	High vs. Background	1.40 (0.67,2.93)	0.369
Total	1,322				

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	683	All Categories		0.849	DRKYR (p=0.020) EDUC*AGE (p=0.009)
Unknown	290	Unknown vs. Background	0.95 (0.46,1.94)	0.881	
Low	167	Low vs. Background	1.37 (0.65,2.89)	0.411	
High	163	High vs. Background	0.97 (0.44,2.15)	0.948	
Total	1,303				

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 9-26.

Analysis of Interpersonal Sensitivity (SCL-90-R)

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I)[a]	p-Value
a) Minimal (n=464)	Low	116	6.0	1.20 (0.90,1.58)	0.220
	Medium	229	6.1		
	High	119	8.4		
b) Maximal (n=652)	Low	158	3.8	1.22 (0.98,1.52)	0.084
	Medium	328	5.2		
	High	166	9.0		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=455)	1.14 (0.82,1.58)**	0.435**	INIT*EDUC (p=0.040) AGE*DRKYR (p=0.019) AGE*ALC (p=0.018)
d) Maximal (n=640)	1.10 (0.86,1.39)	0.458	DRKYR (p=0.015) EDUC (p=0.026)

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

**Log_2 (initial dioxin)-by-covariate interaction ($0.01<p\leq0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 9-26. (Continued)

Analysis of Interpersonal Sensitivity (SCL-90-R)

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.482[b]
(n=464)	≤18.6	6.2 (65)	6.2 (113)	16.7 (48)	1.43 (0.96,2.14)	0.082[c]
	>18.6	5.7 (53)	4.4 (114)	5.6 (71)	1.16 (0.75,1.78)	0.499[c]
f) Maximal						0.315[b]
(n=652)	≤18.6	4.4 (92)	5.9 (171)	12.5 (72)	1.46 (1.07,1.99)	0.018[c]
	>18.6	4.8 (63)	4.4 (159)	5.3 (95)	1.15 (0.82,1.62)	0.415[c]

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal			0.354[b]	DRKYR (p=0.005)
(n=455)	≤18.6	1.38 (0.91,2.10)	0.128[c]	EDUC (p=0.046)
	>18.6	1.04 (0.66,1.63)	0.878[c]	
h) Maximal			0.260[b]	DRKYR (p=0.007)
(n=640)	≤18.6	1.36 (0.98,1.90)	0.064[c]	EDUC (p=0.043)
	>18.6	1.03 (0.71,1.49)	0.865[c]	

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

[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).

[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 9-26. (Continued)

Analysis of Interpersonal Sensitivity (SCL-90-R)

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	690	5.8	All Categories		0.222
Unknown	294	3.7	Unknown vs. Background	0.63 (0.32,1.25)	0.187
Low	171	5.3	Low vs. Background	0.90 (0.43,1.90)	0.787
High	167	8.4	High vs. Background	1.49 (0.79,2.80)	0.220
Total	1,322				

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	683	All Categories		0.681	DRKYR (p=0.041) EDUC (p<0.001)
Unknown	290	Unknown vs. Background	0.70 (0.35,1.40)	0.311	RACE*AGE (p=0.017)
Low	167	Low vs. Background	0.83 (0.39,1.77)	0.625	
High	163	High vs. Background	1.11 (0.57,2.16)	0.768	
Total	1,303				

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

since tour strata (Table 9-26 [e]: p=0.482). However, within the time less than or equal to 18.6 years stratum, a positive association between current dioxin and interpersonal sensitivity was marginally significant (Est. RR=1.43, p=0.082). The unadjusted percentages of these Ranch Hands with abnormal interpersonal sensitivity T-scores for low, medium, and high current dioxin were 6.2, 6.2, and 16.7 percent. In contrast, for Ranch Hands with over 18.6 years since tour, the association between current dioxin and interpersonal sensitivity was positive but not significant (p=0.499).

Similarly, for the maximal cohort, the unadjusted analysis displayed a nonsignificant current dioxin-by-time since tour interaction (Table 9-26 [f]: p=0.315). There was a significant positive association between current dioxin and interpersonal sensitivity within the less than or equal to 18.6 years time stratum, and a nonsignificant positive association for the over 18.6 years time stratum (≤18.6: Est. RR=1.46, p=0.018; >18.6: Est. RR=1.15, p=0.415). For Ranch Hands with 18.6 years or less since tour, the percentages of abnormal interpersonal sensitivity T-scores for low, medium, and high current dioxin were 4.4, 5.9, and 12.5 percent.

After adjusting for education and lifetime alcohol history, both the minimal and the maximal analyses exhibited a nonsignificant current dioxin-by-time since tour interaction (Table 9-26 [g] and [h]: p=0.354 and p=0.260, respectively). Under the maximal assumption, there was a marginally significant positive association between current dioxin and interpersonal sensitivity for the less than or equal to 18.6 years time stratum (Table 9-26 [h]: Adj. RR=1.36, p=0.064).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

Neither the unadjusted nor the adjusted analysis of categorized current dioxin and interpersonal sensitivity detected a significant difference among the prevalence rates of abnormal interpersonal sensitivity T-scores of the four current dioxin categories (Table 9-26 [i] and [j]: p=0.222 and p=0.681, respectively).

Obsessive-Compulsive Behavior—SCL-90-R

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

A marginally significant positive association was detected between initial dioxin and the SCL-90-R obsessive-compulsive behavior variable for the unadjusted minimal analysis (Table 9-27 [a]: Est. RR=1.24, p=0.080). This association can be seen in the increasing percentages of Ranch Hands with this type of behavior for increasing levels of initial dioxin (low, 7.8%; medium, 8.7%; high, 11.8%). Under the maximal assumption, a significant association between initial dioxin and obsessive-compulsive behavior in Ranch Hands was found for the unadjusted analysis (Table 9-27 [b]: Est. RR=1.36, p=0.002) with similarly increasing prevalence rates of 3.8, 6.4, and 13.3 percent for the low, medium, and high levels of initial dioxin.

After adjusting for education, a race-by-age interaction, and an age-by-lifetime alcohol history interaction, the association between initial dioxin and the percentage of Ranch Hands with obsessive-compulsive behavior was nonsignificant (Table 9-27 [c]: p=0.359). For the

TABLE 9-27.

Analysis of Obsessive-Compulsive Behavior (SCL-90-R)

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=464)	Low	116	7.8	1.24 (0.98,1.58)	0.080
	Medium	229	8.7		
	High	119	11.8		
b) Maximal (n=652)	Low	158	3.8	1.36 (1.12,1.65)	0.002
	Medium	328	6.4		
	High	166	13.3		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=455)	1.13 (0.87,1.47)	0.359	EDUC (p=0.102) RACE*AGE (p=0.038) AGE*DRKYR (p=0.004)
d) Maximal (n=640)	1.23 (1.00,1.52)	0.054	DRKYR (p=0.087) EDUC (p=0.039) RACE*AGE (p=0.020)

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

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 9-27. (Continued)

Analysis of Obsessive-Compulsive Behavior (SCL-90-R)

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.283[b]
(n=464)	≤18.6	9.2 (65)	8.9 (113)	12.5 (48)	1.07 (0.72,1.61)	0.730[c]
	>18.6	5.7 (53)	7.9 (114)	12.7 (71)	1.42 (1.03,1.96)	0.031[c]
f) Maximal						0.999[b]
(n=652)	≤18.6	2.2 (92)	8.8 (171)	9.7 (72)	1.37 (1.01,1.87)	0.043[c]
	>18.6	4.8 (63)	6.9 (159)	11.6 (95)	1.37 (1.06,1.78)	0.018[c]

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal			0.350[b]	EDUC (p=0.137)
(n=455)	≤18.6	0.95 (0.61,1.46)	0.806[c]	AGE*DRKYR (p=0.003)
	>18.6	1.23 (0.86,1.74)	0.253[c]	
h) Maximal			0.852[b]	DRKYR (p=0.083)
(n=640)	≤18.6	1.25 (0.90,1.74)	0.188[c]	EDUC (p=0.038)
	>18.6	1.20 (0.91,1.59)	0.199[c]	RACE*AGE (p=0.020)

[a]Relative risk for a twofold increase in dioxin.
[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).
[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 9-27. (Continued)

Analysis of Obsessive-Compulsive Behavior (SCL-90-R)

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	690	6.4	All Categories		0.052
Unknown	294	4.4	Unknown vs. Background	0.68 (0.36,1.28)	0.232
Low	171	8.8	Low vs. Background	1.41 (0.77,2.60)	0.269
High	167	10.8	High vs. Background	1.77 (1.00,3.16)	0.051
Total	1,322				

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	685	All Categories		0.240	RACE*EDUC (p=0.035)
Unknown	293	Unknown vs. Background	0.71 (0.37,1.34)	0.291	
Low	169	Low vs. Background	1.32 (0.71,2.45)	0.378	
High	166	High vs. Background	1.45 (0.80,2.63)	0.221	
Total	1,313				

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

maximal cohort, the adjustment for education, lifetime alcohol history, and a race-by-age interaction caused the same association to become marginally significant (Table 9-27 [d]: Adj. RR=1.23, p=0.054).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

In the minimal unadjusted analysis of the SCL-90-R obsessive-compulsive behavior variable, the current dioxin-by-time since tour interaction was not significant (Table 9-27 [e]: p=0.283). However, for Ranch Hands with time over 18.6 years, there was a significant positive association between current dioxin and the percentage of abnormal obsessive-compulsive behavior T-scores (Est. RR=1.42, p=0.031). This direct association can be seen in the increasing prevalence rates of Ranch Hands with obsessive-compulsive behavior for increasing levels of dioxin (low, 5.7%; medium, 7.9%; high, 12.7%).

Under the maximal assumption, the unadjusted analysis detected a nonsignificant current dioxin-by-time since tour interaction (Table 9-27 [f]: p=0.999). The time less than or equal to 18.6 years stratum displayed a significant positive association between current dioxin and obsessive-compulsive behavior (Table 9-27 [f]: Est. RR=1.37, p=0.043) supported by increasing percentages of obsessive-compulsive behavior of 2.2, 8.8, and 9.7 percent for the low, medium, and high levels of current dioxin. The time over 18.6 years stratum also exhibited a significant positive association with dioxin (Table 9-27 [f]: Est. RR=1.37, p=0.018). The frequencies of participants with obsessive-compulsive behavior increased with increasing levels of current dioxin for this time stratum (low, 4.8%; medium, 6.9%; high, 11.6%).

After adjusting the minimal analysis for education and an age-by-lifetime alcohol history interaction and adjusting the maximal analysis for education, lifetime alcohol history, and a race-by-age interaction, neither analysis detected any significant associations between current dioxin and obsessive-compulsive behavior (Table 9-27 [g] and [h]: p>0.15 for each analysis).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In the unadjusted analysis of the SCL-90-R obsessive-compulsive behavior variable, the contrast of the four current dioxin categories was marginally significant (Table 9-27 [i]: p=0.052). The percentages of abnormal obsessive-compulsive behavior T-scores for the background, unknown, low, and high current dioxin categories were 6.4, 4.4, 8.8, and 10.8 percent. A marginally significant difference was found between the prevalence rates of obsessive-compulsive behavior for the Ranch Hands in the high category and the Comparisons in the background category (Table 9-27 [i]: Est. RR=1.77, 95% C.I.: [1.00,3.16], p=0.051).

The adjustment for a race-by-education interaction caused the results of the analyses to become nonsignificant both overall and for individual contrasts between categories (Table 9-27 [j]: p>0.20 for each analysis).

Paranoid Ideation—SCL-90-R

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

In both the unadjusted and the adjusted analyses, the association between initial dioxin and the frequency of Ranch Hands suffering from paranoid ideation was nonsignificant under both assumptions (Table 9-28 [a-d]: $p>0.25$ for each analysis).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

Similar to the initial dioxin analyses, the unadjusted and adjusted current dioxin and time since tour analyses of paranoid ideation displayed nonsignificant results for both the minimal and the maximal cohorts (Table 9-28 [e-h]: $p>0.15$ for each analysis).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In both the unadjusted and adjusted analyses of categorized current dioxin and paranoid ideation, the overall contrast of the four current dioxin categories was nonsignificant (Table 9-28 [i] and [j]: $p>0.45$ for both analyses).

Phobic Anxiety—SCL-90-R

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

The unadjusted analysis under both minimal and maximal assumptions displayed a nonsignificant association between initial dioxin and phobic anxiety (Table 9-29 [a] and [b]: $p=0.585$ and $p=0.115$, respectively).

After adjustment for covariate information, the results of both the minimal and the maximal analyses remained nonsignificant (Table 9-29 [c] and [d]: $p=0.912$ and $p=0.493$).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

For both the minimal and the maximal cohorts, the unadjusted analysis detected a nonsignificant current dioxin-by-time since tour interaction (Table 9-29 [e] and [f]: $p=0.222$ and $p=0.764$, respectively). The association between current dioxin and phobic anxiety was also nonsignificant within each time stratum.

In the adjusted analysis, there was a significant interaction of current dioxin, time since tour, and race under both the minimal and the maximal assumptions (Table 9-29 [g] and [h]: $p=0.012$ and $p=0.015$). To investigate this interaction, associations between phobic anxiety and current dioxin are presented separately for each time and race stratum in Appendix Table H-1.

Under the minimal assumption, the Black stratum contained only one Ranch Hand with phobic anxiety in the time less than or equal to 18.6 years stratum, and he was in the medium dioxin category. In the time over 18.6 years stratum, two Black Ranch Hands in the low dioxin category had an abnormal phobic anxiety T-score. Due to the sparse number of abnormalities in the Black stratum, the adjusted relative risks, confidence intervals, and

TABLE 9-28.

Analysis of Paranoid Ideation (SCL-90-R)

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=464)	Low	116	5.2	0.81 (0.54,1.22)	0.302
	Medium	229	4.4		
	High	119	3.4		
b) Maximal (n=652)	Low	158	3.2	0.91 (0.67,1.22)	0.511
	Medium	328	4.3		
	High	166	4.2		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=459)	0.81 (0.54,1.22)	0.293	DRKYR (p=0.094)
d) Maximal (n=644)	0.86 (0.64,1.17)	0.324	AGE (p=0.098) ALC (p=0.086) DRKYR (p=0.128)

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

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 9-23. (Continued)

Analysis of Paranoid Ideation (SCL-90-R)

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.474[b]
(n=464)	≤18.6	6.2 (65)	5.3 (113)	8.3 (48)	0.96 (0.57,1.61)	0.865[c]
	>18.6	1.9 (53)	4.4 (114)	0.0 (71)	0.68 (0.31,1.51)	0.344[c]
f) Maximal						0.206[b]
(n=652)	≤18.6	3.3 (92)	5.9 (171)	5.6 (72)	1.12 (0.77,1.64)	0.561[c]
	>18.6	4.8 (63)	3.1 (159)	1.1 (95)	0.74 (0.42,1.28)	0.277[c]

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal			0.546[b]	DRKYR (p=0.057)
(n=459)	≤18.6	0.95 (0.57,1.61)	0.860[c]	
	>18.6	0.72 (0.34,1.54)	0.402[c]	
h) Maximal			0.191[b]	ALC (p=0.071)
(n=648)	≤18.6	1.12 (0.77,1.64)	0.550[c]	
	>18.6	0.73 (0.42,1.27)	0.263[c]	

[a]Relative risk for a twofold increase in dioxin.
[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).
[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).
Note: Minimal--Low: >10-14.65 ppt; [illegible] 14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: [illegible] ppt; High: >33.3 ppt.

TABLE 9-23. (Continued)

Analysis of Paranoid Ideation (SCL-90-R)

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	690	3.5	All Categories		0.645
Unknown	294	3.1	Unknown vs. Background	0.88 (0.40,1.91)	0.740
Low	171	5.3	Low vs. Background	1.54 (0.70,3.38)	0.280
High	167	3.0	High vs. Background	0.86 (0.32,2.28)	0.756
Total	1,322				

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	683	All Categories		0.490	RACE (p=0.150) DRKYR (p=0.036)
Unknown	290	Unknown vs. Background	0.96 (0.44,2.12)	0.922	EDUC*AGE (p=0.036)
Low	167	Low vs. Background	1.60 (0.72,3.56)	0.246	
High	163	High vs. Background	0.67 (0.25,1.85)	0.444	
Total	1,303				

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 9-29.

Analysis of Phobic Anxiety (SCL-90-R)

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=464)	Low	116	6.9	1.08 (0.82,1.42)	0.585
	Medium	229	7.9		
	High	119	8.4		
b) Maximal (n=652)	Low	158	3.8	1.19 (0.96,1.46)	0.115
	Medium	328	7.0		
	High	166	9.0		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=455)	0.98 (0.73,1.32)	0.912	EDUC (p=0.066) AGE*DRKYR (p=0.020)
d) Maximal (n=648)	1.08 (0.86,1.36)	0.493	EDUC (p=0.028)

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

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 9-29. (Continued)

Analysis of Phobic Anxiety (SCL-90-R)

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.222[b]
(n=464)	≤18.6	7.7 (65)	9.7 (113)	6.3 (48)	0.89 (0.56,1.42)	0.628[c]
	>18.6	5.7 (53)	6.1 (114)	9.9 (71)	1.28 (0.89,1.82)	0.178[c]
f) Maximal						0.764[b]
(n=652)	≤18.6	2.2 (92)	8.8 (171)	5.6 (72)	1.23 (0.88,1.71)	0.232[c]
	>18.6	7.9 (63)	5.7 (159)	9.5 (95)	1.15 (0.87,1.52)	0.337[c]

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal			0.283**[b]	CURR*TIME*RACE (p=0.012)
(n=455)	≤18.6	0.86 (0.52,1.41)**	0.547**[c]	EDUC (p=0.113)
	>18.6	1.20 (0.81,1.78)**	0.365**[c]	AGE*DRKYR (p=0.019)
h) Maximal			0.705**[b]	CURR*TIME*RACE (p=0.015)
(n=640)	≤18.6	1.13 (0.79,1.62)**	0.509**[c]	DRKYR (p=0.135)
	>18.6	1.03 (0.76,1.41)**	0.841**[c]	EDUC (p=0.029) RACE*AGE (p=0.043)

[a]Relative risk for a twofold increase in dioxin.
[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).
[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).
**Log_2 (current dioxin)-by-time-by-covariate interaction ($0.01<p\leq0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction.
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 9-29. (Continued)

Analysis of Phobic Anxiety (SCL-90-R)

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	690	6.8	All Categories		0.042
Unknown	294	3.1	Unknown vs. Background	0.43 (0.21,0.89)	0.024
Low	171	8.2	Low vs. Background	1.22 (0.66,2.27)	0.531
High	167	7.8	High vs. Background	1.15 (0.61,2.19)	0.659
Total	1,322				

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	685	All Categories		0.092	EDUC*AGE (p=0.033)
Unknown	293	Unknown vs. Background	0.45 (0.22,0.94)	0.033	
Low	169	Low vs. Background	1.19 (0.63,2.22)	0.595	
High	166	High vs. Background	0.90 (0.46,1.77)	0.764	
Total	1,313				

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

p-values are not presented. The analysis of the non-Black stratum detected a nonsignificant current dioxin-by-time since tour interaction (Appendix Table H-1: p=0.114). The association between current dioxin and phobic anxiety was also nonsignificant within each time stratum.

In the maximal analysis, the Black stratum contained only one Ranch Hand with phobic anxiety in the less than or equal to 18.6 years time stratum and two in the over 18.6 years time stratum. All three of these Ranch Hands were in the medium dioxin category, and for the same reason as stated above, the relative risks, confidence intervals, and p-values are not presented. For the non-Black stratum, the current dioxin-by-time since tour interaction was nonsignificant (Appendix Table H-1: p=0.980), and the association between current dioxin and phobic anxiety was also nonsignificant within each time stratum.

After deletion of the current dioxin-by-time-by-race interaction, both the minimal and the maximal analyses exhibited nonsignificant results (Table 9-29 [g] and [h]: p>0.25 for each analysis).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In the unadjusted analysis of Ranch Hands and Comparisons by current dioxin category, a significant difference was found in the prevalence of abnormal phobic anxiety T-scores among the four categories (Table 9-29 [i]: p=0.042). The percentages of abnormal phobic anxiety T-scores for the background, unknown, low, and high current dioxin categories were 6.8, 3.1, 8.2, and 7.8 percent. The percentage of abnormal T-scores for phobic anxiety was significantly lower for the group of Ranch Hands in the unknown category than for the Comparisons in the background category (Est. RR=0.43, 95% C.I.: [0.21,0.89], p=0.024).

After adjusting for an education-by-age interaction, the overall test for differences among the four current dioxin categories was marginally significant (Table 9-29 [j]: p=0.092). Consistent with the unadjusted results, the prevalence rate of phobic anxiety was still significantly lower for the Ranch Hands in the unknown category than for the Comparisons in the background category (Adj. RR=0.45, 95% C.I.: [0.22,0.94], p=0.033).

Psychoticism—SCL-90-R

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Under the minimal assumption, the unadjusted analysis detected a nonsignificant association between initial dioxin and the SCL-90-R psychoticism variable (Table 9-30 [a]: p=0.144). The maximal unadjusted analysis, however, did find a significant positive association (Table 9-30 [b]: Est. RR=1.25, p=0.022) supported by increasing percentages of psychoticism in Ranch Hands for increasing levels of initial dioxin (low, 6.3%; medium, 7.9%; high, 12.1%).

The adjusted analysis for the minimal cohort exhibited a nonsignificant association between initial dioxin and psychoticism (Table 9-30 [c]: p=0.397). For the maximal cohort, the adjustment for education and lifetime alcohol history reduced the significance of the

TABLE 9-30.

Analysis of Psychoticism (SCL-90-R)

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=464)	Low	116	10.3	1.20 (0.95,1.51)	0.144
	Medium	229	8.3		
	High	119	12.6		
b) Maximal (n=652)	Low	158	6.3	1.25 (1.04,1.50)	0.022
	Medium	328	7.9		
	High	166	12.1		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=459)	1.12 (0.86,1.46)	0.397	AGE*DRKYR (p<0.001) AGE*ALC (p=0.004) DRKYR*ALC (p<0.001)
d) Maximal (n=640)	1.19 (0.98,1.44)	0.089	DRKYR (p=0.073) EDUC (p=0.042)

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

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 9-30. (Continued)

Analysis of Psychoticism (SCL-90-R)

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.661[b]
(n=464)	≤18.6	7.7 (65)	8.9 (113)	12.5 (48)	1.10 (0.73,1.66)	0.655[c]
	>18.6	13.2 (53)	7.9 (114)	12.7 (71)	1.23 (0.91,1.67)	0.182[c]
f) Maximal						0.756[b]
(n=652)	≤18.6	4.4 (92)	7.6 (171)	11.1 (72)	1.27 (0.94,1.73)	0.122[c]
	>18.6	7.9 (63)	9.4 (159)	11.6 (95)	1.20 (0.94,1.53)	0.147[c]

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal			0.967[b]	AGE*DRKYR (p<0.001)
(n=459)	≤18.6	1.08 (0.70,1.67)	0.731[c]	AGE*ALC (p=0.004)
	>18.6	1.09 (0.76,1.57)	0.632[c]	DRKYR*ALC (p<0.001)
h) Maximal			0.882[b]	DRKYR (p=0.076)
(n=640)	≤18.6	1.20 (0.87,1.65)	0.272[c]	EDUC (p=0.040)
	>18.6	1.16 (0.90,1.49)	0.241[c]	

[a]Relative risk for a twofold increase in dioxin.
[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).
[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 9-30. (Continued)

Analysis of Psychoticism (SCL-90-R)

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	690	8.3	All Categories		0.278
Unknown	294	6.1	Unknown vs. Background	0.72 (0.42,1.25)	0.249
Low	171	8.2	Low vs. Background	0.99 (0.54,1.82)	0.975
High	167	11.4	High vs. Background	1.43 (0.82,2.47)	0.206
Total	1,322				

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	685	All Categories		0.704	AGE (p=0.101) ALC (p=0.008) RACE*EDUC (p=0.005)
Unknown	291	Unknown vs. Background	0.78 (0.45,1.37)	0.391	
Low	167	Low vs. Background	0.99 (0.53,1.83)	0.962	
High	166	High vs. Background	1.19 (0.67,2.10)	0.555	
Total	1,309				

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

positive association between initial dioxin and psychoticism to a marginal level (Table 9-30 [d]: Adj. RR=1.19, p=0.089).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

In the unadjusted analysis of psychoticism, under both the minimal and maximal assumptions, the interactions between current dioxin and time since tour were not significant (Table 9-30 [e] and [f]: p=0.661 and p=0.756, respectively). The association between current dioxin and psychoticism was also nonsignificant within the time strata for both minimal and maximal cohorts.

These findings did not change after adjusting for covariate information (Table 9-30 [g] and [h]: p>0.20 for each analysis).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In both the unadjusted and adjusted analyses of the SCL-90-R psychoticism variable, the simultaneous contrast of the four current dioxin categories was not significant (Table 9-30 [i] and [j]: p=0.278 and p=0.704, respectively).

Somatization—SCL-90-R

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

The unadjusted analysis of the SCL-90-R somatization variable displayed a nonsignificant association with initial dioxin in the minimal analysis (Table 9-31 [a]: p=0.634). The maximal unadjusted analysis detected a marginally significant positive association between initial dioxin and somatization (Table 9-31 [b]: Est. RR=1.19, p=0.064). The prevalence rates for somatization in Ranch Hands for the low, medium, and high initial dioxin levels were 6.3, 9.5, and 13.9 percent.

After adjusting for covariate information, the result of the minimal analysis remained nonsignificant (Table 9-31 [c]: p=0.810). The adjustment for education and age under the maximal assumption caused the association between initial dioxin and somatization to become nonsignificant (Table 9-31 [d]: p=0.348).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

In the unadjusted analysis of the SCL-90-R somatization variable based on current dioxin and time since tour, the minimal cohort exhibited a significant current dioxin-by-time interaction (Table 9-31 [e]: p=0.015). A nonsignificant negative association between somatization and current dioxin was found for Ranch Hands with 18.6 years or less since tour (p=0.116), and a marginally significant positive association was displayed for Ranch Hands with more than 18.6 years since tour (Est. RR=1.33, p=0.061). For the earlier tour stratum (time>18.6 years), the prevalence rates of abnormal somatization T-scores were 9.4%, 7.9%, and 16.9% for low, medium, and high current dioxin.

TABLE 9-31.

Analysis of Somatization (SCL-90-R)

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=464)	Low	116	14.7	1.06 (0.84,1.33)	0.634
	Medium	229	8.7		
	High	119	13.5		
b) Maximal (n=652)	Low	158	6.3	1.19 (0.99,1.41)	0.064
	Medium	328	9.5		
	High	166	13.9		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=455)	1.03 (0.80,1.32)	0.810	EDUC (p=0.028) AGE*DRKYR (p=0.010)
d) Maximal (n=648)	1.10 (0.90,1.34)	0.348	AGE (p=0.091) EDUC (p<0.001)

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

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 9-31. (Continued)

Analysis of Somatization (SCL-90-R)

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.015[b]
(n=464)	≤18.6	15.4 (65)	11.5 (113)	8.3 (48)	0.70 (0.45,1.09)	0.116[c]
	>18.6	9.4 (53)	7.9 (114)	16.9 (71)	1.33 (0.99,1.79)	0.061[c]
f) Maximal						0.620[b]
(n=652)	≤18.6	3.3 (92)	12.3 (171)	8.3 (72)	1.09 (0.81,1.47)	0.554[c]
	>18.6	11.1 (63)	8.2 (159)	14.7 (95)	1.20 (0.95,1.52)	0.122[c]

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal			0.025[b]	EDUC*AGE (p=0.037)
(n=455)	≤18.6	0.73 (0.46,1.15)	0.175[c]	AGE*DRKYR (p=0.008)
	>18.6	1.33 (0.96,1.84)	0.084[c]	
h) Maximal			0.608**[b]	CURR*TIME*ALC (p=0.036)
(n=644)	≤18.6	1.02 (0.74,1.41)**	0.916**[c]	AGE (p=0.106)
	>18.6	1.13 (0.88,1.46)**	0.349**[c]	EDUC (p<0.001)

[a]Relative risk for a twofold increase in dioxin.
[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).
[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).
**Log_2 (current dioxin)-by-time-by-covariate interaction ($0.01<p\leq0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction.
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 9-31. (Continued)

Analysis of Somatization (SCL-90-R)

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	690	7.7	All Categories		0.323
Unknown	294	7.5	Unknown vs. Background	0.97 (0.58,1.63)	0.915
Low	171	9.4	Low vs. Background	1.24 (0.69,2.23)	0.471
High	167	12.0	High vs. Background	1.64 (0.95,2.82)	0.077
Total	1,322				

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	685	All Categories		0.597**	DXCAT*RACE (p=0.027)
Unknown	293	Unknown vs. Background	1.05 (0.62,1.77)**	0.857**	AGE (p=0.037)
Low	169	Low vs. Background	1.16 (0.64,2.09)**	0.626**	EDUC (p=0.002)
High	166	High vs. Background	1.49 (0.84,2.64)**	0.168**	
Total	1,313				

**Categorized current dioxin-by-covariate interaction ($0.01<p\leq0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction.

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

For the maximal assumption, the unadjusted analysis displayed a nonsignificant current dioxin-by-time since tour interaction (Table 9-31 [f]: p=0.620), and the association between current dioxin and somatization was also nonsignificant within each time stratum.

The current dioxin-by-time interaction remained significant for the minimal analysis after adjustment for covariate information (Table 9-31 [g]: p=0.025). Also, for the time less than or equal to 18.6 years stratum, the negative association between current dioxin and somatization remained nonsignificant (Adj. RR=0.73, p=0.175), and for the time over 18.6 years stratum, the positive association was again marginally significant (Adj RR=1.33, p=0.084).

The adjusted maximal analysis detected a significant current dioxin-by-time-by-current alcohol use interaction (Table 9-31 [h]: p=0.036). To investigate this interaction the analyses are presented separately for each current alcohol use and time stratum (Appendix Table H-1). For those Ranch Hands who drank one drink or less each day, the interaction of current dioxin and time since tour was nonsignificant (p=0.460). Within the less than or equal to 18.6 years time stratum, there was a nonsignificant positive association between current dioxin and somatization (Adj. RR=1.07, p=0.702), and for the time greater than 18.6 years stratum, there was a marginally significant positive association (Adj. RR=1.27, p=0.094). For Ranch Hands who drank more than one drink each day, the interaction between current dioxin and time was nonsignificant (p=0.459), and there was a nonsignificant negative association between current dioxin and somatization within each time stratum (≤18.6: Adj. RR=0.85, p=0.651; >18.6: Adj. RR=0.56, p=0.212).

After deletion of the current dioxin-by-time-by-current alcohol use interaction from the model, the maximal adjusted analysis exhibited a nonsignificant current dioxin-by-time interaction (Table 9-31 [h]: p=0.608).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In the unadjusted analysis of the SCL-90-R somatization variable, the test for overall differences in the prevalence rates of somatization of the four categories was nonsignificant (Table 9-31 [i]: p=0.323). However, the tests of individual contrasts among these groups found the frequency of somatization to be marginally higher for Ranch Hands in the high category than for the Comparisons in the background category (Table 9-31 [i]: Est. RR=1.64, 95% C.I.: [0.95,2.82], p=0.077; background, 7.7%; high, 12.0%).

The adjusted analysis of the SCL-90-R somatization variable detected a significant categorized current dioxin-by-race interaction (Table 9-31 [j]: p=0.027). To examine this interaction, stratified analyses are presented for Blacks and non-Blacks (Appendix Table H-1). For the Black stratum, there were only six Comparisons in the background category (14.3%) and three Ranch Hands in the unknown category (30.0%) who had abnormal somatization T-scores. The overall contrast of the four current dioxin categories was significant (p=0.048); however, the contrast of the Ranch Hands in the unknown category versus the Comparisons in the background category was not significant. For the non-Black stratum, the simultaneous contrast of the four current dioxin categories was nonsignificant (p=0.180). The percentages of abnormal somatization T-scores for the background,

unknown, low, and high current dioxin categories were 7.3, 6.7, 10.1, and 12.[illegible] percent. The contrast of the Ranch Hands in the high category versus the Comparisons in the background category was marginally significant (Adj. RR=1.69, 95% C.I.: [0.95,3.02], p=0.076).

After deleting the interaction from the model, the adjusted analysis of the SCL 90-R somatization variable did not detect a significant difference in the percentage of abnormal somatization T-scores of the four current dioxin categories (Table 9-31 [j]: p>0.15 for each analysis).

Global Severity Index—SCL-90-R

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

In the unadjusted analysis of the global severity index, there was a marginally significant positive association with initial dioxin for the minimal cohort and a significant association with initial dioxin for the maximal cohort (Table 9-32 [a] and [b]: Est. RR=1.25, p=0.073 and Est. RR=1.27, p=0.013, respectively). The relative frequency of Ranch Hands in the minimal cohort with an abnormal global severity index was nearly the same for the low and medium initial dioxin levels (8.6% and 8.3%, respectively). However, the frequency at the high initial dioxin level was greater (13.5%). Similarly, the corresponding frequencies for the maximal cohort were 6.3, 6.4, and 14.5 percent.

After adjusting for age, lifetime alcohol history, and education, neither the minimal nor the maximal analysis found a significant association between initial dioxin and the global severity index (Table 9-32 [c] and [d]: p=0.467 and p=0.294, respectively).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

In the unadjusted analysis of the global severity index based on current dioxin and time since tour, neither the minimal nor the maximal cohort displayed a significant current dioxin-by-time interaction (Table 9-32 [e] and [f]: p=0.301 and p=0.893, respectively). Thus, the positive associations between current dioxin and the global severity index were not statistically different between the two time strata.

In the minimal unadjusted analysis, the association between current dioxin and the global severity index was not significant for the time less than or equal to 18.6 years stratum, but there was a significant positive association for Ranch Hands with over 18.6 years since tour (Table 9-32 [e]: Est. RR=1.11, p=0.609; Est. RR=1.44, p=0.026, respectively). For Ranch Hands with time over 18.6 years since tour, the percentages of abnormal global severity indices for low, medium, and high current dioxin were 7.6, 6.1, and 14.1 percent.

In the maximal unadjusted analysis, there was a marginally significant positive association between current dioxin and the global severity index for both time strata (Table 9-32 [f]: ≤18.6: Est. RR=1.31, p=0.069; >18.6: Est. RR=1.28, p=0.061). Within the time less than or equal to 18.6 years stratum the prevalence rates of an abnormal global severity index for low, medium, and high current dioxin levels were 4.4, 8.8, and 12.5 percent. For the time over 18.6 years stratum the prevalence rates did not increase steadily with increasing current dioxin, but the association was still positive (low, 7.9%; medium, 6.3%; high, 12.6%).

TABLE 9-32.

Analysis of Global Severity Index (SCL-90-R)

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=464)	Low	116	8.6	1.25 (0.98,1.58)	0.073
	Medium	229	8.3		
	High	119	13.5		
b) Maximal (n=652)	Low	158	6.3	1.27 (1.06,1.53)	0.013
	Medium	328	6.4		
	High	166	14.5		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=455)	1.10 (0.85,1.42)	0.467	EDUC (p=0.036) AGE*DRKYR (p=0.004)
d) Maximal (n=640)	1.12 (0.91,1.36)	0.294	EDUC (p=0.006) AGE (p=0.029) DRKYR (p=0.131)

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

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 9-32. (Continued)

Analysis of Global Severity Index (SCL-90-R)

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.301[b]
(n=464)	≤18.6	9.2 (65)	8.9 (113)	16.7 (48)	1.11 (0.75,1.63)	0.609[c]
	>18.6	7.6 (53)	6.1 (114)	14.1 (71)	1.44 (1.04,1.98)	0.026[c]
f) Maximal						0.893[b]
(n=652)	≤18.6	4.4 (92)	8.8 (171)	12.5 (72)	1.31 (0.98,1.75)	0.069[c]
	>18.6	7.9 (63)	6.3 (159)	12.6 (95)	1.28 (0.99,1.64)	0.061[c]

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal			0.338**[b]	CURR*TIME*RACE (p=0.049)
(n=455)	≤18.6	1.02 (0.67,1.55)**	0.915**[c]	EDUC*AGE (p=0.039)
	>18.6	1.33 (0.93,1.89)**	0.122**[c]	AGE*DRKYR (p=0.001)
h) Maximal			0.886[b]	AGE (p=0.040)
(n=640)	≤18.6	1.14 (0.84,1.55)	0.405[c]	DRKYR (p=0.124)
	>18.6	1.11 (0.84,1.46)	0.471[c]	EDUC (p=0.006)

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

[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).

[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).

**Log_2 (current dioxin)-by-time-by-covariate interaction ($0.01<p\leq0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction.

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 9-32. (Continued)

Analysis of Global Severity Index (SCL-90-R)

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	690	6.1	All Categories		0.025
Unknown	294	5.1	Unknown vs. Background	0.83 (0.45,1.52)	0.545
Low	171	7.6	Low vs. Background	1.27 (0.67,2.42)	0.469
High	167	12.6	High vs. Background	2.22 (1.28,3.86)	0.005
Total	1,322				

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	685	All Categories		0.333	AGE (p=0.016) ALC (p=0.019)
Unknown	291	Unknown vs. Background	0.92 (0.50,1.71)	0.803	EDUC (p=0.003)
Low	167	Low vs. Background	1.22 (0.64,2.35)	0.546	
High	166	High vs. Background	1.66 (0.93,2.97)	0.084	
Total	1,309				

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

Under the minimal assumption, the adjusted analysis detected a significant current dioxin-by-time-by-race interaction (Table 9-32 [g]: p=0.049). To examine this interaction, stratified analyses are presented for each race stratum (Appendix Table H-1). The stratified analyses did not exhibit a significant interaction between current dioxin and time since tour for either the Black or the non-Black stratum (p=0.176 and p=0.221). However, within the non-Black stratum, there was a significant positive association between current dioxin and the global severity index for Ranch Hands with time over 18.6 years (Adj. RR=1.46, p=0.046), and a nonsignificant positive association for Ranch Hands with 18.6 years or less since tour (Adj. RR=1.04, p=0.866). The Black stratum contained only four Ranch Hands with an abnormal global severity index (none of whom were in the high current dioxin category).

After deletion of the current dioxin-by-time-by-race interaction, the minimal adjusted analysis exhibited a nonsignificant current dioxin-by-time since tour interaction (Table 9-32 [g]: p=0.338). The association between current dioxin and the global severity index was also nonsignificant within each time stratum. Under the maximal assumption, the adjusted analysis also displayed a nonsignificant interaction between current dioxin and time (Table 9-32 [h]: p=0.886) as well as nonsignificant associations within time strata.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The analysis of categorized current dioxin found significant differences in the percentage of abnormal scores on the global severity index for the four current dioxin categories (Table 9-32 [i]: p=0.025). The frequencies of abnormal global severity indices for the background, unknown, low, and high current dioxin categories were 6.1, 5.1, 7.6, and 12.6 percent. Specifically, the percentage of participants with an abnormal global severity index was significantly higher for the Ranch Hands in the high category than for the Comparisons in the background category (Table 9-32 [i]: Est. RR=2.22, 95% C.I.: [1.28,3.86], p=0.005).

After adjusting for education, age, and current alcohol use, the contrast of the four current dioxin categories did not detect any significant differences among the prevalence rates of an abnormal global severity index (Table 9-32 [j]: p=0.333). However, the contrast of the Ranch Hands in the high category versus the Comparisons in the background category was marginally significant (Table 9-32 [j]: Adj. RR=1.66, 95% C.I.: [0.93,2.97], p=0.084) with Ranch Hands having a higher risk of abnormal global severity indices.

Positive Symptom Total—SCL-90-R

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

The unadjusted analysis under the minimal assumption detected a marginally significant positive association between initial dioxin and the positive symptom total for Ranch Hands (Table 9-33 [a]: Est. RR=1.25, p=0.079). The associated relative frequencies of Ranch Hands with an abnormal positive symptom total for low, medium, and high initial dioxin categories were 6.9, 7.4, and 12.6 percent. For the maximal assumption, the unadjusted analysis displayed a significant positive association between initial dioxin and the positive symptom total (Table 9-33 [b]: Est. RR=1.23, p=0.043). The percentages of abnormalities for this cohort decreased from low to medium initial dioxin categories and then increased for the high initial dioxin category (low, 7.0%; medium, 5.5%; high, 13.3%).

TABLE 9-33.

Analysis of Positive Symptom Total (SCL-90-R)

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I)[a]	p-Value
a) Minimal (n=464)	Low	116	6.9	1.25 (0.98,1.61)	0.079
	Medium	229	7.4		
	High	119	12.6		
b) Maximal (n=652)	Low	158	7.0	1.23 (1.01,1.49)	0.043
	Medium	328	5.5		
	High	166	13.3		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=455)	1.12 (0.86,1.47)	0.398	EDUC*AGE (p=0.032) AGE*DRKER (p=0.003)
d) Maximal (n=640)	1.08 (0.88,1.34)	0.454	AGE (p=0.038) DRKER (p=0.049) EDUC (p=0.091)

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

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 9-33. (Continued)

Analysis of Positive Symptom Total (SCL-90-R)

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.944[b]
(n=464)	≤18.6	7.7 (65)	7.1 (113)	18.8 (48)	1.29 (0.87,1.89)	0.201[c]
	>18.6	5.7 (53)	6.1 (114)	11.3 (71)	1.31 (0.93,1.85)	0.125[c]
f) Maximal						0.447[b]
(n=652)	≤18.6	5.4 (92)	7.0 (171)	13.9 (72)	1.36 (1.01,1.82)	0.041[c]
	>18.6	7.9 (63)	6.3 (159)	9.5 (95)	1.16 (0.88,1.53)	0.282[c]

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal			0.966[b]	EDUC*AGE (p=0.024)
(n=455)	≤18.6	1.17 (0.77,1.76)	0.462[c]	AGE*DRKYR (p=0.004)
	>18.6	1.18 (0.81,1.72)	0.388[c]	
h) Maximal			0.401[b]	AGE (p=0.057)
(n=640)	≤18.6	1.21 (0.89,1.65)	0.233[c]	EDUC (p=0.046)
	>18.6	1.01 (0.75,1.36)	0.951[c]	DRKYR (p=0.045)

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

[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).

[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 9-33. (Continued)

Analysis of Positive Symptom Total (SCL-90-R)

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	690	6.1	All Categories		0.084
Unknown	294	5.1	Unknown vs. Background	0.83 (0.45,1.52)	0.545
Low	171	7.0	Low vs. Background	1.16 (0.60,2.26)	0.653
High	167	11.4	High vs. Background	1.98 (1.12,3.50)	0.019
Total	1,322				

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	685	All Categories		0.429	AGE (p=0.091) ALC (p=0.012) EDUC (p=0.091)
Unknown	291	Unknown vs. Background	0.92 (0.50,1.70)	0.785	
Low	167	Low vs. Background	1.19 (0.61,2.34)	0.608	
High	166	High vs. Background	1.60 (0.88,2.92)	0.123	
Total	1,309				

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

After adjusting for an education-by-age interaction and an age-by-lifetime alcohol history interaction, the association between initial dioxin and the positive symptom total became nonsignificant for the minimal analysis (Table 9-33 [c]: p=0.398). Similarly, adjustment for age, lifetime alcohol history, and education caused the results of the maximal analysis to also become nonsignificant (Table 9-33 [d]: p=0.454).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

In the unadjusted analysis based on current dioxin and time since tour, neither the minimal nor the maximal cohort displayed a significant current dioxin-by-time interaction (Table 9-33 [e] and [f]: p=0.944 and p=0.447, respectively). However, for the maximal assumption, a significant increasing association between the positive symptom total and current dioxin was found for Ranch Hands with 18.6 years or less since tour (Table 9-33 [f]: Est. RR=1.36, p=0.041). Within this time stratum, the abnormal positive symptom total frequencies for low, medium, and high current dioxin were 5.4, 7.0, and 13.9 percent.

Consistent with the initial dioxin analyses, the adjustment for the same covariates caused no significant results to be found in either the minimal or the maximal adjusted analysis of the positive symptom total (Table 9-33 [g] and [h]: p>0.20 for each analysis).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In the unadjusted analysis of the positive symptom total, the contrast of the four current dioxin categories was marginally significant (Table 9-33 [i]: p=0.084). The frequencies of abnormal positive symptom totals for the background, unknown, low, and high current dioxin categories were 6.1, 5.1, 7.0, and 11.4 percent. Specifically, the analysis found Ranch Hands in the high category had a significantly higher percentage of abnormal positive symptom totals than the Comparisons in the background category (Table 9-33 [i]: Est. RR=1.98, 95% C.I.: [1.12,3.50], p=0.019).

After adjusting for education, age, and current alcohol use, the analysis found no differences regarding the positive symptom total among the four categories (Table 9-33 [j]: p>0.10 for each analysis).

Positive Symptom Distress Index—SCL-90-R

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Neither the unadjusted minimal nor maximal analysis detected a significant association between initial dioxin and the positive symptom distress index of Ranch Hands (Table 9-34 [a] and [b]: p=0.922 and p=0.187, respectively).

After adjusting for lifetime alcohol history and current alcohol use, the minimal and maximal adjusted analyses displayed consistently nonsignificant results (Table 9-34 [c] and [d]: p=0.896 and p=0.164, respectively).

TABLE 9-34.

Analysis of Positive Symptom Distress Index (SCL-90-R)

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I)[a]	p-Value
a) Minimal (n=464)	Low	116	10.3	1.01 (0.80,1.28)	0.922
	Medium	229	11.8		
	High	119	10.9		
b) Maximal (n=652)	Low	158	7.0	1.13 (0.94,1.35)	0.187
	Medium	328	11.6		
	High	166	9.6		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=459)	1.02 (0.80,1.29)	0.896	ALC (p=0.070) DRKYR (p=0.011)
d) Maximal (n=644)	1.14 (0.95,1.37)	0.164	ALC (p=0.133) DRKYR (p=0.023)

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

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 9-34. (Continued)

Analysis of Positive Symptom Distress Index (SCL-90-R)

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.643[b]
(n=464)	≤18.6	7.7 (65)	16.8 (113)	8.3 (48)	0.95 (0.65,1.39)	0.787[c]
	>18.6	11.3 (53)	7.9 (114)	12.7 (71)	1.07 (0.77,1.48)	0.691[c]
f) Maximal						0.783[b]
(n=652)	≤18.6	6.5 (92)	12.3 (171)	11.1 (72)	1.16 (0.88,1.52)	0.291[c]
	>18.6	7.9 (63)	9.4 (159)	10.5 (95)	1.10 (0.85,1.41)	0.465[c]

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal			0.518[b]	RACE (p=0.147)
(n=459)	≤18.6	0.93 (0.63,1.36)	0.705[c]	DRKYR (p=0.007)
	>18.6	1.10 (0.79,1.51)	0.581[c]	ALC (p=0.084)
h) Maximal			0.796[b]	ALC (p=0.128)
(n=644)	≤18.6	1.17 (0.89,1.55)	0.254[c]	DRKYR (p=0.017)
	>18.6	1.12 (0.87,1.44)	0.392[c]	

[a]Relative risk for a twofold increase in dioxin.
[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).
[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 9-34. (Continued)

Analysis of Positive Symptom Distress Index (SCL-90-R)

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	690	8.6	All Categories		0.076
Unknown	294	5.8	Unknown vs. Background	0.66 (0.38,1.15)	0.139
Low	171	12.3	Low vs. Background	1.50 (0.88,2.54)	0.135
High	167	10.8	High vs. Background	1.29 (0.74,2.26)	0.367
Total	1,322				

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	690	All Categories		0.076	--
Unknown	294	Unknown vs. Background	0.66 (0.38,1.15)	0.139	
Low	171	Low vs. Background	1.50 (0.88,2.54)	0.135	
High	167	High vs. Background	1.29 (0.74,2.26)	0.367	
Total	1,322				

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

In both the minimal and maximal unadjusted and adjusted analyses, the current dioxin-by-time since tour interaction and the association between current dioxin and the positive symptom distress index within each time stratum were nonsignificant (Table 9-34 [e-h]: $p>0.25$ for each analysis).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The unadjusted analysis with categorized current dioxin found a marginally significant difference in the percentage of Ranch Hands described as abnormal for the positive symptom distress index of the four current dioxin categories (Table 9-34 [i]: $p=0.076$). However, no significant differences were detected between the background group of Comparisons and any of the three categories of Ranch Hands. The percentages of participants with an abnormal positive symptom distress index for the background, unknown, low, and high current dioxin categories were 8.6, 5.8, 12.3, and 10.8 percent.

In the adjusted analysis, none of the candidate covariates were retained in the model; thus, the relative risks and associated p-values for the adjusted analysis (Table 9-34 [j]) are identical to the unadjusted results (Table 9-34 [i]).

Schizoid Score—MCMI

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

The schizoid score of the MCMI displayed a significant positive association with initial dioxin for both the unadjusted minimal and the unadjusted maximal analyses (Table 9-35 [a] and [b]: $p<0.001$ for both analyses). The unadjusted mean schizoid scores for the minimal cohort for the low, medium, and high initial dioxin categories were 22.9, 25.1, and 28.6. For the maximal cohort, the corresponding mean scores were 23.0, 24.3, and 27.0, respectively.

The adjusted analysis also displayed a significant positive association between the MCMI schizoid score and initial dioxin for both minimal and maximal cohorts (Table 9-35 [c] and [d]: $p=0.002$ for both analyses).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

In the unadjusted analysis based on current dioxin and time since tour, the minimal cohort displayed a marginally significant current dioxin-by-time interaction (Table 9-35 [e]: $p=0.070$). The schizoid score for Ranch Hands with 18.6 years or less since tour exhibited a nonsignificant positive association with current dioxin ($p=0.442$), and for Ranch Hands with time over 18.6 years there was a significant positive association ($p<0.001$). The unadjusted mean scores for the more than 18.6 years stratum for low and medium current dioxin were very similar (23.2 and 24.6). However, for Ranch Hands with high current dioxin, the mean schizoid score was much higher (32.5).

The unadjusted analysis under the maximal assumption also displayed a marginally significant current dioxin-by-time since tour interaction (Table 9-35 [f]: $p=0.054$). Similar to the minimal analysis, there was a nonsignificant positive association between the schizoid

TABLE 9-35.

Analysis of Schizoid Score (MCMI)

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Mean[a]	Slope (Std. Error)[b]	p-Value
a) Minimal	Low	129	22.9	0.077 (0.021)	<0.001
(n=514)	Medium	256	25.1		
(R^2=0.025)	High	129	28.6		
b) Maximal	Low	182	23.0	0.065 (0.016)	<0.001
(n=732)	Medium	368	24.3		
(R^2=0.023)	High	182	27.0		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Initial Dioxin	n	Adj. Mean[a]	Adj. Slope (Std. Error)[b]	p-Value	Covariate Remarks
c) Minimal	Low	128	22.8	0.068 (0.021)	0.002	EDUC (p=0.010)
(n=510)	Medium	254	24.4			
(R^2=0.037)	High	128	27.7			
d) Maximal	Low	179	23.9	0.051 (0.017)	0.002	EDUC (p=0.006)
(n=719)	Medium	362	23.9			AGE*ALC (p=0.037)
(R^2=0.046)	High	178	26.2			AGE*DRKYR (p=0.025)

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm schizoid score versus log_2 dioxin.
Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 9-35. (Continued)

Analysis of Schizoid Score (MCMI)

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Mean[a]/(n) Current Dioxin Low	Medium	High	Slope (Std. Error)[b]	p-Value
e) Minimal						0.070[c]
(n=514)	≤18.6	22.3	25.4	25.0	0.027 (0.034)	0.442[d]
(R^2=0.033)		(72)	(128)	(53)		
	>18.6	23.2	24.6	32.5	0.107 (0.028)	<0.001[d]
		(56)	(129)	(76)		
f) Maximal						0.054[c]
(n=732)	≤18.6	23.3	23.7	25.3	0.029 (0.024)	0.231[d]
(R^2=0.029)		(105)	(190)	(82)		
	>18.6	22.9	24.0	30.3	0.091 (0.021)	<0.001[d]
		(78)	(175)	(102)		

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Mean[a]/(n) Current Dioxin Low	Medium	High	Adj. Slope (Std. Error)[b]	p-Value	Covariate Remarks
g) Minimal						0.074[c]	RACE (p=0.128)
(n=510)	≤18.6	20.8	23.0	22.5	0.015 (0.034)	0.662[d]	EDUC (p=0.008)
(R^2=0.049)		(71)	(127)	(53)			
	>18.6	21.8	22.4	29.3	0.094 (0.028)	0.001[d]	
		(56)	(128)	(75)			
h) Maximal						0.044**[c]	CURR*TIME*DRKYR
(n=719)	≤18.6	24.0**	23.3**	24.6**	0.012 (0.025)**	0.615**[d]	(p=0.040)
(R^2=0.051)		(104)	(186)	(81)			EDUC (p=0.004)
	>18.6	23.4**	23.7**	29.1**	0.077 (0.022)**	<0.001**[d]	
		(77)	(172)	(99)			

[a]Transformed from natural logarithm scale.

[b]Slope and standard error based on natural logarithm schizoid score versus log_2 dioxin.

[c]Test of significance for homogeneity of slopes (current dioxin continuous, time categorized).

[d]Test of significance for slope equal to 0 (current dioxin continuous, time categorized).

**Log_2 (current dioxin)-by-time-by-covariate interaction ($0.01<p\leq0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of this interaction.

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 9-35. (Continued)

Analysis of Schizoid Score (MCMI)

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Mean[a]	Contrast	Difference of Means (95% C.I.)[e]	p-Value[f]
Background	781	23.7	All Categories		<0.001
Unknown	340	22.7	Unknown vs. Background	-1.1 --	0.229
Low	194	24.9	Low vs. Background	1.2 --	0.306
High	184	27.9	High vs. Background	4.2 --	<0.001
Total	1,499		(R^2=0.011)		

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Adj. Mean[a]	Contrast	Difference of Adj. Means (95% C.I.)[e]	p-Value[f]	Covariate Remarks
Background	775	23.7	All Categories		0.027	AGE*ALC (p=0.009)
Unknown	335	23.1	Unknown vs. Background	-0.6 --	0.522	AGE*DRKYR (p=0.017)
Low	190	24.4	Low vs. Background	0.7 --	0.519	ALC*EDUC
High	180	27.0	High vs. Background	3.4 --	0.006	(p=0.037)
Total	1,480		(R^2=0.036)			DRKYR*EDUC (p=0.027)

[a]Transformed from natural logarithm scale.

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

[f]p-value is based on difference of means on natural logarithm scale.

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

score and current dioxin for Ranch Hands with 18.6 years or less since tour (p=0.231) and a significant association for Ranch Hands with more than 18.6 years since tour (p<0.001). The unadjusted mean scores for the earlier tour stratum were nearly the same for low and medium current dioxin (22.9 and 24.0); but the mean score for high current dioxin was greater (30.3).

Consistent with the unadjusted analysis, the adjusted analysis based on the minimal assumption detected a current dioxin-by-time since tour interaction of borderline significance (Table 9-35 [g]: p=0.074). For the 18.6 years or less time stratum, the positive association between the schizoid score and current dioxin remained nonsignificant (p=0.662), while the positive association remained significant for the time greater than 18.6 years stratum (p=0.001).

The adjusted analysis for the maximal cohort detected a significant current dioxin-by-time-by-lifetime alcohol history interaction (Table 9-35 [h]: p=0.040). To examine this interaction, stratified analyses are presented for each lifetime alcohol history and time stratum.

For Ranch Hands with no drink-years, the current dioxin-by-time since tour interaction was not significant (Appendix Table H-1: p=0.136). There was a nonsignificant negative association between current dioxin and the schizoid score for the time less than or equal to 18.6 years stratum (p=0.734) and a significant positive association for the time over 18.6 years stratum (p=0.041). For Ranch Hands in the time over 18.6 years stratum, the adjusted mean schizoid scores were higher for Ranch Hands with low and high current dioxin than for those with medium current dioxin (low, 24.6; medium, 20.1; high, 31.4).

For Ranch Hands who had greater than 0 but less than 40 drink-years, the current dioxin-by-time since tour interaction was marginally significant (Appendix Table H-1: p=0.064). There was a nonsignificant positive association between current dioxin and the schizoid score for Ranch Hands with 18.6 years or less since tour (p=0.702) and a significant positive association for Ranch Hands with time over 18.6 years since tour (p=0.003). For the time greater than 18.6 years stratum, the adjusted mean schizoid scores for Ranch Hands with low and medium current dioxin were nearly the same (22.4 and 22.9, respectively), but the adjusted mean score for those with high current dioxin was much higher (28.7).

For Ranch Hands with greater than 40 drink-years, the current dioxin-by-time since tour interaction was nonsignificant (Appendix Table H-1: p=0.799) and the positive associations between current dioxin and the schizoid score were nonsignificant for both time strata (≤18.6, p=0.643; >18.6, p=0.317).

After deletion of the current dioxin-by-time-by-lifetime alcohol history interaction, the maximal adjusted analysis displayed a significant current dioxin-by-time since tour interaction (Table 9-35 [h]: p=0.044). The positive association between current dioxin and the schizoid score was nonsignificant for the time less than or equal to 18.6 years stratum (p=0.615). However, there was a significant positive association for Ranch Hands with time over 18.6 years (p<0.001). For Ranch Hands in the time over 18.6 years stratum, the adjusted mean schizoid scores for low and medium current dioxin were about the same (23.4 and 23.7) while the mean score was much higher for high current dioxin (29.1).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In the unadjusted analysis of categorized current dioxin, there was an overall significant difference among the mean schizoid scores of the four current dioxin categories (Table 9-35 [i]: $p<0.001$). The unadjusted mean schizoid scores for the background, unknown, low, and high categories were 23.7, 22.7, 24.9, and 27.9. The mean schizoid score for the Ranch Hands in the high current dioxin category was significantly higher than the mean score for the Comparisons in the background current dioxin category ($p<0.001$).

Similarly, in the adjusted analysis of the MCMI schizoid score, the simultaneous contrast of the four current dioxin categories was significant ($p=0.027$). Also, the mean schizoid score for the Ranch Hands in the high current dioxin category remained significantly higher than that of the Comparisons in the background category ($p=0.006$).

Avoidant Score—MCMI

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

The unadjusted analysis of the MCMI avoidant score displayed a significant positive association with initial dioxin for both the minimal and maximal cohorts (Table 9-36 [a] and [b]: $p<0.001$ for each analysis). The unadjusted means for the minimal cohort for the low, medium, and high initial dioxin categories were 15.0, 17.3, and 20.1. For the maximal cohort, the corresponding means were 16.1, 16.1, and 19.4, respectively.

The adjusted analysis of the minimal cohort detected a significant interaction between initial dioxin and education level (Table 9-36 [c]: $p=0.037$). To examine this interaction, separate analyses were performed for each education stratum (Appendix Table H-1). The stratified analyses displayed a nonsignificant positive association between initial dioxin and the MCMI avoidant score for Ranch Hands with a high school level education ($p=0.249$). For Ranch Hands with a college level education, there was a significant positive association between the avoidant score and initial dioxin ($p<0.001$). The adjusted mean scores for this stratum increased steadily for increasing levels of initial dioxin (low, 10.5; medium, 13.4; high, 17.5).

After deletion of the initial dioxin-by-education interaction, the adjusted minimal analysis detected a positive association between initial dioxin and the MCMI avoidant score (Table 9-36 [c]: $p=0.003$). Concurrently, the maximal adjusted analysis also displayed a significant positive association between the MCMI avoidant score and initial dioxin (Table 9-36 [d]: $p=0.038$).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

In the unadjusted analysis of the MCMI avoidant score with current dioxin and time since tour under the minimal assumption, the interaction between current dioxin and time was significant (Table 9-36 [e]: $p=0.028$). A nonsignificant positive association was found for those Ranch Hands with time less than or equal to 18.6 years ($p=0.624$). For Ranch Hands with time over 18.6 years, there was a significant positive association between the avoidant

TABLE 9-36.

Analysis of Avoidant Score (MCMI)

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Mean[a]	Slope (Std. Error)[b]	p-Value
a) Minimal	Low	129	15.0	0.110 (0.029)	<0.001
(n=514)	Medium	256	17.3		
(R^2=0.027)	High	129	20.1		
b) Maximal	Low	182	16.1	0.082 (0.021)	<0.001
(n=732)	Medium	368	16.1		
(R^2=0.020)	High	182	19.4		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Initial Dioxin	n	Adj. Mean[a]	Adj. Slope (Std. Error)[b]	p-Value	Covariate Remarks
c) Minimal	Low	128	14.9**	0.086 (0.029)**	0.003**	INIT*EDUC (p=0.037)
(n=505)	Medium	250	16.1**			DRKYR (p=0.083)
(R^2=0.097)	High	127	18.5**			
d) Maximal	Low	179	17.5	0.046 (0.022)	0.038	DRKYR (p=0.052)
(n=719)	Medium	362	15.6			EDUC (p<0.001)
(R^2=0.066)	High	178	17.8			

[a]Transformed from natural logarithm (X + 1) scale.

[b]Slope and standard error based on natural logarithm (avoidant score + 1) versus log_2 dioxin.

**Log_2 (initial dioxin)-by-covariate interaction ($0.01<p\leq0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of this interaction.

Note: Minimal--Low: 52 93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 9-36. (Continued)

Analysis of Avoidant Score (MCMI)

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Mean[a]/(n) Current Dioxin Low	Medium	High	Slope (Std. Error)[b]	p-Value
e) Minimal						0.028[c]
(n=514)	≤18.6	16.0	16.3	17.0	0.023 (0.047)	0.624[d]
(R^2=0.036)		(72)	(128)	(53)		
	>18.6	15.0	17.1	23.7	0.158 (0.039)	<0.001[d]
		(56)	(129)	(76)		
f) Maximal						0.076[c]
(n=732)	≤18.6	15.1	16.0	17.6	0.033 (0.033)	0.317[d]
(R^2=0.024)		(105)	(190)	(82)		
	>18.6	16.8	16.8	20.3	0.112 (0.029)	<0.001[d]
		(78)	(175)	(102)		

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Mean[a]/(n) Current Dioxin Low	Medium	High	Adj. Slope (Std. Error)[b]	p-Value	Covariate Remarks
g) Minimal						0.029[c]	DRKYR (p=0.096)
(n=505)	≤18.6	15.9	15.3	15.9	0.003 (0.046)	0.951[d]	EDUC (p<0.001)
(R^2=0.098)		(71)	(126)	(53)			
	>18.6	14.9	15.8	22.0	0.133 (0.038)	<0.001[d]	
		(56)	(125)	(74)			
h) Maximal						0.045[c]	DRKYR (p=0.061)
(n=719)	≤18.6	16.3	15.6	16.5	-0.006 (0.033)	0.848[d]	EDUC (p=0.001)
(R^2=0.073)		(104)	(186)	(81)			
	>18.6	17.5	16.4	18.4	0.081 (0.029)	0.006[d]	
		(77)	(172)	(99)			

[a]Transformed from natural logarithm (X + 1) scale.
[b]Slope and standard error based on natural logarithm (avoidant score + 1) versus log_2 dioxin.
[c]Test of significance for homogeneity of slopes (current dioxin continuous, time categorized).
[d]Test of significance for slope equal to 0 (current dioxin continuous, time categorized).
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 9-36. (Continued)

Analysis of Avoidant Score (MCMI)

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Mean[a]	Contrast	Difference of Means (95% C.I.)[e]	p-Value[f]
Background	781	16.3	All Categories		0.035
Unknown	340	15.0	Unknown vs. Background	-1.3 --	0.164
Low	194	16.8	Low vs. Background	0.5 --	0.667
High	184	19.1	High vs. Background	2.8 --	0.032
Total	1,499		(R^2=0.006)		

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Adj. Mean[a]	Contrast	Difference of Adj. Means (95% C.I.)[e]	p-Value[f]	Covariate Remarks
Background	775	16.2	All Categories		0.351	DRKYR (p=0.007) EDUC (p<0.001)
Unknown	335	15.5	Unknown vs. Background	-0.8 --	0.406	
Low	190	16.3	Low vs. Background	0.1 --	0.957	
High	180	18.0	High vs. Background	1.8 --	0.166	
Total	1,480		(R^2=0.029)			

[a]Transformed from natural logarithm (X + 1) scale.

[e]Difference of means after transformation to original scale; confidence interval on difference of means not given because analysis was performed on natural logarithm (X + 1) scale.

[f]p-value is based on difference of means on natural logarithm (X + 1) scale.

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

score and current dioxin ($p<0.001$). For this time stratum, the unadjusted mean scores for low, medium, and high current dioxin were 15.0, 17.1, and 23.7.

The unadjusted maximal analysis detected a marginally significant current dioxin-by-time since tour interaction (Table 9-36 [f]: $p=0.076$). The positive association between current dioxin and the avoidant score was nonsignificant for the time less than or equal to 18.6 years time stratum ($p=0.317$), but there was a significant positive association for Ranch Hands with time over 18.6 years ($p<0.001$). The unadjusted means for the time over 18.6 years stratum for low, medium, and high current dioxin were 16.8, 16.8, and 20.3.

The adjustment for lifetime alcohol history and education had little effect on the analysis of the minimal cohort. The current dioxin-by-time since tour interaction remained significant (Table 9-36 [g]: $p=0.029$). The time less than or equal to 18.6 years stratum displayed a nonsignificant positive association between the avoidant score and current dioxin ($p=0.951$), while for those Ranch Hands with time over 18.6 years, there was a significant positive association ($p<0.001$).

In the maximal cohort analysis, the adjustment for lifetime alcohol history and education caused the current dioxin-by-time since tour interaction to become significant (Table 9-36 [h]: $p=0.045$). For Ranch Hands in the time less than or equal to 18.6 years stratum, there was a nonsignificant negative association between the MCMI avoidant score and current dioxin ($p=0.848$); the positive association for the time over 18.6 years stratum remained significant ($p=0.006$).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The unadjusted analysis of categorized current dioxin detected a significant overall difference in the mean avoidant scores of the four current dioxin categories (Table 9-36 [i]: $p=0.035$). The unadjusted mean scores for the background, unknown, low, and high categories were 16.3, 15.0, 16.8, and 19.1. There were no significant differences found between the Comparisons in the background category and the Ranch Hands in either the unknown or low current dioxin category ($p=0.164$ and $p=0.667$, respectively). The mean avoidant score was found to be significantly higher for the Ranch Hands in the high current dioxin category than for the the Comparisons in the background category ($p=0.032$).

After adjusting for lifetime alcohol history and education, the analysis of the four current dioxin categories found no significant differences in the mean avoidant scores of the four categories (Table 9-36 [j]: $p>0.15$ for each contrast).

Dependent Score—MCMI

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

The MCMI dependent score displayed a significant positive association with initial dioxin for both the unadjusted minimal and the unadjusted maximal analyses (Table 9-37 [a] and [b]: $p=0.027$ and $p=0.009$). The unadjusted mean dependent scores for the minimal cohort were nearly the same for the low and medium initial dioxin categories (40.8 and 40.7), but the mean score was larger for the high initial dioxin category (43.2). For the maximal

TABLE 9-37.

Analysis of Dependent Score (MCMI)

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Mean[a]	Slope (Std. Error)[b]	p-Value
a) Minimal	Low	129	40.8	0.123 (0.056)	0.027
(n=514)	Medium	256	40.7		
(R^2=0.009)	High	129	43.2		
b) Maximal	Low	182	38.8	0.108 (0.041)	0.009
(n=732)	Medium	368	40.6		
(R^2=0.009)	High	182	43.1		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Initial Dioxin	n	Adj. Mean[a]	Adj. Slope (Std. Error)[b]	p-Value	Covariate Remarks
c) Minimal	Low	128	41.6	0.137 (0.058)	0.018	AGE*DRKYR (p=0.005)
(n=505)	Medium	250	41.5			RACE*EDUC (p=0.046)
(R^2=0.049)	High	127	44.7			
d) Maximal	Low	179	42.2	0.091 (0.044)	0.037	EDUC (p=0.007)
(n=719)	Medium	362	41.9			AGE*DRKYR (p=0.005)
(R^2=0.043)	High	178	44.7			ALC*RACE(p=0.032)

[a]Transformed from square root scale.

[b]Slope and standard error based on square root dependent score versus log_2 dioxin.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 9-37. (Continued)

Analysis of Dependent Score (MCMI)

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Mean[a]/(n) Current Dioxin Low	Medium	High	Slope (Std. Error)[b]	p-Value
e) Minimal						0.401[c]
(n=514)	≤18.6	41.4	40.5	41.1	0.060 (0.091)	0.506[d]
(R^2=0.010)		(72)	(128)	(53)		
	>18.6	42.3	40.4	43.9	0.159 (0.074)	0.033[d]
		(56)	(129)	(76)		
f) Maximal						0.541[c]
(n=732)	≤18.6	39.3	39.2	43.9	0.077 (0.064)	0.231[d]
(R^2=0.010)		(105)	(190)	(82)		
	>18.6	38.8	41.5	43.0	0.129 (0.057)	0.023[d]
		(78)	(175)	(102)		

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Mean[a]/(n) Current Dioxin Low	Medium	High	Adj. Slope (Std. Error)[b]	p-Value	Covariate Remarks
g) Minimal						0.477[c]	AGE*DRKYR (p=0.006)
(n=505)	≤18.6	41.9	41.6	43.2	0.097 (0.093)	0.300[d]	RACE*EDUC (p=0.039)
(R^2=0.051)		(71)	(126)	(53)			
	>18.6	42.6	41.0	44.7	0.179 (0.077)	0.020[d]	
		(56)	(125)	(74)			
h) Maximal						0.347[c]	EDUC (p=0.006)
(n=719)	≤18.6	42.5	40.9	45.5	0.051 (0.066)	0.443[d]	AGE*DRKYR (p=0.005)
(R^2=0.045)		(104)	(186)	(81)			ALC*RACE (p=0.030)
	>18.6	40.9	42.9	44.7	0.131 (0.059)	0.026[d]	
		(77)	(172)	(99)			

[a]Transformed from square root scale.

[b]Slope and standard error based on square root dependent score versus log_2 dioxin.

[c]Test of significance for homogeneity of slopes (current dioxin continuous, time categorized).

[d]Test of significance for slope equal to 0 (current dioxin continuous, time categorized).

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 9-37. (Continued)

Analysis of Dependent Score (MCMI)

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Mean[a]	Contrast	Difference of Means (95% C.I.)[e]	p-Value[f]
Background	781	42.1	All Categories		0.033
Unknown	340	39.3	Unknown vs. Background	-2.8 --	0.032
Low	194	39.2	Low vs. Background	-2.9 --	0.066
High	184	43.4	High vs. Background	1.3 --	0.451
Total	1,499		(R^2=0.006)		

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Adj. Mean[a]	Contrast	Difference of Adj. Means (95% C.I.)[e]	p-Value[f]	Covariate Remarks
Background	775	42.2	All Categories		0.115	EDUC (p<0.001) ALC*DRKYR (p=0.004)
Unknown	335	40.2	Unknown vs. Background	-2.0 --	0.133	
Low	190	38.8	Low vs. Background	-3.4 --	0.037	
High	180	42.3	High vs. Background	0.1 --	0.944	
Total	1 480		(R^2=0.022)			

[a]Transformed from square root scale.

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

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

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

cohort, the corresponding mean scores for the low, medium, and high initial dioxin categories were 38.8, 40.6, and 43.1.

The adjusted analysis also displayed a significant positive association between the MCMI dependent score and initial dioxin for both the minimal and maximal cohorts (Table 9-37 [c] and [d]: p=0.018 and p=0.037).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

In the unadjusted analysis, under both the minimal and maximal assumptions, the interaction between current dioxin and time since tour was not significant (Table 9-37 [e] and [f]: p=0.401 and p=0.541, respectively); thus, the slopes for the two time strata did not differ significantly. Under the minimal assumption, a significant positive association was found between the MCMI dependent score and current dioxin for Ranch Hands with time over 18.6 years (Table 9-37 [e]: p=0.033). For these Ranch Hands, the mean dependent scores for low, medium, and high current dioxin were 42.3, 40.4, and 43.9.

Based on the maximal assumption, the unadjusted analysis detected a significant positive association between the MCMI dependent score and current dioxin for Ranch Hands with time over 18.6 years (Table 9-37 [f]: p=0.023). The mean dependent scores became larger for increasing levels of current dioxin for Ranch Hands in this time stratum (low, 38.8; medium, 41.5; high 43.0).

In the adjusted analysis based on both the minimal and maximal assumptions, the interaction between current dioxin and time was nonsignificant (Table 9-37 [g] and [h]: p=0.477 and p=0.347, respectively). In both the minimal and maximal cohorts, there were significant positive associations between current dioxin and the dependent score for the time over 18.6 years stratum (p=0.020 and p=0.026, respectively).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In the unadjusted analysis, the mean MCMI dependent scores were significantly different for the four current dioxin categories (Table 9-37 [i]: p=0.033). The unadjusted mean scores for the background, unknown, low, and high current dioxin categories were 42.1, 39.3, 39.2, and 43.4. The mean dependent score for the Ranch Hands in the unknown current dioxin category was significantly lower than the mean score for the Comparisons in the background category (p=0.032). There was also a marginally significant difference between the mean dependent scores of the Comparisons and the mean score of the Ranch Hands in the low current dioxin level category (p=0.066) with the Ranch Hands having a lower mean score than the Comparisons. The mean score of the Ranch Hands in the high category did not differ significantly from that of the Comparisons in the background category (p=0.451).

After adjusting for education and a current alcohol use-by-lifetime alcohol history interaction, the analysis of categorized current dioxin did not find any significant differences in the mean dependent scores of the four current dioxin categories (Table 9-37 [j]: p=0.115). However, the individual analysis of the low versus background categories found the mean

dependent score of the Ranch Hands in the low current dioxin category to be significantly lower than that of the Comparisons in the background category (p=0.037).

Histrionic Score—MCMI

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

In the unadjusted analysis of the MCMI histrionic score, there was a significant negative association with initial dioxin under both the minimal and the maximal assumptions (Table 9-38 [a] and [b]: p=0.003 and p=0.002). In the minimal cohort, the unadjusted mean histrionic scores for the low, medium, and high initial dioxin categories were 63.9, 63.4, and 59.8. In the maximal cohort, the corresponding mean scores were 64.1, 63.9, and 60.9, respectively.

After adjusting for covariate information, a significant negative association remained between initial dioxin and the MCMI histrionic score in both the minimal and maximal cohorts (Table 9-38 [c] and [d]: p=0.011 and p=0.037).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

In the unadjusted analysis of the MCMI histrionic score with current dioxin and time since tour, there was a marginally significant current dioxin-by-time interaction under both the minimal and maximal assumptions (Table 9-38 [e] and [f]: p=0.099 and p=0.073). For the minimal cohort, the negative association between current dioxin and the MCMI histrionic score was not significant for those Ranch Hands with 18.6 years or less since their tour (p=0.616), but the negative association was significant for the time over 18.6 years stratum (p=0.001). For the time over 18.6 years stratum, the unadjusted mean histrionic score for low, medium, and high current dioxin were 65.4, 62.7, and 58.4.

The unadjusted maximal analysis also found a nonsignificant association between current dioxin and the histrionic score for the time less than or equal to 18.6 years stratum (Table 9-38 [f]: p=0.513), and a significant negative association for the time over 18.6 years stratum (p<0.001). The unadjusted mean scores for the time over 18.6 years stratum were nearly the same for low and medium current dioxin (64.0 and 64.1), while the mean score for high current dioxin was lower (59.8).

After adjusting for age, race, lifetime alcohol history, and education, the analysis of the minimal cohort detected a nonsignificant current dioxin-by-time since tour interaction (Table 9-38 [g]: p=0.112). For the time over 18.6 years stratum, there was a significant negative association between current dioxin and the histrionic score (p=0.006).

The adjusted analysis of the maximal cohort displayed a significant current dioxin-by-time-by-race interaction (Table 9-38 [h]: p=0.009). To investigate this interaction, separate analyses are presented for each race and time stratum. The analysis of the Black stratum exhibited a significant current dioxin-by-time since tour interaction (Appendix Table H-1: p=0.003). Within the time less than or equal to 18.6 years stratum, there was a significant positive association between current dioxin and the histrionic score (p=0.001). The adjusted mean scores for this stratum for low, medium, and high current dioxin were 57.6, 72.4, and

TABLE 9-38.

Analysis of Histrionic Score (MCMI)

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Mean[a]	Slope (Std. Error)[b]	p-Value
a) Minimal	Low	129	63.9	-192.7 (63.7)	0.003
(n=514)	Medium	256	63.4		
(R^2=0.018)	High	129	59.8		
b) Maximal	Low	182	64.1	-150.8 (47.9)	0.002
(n=732)	Medium	368	63.9		
(R^2=0.013)	High	182	60.9		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Initial Dioxin	n	Adj. Mean[a]	Adj. Slope (Std. Error)[b]	p-Value	Covariate Remarks
c) Minimal	Low	128	68.1	-166.6 (65.4)	0.011	AGE (p=0.043)
(n=505)	Medium	250	68.4			RACE (p<0.001)
(R^2=0.089)	High	127	65.1			DRKYR (p=0.040)
						EDUC (p<0.001)
d) Maximal	Low	179	67.6	-105.1 (50.2)	0.037	AGE (p=0.047)
(n=719)	Medium	362	68.4			RACE (p<0.001)
(R^2=0.074)	High	178	66.2			DRKYR (p=0.028)
						EDUC (p<0.001)

[a]Transformed from square scale.

[b]Slope and standard error based on square histrionic score versus log_2 dioxin.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 9-38. (Continued)

Analysis of Histrionic Score (MCMI)

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Mean[a]/(n) Current Dioxin Low	Medium	High	Slope (Std. Error)[b]	p-Value
e) Minimal						0.099[c]
(n=514)	≤18.6	63.8	63.5	61.6	-52.0 (103.7)	0.616[d]
(R^2=0.022)		(72)	(128)	(53)		
	>18.6	65.4	62.7	58.4	-274.0 (85.0)	0.001[d]
		(56)	(129)	(76)		
f) Maximal						0.073[c]
(n=732)	≤18.6	63.5	64.1	62.3	-48.6 (74.3)	0.513[d]
(R^2=0.017)		(105)	(190)	(82)		
	>18.6	64.0	64.1	59.8	-226.9 (65.7)	<0.001[d]
		(78)	(175)	(102)		

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Mean[a]/(n) Current Dioxin Low	Medium	High	Adj. Slope (Std. Error)[b]	p-Value	Covariate Remarks
g) Minimal						0.112[c]	AGE (p=0.064)
(n=505)	≤18.6	68.3	68.7	66.8	-32.0 (105.0)	0.760[d]	RACE (p<0.001)
(R^2=0.094)		(71)	(126)	(53)			DRKYR (p=0.043)
	>18.6	69.5	67.5	63.9	-240.6 (86.4)	0.006[d]	EDUC (p<0.001)
		(56)	(125)	(74)			
h) Maximal						****	CURR*TIME*RACE (p=0.009)
(n=719)	≤18.6	****	****	****	****	****	DRKYR (p=0.055)
(R^2=0.099)		(104)	(186)	(81)			EDUC (p<0.001)
	>18.6	****	****	****	****	****	AGE*RACE (p=0.036)
		(77)	(172)	(99)			

[a]Transformed from square scale.

[b]Slope and standard error based on square histrionic score versus log_2 dioxin.

[c]Test of significance for homogeneity of slopes (current dioxin continuous, time categorized).

[d]Test of significance for slope equal to 0 (current dioxin continuous, time categorized).

****Log_2 (current dioxin)-by-time-by-covariate interaction ($p \leq 0.01$); adjusted mean, adjusted slope, standard error, and p-value not presented.

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 9-38. (Continued)

Analysis of Histrionic Score (MCMI)

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Mean[a]	Contrast	Difference of Means (95% C.I.)[e]	p-Value[f]
Background	781	64.4	All Categories		0.014
Unknown	340	64.6	Unknown vs. Background	0.2 --	0.806
Low	194	63.2	Low vs. Background	-1.2 --	0.287
High	184	60.9	High vs. Background	-3.5 --	0.003
Total	1,499		(R^2=0.007)		

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Adj. Mean[a]	Contrast	Difference of Adj. Means (95% C.I.)[e]	p-Value[f]	Covariate Remarks
Background	775	66.8	All Categories		0.132	RACE (p<0.001)
						AGE*DRKYR (p=0.021)
Unknown	335	66.7	Unknown vs. Background	-0.1 --	0.896	ALC*EDUC (p=0.036)
Low	190	66.0	Low vs. Background	-0.7 --	0.492	DRKYR*EDUC (p=0.006)
High	180	64.2	High vs. Background	-2.6 --	0.020	
Total	1,480		(R^2=0.053)			

[a]Transformed from square scale.

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

[f]p-value is based on difference of means on square scale.

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

83.2. For the time over 18.6 years stratum, there was a nonsignificant negative association (p=0.656).

The analysis of the non-Black stratum detected a marginally significant current dioxin-by-time since tour interaction (Appendix Table H-1: p=0.057). For the time less than or equal to 18.6 years stratum, there was a nonsignificant negative association between current dioxin and the MCMI histrionic score (p=0.871), but there was a significant negative association for those Ranch Hands with time since tour greater than 18.6 years (p=0.003).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In the unadjusted analysis of the MCMI histrionic score, the overall contrast of the four current dioxin categories was significant (Table 9-38 [i]: p=0.014). The unadjusted mean histrionic scores for the background, unknown, low, and high current dioxin categories were 64.4, 64.6, 63.2, and 60.9. The contrasts of the mean histrionic scores of the unknown versus background and low versus background current dioxin categories were not statistically significant (p=0.806 and p=0.287). However, the mean score of the Ranch Hands in the high current dioxin category was significantly lower than the mean score of the Comparisons in the background category (p=0.003).

After adjusting for race, an age-by-lifetime alcohol history interaction, a current alcohol use-by-education interaction, and a lifetime alcohol history-by-education interaction, the analysis did not detect a significant overall difference among the mean histrionic scores of the four current dioxin categories (Table 9-38 [j]: p=0.132). However, the mean histrionic score for the Ranch Hands in the high current dioxin category was significantly lower than that of the Comparisons in the background category (p=0.020).

Narcissistic Score—MCMI

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

The unadjusted analysis of both the minimal and the maximal cohorts detected a significant negative association between initial dioxin and the MCMI narcissistic score (Table 9-39 [a] and [b]: p=0.007 and p=0.003, respectively). The unadjusted mean narcissistic scores for the minimal cohort for the low, medium, and high initial dioxin categories were 63.5, 65.3, and 60.8. The corresponding unadjusted mean scores for the maximal cohort were 65.1, 65.0, and 62.0, respectively.

After the adjustment for race, current alcohol use, and education, the minimal analysis detected a marginally significant negative association between initial dioxin and the MCMI narcissistic score (Table 9-39 [c]: p=0.053). The adjustment for covariate information did not affect the significance of the negative association in the maximal analysis (Table 9-39 [d]: p=0.012).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

In the unadjusted analysis, under both the minimal and maximal assumptions, the interactions between current dioxin and time since tour were not significant (Table 9-39 [e]

TABLE 9-39.

Analysis of Narcissistic Score (MCMI)

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Mean	Slope (Std. Error)[a]	p-Value
a) Minimal	Low	129	63.5	-1.454 (0.534)	0.007
(n=514)	Medium	256	65.3		
(R^2=0.014)	High	129	60.8		
b) Maximal	Low	182	65.1	-1.206 (0.403)	0.003
(n=732)	Medium	368	65.0		
(R^2=0.012)	High	182	62.0		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Initial Dioxin	n	Adj. Mean	Adj. Slope (Std. Error)[a]	p-Value	Covariate Remarks
c) Minimal	Low	128	66.5	-1.051 (0.542)	0.053	RACE (p=0.008)
(n=508)	Medium	252	69.1			ALC (p=0.080)
(R^2=0.040)	High	128	65.2			EDUC (p=0.028)
d) Maximal	Low	179	68.5	-1.082 (0.430)	0.012	DRKYR (p=0.140)
(n=719)	Medium	362	68.9			AGE*EDUC (p=0.045)
(R^2=0.048)	High	178	66.2			ALC*RACE (p=0.037)

[a]Slope and standard error based on narcissistic score versus log_2 dioxin.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 9-39. (Continued)

Analysis of Narcissistic Score

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Mean/(n) Current Dioxin Low	Medium	High	Slope (Std. Error)[a]	p-Value
e) Minimal						0.217[b]
(n=514)	≤18.6	65.2	65.9	63.1	-0.352 (0.868)	0.686[c]
(R^2=0.021)		(72)	(128)	(53)		
	>18.6	62.1	64.1	59.5	-1.741 (0.712)	0.015[c]
		(56)	(129)	(76)		
f) Maximal						0.153[b]
(n=732)	≤18.6	65.0	66.3	63.7	-0.376 (0.625)	0.548[c]
(R^2=0.017)		(105)	(190)	(82)		
	>18.6	64.7	63.8	60.8	-1.569 (0.553)	0.005[c]
		(78)	(175)	(102)		

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Mean/(n) Current Dioxin Low	Medium	High	Adj. Slope (Std. Error)[a]	p-Value	Covariate Remarks
g) Minimal						0.223[b]	RACE (p=0.005)
(n=508)	≤18.6	68.4	69.8	67.5	0.056 (0.869)	0.948[c]	ALC (p=0.078)
(R^2=0.049)		(71)	(127)	(53)			EDUC (p=0.022)
	>18.6	65.3	67.8	63.8	-1.307 (0.718)	0.069[c]	
		(56)	(126)	(75)			
h) Maximal						0.080[b]	AGE*EDUC (p=0.042)
(n=719)	≤18.6	68.2	70.0	68.0	-0.055 (0.649)	0.933[c]	DRKYR*RACE (p=0.022)
(R^2=0.055)		(104)	(186)	(81)			
	>18.6	68.5	67.5	64.8	-1.517 (0.575)	0.009[c]	
		(77)	(172)	(99)			

[a]Slope and standard error based on narcissistic score versus log_2 dioxin.

[b]Test of significance for homogeneity of slopes (current dioxin continuous, time categorized).

[c]Test of significance for slope equal to 0 (current dioxin continuous, time categorized).

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 9-39. (Continued)

Analysis of Narcissistic Score (MCMI)

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Mean	Contrast	Difference of Means (95% C.I.)	p-Value
Background	781	64.0	All Categories		0.025
Unknown	340	66.0	Unknown vs. Background	2.0 (0.0,3.9)	0.048
Low	194	65.5	Low vs. Background	1.5 (-0.9,3.9)	0.225
High	184	62.1	High vs. Background	-1.9 (-4.4,0.5)	0.122
Total	1,499		(R^2=0.006)		

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Adj. Mean	Contrast	Difference of Adj. Means (95% C.I.)	p-Value	Covariate Remarks
Background	775	66.7	All Categories		0.084	RACE (p<0.001) DRKYR (p=0.078) EDUC (p=0.002)
Unknown	335	68.5	Unknown vs. Background	1.8 (-0.2,3.7)	0.075	
Low	190	68.5	Low vs. Background	1.8 (-0.6,4.2)	0.145	
High	180	65.6	High vs. Background	-1.2 (-3.6,1.3)	0.361	
Total	1,480		(R^2=0.021)			

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

and [f]: p=0.217 and p=0.153, respectively). Under the minimal assumption, a significant negative association between current dioxin and the narcissistic score was found for Ranch Hands with time over 18.6 years (Table 9-39 [e]: p=0.015). For these Ranch Hands, the mean narcissistic scores for low, medium, and high current dioxin were 62.1, 64.1, and 59.5.

Under the maximal assumption, the unadjusted analysis detected a significant negative association between current dioxin and the narcissistic score for Ranch Hands with over 18.6 years since tour (Table 9-39 [f]: p=0.005). The unadjusted mean scores for these Ranch Hands decreased as current dioxin increased (low, 64.7; medium, 63.8; high, 60.8).

After adjusting for race, current alcohol use, and education, the minimal analysis displayed a nonsignificant current dioxin-by-time since tour interaction (Table 9-39 [g]: p=0.223). For Ranch Hands with time over 18.6 years, there was a marginally significant negative association between current dioxin and the MCMI narcissistic score (p=0.069).

After adjusting for an age-by-education interaction and a lifetime alcohol history-by-race interaction, the current dioxin-by-time since tour interaction was marginally significant for the maximal cohort (Table 9-39 [h]: p=0.080). For those Ranch Hands with time less than or equal to 18.6 years, there was a nonsignificant positive association between current dioxin and the narcissistic score (p=0.933). However, there was a significant negative association for Ranch Hands with over 18.6 years since their tour (p=0.009).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The analysis of categorized current dioxin detected a significant difference in the mean narcissistic scores of the four current dioxin categories (Table 9-39 [i]: p=0.025). The unadjusted mean scores for the background, unknown, low, and high current dioxin categories were 64.0, 66.0, 65.5, and 62.1. The mean narcissistic score for Ranch Hands in the unknown category was significantly higher than the mean score for Comparisons in the background category (p=0.048). Neither the low versus background nor the high versus background contrast was significant (p=0.225 and p=0.122).

After adjusting for race, lifetime alcohol history, and education, there was a marginally significant difference in the mean narcissistic scores of the four current dioxin categories (Table 9-39 [j]: p=0.084). The adjusted mean narcissistic scores for the background, unknown, low, and high current dioxin categories were 66.7, 68.5, 68.5, and 65.6. A marginally significant difference was detected between the mean score of Comparisons in the background category and Ranch Hands in the unknown category (p=0.075) with the Ranch Hands having a higher mean narcisstic score. No other significant differences in mean narcissistic scores were found (low versus background: p=0.145; high versus background: p=0.361).

Antisocial Score—MCMI

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

In the unadjusted analysis of the MCMI antisocial score, there was a nonsignificant association with initial dioxin under the minimal and maximal assumptions (Table 9-40 [a] and [b]: p=0.417 and p=0.643).

In the adjusted analysis, there were significant interactions between initial dioxin and current alcohol use under both the minimal and the maximal assumptions (Table 9-40 [c] and [d]: p=0.022 and p=0.005). To examine these interactions, associations between the antisocial score and initial dioxin are presented separately for each current alcohol use stratum.

In the minimal analysis, there was a nonsignificant negative association between initial dioxin and the antisocial score for Ranch Hands who had less than one drink per day and a nonsignificant positive association for those who drank between one and four drinks per day (Appendix Table H-1: p=0.685 and p=0.513). For those who drank more than four drinks per day, there was a significant negative association (p=0.023). Within this stratum, the adjusted mean antisocial scores for the low, medium, and high initial dioxin categories were 54.2, 38.6, and 25.2. After deletion of the initial dioxin-by-current alcohol use from the model, there was a nonsignificant negative association between initial dioxin and the antisocial score for the minimal cohort (Table 9-40 [c]: p=0.238).

Under the maximal assumption, there was a nonsignificant negative association between initial dioxin and the antisocial score for Ranch Hands who drank less than one drink per day and for Ranch Hands who drank between one and four drinks per day (Appendix Table H-1: p=0.993 and p=0.642, respectively). For Ranch Hands who drank more than four drinks per day, there was a significant negative association between initial dioxin and the MCMI antisocial score (p<0.001). The adjusted mean scores for this stratum decreased steadily for increasing levels of initial dioxin (low, 82.6; medium, 65.5; high, 37.5).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

In both the unadjusted and adjusted minimal and maximal analyses, the current dioxin-by-time since tour interactions and the associations between current dioxin and the MCMI antisocial score within each time stratum were nonsignificant (Table 9-40 [e-h]: p>0.25 for each analysis).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The unadjusted analysis of the four current dioxin categories detected a marginally significant difference among the mean antisocial scores of the four categories (Table 9-40 [i]: p=0.074). The unadjusted mean scores for the background, unknown, low, and high current dioxin categories were 59.6, 61.6, 63.3, and 61.2. The mean antisocial score of the Ranch Hands in the low current dioxin category was significantly higher than the mean score of the Comparisons in the background category (p=0.016).

TABLE 9-40.

Analysis of Antisocial Score (MCMI)

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Mean	Slope (Std. Error)[a]	p-Value
a) Minimal	Low	129	60.3	-0.557 (0.685)	0.417
(n=514)	Medium	256	62.7		
(R^2=0.001)	High	129	61.0		
b) Maximal	Low	182	60.6	-0.236 (0.508)	0.643
(n=732)	Medium	368	62.2		
(R^2<0.001)	High	182	61.1		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Initial Dioxin	n	Adj. Mean	Adj. Slope (Std. Error)[a]	p-Value	Covariate Remarks
c) Minimal	Low	129	60.3**	-0.860 (0.727)**	0.238**	INIT*ALC (p=0.022)
(n=509)	Medium	252	62.1**			AGE*ALC (p=0.008)
(R^2=0.039)	High	128	60.1**			ALC*RACE (p=0.007)
						ALC*DRKYR (p=0.035)
d) Maximal	Low	180	****	****	****	INIT*ALC (p=0.005)
(n=724)	Medium	365	****			AGE (p=0.048)
(R^2=0.021)	High	179	****			DRKYR (p=0.022)

[a]Slope and standard error based on antisocial score versus log_2 dioxin.

**Log_2 (initial dioxin)-by-covariate interaction ($0.01<p\leq0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of this interaction.

****Log_2 (initial dioxin)-by-covariate interaction ($p\leq0.01$); adjusted mean, adjusted slope, standard error, and p-value not presented.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 9-40. (Continued)

Analysis of Antisocial Score (MCMI)

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Mean/(n) Current Dioxin Low	Medium	High	Slope (Std. Error)[a]	p-Value
e) Minimal						0.323[b]
(n=514)	≤18.6	61.2	63.4	64.0	0.526 (1.116)	0.638[c]
(R^2=0.006)		(72)	(128)	(53)		
	>18.6	58.6	61.6	60.0	-0.901 (0.915)	0.325[c]
		(56)	(129)	(76)		
f) Maximal						0.378[b]
(n=732)	≤18.6	60.7	63.6	62.3	0.450 (0.789)	0.568[c]
(R^2=0.004)		(105)	(190)	(82)		
	>18.6	59.7	61.0	60.3	-0.478 (0.698)	0.493[c]
		(78)	(175)	(102)		

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Mean/(n) Current Dioxin Low	Medium	High	Adj. Slope (Std. Error)[a]	p-Value	Covariate Remarks
g) Minimal						0.407[b]	DRKYR (p=0.056)
(n=509)	≤18.6	61.7	63.5	63.9	0.428 (1.145)	0.709[c]	AGE*ALC (p=0.043)
(R^2=0.025)		(72)	(127)	(53)			
	>18.6	57.9	61.7	60.4	-0.771 (0.951)	0.418[c]	
		(56)	(126)	(75)			
h) Maximal						0.380[b]	AGE (p=0.080)
(n=724)	≤18.6	60.8	63.6	61.8	0.162 (0.807)	0.841[c]	DRKYR (p=0.028)
(R^2=0.013)		(104)	(189)	(81)			
	>18.6	60.1	61.5	59.5	-0.765 (0.718)	0.286[c]	
		(77)	(173)	(100)			

[a]Slope and standard error based on antisocial score versus log_2 dioxin.

[b]Test of significance for homogeneity of slopes (current dioxin continuous, time categorized).

[c]Test of significance for slope equal to 0 (current dioxin continuous, time categorized).

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 9-40. (Continued)

Analysis of Antisocial Score (MCMI)

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Mean	Contrast	Difference of Means (95% C.I.)	p-Value
Background	781	59.6	All Categories		0.074
Unknown	340	61.6	Unknown vs. Background	2.0 (-0.5,4.4)	0.117
Low	194	63.3	Low vs. Background	3.7 (0.7,6.8)	0.016
High	184	61.2	High vs. Background	1.6 (-1.5,4.8)	0.300
Total	1,499		(R^2=0.005)		

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Adj. Mean	Contrast	Difference of Adj. Means (95% C.I.)	p-Value	Covariate Remarks
Background	780	59.6**	All Categories		0.061**	DXCAT*ALC (p=0.014) DRKYR (p=0.005)
Unknown	337	61.6**	Unknown vs. Background	2.0 (-0.4,4.[illegible])**	0.107**	AGE*ALC (p=0.015)
Low	192	63.5**	Low vs. Background	3.9 (0.9,7.0)**	0.012**	
High	181	60.9**	High vs. Background	1.3 (-1.8,4.5)**	0.405**	
Total	1,490		(R^2=0.020)			

**Categorized current dioxin-by-covariate interaction ($0.01<p\leq0.05$); adjusted mean, confidence interval, and p-value derived from a model fitted after deletion of this interaction.

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

The adjusted analysis detected a significant interaction between categorized current dioxin and current alcohol use (Table 9-40 [j]: p=0.014). After stratifying by current alcohol use, there was a marginally significant difference found among the mean antisocial scores of the four current dioxin categories for participants who drank one or fewer drinks per day (Appendix Table H-1: p=0.076). The mean adjusted antisocial scores for the background, unknown, low, and high current dioxin categories were 59.5, 61.6, 63.4, and 62.1. Specifically, the mean antisocial score of the low category was significantly higher than the mean score of the background category (p=0.024).

For participants who drank more than one but less than or equal to four drinks per day, there were no significant differences found among the adjusted mean antisocial scores of the four current dioxin categories (Appendix Table H-1: p=0.820). The adjusted mean scores for the background, unknown, low, and high categories were 60.5, 60.3, 63.9, and 60.5.

The adjusted mean antisocial scores of the four current dioxin categories were found to differ significantly for the participants who drank more than four drinks per day (Appendix Table H-1: p=0.003). The adjusted mean scores for the background, unknown, low, and high categories were 59.0, 75.0, 69.6, and 38.0. Thus, the mean antisocial score of the Ranch Hands in the unknown current dioxin category was significantly higher than the mean score of the Comparisons in the background category (p=0.049) and Ranch Hands in the high category had a significantly lower mean antisocial score than the Comparisons in the background category (p=0.010).

After deletion of the current dioxin-by-current alcohol use interaction from the model, the analysis of categorized current dioxin detected a marginally significant difference among the mean antisocial scores of the four categories (Table 9-40 [j]: p=0.061). The mean score of the low category was found to be significantly higher than the mean score of the background category (p=0.012).

Compulsive Score—MCMI

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

The unadjusted analysis under both the minimal and the maximal assumption displayed nonsignificant associations between the MCMI compulsive score and initial dioxin (Table 9-41 [a] and [b]: p=0.193 and p=0.178, respectively). After the adjustment for covariate information, the associations were still nonsignificant for both the minimal and the maximal cohorts (Table 9-41 [c] and [d]: p=0.976 and p=0.580).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

In the unadjusted analysis of the MCMI compulsive score, under both the minimal and maximal assumptions, the interactions between current dioxin and time since tour were not significant (Table 9-41 [e] and [f]: p=0.576 and p=0.832, respectively). The associations between current dioxin and the compulsive score were also nonsignificant within the time strata for both minimal and maximal cohorts.

TABLE 9-41.

Analysis of Compulsive Score (MCMI)

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Mean[a]	Slope (Std. Error)[b]	p-Value
a) Minimal	Low	129	69.2	-58.779 (45.095)	0.193
(n=514)	Medium	256	68.5		
(R^2=0.003)	High	129	68.0		
b) Maximal	Low	182	68.9	-42.347 (31.425)	0.178
(n=732)	Medium	368	68.9		
(R^2=0.002)	High	182	67.8		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Initial Dioxin	n	Adj. Mean[a]	Adj. Slope (Std. Error)[b]	p-Value	Covariate Remarks
c) Minimal	Low	129	68.7	1.385 (45.155)	0.976	AGE (p<0.001)
(n=509)	Medium	252	68.5			DRKYR (p<0.001)
(R^2=0.080)	High	128	68.7			
d) Maximal	Low	179	68.6	18.043 (32.578)	0.580	DRKYR (p<0.001)
(n=719)	Medium	362	68.8			AGE*EDUC
(R^2=0.071)	High	178	68.9			(p=0.048)

[a]Transformed from square scale.

[b]Slope and standard error based on square compulsive score versus log_2 dioxin.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 9-41. (Continued)

Analysis of Compulsive Score (MCMI)

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Mean[a]/(n) Current Dioxin Low	Medium	High	Slope (Std. Error)[b]	p-Value
e) Minimal						0.576[c]
(n=514)	≤18.6	69.1	68.4	67.7	-35.019 (73.555)	0.634[d]
(R^2=0.005)		(72)	(128)	(53)		
	>18.6	69.4	68.8	67.8	-88.219 (60.291)	0.144[d]
		(56)	(129)	(76)		
f) Maximal						0.832[c]
(n=732)	≤18.6	69.5	68.2	68.5	-42.543 (48.816)	0.384[d]
(R^2=0.003)		(105)	(190)	(82)		
	>18.6	69.2	69.0	67.8	-56.414 (43.184)	0.192[d]
		(78)	(175)	(102)		

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Mean[a]/(n) Current Dioxin Low	Medium	High	Adj. Slope (Std. Error)[b]	p-Value	Covariate Remarks
g) Minimal						0.476[c]	AGE (p<0.001)
(n=505)	≤18.6	68.1	68.6	68.9	65.987 (72.879)	0.366[d]	DRKYR (p<0.001)
(R^2=0.089)		(71)	(126)	(53)			EDUC (p=0.129)
	>18.6	69.1	68.9	68.8	0.742 (60.259)	0.990[d]	
		(56)	(125)	(74)			
h) Maximal						0.963[c]	DRKYR (p<0.001)
(n=719)	≤18.6	69.3	68.1	69.4	16.780 (49.397)	0.734[d]	AGE*EDUC (p=0.047)
(R^2=0.071)		(104)	(186)	(81)			
	>18.6	68.3	69.0	69.0	13.836 (43.818)	0.752[d]	
		(77)	(172)	(99)			

[a]Transformed from square scale.

[b]Slope and standard error based on square compulsive score versus log_2 dioxin.

[c]Test of significance for homogeneity of slopes (current dioxin continuous, time categorized).

[d]Test of significance for slope equal to 0 (current dioxin continuous, time categorized).

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 9-41. (Continued)

Analysis of Compulsive Score (MCMI)

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Mean[a]	Contrast	Difference of Means (95% C.I.)[e]	p-Value[f]
Background	781	68.4	All Categories		0.838
Unknown	340	68.7	Unknown vs. Background	0.3 --	0.621
Low	194	68.7	Low vs. Background	0.3 --	0.641
High	184	68.1	High vs. Background	-0.3 --	0.621
Total	1,499		(R^2<0.001)		

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Adj. Mean[a]	Contrast	Difference of Adj. Means (95% C.I.)[e]	p-Value[f]	Covariate Remarks
Background	775	68.5	All Categories		0.962	AGE*DRKYR (p<0.001) AGE*EDUC (p=0.020)
Unknown	335	68.6	Unknown vs. Background	0.1 --	0.829	
Low	190	68.7	Low vs. Background	0.2 --	0.730	
High	180	68.8	High vs. Background	0.3 --	0.641	
Total	1,480		(R^2=0.056)			

[a]Transformed from square scale.

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

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

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

These findings did not change after adjusting for covariate information (Table 9-41 [g] and [h]: $p>0.35$ for each analysis).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In both the unadjusted and the adjusted analysis of categorized current dioxin, there were no significant differences detected among the mean MCMI compulsive scores of the four current dioxin categories (Table 9-41 [i] and [j]: $p>0.60$ for each analysis).

Passive-Aggressive Score—MCMI

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

The unadjusted analysis of the MCMI passive-aggressive score detected significant positive associations with initial dioxin for both the minimal and the maximal cohorts (Table 9-42 [a] and [b]: $p=0.046$ and $p<0.001$). In the minimal analysis, the unadjusted mean passive-aggressive scores for the low, medium, and high initial dioxin categories were 18.7, 20.3, and 21.2. The corresponding mean scores for the maximal cohort were 17.3, 18.9, and 21.5, respectively.

After the adjustment for age, lifetime alcohol history, and education, the minimal analysis detected a nonsignificant positive association between initial dioxin and the passive-aggressive score (Table 9-42 [c]: $p=0.950$). Similarly, after adjustment for age, race, lifetime alcohol history, and a current alcohol use-by-education interaction, the maximal analysis also exhibited a nonsignificant positive association between initial dioxin and the passive-aggressive score (Table 9-42 [d]: $p=0.295$).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

In the unadjusted analysis of the minimal cohort, the current dioxin-by-time since tour interaction was nonsignificant (Table 9-42 [e]: $p=0.371$). Within the over 18.6 years time stratum, there was a significant positive association between current dioxin and the passive-aggressive score ($p=0.037$). The unadjusted mean scores for Ranch Hands with time greater than 18.6 years increased steadily for increasing levels of current dioxin (low, 17.8; medium, 20.5; high, 21.4).

Based upon the maximal assumption, the unadjusted analysis again displayed a nonsignificant current dioxin-by-time since tour interaction (Table 9-42 [f]: $p=0.768$). However, both time strata exhibited a significant positive association between current dioxin and the passive-aggressive score (≤18.6 years: $p=0.044$; >18.6 years: $p=0.007$). The unadjusted mean scores for the time less than or equal to 18.6 years stratum for low, medium, and high current dioxin were 16.2, 20.1, and 19.7. For the time over 18.6 years stratum, the unadjusted mean passive-aggressive scores increased for increasing current dioxin levels (low, 16.8; medium, 19.6; high, 20.9).

TABLE 9-42.

Analysis of Passive-Aggressive Score (MCMI)

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Mean[a]	Slope (Std. Error)[b]	p-Value
a) Minimal	Low	129	18.7	0.130 (0.065)	0.046
(n=514)	Medium	256	20.3		
(R^2=0.008)	High	129	21.2		
b) Maximal	Low	182	17.3	0.156 (0.046)	<0.001
(n=732)	Medium	368	18.9		
(R^2=0.015)	High	182	21.5		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Initial Dioxin	n	Adj. Mean[a]	Adj. Slope (Std. Error)[b]	p-Value	Covariate Remarks
c) Minimal	Low	128	19.7	0.004 (0.066)	0.950	AGE (p<0.001)
(n=503)	Medium	250	19.7			DRKYR (p<0.001)
(R^2=0.080)	High	127	19.0			EDUC (p=0.003)
d) Maximal	Low	179	20.6	0.050 (0.048)	0.295	AGE (p<0.001)
(n=719)	Medium	362	21.0			RACE (p=0.056)
(R^2=0.096)	High	178	21.4			DRKYR (p<0.001)
						ALC*EDUC (p=0.031)

[a]Transformed from square root scale.

[b]Slope and standard error based on square root passive-aggressive score versus log_2 dioxin.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 9-42. (Continued)

Analysis of Passive-Aggressive Score (MCMI)

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Mean[a]/(n) Current Dioxin Low	Medium	High	Slope (Std. Error)[b]	p-Value
e) Minimal						0.371[c]
(n=514)	≤18.6	18.6	20.2	21.7	0.059 (0.106)	0.578[d]
(R^2=0.009)		(72)	(128)	(53)		
	>18.6	17.8	20.5	21.4	0.182 (0.087)	0.037[d]
		(56)	(129)	(76)		
f) Maximal						0.768[c]
(n=732)	≤18.6	16.2	20.1	19.7	0.145 (0.072)	0.044[d]
(R^2=0.016)		(105)	(190)	(82)		
	>18.6	16.8	19.6	20.9	0.174 (0.064)	0.007[d]
		(78)	(175)	(102)		

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Mean[a]/(n) Current Dioxin Low	Medium	High	Adj. Slope (Std. Error)[b]	p-Value	Covariate Remarks
g) Minimal						0.324[c]	AGE (p<0.001)
(n=505)	≤18.6	19.8	19.4	18.9	-0.089 (0.106)	0.401[d]	DRKYR (p<0.001)
(R^2=0.082)		(71)	(126)	(53)			EDUC (p=0.003)
	>18.6	18.9	20.1	19.5	0.042 (0.088)	0.630[d]	
		(56)	(125)	(74)			
h) Maximal						0.823[c]	AGE (p<0.001)
(n=719)	≤18.6	19.0	21.9	19.5	0.033 (0.073)	0.646[d]	RACE (p=0.059)
(R^2=0.096)		(104)	(186)	(81)			DRKYR (p<0.001)
	>18.6	20.8	21.8	20.2	0.054 (0.064)	0.399[d]	ALC*EDUC (p=0.032)
		(77)	(172)	(99)			

[a]Transformed from square root scale.

[b]Slope and standard error based on square root passive-aggressive score versus log_2 dioxin.

[c]Test of significance for homogeneity of slopes (current dioxin continuous, time categorized).

[d]Test of significance for slope equal to 0 (current dioxin continuous, time categorized).

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 9-42. (Continued)

Analysis of Passive-Aggressive Score (MCMI)

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Mean[a]	Contrast	Difference of Means (95% C.I.)[e]	p-Value[f]
Background	781	19.0	All Categories		0.054
Unknown	340	17.6	Unknown vs. Background	-1.4 –	0.132
Low	194	20.8	Low vs. Background	1.8 –	0.128
High	184	20.4	High vs. Background	1.4 –	0.268
Total	1,499		(R^2=0.005)		

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Adj. Mean[a]	Contrast	Difference of Adj. Means (95% C.I.)[e]	p-Value[f]	Covariate Remarks
Background	775	18.9**	All Categories		0.248**	DXCAT*AGE (p=0.031) DRKYR (p<0.001)
Unknown	335	18.0**	Unknown vs. Background	-0.9 –**	0.315**	EDUC (p=0.037)
Low	190	20.[illegible]**	Low vs. Background	1.8 –**	0.138**	
High	180	18.9**	High vs. Background	0.0 –**	0.965**	
Total	1,480		(R^2=0.051)			

[a]Transformed from square root scale.

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

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

**Categorized current dioxin-by-covariate interaction ($0.01<p\leq0.05$); adjusted mean, confidence interval, and p-value derived from a model fitted after deletion of this interaction.

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

After the adjustment for covariate information, the interactions between current dioxin and time remained nonsignificant (Table 9-42 [g] and [h]: p=0.324 and p=0.823, respectively). The associations between current dioxin and the passive-aggressive score became nonsignificant within both time strata for the minimal cohort after age, lifetime alcohol history, and education were retained in the model. Similarly, after adjustment for age, race, lifetime alcohol history, and a current alcohol use-by-education interaction in the maximal analysis, the associations between current dioxin and the passive-aggressive score became nonsignificant.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In the unadjusted analysis, there was a marginally significant difference among the mean passive-aggressive scores of the four current dioxin categories (Table 9-42 [i]: p=0.054). However, the mean score of the background group of Comparisons did not differ significantly from the mean score of the unknown, low, or high current dioxin categories (p=0.132, p=0.128, and p=0.268, respectively). The unadjusted mean scores for the background, unknown, low, and high current dioxin categories were 19.0, 17.6, 20.8, and 20.4.

The adjusted analysis of the MCMI passive-aggressive score detected a significant interaction between categorized current dioxin and age (Table 9-42 [j]: p=0.031). To examine this interaction, adjusted analyses were performed for Ranch Hands and Comparisons born in or after 1942 and for those born before 1942. For the younger participants, the overall contrast of the four current dioxin categories was significant (Appendix Table H-1: p=0.004). For these participants, the mean passive-aggressive scores for the background, unknown, low, and high categories were 19.5, 19.7, 26.7, and 20.9. The contrast of the Ranch Hands in the low category versus the Comparisons in the background category was also significant (p<0.001) with the Ranch Hands having a higher mean passive-aggressive score than the Comparisons. In fact, the Ranch Hands in the unknown, low, and high categories had higher mean adjusted passive-aggressive scores than the Comparisons in the background category.

For the older participants (born before 1942), the simultaneous contrast of the four current dioxin categories was not significant (Appendix Table H-1: p=0.450). The mean adjusted passive-aggressive scores for these participants in the background, unknown, low, and high categories were 18.4, 16.8, 16.8, and 17.8. Unlike the analysis of the younger participants, the older Comparisons in the background category had a higher mean adjusted passive-aggressive score than the older Ranch Hands in the unknown, low, and high categories.

After deletion of the interaction from the model and adjusting only for lifetime alcohol history and education, the adjusted analysis of the passive-aggressive score and categorized current dioxin was not significant (Table 9-42 [j]: p=0.243).

Schizotypal Score—MCMI

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

The unadjusted analysis of both the minimal and the maximal cohort displayed a significant positive association between initial dioxin and the MCMI schizotypal score (Table 9-43 [a] and [b]: $p<0.001$ and $p<0.001$, respectively). The unadjusted mean schizotypal scores for the minimal analysis for the low, medium, and high initial dioxin categories were 31.9, 34.8, and 39.1. For the maximal cohort, the corresponding mean scores were 32.2, 33.2, and 38.1, respectively.

The adjustment for covariate information did not change the significance of the positive association between initial dioxin and the schizotypal score for either the minimal or the maximal cohort analysis (Table 9-43 [c] and [d]: $p<0.001$ and $p=0.001$).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

In the unadjusted analysis of the MCMI schizotypal score with current dioxin and time since tour under the minimal assumption, the interaction between current dioxin and time was not significant (Table 9-43 [e]: $p=0.264$). A significant positive association between current dioxin and the schizotypal score was found for Ranch Hands with time over 18.6 years ($p<0.001$). The unadjusted mean scores for this time stratum became larger for increasing levels of current dioxin (low, 33.6; medium, 34.7; high, 41.8).

Under the maximal assumption, the unadjusted analysis detected a nonsignificant current dioxin-by-time since tour interaction (Table 9-43 [f]: $p=0.290$). Thus, the positive relationships between current dioxin and the schizotypal score did not differ significantly for the two time strata. Within each time stratum, there was a significant positive association between current dioxin and the schizotypal score (≤ 18.6: $p=0.037$; >18.6: $p<0.001$). The unadjusted mean scores for the time less than or equal to 18.6 years stratum for low, medium, and high current dioxin were 31.7, 32.1, and 36.6. The corresponding mean scores for the time over 18.6 years stratum were 32.4, 34.4, and 39.8.

After adjusting for education, both the minimal and the maximal analysis displayed a nonsignificant current dioxin-by-time since tour interaction (Table 9-43 [g] and [h]: $p=0.296$ and $p=0.225$, respectively). Under both the minimal and the maximal assumptions, there was a significant positive association between current dioxin and the MCMI schizotypal score for Ranch Hands with time over 18.6 years ($p=0.002$ for both analyses).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In the analysis of categorized current dioxin, a significant difference was detected among the mean schizotypal scores of the participants in the four current dioxin categories (Table 9-43 [i]: $p=0.003$). The unadjusted mean scores for the background, unknown, low, and high current dioxin categories were 33.9, 31.9, 34.0, and 38.4. The mean schizotypal scores of the Ranch Hands in the unknown and low categories did not differ significantly from the mean score of the background category of Comparisons (unknown versus background: $p=0.114$; low versus background: $p=0.914$). However, the mean schizotypal score for the Ranch Hands in

TABLE 9-43.

Analysis of Schizotypal Score (MCMI)

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Mean	Slope (Std. Error)[a]	p-Value
a) Minimal	Low	129	31.9	2.836 (0.667)	<0.001
(n=514)	Medium	256	34.8		
(R^2=0.034)	High	129	39.1		
b) Maximal	Low	182	32.2	2.298 (0.497)	<0.001
(n=732)	Medium	368	33.2		
(R^2=0.028)	High	182	38.1		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Initial Dioxin	n	Adj. Mean	Adj. Slope (Std. Error)[a]	p-Value	Covariate Remarks
c) Minimal	Low	128	31.8	2.448 (0.670)	<0.001	EDUC (p<0.001)
(n=510)	Medium	254	33.6			
(R^2=0.062)	High	128	37.8			
d) Maximal	Low	181	33.6	1.681 (0.516)	0.001	EDUC (p<0.001)
(n=727)	Medium	365	32.7			
(R^2=0.050)	High	181	36.7			

[a]Slope and standard error based on schizotypal score versus log_2 dioxin.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 9-43. (Continued)

Analysis of Schizotypal Score (MCMI)

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Mean/(n) Current Dioxin Low	Medium	High	Slope (Std. Error)[a]	p-Value
e) Minimal						0.264[b]
(n=514)	≤18.6	31.0	34.6	35.3	1.724 (1.088)	0.114[c]
(R^2=0.036)		(72)	(128)	(53)		
	>18.6	33.6	34.7	41.8	3.296 (0.891)	<0.001[c]
		(56)	(129)	(76)		
f) Maximal						0.290[b]
(n=732)	≤18.6	31.7	32.1	36.6	1.610 (0.771)	0.037[c]
(R^2=0.031)		(105)	(190)	(82)		
	>18.6	32.4	34.4	39.8	2.701 (0.682)	<0.001[c]
		(78)	(175)	(102)		

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Mean/(n) Current Dioxin Low	Medium	High	Adj. Slope (Std. Error)[a]	p-Value	Covariate Remarks
g) Minimal						0.296[b]	EDUC (p<0.001)
(n=510)	≤18.6	30.7	33.5	34.0	1.397 (1.081)	0.197[c]	
(R^2=0.064)		(71)	(127)	(53)			
	>18.6	33.8	33.4	40.5	2.855 (0.893)	0.002[c]	
		(56)	(128)	(75)			
h) Maximal						0.225[b]	EDUC (p<0.001)
(n=727)	≤18.6	33.0	31.6	35.4	0.904 (0.784)	0.250[c]	
(R^2=0.054)		(105)	(187)	(82)			
	>18.6	33.3	34.1	38.2	2.148 (0.691)	0.002[c]	
		(78)	(174)	(101)			

[a]Slope and standard error based on schizotypal score versus log_2 dioxin.

[b]Test of significance for homogeneity of slopes (current dioxin continuous, time categorized).

[c]Test of significance for slope equal to 0 (current dioxin continuous, time categorized).

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 9-43. (Continued)

Analysis of Schizotypal Score (MCMI)

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Mean	Contrast	Difference of Means (95% C.I.)	p-Value
Background	781	33.9	All Categories		0.003
Unknown	340	31.9	Unknown vs. Background	-1.9 (-4.3,0.5)	0.114
Low	194	34.0	Low vs. Background	0.2 (-2.8,3.1)	0.914
High	184	38.4	High vs. Background	4.5 (1.5,7.5)	0.004
Total	1,499		(R^2=0.009)		

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Adj. Mean	Contrast	Difference of Adj. Means (95% C.I.)	p-Value	Covariate Remarks
Background	775	33.9	All Categories		0.053	DRKYR (p=0.063) EDUC (p<0.001)
Unknown	335	32.5	Unknown vs. Background	-1.4 (-3.8,1.0)	0.251	
Low	190	33.5	Low vs. Background	-0.4 (-3.4,2.6)	0.788	
High	180	37.3	High vs. Background	3.4 (0.4,6.5)	0.029	
Total	1,480		(R^2=0.024)			

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

the high current dioxin category was significantly higher than the mean score for the Comparisons in the background category (p=0.004).

After the adjustment for lifetime alcohol history and education, there was only a marginally significant difference detected in the mean schizotypal scores of the four current dioxin categories (Table 9-43 [j]: p=0.053). Concurrent with the results of the unadjusted analysis, the mean score of the Ranch Hands in the high current dioxin category was significantly higher than that of the Comparisons in the background category (p=0.029).

Borderline Score—MCMI

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

The unadjusted analysis under the minimal assumption displayed a nonsignificant association between initial dioxin and the MCMI borderline score (Table 9-44 [a]: p=0.202). The maximal unadjusted analysis of the borderline score detected a significant positive association with initial dioxin (Table 9-44 [b]: p=0.028). For the maximal cohort, the unadjusted mean borderline scores became larger for increasing levels of initial dioxin (low, 31.2; medium, 32.5; high, 33.6).

In the adjusted minimal analysis, the association between initial dioxin and the borderline score remained nonsignificant (Table 9-44 [c]: p=0.333). Under the maximal assumption, the adjusted analysis detected a significant interaction between initial dioxin and education (Table 9-44 [d]: p=0.021). To examine this interaction separate analyses are presented for each education-level stratum. For Ranch Hands with a college education, there was a significant increasing association between initial dioxin and the borderline score (Appendix Table H-1: p=0.021). The adjusted mean scores for the low, medium, and high initial dioxin categories were 31.1, 32.4, and 37.8. In contrast, for Ranch Hands with a high school education, the analysis displayed a nonsignificant negative association (Appendix Table H-1: p=0.373).

After deletion of the initial dioxin-by-education interaction, the maximal adjusted analysis exhibited a nonsignificant association between initial dioxin and the MCMI borderline score (Table 9-44 [d]: p=0.388).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

The unadjusted analysis of the MCMI borderline score based on current dioxin and time since tour did not detect a significant current dioxin-by-time interaction for either the minimal or the maximal cohort (Table 9-44 [e] and [f]: p=0.311 and p=0.809). In the minimal analysis, the association between current dioxin and the borderline score was also nonsignificant within each time stratum. However, for the maximal cohort, there was a marginally significant positive association between current dioxin and the borderline score for those Ranch Hands with time over 18.6 years (Table 9-44 [f]: p=0.072). The unadjusted mean scores for this time stratum for low, medium, and high current dioxin were 30.5, 33.5, and 33.3.

TABLE 9-44.

Analysis of Borderline Score (MCMI)

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Mean	Slope (Std. Error)[a]	p-Value
a) Minimal	Low	129	33.2	0.794 (0.622)	0.202
(n=514)	Medium	256	32.8		
(R^2=0.003)	High	129	34.0		
b) Maximal	Low	182	31.2	0.991 (0.451)	0.028
(n=732)	Medium	368	32.5		
(R^2=0.007)	High	182	33.6		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Initial Dioxin	n	Adj. Mean	Adj. Slope (Std. Error)[a]	p-Value	Covariate Remarks
c) Minimal	Low	128	36.1	0.611 (0.631)	0.333	RACE (p=0.022)
(n=505)	Medium	250	35.2			DRKYR (p=0.049)
(R^2=0.033)	High	127	36.5			EDUC (p=0.036)
d) Maximal	Low	179	35.8**	0.405 (0.469)**	0.388**	INIT*EDUC (p=0.021)
(n=719)	Medium	362	35.0**			RACE (p=0.019)
(R^2=0.046)	High	178	35.6**			DRKYR (p=0.135)

[a]Slope and standard error based on borderline score versus log_2 dioxin.

**Log_2 (initial dioxin)-by-covariate interaction ($0.01<p\leq0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of this interaction.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 9-44. (Continued)

Analysis of Borderline Score (MCMI)

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Mean/(n) Current Dioxin Low	Medium	High	Slope (Std. Error)[a]	p-Value
e) Minimal						0.311[b]
(n=514)	≤18.6	33.5	33.3	32.2	-0.016 (1.015)	0.988[c]
(R^2=0.005)		(72)	(128)	(53)		
	>18.6	33.1	32.1	35.3	1.315 (0.832)	0.115[c]
		(56)	(129)	(76)		
f) Maximal						0.809[b]
(n=732)	≤18.6	30.1	32.6	33.9	0.891 (0.701)	0.204[c]
(R^2=0.007)		(105)	(190)	(82)		
	>18.6	30.5	33.5	33.3	1.118 (0.620)	0.072[c]
		(73)	(175)	(102)		

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Mean/(n) Current Dioxin Low	Medium	High	Adj. Slope (Std. Error)[a]	p-Value	Covariate Remarks
g) Minimal						0.334[b]	RACE (p=0.023)
(n=505)	≤18.6	36.6	36.2	35.2	-0.074 (1.014)	0.942[c]	DRKYR (p=0.040)
(R^2=0.035)		(71)	(126)	(53)			EDUC (p=0.039)
	>18.6	35.8	34.2	37.5	1.189 (0.839)	0.157[c]	
		(56)	(125)	(74)			
h) Maximal						0.739[b]	RACE (p=0.016)
(n=719)	≤18.6	34.1	35.6	36.1	0.314 (0.713)	0.660[c]	DRKYR (p=0.146)
(R^2=0.039)		(104)	(186)	(81)			EDUC (p<0.001)
	>18.6	34.4	35.8	34.9	0.624 (0.628)	0.321[c]	
		(77)	(172)	(99)			

[a]Slope and standard error based on borderline score versus log_2 dioxin.

[b]Test of significance for homogeneity of slopes (current dioxin continuous, time categorized).

[c]Test of significance for slope equal to 0 (current dioxin continuous, time categorized).

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 9-44. (Continued)

Analysis of Borderline Score (MCMI)

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Mean	Contrast	Difference of Means (95% C.I.)	p-Value
Background	781	33.3	All Categories		0.170
Unknown	340	31.0	Unknown vs. Background	-2.4 (-4.5,-0.2)	0.033
Low	194	32.5	Low vs. Background	-0.8 (-3.5,1.9)	0.567
High	184	33.5	High vs. Background	0.2 (-2.5,2.9)	0.882
Total	1,499		(R^2=0.003)		

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Adj. Mean	Contrast	Difference of Adj. Means (95% C.I.)	p-Value	Covariate Remarks
Background	775	33.2**	All Categories		0.415**	DXCAT*EDUC (p=0.033) DRKYR (p=0.003)
Unknown	335	31.5**	Unknown vs. Background	-1.8 (-3.9,0.4)**	0.110**	
Low	190	32.0**	Low vs. Background	-1.2 (-3.9,1.5)**	0.369**	
High	180	32.7**	High vs. Background	-0.6 (-3.3,2.2)**	0.694**	
Total	1,480		(R^2=0.027)			

**Categorized current dioxin-by-covariate interaction ($0.01<p\leq0.05$); adjusted mean, confidence interval, and p-value derived from a model fitted after deletion of this interaction.

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

After adjusting for race, lifetime alcohol history, and education, both the minimal and the maximal analyses found a nonsignificant current dioxin-by-time interaction (Table 9-44 [g] and [h]: p=0.334 and p=0.739, respectively). The association between current dioxin and the borderline score was also nonsignificant within each time stratum.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

There was not a significant overall difference in the mean borderline scores of the four current dioxin categories (Table 9-44 [i]: p=0.170). However, the mean score for the Ranch Hands in the unknown current dioxin category was significantly lower than the mean score for the Comparisons in the background category (p=0.033). The mean borderline scores for the background, unknown, low, and high current dioxin categories were 33.3, 31.0, 32.5, and 33.5.

In the adjusted analysis, there was a significant interaction between categorized current dioxin and education (Table 9-44 [j]: p=0.033). To investigate this interaction, stratified analyses are presented for each education level. For the high school educated participants, there was no significant difference found among the mean borderline scores of the four current dioxin categories (Appendix Table H-1: p=0.578). The adjusted mean borderline scores for the background, unknown, low, and high categories were 34.3, 36.3, 33.8, and 33.6. For those participants with a college level education, there was a significant difference found among the mean borderline scores of the four categories (p=0.022). The mean score of the unknown category was found to be significantly lower than the mean score of those in the background category (p=0.004).

After deletion of the categorized current dioxin-by-education interaction from the model and adjusting only for education and lifetime alcohol history, there were no significant differences detected among the mean borderline scores of the four current dioxin categories (Table 9-44 [j]: p=0.415).

Paranoid Score—MCMI

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Neither the unadjusted minimal nor maximal analysis detected a significant association between initial dioxin and the MCMI paranoid score (Table 9-45 [a] and [b]: p=0.675 and p=0.729, respectively).

The results of the adjusted analyses were consistently nonsignificant for the minimal and maximal cohorts (Table 9-45 [c] and [d]: p=0.413 and p=0.960).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

In the unadjusted analysis of the MCMI paranoid score under both the minimal and maximal assumptions, the interactions between current dioxin and time since tour were not significant (Table 9-45 [e] and [f]: p=0.979 and p=0.891, respectively). The associations between current dioxin and the paranoid score were also nonsignificant within each time stratum for both minimal and maximal cohorts.

TABLE 9-45.

Analysis of Paranoid Score (MCMI)

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Mean	Slope (Std. Error)[a]	p-Value
a) Minimal	Low	129	51.8	0.227 (0.539)	0.675
(n=514)	Medium	256	53.7		
(R^2<0.001)	High	129	53.3		
b) Maximal	Low	182	52.9	0.139 (0.400)	0.729
(n=732)	Medium	368	53.1		
(R^2<0.001)	High	182	53.2		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Initial Dioxin	n	Adj. Mean	Adj. Slope (Std. Error)[a]	p-Value	Covariate Remarks
c) Minimal	Low	129	53.8	0.457 (0.557)	0.413	RACE (p=0.080)
(n=512)	Medium	254	55.8			AGE*ALC (p=0.045)
(R^2=0.021)	High	129	55.8			
d) Maximal	Low	181	56.8	-0.021 (0.418)	0.960	RACE (p=0.004)
(n=727)	Medium	365	56.0			EDUC (p=0.086)
(R^2=0.016)	High	181	56.1			

[a]Slope and standard error based on paranoid score versus log_2 dioxin.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 9-45. (Continued)

Analysis of Paranoid Score (MCMI)

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Mean/(n) Current Dioxin Low	Medium	High	Slope (Std. Error)[a]	p-Value
e) Minimal						0.979[b]
(n=514)	≤18.6	54.7	54.3	54.8	0.522 (0.876)	0.551[c]
(R^2=0.010)		(72)	(128)	(53)		
	>18.6	49.8	52.2	52.8	0.551 (0.718)	0.443[c]
		(56)	(129)	(76)		
f) Maximal						0.891[b]
(n=732)	≤18.6	53.4	54.2	55.4	0.476 (0.620)	0.443[c]
(R^2=0.008)		(105)	(190)	(82)		
	>18.6	51.1	52.0	52.0	0.362 (0.548)	0.509[c]
		(78)	(175)	(102)		

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Mean/(n) Current Dioxin Low	Medium	High	Adj. Slope (Std. Error)[a]	p-Value	Covariate Remarks
g) Minimal						0.937[b]	RACE (p=0.056)
(n=512)	≤18.6	56.7	56.4	57.5	0.852 (0.900)	0.345[c]	AGE*ALC (p=0.040)
(R^2=0.033)		(72)	(128)	(53)			
	>18.6	51.7	54.2	55.4	0.941 (0.740)	0.204[c]	
		(56)	(127)	(76)			
h) Maximal						0.909[b]	RACE (p=0.004)
(n=727)	≤18.6	57.1	57.3	58.4	0.310 (0.634)	0.626[c]	EDUC (p=0.107)
(R^2=0.024)		(105)	(187)	(82)			
	>18.6	54.9	55.1	54.9	0.214 (0.558)	0.701[c]	
		(78)	(174)	(101)			

[a]Slope and standard error based on paranoid score versus log_2 dioxin.

[b]Test of significance for homogeneity of slopes (current dioxin continuous, time categorized).

[c]Test of significance for slope equal to 0 (current dioxin continuous, time categorized).

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 9-45. (Continued)

Analysis of Paranoid Score (MCMI)

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Mean	Contrast	Difference of Means (95% C.I.)	p-Value
Background	781	51.5	All Categories		0.191
Unknown	340	52.9	Unknown vs. Background	1.3 (-0.6,3.3)	0.187
Low	194	53.6	Low vs. Background	2.0 (-0.4,4.5)	0.104
High	184	53.5	High vs. Background	2.0 (-0.5,4.5)	0.118
Total	1,499		(R^2=0.003)		

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Adj. Mean	Contrast	Difference of Adj. Means (95% C.I.)	p-Value	Covariate Remarks
Background	775	53.3	All Categories		0.202	RACE (p=0.025)
						DRKYR (p=0.121)
Unknown	335	55.2	Unknown vs. Background	1.9 (-0.1,3.9)	0.067	EDUC (p<0.001)
Low	190	55.1	Low vs. Background	1.7 (-0.7,4.2)	0.166	
High	180	54.7	High vs. Background	1.4 (-1.2,3.9)	0.284	
Total	1,480		(R^2=0.022)			

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

These findings did not change after adjusting for covariate information (Table 9-45 [g] and [h]: p>0.20 for each analysis).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In the unadjusted analysis, there were no significant differences in the mean MCMI paranoid scores of the four current dioxin categories (Table 9-45 [i]: p>0.10 for each analysis).

After adjusting for race, lifetime alcohol history, and education, the overall test of differences among the mean paranoid scores of the four current dioxin categories remained nonsignificant (Table 9-45 [j]: p=0.202). However, there was a marginally significant difference detected between the mean paranoid score of the Comparisons in the background category and the mean paranoid score of the Ranch Hands in the unknown current dioxin category (p=0.067). The adjusted mean paranoid scores for the background, unknown, low, and high current dioxin categories were 53.3, 55.2, 55.1, and 54.7.

Anxiety Score—MCMI

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

The unadjusted analysis detected a significant positive association between initial dioxin and the MCMI anxiety score for both minimal and maximal cohorts (Table 9-46 [a] and [b]: p=0.046 and p<0.001). The unadjusted mean anxiety scores under the minimal assumption for the low, medium, and high initial dioxin categoires were 46.8, 47.0 and 49.7. The corresponding mean scores for the maximal cohort were 43.5, 46.6, and 48.5, respectively.

In the adjusted analysis performed under the minimal assumption, there was a significant interaction between initial dioxin and race (Table 9-46 [c]: p=0.017). Separate analyses were performed for the individual race strata. In the Black stratum, there was a significant negative association between initial dioxin the MCMI anxiety score (Appendix Table H-1: p=0.043), and in the non-Black stratum, there was a significant positive association (p=0.036). For the low, medium, and high initial dioxin categories of the Black stratum, the adjusted mean anxiety scores were 54.0, 54.6, and 20.7, respectively. The corresponding means for the low, medium, and high initial dioxin levels in the non-Black stratum were 46.0, 45.8, and 49.5. After deletion of the initial dioxin-by-race interaction from the model and adjusting only for race and education, the positive association between initial dioxin and the anxiety score was only marginally significant (Table 9-46 [c]: p=0.091).

The adjusted analysis also found an initial dioxin-by-race interaction for the maximal cohort (Table 9-46 [d]: p=0.005). The stratified analyses of this interaction displayed a significant negative association between initial dioxin and the anxiety score for the Black stratum (Appendix Table H-1: p=0.016) and a significant positive association for the non-Black stratum (p=0.007). The adjusted mean anxiety scores for the Black stratum decreased with increasing initial dioxin levels (low, 60.8; medium, 55.6; high, 37.7), while the mean scores became larger for increasing initial dioxin for the non-Black stratum (low, 44.5; medium, 45.4; high, 47.6).

TABLE 9-46.

Analysis of Anxiety Score (MCMI)

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Mean	Slope (Std. Error)[a]	p-Value
a) Minimal	Low	129	46.8	1.551 (0.775)	0.046
(n=514)	Medium	256	47.0		
(R^2=0.008)	High	129	49.7		
b) Maximal	Low	182	43.5	1.943 (0.568)	<0.001
(n=732)	Medium	368	46.6		
(R^2=0.016)	High	182	48.5		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Initial Dioxin	n	Adj. Mean	Adj. Slope (Std. Error)[a]	p-Value	Covariate Remarks
c) Minimal	Low	123	48.7**	1.337 (0.788)**	0.091**	INIT*RACE (p=0.017)
(n=510)	Medium	254	48.5**			EDUC (p=0.082)
(R^2=0.027)	High	128	51.1**			
d) Maximal	Low	181	****	****	****	INIT*RACE (p=0.005)
(n=727)	Medium	365	****			EDUC (p=0.004)
(R^2=0.043)	High	181	****			

[a]Slope and standard error based on anxiety score versus log_2 dioxin.

**Log_2 (initial dioxin)-by-covariate interaction ($0.01<p\leq0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of this interaction.

****Log_2 (initial dioxin)-by-covariate interaction ($p\leq0.01$); adjusted mean, adjusted slope, standard error, and p-value not presented.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 9-46. (Continued)

Analysis of Anxiety Score (MCMI)

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Mean/(n) Current Dioxin Low	Medium	High	Slope (Std. Error)[a]	p-Value
e) Minimal						0.155[b]
(n=514)	≤18.6	47.3	47.5	45.8	-0.023 (1.263)	0.985[c]
(R^2=0.010)		(72)	(128)	(53)		
	>18.6	45.4	47.0	52.1	2.307 (1.036)	0.026[c]
		(56)	(129)	(76)		
f) Maximal						0.917[b]
(n=732)	≤18.6	41.0	45.7	48.8	1.838 (0.883)	0.038[c]
(R^2=0.016)		(105)	(190)	(82)		
	>18.6	46.0	47.1	49.6	1.716 (0.781)	0.028[c]
		(78)	(175)	(102)		

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Mean/(n) Current Dioxin Low	Medium	High	Adj. Slope (Std. Error)[a]	p-Value	Covariate Remarks
g) Minimal						0.202[b]	EDUC (p=0.073)
(n=510)	≤18.6	47.0	47.1	45.1	-0.173 (1.267)	0.891[c]	
(R^2=0.015)		(71)	(127)	(53)			
	>18.6	45.5	46.2	51.0	1.915 (1.047)	0.068[c]	
		(56)	(128)	(75)			
h) Maximal						0.914[b]	RACE (p=0.040)
(n=727)	≤18.6	45.3	48.7	51.2	1.267 (0.897)	0.158[c]	EDUC (p=0.003)
(R^2=0.032)		(105)	(187)	(82)			
	>18.6	50.2	49.8	51.3	1.141 (0.790)	0.149[c]	
		(78)	(174)	(101)			

[a]Slope and standard error based on anxiety score versus log_2 dioxin.

[b]Test of significance for homogeneity of slopes (current dioxin continuous, time categorized).

[c]Test of significance for slope equal to 0 (current dioxin continuous, time categorized).

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 9-46. (Continued)

Analysis of Anxiety Score (MCMI)

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Mean	Contrast	Difference of Means (95% C.I.)	p-Value
Background	781	47.2	All Categories		0.038
Unknown	340	44.1	Unknown vs. Background	-3.1 (-5.8,-0.4)	0.023
Low	194	46.4	Low vs. Background	-0.8 (-4.1,2.5)	0.630
High	184	49.3	High vs. Background	2.1 (-1.3,5.5)	0.231
Total	1,499		(R^2=0.006)		

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Adj. Mean	Contrast	Difference of Adj. Means (95% C.I.)	p-Value	Covariate Remarks
Background	776	48.0**	All Categories		0.248**	DXCAT*RACE (p=0.018) AGE*EDUC (p=0.045)
Unknown	338	45.7**	Unknown vs. Background	-2.2 (-4.9,0.5)**	0.107**	
Low	192	46.7**	Low vs. Background	-1.2 (-4.6,2.1)**	0.461**	
High	183	49.2**	High vs. Background	1.3 (-2.2,4.7)**	0.464**	
Total	1,489		(R^2=0.028)			

**Categorized current dioxin-by-covariate interaction ($0.01<p\leq0.05$); adjusted mean, confidence interval, and p-value derived from a model fitted after deletion of this interaction.

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

In the unadjusted analysis of the MCMI anxiety score with current dioxin and time since tour under the minimal assumption, the interaction between current dioxin and time was not significant (Table 9-46 [e]: p=0.155). However, there was a significant positive association between current dioxin and the anxiety score for Ranch Hands with time over 18.6 years (p=0.026). The unadjusted mean anxiety scores for low, medium, and high current dioxin were 45.4, 47.0, and 52.1.

Under the maximal assumption, the unadjusted analysis also exhibited a nonsignificant current dioxin-by-time since tour interaction (Table 9-46 [f]: p=0.917). For Ranch Hands with time less than or equal to 18.6 years, a significant positive association was displayed between the anxiety score and current dioxin (p=0.038). For these individuals, the mean scores for low, medium, and high current dioxin were 41.0, 45.7, and 48.8. Within the time greater than 18.6 years stratum, there was also a significant positive association between current dioxin and the anxiety score (p=0.028). The mean unadjusted scores for this stratum similarly became larger for increasing current dioxin (low, 46.0; medium, 47.1; high, 49.6).

After adjusting for education, the minimal analysis still displayed a nonsignificant current dioxin-by-time since tour interaction (Table 9-46 [g]: p=0.202). Within the time over 18.6 years stratum, the positive association between current dioxin and the anxiety score became only marginally significant (p=0.068). The current dioxin-by-time since tour interaction also remained nonsignificant for the maximal analysis after the retention of race and education in the model (Table 9-46 [h]: p=0.914). The association between current dioxin and the anxiety score was no longer significant for either time stratum.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In the unadjusted analysis of categorized current dioxin, there was a significant difference found among the mean anxiety scores of the participants in the four current dioxin categories (Table 9-46 [i]: p=0.038). The unadjusted mean scores for the background, unknown, low, and high current dioxin categories were 47.2, 44.1, 46.4, and 49.3. The analysis found the mean anxiety score of Ranch Hands in the unknown category to be significantly lower than the mean score of Comparisons in the background category (p=0.023). The mean anxiety scores of the low and high current dioxin categories did not differ significantly from the mean score of those in the background category (p=0.630 and p=0.231).

The adjusted analysis of the MCMI anxiety score revealed a significant interaction between categorized current dioxin and race (Table 9-46 [j]: p=0.018). After stratifying by race, the adjusted analysis for Black participants detected a marginally significant overall difference among the mean anxiety scores of the four current dioxin categories (Appendix Table H-1: p=0.066). The adjusted mean anxiety scores for the background, unknown, low, and high categories were 45.1, 60.7, 54.6, and 41.7. The mean score of the Ranch Hands in the unknown category was significantly higher than the mean score of the Comparisons in the background category (p=0.021).

The adjusted analysis of the non-Black stratum also detected a marginally significant difference among the mean anxiety scores of the four current dioxin categories (Appendix Table H-1: p=0.071). The mean scores for the background, unknown, low, and high categories were 47.2, 44.2, 45.3, and 48.7. In contrast to the analysis of the Black stratum, the mean anxiety score of the unknown category was significantly lower than the mean score of the background category in the non-Black stratum (p=0.032).

After deletion of the interaction from the model and adjusting for race and an age-by-education interaction, there were no significant differences detected in the mean anxiety scores of the four current dioxin categories (Table 9-46 [j]: p=0.248).

Somatoform Score—MCMI

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

In the unadjusted analysis based upon the minimal assumption, the association between initial dioxin and the MCMI somatoform score was not significant (Table 9-47 [a]: p=0.327). However, under the maximal assumption, there was a significant positive association between initial dioxin and the somatoform score (Table 9-47 [b]: p=0.033). The unadjusted mean scores for the low, medium, and high initial dioxin categories of the maximal cohort were 49.1, 51.2, and 51.8. Consistent with the unadjusted results, the adjusted analysis also detected a nonsignificant association between initial dioxin and the somatoform score for the minimal cohort (Table 9-47 [c]: p=0.196) and a significant positive association for the maximal cohort (Table 9-47 [d]: p=0.011).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

Under both the minimal and the maximal assumptions, the unadjusted analysis of the somatoform score exhibited nonsignificant current dioxin-by-time since tour interactions (Table 9-47 [e] and [f]: p=0.683 and p=0.394, respectively). However, for the time less than or equal to 18.6 years stratum of the maximal cohort, there was a marginally significant positive association between current dioxin and the somatoform score (Table 9-47 [f]: p=0.055). For this time stratum, the mean somatoform scores for low, medium, and high current dioxin were 48.2, 50.0, 53.0.

In the adjusted analysis of the somatoform score, the interaction of current dioxin and time since tour was again nonsignificant under the minimal assumption (Table 9-47 [g]: p=0.670) and the maximal assumption (Table 9-47 [h]: p=0.436). Similarly, after adjusting for age, race, and lifetime alcohol history, the time less than or equal to 18.6 years stratum of the maximal cohort displayed a significant positive association between current dioxin and the somatoform score (Table 9-47 [h]: p=0.030).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The unadjusted analysis of categorized current dioxin did not detect a significant overall difference among the mean somatoform scores of the four current dioxin categories (Table 9-47 [i]: p=0.407).

TABLE 9-47.

Analysis of Somatoform Score (MCMI)

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Mean	Slope (Std. Error)[a]	p-Value
a) Minimal	Low	129	51.7	0.617 (0.629)	0.327
(n=514)	Medium	256	50.7		
(R^2=0.002)	High	129	52.9		
b) Maximal	Low	182	49.1	0.981 (0.460)	0.033
(n=732)	Medium	368	51.2		
(R^2=0.006)	High	182	51.8		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Initial Dioxin	n	Adj. Mean	Adj. Slope (Std. Error)[a]	p-Value	Covariate Remarks
c) Minimal	Low	129	54.3	0.811 (0.627)	0.196	RACE (p=0.038)
(n=509)	Medium	252	53.4			DRKYR (p=0.050)
(R^2=0.017)	High	128	56.0			
d) Maximal	Low	180	52.5	1.199 (0.471)	0.011	AGE (p=0.123)
(n=724)	Medium	365	54.1			RACE (p=0.008)
(R^2=0.022)	High	179	55.6			DRKYR (p=0.040)

[a]Slope and standard error based on somatoform score versus log_2 dioxin.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 9-47. (Continued)

Analysis of Somatoform Score (MCMI)

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Mean/(n) Current Dioxin Low	Medium	High	Slope (Std. Error)[a]	p-Value
e) Minimal						0.683[b]
(n=514)	≤18.6	52.3	51.4	50.3	0.374 (1.026)	0.716[c]
(R^2=0.003)		(72)	(128)	(53)		
	>18.6	51.2	50.3	54.0	0.915 (0.841)	0.277[c]
		(56)	(129)	(76)		
f) Maximal						0.394[b]
(n=732)	≤18.6	48.2	50.0	53.0	1.374 (0.714)	0.055[c]
(R^2=0.008)		(105)	(190)	(82)		
	>18.6	51.1	51.1	52.5	0.560 (0.632)	0.375[c]
		(78)	(175)	(102)		

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Mean/(n) Current Dioxin Low	Medium	High	Adj. Slope (Std. Error)[a]	p-Value	Covariate Remarks
g) Minimal						0.670[b]	RACE (p=0.041)
(n=509)	≤18.6	54.7	53.8	53.3	0.494 (1.019)	0.628[c]	DRKYR (p=0.055)
(R^2=0.018)		(72)	(127)	(53)			
	>18.6	54.4	53.0	56.9	1.056 (0.836)	0.207[c]	
		(56)	(126)	(75)			
h) Maximal						0.436[b]	AGE (p=0.134)
(n=724)	≤18.6	51.6	53.3	56.7	1.581 (0.726)	0.030[c]	RACE (p=0.008)
(R^2=0.023)		(104)	(189)	(81)			DRKYR (p=0.041)
	>18.6	54.2	54.0	56.6	0.840 (0.645)	0.193[c]	
		(77)	(173)	(100)			

[a]Slope and standard error based on somatoform score versus log_2 dioxin.

[b]Test of significance for homogeneity of slopes (current dioxin continuous, time categorized).

[c]Test of significance for slope equal to 0 (current dioxin continuous, time categorized).

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 9-47. (Continued)

Analysis of Somatoform Score (MCMI)

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Mean	Contrast	Difference of Means (95% C.I.)	p-Value
Background	781	51.1	All Categories		0.407
Unknown	340	50.2	Unknown vs. Background	-0.9 (-3.1,1.4)	0.445
Low	194	50.1	Low vs. Background	-0.9 (-3.7,1.8)	0.500
High	184	52.7	High vs. Background	1.6 (-1.2,4.4)	0.260
Total	1,499		(R^2=0.002)		

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Adj. Mean	Contrast	Difference of Adj. Means (95% C.I.)	p-Value	Covariate Remarks
Background	775	52.4**	All Categories		0.438**	DXCAT*ALC (p=0.019)
						DXCAT*DRKYR (p=0.007)
Unknown	335	51.9**	Unknown vs. Background	-0.5 (-2.7,1.8)**	0.675**	RACE (p=0.113)
Low	190	51.0**	Low vs. Background	-1.4 (-4.1,1.4)**	0.334**	EDUC (p=0.029)
High	180	53.9**	High vs. Background	1.5 (-1.3,4.4)**	0.296**	AGE*DRKYR (p=0.016)
Total	1,480		(R^2=0.024)			

**Categorized current dioxin-by-covariate interaction ($0.01<p\leq0.05$); adjusted mean, confidence interval, and p-value derived from a model fitted after deletion of this interaction.

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

The adjusted analysis detected significant interactions between categorized current dioxin and current alcohol use and between categorized current dioxin and lifetime alcohol history (Table 9-47 [j]: p=0.019 and p=0.007, respectively). To investigate these interactions, Appendix Table H-1 presents separate analyses for each of four current alcohol use and lifetime alcohol history combination strata (i.e., ≤1 drink/day, ≤40 drink-years; ≤1 drink/day, >40 drink-years; >1 drink/day, ≤40 drink-years; >1 drink/day, and >40 drink years).

The contrasts of the four current dioxin categories were not significant for any of the stratified analyses (Appendix Table H-1: p>0.10 for each analysis). However, the adjusted mean somatoform score of the low category was significantly lower than the mean of the background category (p=0.044) for participants who drank less than or equal to one drink per day but who had more than 40 drink-years. The contrast of the high versus background categories was also marginally significant for this stratum with the mean of the background category again higher (p=0.094). The mean somatoform scores for this stratum were 56.0, 55.2, 47.4, and 49.0 for the background, unknown, low, and high current dioxin categories.

The analysis of the participants who drank more than one drink per day but had 40 drink-years or less detected a marginally significant difference between the mean somatoform score of the Comparisons in the background category and of the Ranch Hands in the high category (Appendix Table H-1: p=0.077). The adjusted mean somatoform scores for this stratum were 48.3, 53.5, 52.0, and 58.4 for the background, unknown, low, and high current dioxin categories.

After deletion of the interaction from the model and adjusting only for race, current alcohol use, education, and an age-by-lifetime alcohol history interaction, there were no significant differences detected among the mean somatoform scores of the four current dioxin categories (Table 9-47 [j]: p=0.438).

Hypomania Score—MCMI

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Based upon the minimal assumption, the unadjusted analysis detected a marginally significant negative association between initial dioxin and the MCMI hypomania score (Table 9-48 [a]: p=0.054). The unadjusted mean scores for the low, medium, and high initial dioxin categories were 21.6, 22.0, and 17.6. For the maximal assumption, there was a nonsignificant negative association between initial dioxin and the hypomania score (Table 9-48 [b]: p=0.133).

Under the minimal assumption, there was a significant interaction between initial dioxin and race (Table 9-48 [c]: p=0.013). To examine this interaction, Blacks and non-Blacks were analyzed separately. For the Black stratum, there was a significant positive association between initial dioxin and the hypomania score (Appendix Table H-1: p=0.036); and for the non-Black stratum, there was a significant negative association (p=0.025). The adjusted mean hypomania scores for the Black stratum were 21.0, 25.8, and 46.6 for the low, medium, and high initial dioxin categories. The corresponding means for the non-Black stratum were 21.7, 22.8, and 17.2. After deletion of the initial dioxin-by-race interaction from

TABLE 9-48.

Analysis of Hypomania Score (MCMI)

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Mean[a]	Slope (Std. Error)[b]	p-Value
a) Minimal	Low	129	21.6	-0.189 (0.097)	0.054
(n=514)	Medium	256	22.0		
(R^2=0.007)	High	129	17.6		
b) Maximal	Low	182	20.7	-0.108 (0.072)	0.133
(n=732)	Medium	368	21.8		
(R^2=0.003)	High	182	19.1		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Initial Dioxin	n	Adj. Mean[a]	Adj. Slope (Std. Error)[b]	p-Value	Covariate Remarks
c) Minimal	Low	128	23.2**	-0.186 (0.102)**	0.069**	INIT*RACE (p=0.013)
(n=505)	Medium	250	24.8**			DRKYR (p=0.013)
(R^2=0.052)	High	127	19.5**			EDUC (p=0.109)
						AGE*RACE (p=0.013)
d) Maximal	Low	179	22.0**	-0.090 (0.076)**	0.236**	INIT*RACE (p=0.039)
(n=719)	Medium	362	24.1**			DRKYR (p=0.002)
(R^2=0.045)	High	178	21.4**			EDUC (p=0.056)
						AGE*RACE (p=0.007)

[a]Transformed from square root scale.

[b]Slope and standard error based on square root hypomania score versus log_2 dioxin.

**Log_2 (initial dioxin)-by-covariate interaction ($0.01<p\leq0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of this interaction.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 9-43. (Continued)

Analysis of Hypomania Score
(MCMI)

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Mean[a]/(n) Current Dioxin Low	Medium	High	Slope (Std. Error)[b]	p-Value
e) Minimal						0.674[c]
(n=514)	≤18.6	23.0	21.4	19.3	-0.136 (0.159)	0.394[d]
(R^2=0.008)		(72)	(128)	(53)		
	>18.6	21.0	21.9	16.6	-0.222 (0.130)	0.089[d]
		(56)	(129)	(76)		
f) Maximal						0.237[c]
(n=732)	≤18.6	20.4	21.9	19.1	-0.017 (0.111)	0.875[d]
(R^2=0.005)		(105)	(190)	(82)		
	>18.6	22.5	22.0	17.7	-0.193 (0.098)	0.050[d]
		(78)	(175)	(102)		

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Mean[a]/(n) Current Dioxin Low	Medium	High	Adj. Slope (Std. Error)[b]	p-Value	Covariate Remarks
g) Minimal						0.782[c]	AGE (p=0.060)
(n=505)	≤18.6	27.7	25.4	22.5	-0.182 (0.164)	0.268[d]	RACE (p=0.123)
(R^2=0.034)		(71)	(126)	(53)			DRKYR (p=0.013)
	>18.6	24.1	26.6	20.0	-0.239 (0.135)	0.078[d]	EDUC (p=0.097)
		(56)	(125)	(74)			
h) Maximal						0.162[c]	DRKYR (p=0.003)
(n=719)	≤18.6	21.5	24.0	21.5	0.002 (0.115)	0.985[d]	EDUC (p=0.049)
(R^2=0.042)		(104)	(186)	(81)			AGE*RACE (p=0.029)
	>18.6	25.9	24.5	19.8	-0.203 (0.101)	0.045[d]	
		(77)	(172)	(99)			

[a]Transformed from square root scale.

[b]Slope and standard error based on square root hypomania score versus log_2 dioxin.

[c]Test of significance for homogeneity of slopes (current dioxin continuous, time categorized).

[d]Test of significance for slope equal to 0 (current dioxin continuous, time categorized).

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 9-48. (Continued)

Analysis of Hypomania Score (MCMI)

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Mean[a]	Contrast	Difference of Means (95% C.I.)[e]	p-Value[f]
Background	781	21.9	All Categories		0.251
Unknown	340	22.4	Unknown vs. Background	0.5 –	0.742
Low	194	22.4	Low vs. Background	0.5 –	0.795
High	184	18.3	High vs. Background	-3.5 –	0.071
Total	1,499		(R^2=0.003)		

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Adj. Mean	Contrast	Difference of Adj. Means (95% C.I.)	p-Value	Covariate Remarks
Background	775	****	All Categories		****	DXCAT*RACE (p=0.004) AGE (p=0.048)
Unknown	335	****	Unknown vs. Background	****	****	DRKYR (p=0.002)
Low	190	****	Low vs. Background	****	****	EDUC (p=0.009)
High	180	****	High vs. Background	****	****	
Total	1,480		(R^2=0.025)			

[a]Transformed from square root scale.

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

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

****Categorized current dioxin-by-covariate interaction ($p \leq 0.01$); adjusted mean, confidence interval, and p-value not presented.

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

the model, there was only a marginally significant negative association between initial dioxin and the hypomania score (Table 9-48 [c]: p=0.069).

The adjusted analysis under the maximal assumption also detected a significant initial dioxin-by-race interaction (Table 9-48 [d]: p=0.039). This interaction was also investigated by stratifying the Ranch Hands by race, and the results were similar to those of the minimal cohort. There was a marginally significant positive association between initial dioxin and the hypomania score in the Black stratum (Appendix Table H-1: p=0.065) and a nonsignificant negative association in the non-Black stratum (p=0.135). The adjusted means for the low, medium, and high initial dioxin categories were 20.7, 20.2, and 49.6 for the Black stratum and 19.9, 22.3, and 18.5 for the non-Black stratum. After deletion of the initial dioxin-by-race interaction, the association between initial dioxin and the MCMI hypomania score was nonsignificant (Table 9-48 [d]: p=0.236).

Model 2: Ranch Hands - Log_2 (Initial Dioxin)

In the unadjusted analysis of the MCMI hypomania score, the interaction of current dioxin and time since tour was not significant for either the minimal or the maximal cohort (Table 9-48 [e] and [f]: p=0.674 and p=0.237). However, under the minimal assumption, the negative association between current dioxin and the hypomania score was marginally significant for the time greater than 18.6 years stratum (Table 9-48 [e]: p=0.089). The unadjusted mean hypomania scores for this stratum were 21.0, 21.9, and 16.6 for low, medium, and high current dioxin. Also, under the maximal assumption, there was a significant negative association between current dioxin and the hypomania score for the time over 18.6 years stratum (Table 9-48 [f]: p=0.050). The unadjusted mean hypomania scores for this stratum decreased steadily for increasing levels of current dioxin (low, 22.5; medium, 22.0; high, 17.7).

After adjusting for covariate information, the current dioxin-by-time since tour interaction remained nonsignificant for both the minimal and the maximal cohort (Table 9-48 [g] and [h]: p=0.782 and p=0.162). Consistent with the unadjusted results, there was a marginally significant negative association between current dioxin and the hypomania score for the time greater than 18.6 years stratum of the minimal cohort (Table 9-48 [g]: p=0.078). Likewise, there was a significant negative association for the same time stratum under the maximal assumption (Table 9-48 [h]: p=0.045).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The unadjusted analysis of categorized current dioxin did not detect a significant overall difference among the mean hypomania scores of the four current dioxin categories (Table 9-48 [i]: p=0.251). However, the analysis displayed a marginally significant difference between the mean score of the Comparisons in the background category and the mean score of the Ranch Hands in the high category (p=0.071). The unadjusted mean hypomania scores for the background, unknown, low, and high categories were 21.9, 22.4, 22.4, and 18.3.

The adjusted analysis detected a significant interaction between categorized current dioxin and race (Table 9-48 [j]: p=0.004). To examine this interaction, the participants were

stratified by race and analyzed separately. For the Black stratum, the test for overall differences among the four mean hypomania scores was significant (Appendix Table H-1: p=0.013). The adjusted mean hypomania scores for the Black stratum were 24.0, 42.1, 16.7, and 54.3 for the background, unknown, low, and high current dioxin categories. The mean score of the unknown category was marginally higher than the mean score of the background category (p=0.063) and the mean score of the high category was significantly higher than that of the background category (p=0.015).

The adjusted analysis of the non-Black stratum did not detect a significant overall difference among the mean hypomania scores of the four current dioxin categories (Appendix Table H-1: p=0.125). However, the mean hypomania score of the high current dioxin category was significantly lower than the mean score of the background category (p=0.039). The adjusted mean hypomania scores for the background, unknown, low, and high current dioxin categories of the non-Black stratum were 21.7, 21.6, 23.3, and 17.5.

Dysthymia Score—MCMI

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

In the unadjusted analysis of the MCMI dysthymia score, there was not a significant association with initial dioxin for the minimal assumption (Table 9-49 [a]: p=0.184). Based on the maximal assumption, there was a significant positive association between initial dioxin and the dysthymia score (Table 9-49 [b]: p=0.031). The unadjusted mean dysthymia scores for the low, medium, and high initial dioxin categories of the maximal cohort were 48.0, 48.8, and 51.6.

The adjusted analysis of the dysthymia score detected significant initial dioxin-by-race interactions for both the minimal and maximal cohorts (Table 9-49 [c] and [d]: p=0.002 and p=0.008). Separate analyses were performed for Black and non-Black participants (Appendix Table H-1). The stratified analysis of the minimal cohort displayed a significant negative association between the dysthymia score and initial dioxin in the Black stratum (p=0.006) and a marginally significant positive association for the non-Black stratum (p=0.061). The adjusted mean dysthymia scores for the Black stratum were nearly the same for the low and medium initial dioxin categories and decreased for the high category (low, 55.2; medium, 52.1; high, 21.3). In contrast, the adjusted mean dysthymia scores for the non-Black stratum were again nearly the same for the low and medium categories but increased for the high category (low, 49.8; medium, 49.3; high, 52.9).

Similarly, for the maximal assumption, there was a significant negative association between initial dioxin and the dysthymia score for the Black stratum (Appendix Table H-1: p=0.024) and a significant positive association for the non-Black stratum (p=0.010). The adjusted mean dysthymia scores for the low, medium, and high initial dioxin categoires of the Black stratum were 45.0, 55.2, and 34.9. The corresponding mean scores for the non-Black stratum were 48.0, 48.3, and 52.3.

TABLE 9-49.

Analysis of Dysthymia Score (MCMI)

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Mean	Slope (Std. Error)[a]	p-Value
a) Minimal	Low	129	50.3	1.052 (0.791)	0.184
(n=514)	Medium	256	49.5		
(R^2=0.003)	High	129	52.1		
b) Maximal	Low	182	48.0	1.293 (0.597)	0.031
(n=732)	Medium	368	48.8		
(R^2=0.006)	High	182	51.6		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Initial Dioxin	n	Adj. Mean	Adj. Slope (Std. Error)	p-Value	Covariate Remarks
c) Minimal	Low	129	****	****	****	INIT*RACE (p=0.002)
(n=514)	Medium	256	****			
(R^2=0.022)	High	129	****			
d) Maximal	Low	182	****	****	****	INIT*RACE (p=0.008)
(n=732)	Medium	368	****			
(R^2=0.016)	High	182	****			

[a]Slope and standard error based on dysthymia score versus log_2 dioxin.

****Log_2 (initial dioxin)-by-covariate interaction ($p \leq 0.01$); adjusted mean, adjusted slope, standard error, and p-value not presented.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 9-49. (Continued)

Analysis of Dysthymia Score (MCMI)

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Mean/(n) Current Dioxin Low	Medium	High	Slope (Std. Error)[a]	p-Value
e) Minimal						0.576[b]
(n=514)	≤18.6	49.3	49.5	48.5	0.328 (1.290)	0.799[c]
(R^2=0.005)		(72)	(128)	(53)		
	>18.6	50.7	50.5	53.5	1.262 (1.058)	0.233[c]
		(56)	(129)	(76)		
f) Maximal						0.616[b]
(n=732)	≤18.6	48.0	47.5	50.7	0.886 (0.927)	0.340[c]
(R^2=0.008)		(105)	(190)	(82)		
	>18.6	47.3	50.7	52.1	1.507 (0.820)	0.067[c]
		(78)	(175)	(102)		

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Mean/(n) Current Dioxin Low	Medium	High	Adj. Slope (Std. Error)[a]	p-Value	Covariate Remarks
g) Minimal						0.576[b]	- -
(n=514)	≤18.6	49.3	49.5	48.5	0.328 (1.290)	0.799[c]	
(R^2=0.005)		(72)	(128)	(53)			
	>18.6	50.7	50.5	53.5	1.262 (1.058)	0.233[c]	
		(56)	(129)	(76)			
h) Maximal						0.616[b]	- -
(n=732)	≤18.6	48.0	47.5	50.7	0.886 (0.927)	0.340[c]	
(R^2=0.008)		(105)	(190)	(82)			
	>18.6	47.3	50.7	52.1	1.507 (0.820)	0.067[c]	
		(78)	(175)	(102)			

[a]Slope and standard error based on dysthymia score versus log_2 dioxin.

[b]Test of significance for homogeneity of slopes (current dioxin continuous, time categorized).

[c]Test of significance for slope equal to 0 (current dioxin continuous, time categorized).

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 9-49. (Continued)

Analysis of Dysthymia Score (MCMI)

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Mean	Contrast	Difference of Means (95% C.I.)	p-Value
Background	781	49.7	All Categories		0.159
Unknown	340	47.1	Unknown vs. Background	-2.5 (-5.4,0.3)	0.078
Low	194	49.4	Low vs. Background	-0.3 (-3.8,3.2)	0.886
High	184	51.5	High vs. Background	1.8 (-1.8,5.4)	0.329
Total	1,499		(R^2=0.003)		

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Adj. Mean	Contrast	Difference of Adj. Means (95% C.I.)	p-Value	Covariate Remarks
Background	776	49.4**	All Categories		0.450**	DXCAT*RACE (p=0.042)
						ALC (p=0.144)
Unknown	336	47.5**	Unknown vs. Background	-1.9 (-4.8,1.0)**	0.191**	EDUC (p=0.031)
Low	190	48.7**	Low vs. Background	-0.7 (-4.2,2.8)**	0.699**	
High	183	50.5**	High vs. Background	1.1 (-2.5,4.8)**	0.535**	
Total	1,485		(R^2=0.013)			

**Categorized current dioxin-by-covariate interaction ($0.01<p\leq0.05$); adjusted mean, confidence interval, and p-value derived from a model fitted after deletion of this interaction.

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

Under the minimal assumption, the unadjusted analysis of the MCMI dysthymia score contained a nonsignificant interaction between current dioxin and time since tour (Table 9-49 [e]: p=0.576). Under the maximal assumption, the unadjusted analysis also displayed a nonsignificant current dioxin-by-time interaction (Table 9-49 [f]: p=0.616). However, for Ranch Hands in the time greater than 18.6 years stratum of the maximal cohort, there was a marginally significant positive association between current dioxin and the dysthymia score (p=0.067). For this time strata, the unadjusted mean dysthymia scores for low, medium, and high current dioxin were 47.3, 50.7, and 52.1.

None of the candidate covariates was retained in the adjusted model for either the minimal or the maximal cohort; thus, the adjusted results (Table 9-49 [g] and [h]) are identical to the unadjusted results.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The unadjusted analysis of categorized current dioxin did not detect an overall significant difference among the mean dysthymia scores of the four current dioxin categories (Table 9-49 [i]: p=0.159). However, there was a marginally significant difference between the mean score of the Comparisons in the background category and the mean score of the Ranch Hands in the unknown category (p=0.078). The unadjusted mean dysthymia scores for the background, unknown, low, and high current dioxin categories were 49.7, 47.1, 49.4, and 51.5.

In the adjusted analysis, there was a significant interaction between categorized current dioxin and race (Table 9-49 [j]: p=0.042). After stratifying the participants by race, the adjusted analysis displayed a marginally significant overall difference among the mean dysthymia scores for the Black stratum (Appendix Table H-1: p=0.097). Specifically, the mean score of the Ranch Hands in the high category was marginally lower than the mean score of the Comparisons in the background category (p=0.085). In the non-Black stratum, the analysis did not detect a significant difference among the mean dysthymia scores of the four current dioxin categories (p=0.211). In the Black stratum, the mean score for the high current dioxin category was much lower than the mean scores of the other three categories (background, 48.1; unknown, 55.2; low, 56.8; high, 33.4). Contrastingly, for the non-Black stratum, the mean score of the high category was higher than the mean scores of the other three categories (background, 49.7; unknown, 47.4; low, 48.4; high, 51.5).

After deletion of the categorized current dioxin-by-race interaction from the model, no significant differences were found among the mean dysthymia scores of the four current dioxin categories (Table 9-49 [j]: p=0.450).

Alcohol Abuse Score—MCMI

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

In the unadjusted analysis of the MCMI alcohol abuse score, there was no significant association with initial dioxin under either the minimal or the maximal assumption (Table 9-50 [a] and [b]: p=0.781 and p=0.588).

The adjusted analysis also exhibited nonsignificant associations between initial dioxin and the alcohol abuse score for both the minimal and maximal cohorts (Table 9-50 [c] and [d]: p=0.921 and p=0.440, respectively).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

In both the unadjusted and adjusted minimal and maximal analyses, the current dioxin-by-time since tour interactions and the associations between current dioxin and the MCMI alcohol abuse score within each time stratum were nonsignificant (Table 9-50 [e-h]: p>0.15 for each analysis).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The unadjusted analysis did not detect a significant difference among the mean alcohol abuse scores of the four current dioxin categories (Table 9-50 [i]: p=0.898).

The adjusted analysis displayed a significant interaction between categorized current dioxin and race (Table 9-50 [j]: p=0.004). To examine this interaction, the participants were stratified by race and analyzed separately (Appendix Table H-1). In the Black stratum, there was a significant difference among the mean alcohol abuse scores of the four current dioxin categories (Appendix Table H-1: p=0.010). Specifically, the mean scores of the unknown and high current dioxin categories were significantly higher than the mean score of the background category (p=0.008 and p=0.012, respectively). T mean alcohol abuse score of the background category was the lowest of the four categorie. ackground, 30.1; unknown, 44.2; low, 36.7; high, 45.9).

In the non-Black stratum, the mean alcohol abuse scores of the four current dioxin categories were not significantly different (p=0.458). In this stratum, the mean score of the background category was the highest of the four categories (background, 31.4; unknown, 30.5; low, 30.5; high, 29.4).

Drug Abuse Score—MCMI

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

In both the unadjusted and the adjusted minimal and maximal analyses, the associations between initial dioxin and the MCMI drug abuse score were nonsignificant (Table 9-51 [a-d]: p>0.35).

TABLE 9-50.

Analysis of Alcohol Abuse Score (MCMI)

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Mean	Slope (Std. Error)[a]	p-Value
a) Minimal	Low	129	31.1	0.171 (0.615)	0.781
(n=514)	Medium	256	30.6		
(R^2<0.001)	High	129	31.6		
b) Maximal	Low	182	30.5	0.244 (0.451)	0.588
(n=732)	Medium	368	30.6		
(R^2<0.001)	High	182	31.5		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Initial Dioxin	n	Adj. Mean	Adj. Slope (Std. Error)[a]	p-Value	Covariate Remarks
c) Minimal	Low	128	35.2	-0.061 (0.615)	0.921	RACE (p=0.002)
(n=510)	Medium	254	34.3			EDUC (p=0.005)
(R^2=0.036)	High	128	35.2			
d) Maximal	Low	181	36.8	-0.357 (0.461)	0.440	RACE (p<0.001)
(n=727)	Medium	365	35.0			EDUC (p<0.001)
(R^2=0.045)	High	181	35.3			

[a]Slope and standard error based on alcohol abuse score versus log_2 dioxin.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 9-50. (Continued)

Analysis of Alcohol Abuse (MCMI)

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Mean/(n) Current Dioxin Low	Medium	High	Slope (Std. Error)[a]	p-Value
e) Minimal						0.325[b]
(n=514)	≤18.6	32.5	30.2	29.8	-0.668 (1.003)	0.506[c]
(R^2=0.002)		(72)	(128)	(53)		
	>18.6	29.4	31.0	33.1	0.609 (0.822)	0.459[c]
		(56)	(129)	(76)		
f) Maximal						0.384[b]
(n=732)	≤18.6	30.8	30.8	29.8	-0.230 (0.700)	0.742[c]
(R^2=0.002)		(105)	(190)	(82)		
	>18.6	29.0	31.5	32.0	0.583 (0.619)	0.347[c]
		(78)	(175)	(102)		

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Mean/(n) Current Dioxin Low	Medium	High	Adj. Slope (Std. Error)[a]	p-Value	Covariate Remarks
g) Minimal						0.455[b]	RACE (p=0.002)
(n=510)	≤18.6	36.4	33.8	33.7	-0.727 (0.992)	0.464[c]	EDUC (p=0.004)
(R^2=0.037)		(71)	(127)	(53)			
	>18.6	33.5	34.5	36.3	0.228 (0.819)	0.781[c]	
		(56)	(128)	(75)			
h) Maximal						0.384[b]	AGE (p=0.146)
(n=727)	≤18.6	36.4	35.0	32.9	-1.011 (0.714)	0.157[c]	RACE (p<0.001)
(R^2=0.049)		(105)	(187)	(82)			EDUC (p<0.001)
	>18.6	35.0	36.0	34.6	-0.213 (0.630)	0.736[c]	
		(78)	(174)	(101)			

[a]Slope and standard error based on alcohol abuse score versus log_2 dioxin.

[b]Test of significance for homogeneity of slopes (current dioxin continuous, time categorized).

[c]Test of significance for slope equal to 0 (current dioxin continuous, time categorized).

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 9-50. (Continued)

Analysis of Alcohol Abuse Score (MCMI)

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Mean	Contrast	Difference of Means (95% C.I.)	p-Value
Background	781	31.3	All Categories		0.898
Unknown	340	30.5	Unknown vs. Background	-0.8 (-3.0,1.3)	0.443
Low	194	31.0	Low vs. Background	-0.3 (-2.9,2.3)	0.810
High	184	31.0	High vs. Background	-0.3 (-3.0,2.4)	0.811
Total	1,499		(R^2<0.001)		

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Adj. Mean	Contrast	Difference of Adj. Means (95% C.I.)	p-Value	Covariate Remarks
Background	776	****	All Categories		****	DXCAT*RACE (p=0.004) EDUC (p<0.001)
Unknown	338	****	Unknown vs. Background	****	****	
Low	192	****	Low vs. Background	****	****	
High	183	****	High vs. Background	****	****	
Total	1,489		(R^2=0.023)			

****Categorized current dioxin-by-covariate interaction ($p \leq 0.01$); adjusted mean, confidence interval, and p-value not presented.

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 9-51.

Analysis of Drug Abuse Score (MCMI)

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Mean	Slope (Std. Error)[a]	p-Value
a) Minimal	Low	129	46.4	-0.501 (0.734)	0.495
(n=514)	Medium	256	49.4		
(R^2<0.001)	High	129	46.0		
b) Maximal	Low	182	45.6	0.151 (0.549)	0.783
(n=732)	Medium	368	48.1		
(R^2<0.001)	High	182	47.2		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Initial Dioxin	n	Adj. Mean	Adj. Slope (Std. Error)[a]	p-Value	Covariate Remarks
c) Minimal	Low	129	51.7	-0.670 (0.752)	0.373	AGE (p=0.080)
(n=509)	Medium	252	54.9			RACE (p=0.001)
(R^2=0.045)	High	128	51.4			DRKYR (p=0.003)
d) Maximal	Low	180	51.7	-0.220 (0.555)	0.692	AGE (p=0.011)
(n=724)	Medium	365	53.6			RACE (p<0.001)
(R^2=0.044)	High	179	51.9			DRKYR (p<0.001)

[a]Slope and standard error based on drug abuse score versus log_2 dioxin.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 9-51. (Continued)

Analysis of Drug Abuse Score (MCMI)

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Mean/(n) Current Dioxin Low	Medium	High	Slope (Std. Error)[a]	p-Value
e) Minimal						0.247[b]
(n=514)	≤18.6	48.2	50.9	49.0	0.963 (1.191)	0.419[c]
(R^2=0.012)		(72)	(128)	(53)		
	>18.6	45.4	47.4	43.9	-0.823 (0.976)	0.399[c]
		(56)	(129)	(76)		
f) Maximal						0.204[b]
(n=732)	≤18.6	45.9	49.6	50.3	1.274 (0.850)	0.134[c]
(R^2=0.009)		(105)	(190)	(82)		
	>18.6	42.9	47.3	45.1	-0.169 (0.752)	0.822[c]
		(78)	(175)	(102)		

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Mean/(n) Current Dioxin Low	Medium	High	Adj. Slope (Std. Error)[a]	p-Value	Covariate Remarks
g) Minimal						0.223[b]	RACE (p<0.001)
(n=509)	≤18.6	53.8	57.0	55.7	1.261 (1.176)	0.284[c]	DRKYR (p=0.003)
(R^2=0.053)		(72)	(127)	(53)			
	>18.6	49.9	52.9	50.0	-0.590 (0.965)	0.541[c]	
		(56)	(126)	(75)			
h) Maximal						0.160[b]	AGE (p=0.040)
(n=724)	≤18.6	51.9	55.1	55.4	0.963 (0.854)	0.260[c]	RACE (p<0.001)
(R^2=0.051)		(104)	(189)	(81)			DRKYR (p<0.001)
	>18.6	50.1	52.8	49.7	-0.607 (0.758)	0.424[c]	
		(77)	(173)	(100)			

[a]Slope and standard error based on drug abuse score versus log_2 dioxin.

[b]Test of significance for homogeneity of slopes (current dioxin continuous, time categorized).

[c]Test of significance for slope equal to 0 (current dioxin continuous, time categorized).

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 9-51. (Continued)

Analysis of Drug Abuse Score (MCMI)

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Mean	Contrast	Difference of Means (95% C.I.)	p-Value
Background	781	48.2	All Categories		0.746
Unknown	340	47.2	Unknown vs. Background	-1.0 (-3.5,1.5)	0.429
Low	194	48.9	Low vs. Background	0.7 (-2.4,3.8)	0.659
High	184	47.4	High vs. Background	-0.8 (-4.0,2.4)	0.619
Total	1,499		(R^2=0.001)		

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Adj. Mean	Contrast	Difference of Adj. Means (95% C.I.)	p-Value	Covariate Remarks
Background	780	51.7	All Categories		0.769	AGE (p=0.023) RACE (p<0.001)
Unknown	337	51.3	Unknown vs. Background	-0.4 (-2.9,2.1)	0.761	DRKYR (p<0.001)
Low	192	52.6	Low vs. Background	0.9 (-2.1,4.0)	0.552	
High	181	50.5	High vs. Background	-1.1 (-4.3,2.1)	0.486	
Total	1,490		(R^2=0.023)			

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

The unadjusted analysis of the MCMI drug abuse score did not detect a significant current dioxin-by-time since tour interaction in either the minimal or the maximal analysis (Table 9-51 [e] and [f]: p=0.247 and p=0.204). The association between current dioxin and the drug abuse score was also nonsignificant within each time stratum under both minimal and maximal assumptions.

The adjustment for covariate information did not change the lack of significance of the unadjusted results (Table 9-51 [g] and [h]: p>0.15 for each analysis).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

Neither the unadjusted nor the adjusted analysis of categorized current dioxin detected a significant difference among the mean drug abuse scores of the four current dioxin categories (Table 9-51 [i] and [j]: p=0.746 and p=0.769, respectively).

Psychotic Thinking Score—MCMI

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

In the unadjusted analysis of the MCMI psychotic thinking score, there were significant positive associations with initial dioxin under both the minimal and the maximal assumptions (Table 9-52 [a] and [b]: p<0.001 for both analyses). Based on the minimal assumption, the mean psychotic thinking scores for Ranch Hands in the low, medium, and high initial dioxin categories were 28.1, 32.9, and 36.5. The corresponding means under the maximal assumption were 30.6, 30.3, and 36.1, respectively.

The adjusted analysis also found significant positive associations between initial dioxin and the MCMI psychotic thinking score for both the minimal and the maximal cohorts (Table 9-52 [c] and [d]: p=0.001 and p=0.021).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

The unadjusted analysis of the psychotic thinking score detected marginally significant interactions between current dioxin and time since tour under both the minimal and the maximal assumptions (Table 9-52 [e] and [f]: p=0.059 and p=0.083). Also, under both assumptions, there were significant positive associations between current dioxin and the psychotic thinking score for Ranch Hands with more than 18.6 years since the end of their tour (Table 9-52 [e] and [f]: p<0.001 for both analyses). The mean psychotic thinking scores of Ranch Hands having greater than 18.6 years since tour for low, medium, and high current dioxin were 25.6, 32.5, and 38.5 under the minimal assumption and 27.6, 30.4, and 37.4, respectively, under the maximal assumption.

The adjustment for race and education had very little effect on the results of the analysis of the psychotic thinking score with current dioxin and time since tour. Under both the minimal and the maximal assumptions, there were marginally significant current dioxin-by-time since tour interactions (Table 9-52 [g] and [h]: p=0.074 and p=0.057). Also, for Ranch

TABLE 9-52.

Analysis of Psychotic Thinking Score (MCMI)

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Mean	Slope (Std. Error)[a]	p-Value
a) Minimal	Low	129	28.1	2.866 (0.725)	<0.001
(n=514)	Medium	256	32.9		
(R^2=0.030)	High	129	36.5		
b) Maximal	Low	182	30.6	2.147 (0.534)	<0.001
(n=732)	Medium	368	30.3		
(R^2=0.022)	High	182	36.1		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Initial Dioxin	n	Adj. Mean	Adj. Slope (Std. Error)[a]	p-Value	Covariate Remarks
c) Minimal	Low	128	30.4	2.343 (0.716)	0.001	RACE (p=0.094)
(n=510)	Medium	254	33.9			EDUC (p<0.001)
(R^2=0.096)	High	128	37.4			
d) Maximal	Low	181	36.1	1.266 (0.545)	0.021	RACE (p=0.033)
(n=727)	Medium	365	32.9			EDUC (p<0.001)
(R^2=0.072)	High	181	37.5			

[a]Slope and standard error based on psychotic thinking score versus log_2 dioxin.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 9-52. (Continued)

Analysis of Psychotic Thinking Score (MCMI)

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Mean/(n) Current Dioxin Low	Medium	High	Slope (Std. Error)[a]	p-Value
e) Minimal						0.059[b]
(n=514)	≤18.6	29.6	33.9	32.8	1.324 (1.178)	0.262[c]
(R^2=0.038)		(72)	(128)	(53)		
	>18.6	25.6	32.5	38.5	4.209 (0.966)	<0.001[c]
		(56)	(129)	(76)		
f) Maximal						0.083[b]
(n=732)	≤18.6	29.4	31.5	35.9	1.262 (0.826)	0.127[c]
(R^2=0.028)		(105)	(109)	(82)		
	>18.6	27.6	30.4	37.4	3.179 (0.731)	<0.001[c]
		(78)	(175)	(102)		

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Mean/(n) Current Dioxin Low	Medium	High	Adj. Slope (Std. Error)[a]	p-Value	Covariate Remarks
g) Minimal						0.074[b]	RACE (p=0.100)
(n=510)	≤18.6	31.4	35.0	33.7	0.933 (1.151)	0.418[c]	EDUC (p<0.001)
(R^2=0.103)		(71)	(127)	(53)			
	>18.6	28.3	33.2	39.1	3.586 (0.950)	<0.001[c]	
		(56)	(128)	(75)			
h) Maximal						0.057[b]	RACE (p=0.035)
(n=727)	≤18.6	34.4	33.9	37.4	0.307 (0.828)	0.711[c]	EDUC (p<0.001)
(R^2=0.079)		(105)	(187)	(82)			
	>18.6	32.2	33.0	38.4	2.363 (0.729)	0.001[c]	
		(78)	(174)	(101)			

[a]Slope and standard error based on psychotic thinking score versus log_2 dioxin.

[b]Test of significance for homogeneity of slopes (current dioxin continuous, time categorized).

[c]Test of significance for slope equal to 0 (current dioxin continuous, time categorized).

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 9-52. (Continued)

Analysis of Psychotic Thinking Score (MCMI)

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Mean	Contrast	Difference of Means (95% C.I.)	p-Value
Background	781	32.6	All Categories		0.004
Unknown	340	30.1	Unknown vs. Background	-2.5 (-5.0,0.0)	0.053
Low	194	31.9	Low vs. Background	-0.7 (-3.9,2.4)	0.643
High	184	36.7	High vs. Background	4.1 (0.9,7.3)	0.012
Total	1,499		(R^2=0.009)		

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Adj. Mean	Contrast	Difference of Adj. Means (95% C.I.)	p-Value	Covariate Remarks
Background	775	34.4	All Categories		0.215	AGE (p=0.106) RACE (p=0.106)
Unknown	335	32.8	Unknown vs. Background	-1.6 (-4.1,1.0)	0.223	DRKYR (p=0.004)
Low	190	33.1	Low vs. Background	-1.3 (-4.5,1.8)	0.400	EDUC (p<0.001)
High	180	36.4	High vs. Background	2.0 (-1.2,5.3)	0.220	
Total	1,480		(R^2=0.045)			

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

Hands with greater than 18.6 years since the end of their tour, there were significant positive associations between current dioxin and the psychotic thinking score for both the minimal and maximal cohorts (Table 9-52 [g] and [h]: $p<0.001$ and $p=0.001$).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In the unadjusted analysis of the MCMI psychotic thinking score with Ranch Hands and Comparisons by current dioxin category, the contrast of the four current dioxin categories was significant (Table 9-52 [i]: $p=0.004$). The unadjusted mean psychotic thinking scores for the background, unknown, low, and high current dioxin categories were 32.6, 30.1, 31.9, and 36.7. The contrast of the mean psychotic thinking scores of the unknown category versus the background category was marginally significant ($p=0.053$). Also, the difference between the mean psychotic thinking scores of the high category and the background category was significant ($p=0.012$).

After adjusting for age, race, lifetime alcohol history, and education, there was no significant difference detected among the mean psychotic thinking scores of the four current dioxin categories (Table 9-52 [j]: $p=0.215$).

Psychotic Depression Score—MCMI

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

The unadjusted analysis of the MCMI psychotic depression score detected significant positive associations with initial dioxin under both the minimal and maximal assumptions (Table 9-53 [a] and [b]: $p=0.005$ and $p<0.001$). The unadjusted mean psychotic depression scores for the minimal cohort were 22.4, 23.4, and 26.7 for the low, medium, and high initial dioxin categories. The corresponding means for the maximal cohort were 22.0, 22.1, and 26.5.

The minimal adjusted analysis also displayed a significant positive association between the psychotic depression score and initial dioxin (Table 9-53 [c]: $p=0.035$). After adjusting for race, lifetime alcohol history, and education, the maximal analysis detected only a marginally significant positive relationship between initial dioxin and the MCMI psychotic depression score (Table 9-53 [d]: $p=0.081$).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

In the unadjusted analysis of the psychotic depression score with current dioxin and time since tour, the current dioxin-by-time interaction was not significant for either the minimal or the maximal cohort (Table 9-53 [e] and [f]: $p=0.262$ and $p=0.195$). However, there were significant positive associations between current dioxin and the psychotic depression score for Ranch Hands with more than 18.6 years since tour under both the minimal and maximal assumptions (Table 9-53 [e] and [f]: $p=0.006$ and $p<0.001$). In the minimal cohort, the mean psychotic depression scores for Ranch Hands with early tours for low, medium, and high current dioxin were 21.8, 23.6, and 28.0. Under the maximal assumption, the mean psychotic depression scores also became larger with increasing current dioxin levels for this time stratum (low, 19.1; medium, 22.9; high, 27.1).

TABLE 9-53.

Analysis of Psychotic Depression Score (MCMI)

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Mean	Slope (Std. Error)[a]	p-Value
a) Minimal	Low	129	22.4	2.122 (0.746)	0.005
(n=514)	Medium	256	23.4		
(R^2=0.016)	High	129	26.7		
b) Maximal	Low	182	22.0	1.842 (0.537)	<0.001
(n=732)	Medium	368	22.1		
(R^2=0.016)	High	182	26.5		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Initial Dioxin	n	Adj. Mean	Adj. Slope (Std. Error)[a]	p-Value	Covariate Remarks
c) Minimal	Low	128	24.7	1.567 (0.741)	0.035	RACE (p=0.114)
(n=505)	Medium	250	24.6			ALC (p=0.125)
(R^2=0.082)	High	127	27.6			DRKYR (p=0.020)
						EDUC (p<0.001)
d) Maximal	Low	179	27.3	0.963 (0.551)	0.081	RACE (p=0.040)
(n=719)	Medium	362	24.6			DRKYR (p=0.007)
(R^2=0.070)	High	178	27.9			EDUC (p<0.001)

[a]Slope and standard error based on psychotic depression score versus log_2 dioxin.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 9-33. (Continued)

Analysis of Psychotic Depression Score (MCMI)

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Mean/(n) Current Dioxin Low	Medium	High	Slope (Std. Error)[a]	p-Value
e) Minimal						0.262[b]
(n=514)	≤18.6	22.5	23.3	25.2	0.988 (1.217)	0.417[c]
(R^2=0.017)		(72)	(128)	(53)		
	>18.6	21.8	23.6	28.0	2.755 (0.997)	0.006[c]
		(56)	(129)	(76)		
f) Maximal						0.195[b]
(n=732)	≤18.6	20.7	23.4	24.9	1.128 (0.833)	0.176[c]
(R^2=0.019)		(105)	(190)	(82)		
	>18.6	19.1	22.9	27.1	2.571 (0.737)	<0.001[c]
		(78)	(175)	(102)		

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Mean/(n) Current Dioxin Low	Medium	High	Adj. Slope (Std. Error)[a]	p-Value	Covariate Remarks
g) Minimal						0.352[b]	RACE (p=0.127)
(n=505)	≤18.6	24.8	24.7	26.5	0.670 (1.192)	0.574[c]	ALC (p=0.124)
(R^2=0.083)		(71)	(126)	(53)			DRKYR (p=0.018)
	>18.6	23.8	24.5	28.6	2.101 (0.986)	0.034[c]	EDUC (p<0.001)
		(56)	(125)	(74)			
h) Maximal						0.180[b]	RACE (p=0.042)
(n=719)	≤18.6	25.6	26.0	27.0	0.303 (0.837)	0.717[c]	DRKYR (p=0.005)
(R^2=0.074)		(104)	(186)	(81)			EDUC (p<0.001)
	>18.6	23.2	25.3	27.5	1.769 (0.737)	0.017[c]	
		(77)	(172)	(99)			

[a]Slope and standard error based on psychotic depression versus log_2 dioxin.

[b]Test of significance for homogeneity of slopes (current dioxin continuous, time categorized).

[c]Test of significance for slope equal to 0 (current dioxin continuous, time categorized).

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 9-53. (Continued)

Analysis of Psychotic Depression Score (MCMI)

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Mean	Contrast	Difference of Means (95% C.I.)	p-Value
Background	781	23.6	All Categories		0.070
Unknown	340	21.4	Unknown vs. Background	-2.2 (-4.7,0.3)	0.091
Low	194	22.8	Low vs. Background	-0.8 (-3.9,2.4)	0.633
High	184	26.1	High vs. Background	2.6 (-0.7,5.8)	0.119
Total	1,499		(R^2=0.005)		

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Adj. Mean	Contrast	Difference of Adj. Means (95% C.I.)	p-Value	Covariate Remarks
Background	775	23.5	All Categories		0.475	DRKYR (p=0.002)
Unknown	335	22.1	Unknown vs. Background	-1.4 (-4.0,1.1)	0.274	AGE*RACE (p=0.042) ALC*EDUC (p=0.033)
Low	190	22.5	Low vs. Background	-1.0 (-4.1,2.2)	0.543	
High	180	24.8	High vs. Background	1.3 (-2.0,4.5)	0.450	
Total	1,480		(R^2=0.040)			

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

The adjusted analysis also did not detect a significant interaction between current dioxin and the MCMI psychotic depression score under either assumption (Table 9-53 [e] and [f]: p=0.352 and p=0.180). Similar to the unadjusted results, the adjusted analysis displayed significant positive associations between current dioxin and the psychotic depression score for Ranch Hands with greater than 18.6 years since tour under both the minimal and maximal assumptions (Table 9-53 [g] and [h]: p=0.034 and p=0.017).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In the unadjusted analysis of the MCMI psychotic depression score, the overall contrast of the four current dioxin categories was marginally significant (Table 9-53 [i]: p=0.070). The mean psychotic depression scores for the background, unknown, low, and high current dioxin categories were 23.6, 21.4, 22.8, and 26.1. The contrast of Ranch Hands in the unknown current dioxin category versus Comparisons in the background category was marginally significant (p=0.091) with the Ranch Hands having a lower mean psychotic depression score.

After adjusting for lifetime alcohol history, an age-by-race interaction, and a current alcohol use-by-education interaction, the analysis did not detect a significant overall difference among the mean MCMI psychotic depression scores of the four current dioxin categories (Table 9-53 [j]: p=0.475).

Psychotic Delusion Score—MCMI

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Based on the minimal assumption, the unadjusted analysis displayed a nonsignificant association between initial dioxin and the MCMI psychotic delusion score (Table 9-54 [a]: p=0.141). However, under the maximal assumption, there was a marginally significant positive relationship between initial dioxin and the psychotic delusion score (Table 9-54 [b]: p=0.065). The mean psychotic delusion scores became larger for increasing levels of current dioxin (low, 42.3; medium, 43.9; high, 46.0).

The minimal analysis of the psychotic delusion score remained nonsignificant after adjustment for covariate information (Table 9-54 [c]: p=0.282). After the adjustment for race, education, and an age-by-lifetime alcohol history interaction, the association between initial dioxin and the psychotic delusion score was also nonsignificant under the maximal assumption (Table 9-54 [d]: p=0.368).

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

The unadjusted analysis of the psychotic delusion score with current dioxin and time since tour did not detect a significant current dioxin-by-time interaction for either the minimal or the maximal cohort (Table 9-54 [e] and [f]: p=0.218 and p=0.271). For Ranch Hands with greater than 18.6 years since tour, there were significant positive associations between current dioxin and the psychotic delusion score under both the minimal and maximal assumptions (Table 9-54 [e] and [f]: p=0.041 and p=0.020). In the minimal cohort, the mean psychotic delusion scores for Ranch Hands with more than 18.6 years since the end of their

TABLE 9-54.

Analysis of Psychotic Delusion Score (MCMI)

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Mean	Slope (Std. Error)[a]	p-Value
a) Minimal	Low	129	41.9	1.050 (0.713)	0.141
(n=514)	Medium	256	45.3		
(R^2=0.004)	High	129	45.8		
b) Maximal	Low	182	42.3	0.982 (0.531)	0.065
(n=732)	Medium	368	43.9		
(R^2=0.005)	High	182	46.0		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Initial Dioxin	n	Adj. Mean	Adj. Slope (Std. Error)[a]	p-Value	Covariate Remarks
c) Minimal	Low	128	41.8	0.774 (0.718)	0.282	ALC (p=0.062)
(n=508)	Medium	252	44.8			EDUC (p=0.002)
(R^2=0.029)	High	128	44.9			
d) Maximal	Low	179	46.2	0.508 (0.564)	0.368	RACE (p=0.085)
(n=719)	Medium	362	46.1			EDUC (p<0.001)
(R^2=0.039)	High	178	47.8			AGE*DRKYR (p=0.012)

[a]Slope and standard error based psychotic delusion score versus log_2 dioxin.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 9-54. (Continued)

Analysis of Psychotic Delusion Score (MCMI)

Ranch Hands - Log_2 (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Mean/(n) Current Dioxin Low	Medium	High	Slope (Std. Error)[a]	p-Value
e) Minimal						0.218[b]
(n=514)	≤18.6	44.4	45.3	45.3	0.096 (1.161)	0.934[c]
(R^2=0.009)		(72)	(128)	(53)		
	>18.6	38.8	45.2	46.3	1.947 (0.952)	0.041[c]
		(56)	(129)	(76)		
f) Maximal						0.271[b]
(n=732)	≤18.6	43.3	44.7	45.6	0.487 (0.823)	0.554[c]
(R^2=0.009)		(105)	(190)	(82)		
	>18.6	40.7	43.2	46.1	1.698 (0.728)	0.020[c]
		(78)	(175)	(102)		

Ranch Hands - Log_2 (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Mean/(n) Current Dioxin Low	Medium	High	Adj. Slope (Std. Error)[a]	p-Value	Covariate Remarks
g) Minimal						0.267[b]	ALC (p=0.066)
(n=508)	≤18.6	44.2	44.5	44.3	-0.127 (1.156)	0.912[c]	EDUC (p=0.002)
(R^2=0.032)		(71)	(127)	(53)			
	>18.6	39.0	44.9	45.5	1.531 (0.957)	0.110[c]	
		(56)	(126)	(75)			
h) Maximal						0.180[b]	RACE (p=0.086)
(n=719)	≤18.6	46.9	46.6	46.9	-0.153 (0.855)	0.858[c]	EDUC (p<0.001)
(R^2=0.042)		(104)	(186)	(81)			AGE*DRKYR (p=0.012)
	>18.6	43.8	46.1	47.9	1.320 (0.756)	0.081[c]	
		(77)	(172)	(99)			

[a]Slope and standard error based on psychotic delusion score versus log_2 dioxin.

[b]Test of significance for homogeneity of slopes (current dioxin continuous, time categorized).

[c]Test of significance for slope equal to 0 (current dioxin continuous, time categorized).

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 9-54. (Continu

Analysis of Psychotic Delusion (MCMI)

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Mean	Contrast	Difference of Means (95% C.I.)	p-Value
Background	781	42.1	All Categories		0.076
Unknown	340	43.1	Unknown vs. Background	0.9 (-1.7,3.5)	0.497
Low	194	45.1	Low vs. Background	3.0 (-0.3,6.2)	0.073
High	184	45.9	High vs. Background	3.7 (0.4,7.0)	0.026
Total	1,499		(R^2=0.005)		

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Adj. Mean	Contrast	Difference of Adj. Means (95% C.I.)	p-Value	Covariate Remarks
Background	775	44.2	All Categories		0.213	RACE (p=0.062) AGE*ALC (p=0.004)
Unknown	335	46.1	Unknown vs. Background	1.8 (-1.8,4.5)	0.166	AGE*DRKYR (p=0.030)
Low	190	46.7	Low vs. Background	2.5 (-0.7,5.7)	0.125	ALC*DRKYR (p=0.036)
High	180	46.7	High vs. Background	2.5 (-0.8,5.8)	0.144	ALC*EDUC (p=0.010)
Total	1,480		(R^2=0.045)			

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

tour were 38.8, 45.2, and 46.3 for low, medium, and high current dioxin. The corresponding mean psychotic delusion scores for the same time stratum of the maximal cohort were 40.7, 43.2, and 46.1, respectively.

After adjusting the minimal analysis for current alcohol use and education, the interaction between current dioxin and time since tour remained nonsignificant (Table 9-54 [g]: p=0.267). Under the maximal assumption the current dioxin-by-time interaction was also nonsignificant (Table 9-54 [h]: p=0.180), but for Ranch Hands with more than 18.6 years since the end of their tour, there was a marginally significant positive association between current dioxin and the psychotic delusion score (p=0.081).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In the unadjusted analysis of the psychotic delusion score, the contrast of the four current dioxin categories was marginally significant (Table 9-54 [i]: p=0.076). The mean psychotic delusion scores for the background, unknown, low, and high current dioxin categories were 42.1, 43.1, 45.1, and 45.9. The contrast of the Ranch Hands in the low category versus the Comparisons in the background category was marginally significant (p=0.073) with the Ranch Hands having a higher mean psychotic delusion score than the Comparisons. Also, the mean psychotic delusion score of the Ranch Hands in the high current dioxin category was significantly higher than the mean score of the Comparisons in the background category (p=0.026).

After adjusting for race and several significant covariate interactions, the analysis of the psychotic delusion score for the four current dioxin categories was not significant (Table 9-54 [j]: p=0.213).

DISCUSSION

Prior to the 1982 Baseline study, little scientifically validated information existed regarding the relationship between dioxin exposure and disturbances of cognition and emotions in man. The Baseline and 1985 examinations attempted to explore these possible relationships using well-established questionnaires, personality inventories, and neuropsychological assessment techniques. These instruments included the Cornell Medical Index (CMI), the MMPI, and the HRB.

In the 1982 Baseline study, the analysis of extensive data generated by the CMI, MMPI, and HRB revealed few statistically significant differences between the Ranch Hand and Comparison groups. More specifically, the two groups did not differ significantly on several tests of cognitive (cerebral) function. The Ranch Hand group reported a moderately greater number of diffuse medical (somatic) complaints on the CMI. They also registered higher (but not statistically significant) scores on the MMPI scales that are influenced most heavily by physical complaints such as generalized feelings of lassitude and malaise, energy loss, and mental and physical slowing.

There were no compelling Ranch Hand-Comparison group test differences observed during the 1985 examination. Nevertheless, the possibility of a relationship between dioxin

exposure and the subsequent development of psychological or psychophysiological disorders could not be entirely ruled out.

To promote maximum compliance among the subjects, the 1987 examination included the SCL-90-R and MCMI evaluations. The SCL-90-R is a 90-item checklist of physical and mental symptoms that provides a reasonable measure of health-related concerns and associated anxiety, depression, and general emotional discomfort. The MCMI provided backup measures of depression, anxiety, somatization, and hypochondriasis for the SCL-90-R, while also screening for personality disorders and major psychiatric syndromes including psychoses. Both the SCL-90-R and the MCMI have been extensively used in research and some clinical settings requiring economical assessment of psychiatric disorders, physical disability status, and response to specific therapies. In addition, verified histories of psychological disorders and self-reported sleep disorders were also included in the 1987 examination.

The unadjusted initial dioxin analyses revealed several statistically significant results for the verified questionnaire, sleep disorder, and SCL-90-R variables. However, when adjusted for effects of covariate factors (i.e., age, education, alcohol use, and race), none of these results remained significant.

After adjustment for covariate factors, 9 of the 20 MCMI scale results remained statistically significant under either the minimal or the maximal assumption (positive: schizoid, avoidant, dependent, schizotypal, somatoform, psychotic thinking, and psychotic depression scores; negative: histrionic and narcissistic scores). Such results suggest the possibility of a relationship between personality disturbances and/or psychotic disorders and extrapolated initial TCDD levels. However, examination of interview data and a review of MCMI test structure indicates that the MCMI results should be interpreted with caution.

The adjusted analyses of the verified questionnaire findings did not display a statistically significant positive relationship with initial dioxin for psychoses of the type observed on the MCMI psychotic thinking scale. Similarly, verified questionnaire data did not exhibit significant adjusted results on measures of anxiety or neuroses of the type that would be anticipated in a population suffering from the high incidence of personality disturbances implied by the MCMI data.

The number of statistically significant MCMI results may have been inflated by test construction intricacies that have been described by Millon (34) and Choca (35). These investigations revealed substantial (50% to 65%) item overlap for the schizoid, avoidant, dependent, schizotypal, psychotic thinking, and psychotic depression scales. These same scales are also positively correlated at levels ranging from 0.56 to 0.94. Difficulties with overlapping components also extend to the histrionic and narcissistic scales which correlate -0.52 on average with the schizoid, avoidant, schizotypal, and psychotic thinking scales.

The remaining statistically significant MCMI scale result was observed on the somatoform scale. This result does not appear to be related to structural factors. According to the MCMI manual (34), the somatoform scale correlates 0.43 with the somatization scale of the SCL-90-R. The absence of statistically significant results on the somatization or

positive symptom total scales of the SCL-90-R is inconsistent with significant MCMI somatoform scale findings.

Adjusted current dioxin and time since tour analyses for the verified questionnaire and sleep disorder variables were generally not significant. Of the SCL-90-R variables, the anxiety scale was positively related to current dioxin for Ranch Hands with time greater than 18.6 years. For these Ranch Hands, marginally significant results were also observed on the somatization scale of the SCL-90-R and the anxiety scale of the MCMI. The MCMI manual (34) reveals that these two scales correlate with the anxiety scale of the SCL-90-R at 0.67 and 0.52, respectively. Internally consistent results of this type suggest the possibility of latent and now emerging anxiety or psychophysiological disorders. However, additional inspection of the verified questionnaire data did not reveal evidence for significant anxiety disorders.

Review of the adjusted analyses of MCMI data revealed multiple statistically significant results. These results appeared predominantly on the scales with high correlations as described above. The possibility that these findings may be related in part to structural test factors is again noted. However, the majority of significant results on scales designed to reflect personality and psychotic disorders are observed primarily for Ranch Hands with tours more than 18.6 years ago. The possibility of emerging latent disorders is suggested, but inspection of verified questionnaire data and SCL-90-R results failed to reveal corroborating evidence of time-related psychoses or neuroses.

A review of the adjusted findings for the categorized current dioxin analyses of questionnaire and SCL-90-R data revealed only one clearly significant result for Ranch Hands in the high current dioxin category. These participants reported frightening dreams. A recent study (36) revealed that frightening dreams has proved to be one of the more consistent clinical indicators manifested in studies of chronic PTSD. However, in the context of the present study, frightening dreams is not likely to represent a significant dose-related sleep abnormality in that all other indicators of sleep disorders failed to meet the criteria required for statistical significance with TCDD exposure.

The adjusted analyses of the MCMI variables revealed only two statistically significant results in the high current dioxin category. These results were obtained on the schizoid and schizotypal scales. Previously discussed factors of test structure and an absence of any corroborating verified questionnaire data combine to reduce the likelihood that these results are associated with a dose-response effect.

In summary, a tri-model approach was employed to scrutinize several complex relationships between dependent psychological variables and objectively determined TCDD levels. This expanded analysis permitted a more sophisticated and empirical approach to the problem of determining to what extent the body burden of dioxin might be associated with psychological and/or psychophysiological disorders. There was a relatively large number of statistically significant results for the MCMI variables. These findings may be spurious associations due to the interrelatedness of the MCMI scales inherent to the test development structure. These results were not corroborated by the verified questionnaire data results and the SCL-90-R variables. Based on these analyses, the incidence of

psychological and psychosocial disorders appears unrelated to TCDD body burdens in Ranch Hands.

SUMMARY

The psychological assessment was based on analyses of verified psychological disorders; reported sleep disorders; and two psychological instruments, the SCL-90-R and the MCMI, in association with serum dioxin levels. Tables 9-55, 9-56, and 9-57 present the results of these analyses based on initial dioxin for Ranch Hands, current dioxin and time since tour for Ranch Hands, and current dioxin category for Ranch Hands and Comparisons.

Questionnaire: Verified

Five psychological disorders were analyzed in the psychological assessment: psychoses, alcohol dependence, drug dependence, anxiety, and other neuroses. These disorders were self-reported and later verified by a medical record review. Participants with a pre-SEA history of these disorders were excluded from the analyses along with participants with PTSD as determined from the MMPI.

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

In the unadjusted analysis of psychoses, a marginally significant negative association was found with initial dioxin under the minimal assumption. After adjustment for race and education, the negative association between psychoses and initial dioxin became significant (Table 9-55: p=0.042) for the minimal cohort.

There were no significant findings in the analysis of alcohol dependence, and there were only two participants (both Comparisons) with a verified self-reported history of a drug dependence.

In the unadjusted analyses of anxiety and the ICD-9-CM code-based category of "other neuroses," the minimal analyses were nonsignificant, but the maximal analyses detected a significant positive association with initial dioxin for both of these psychological disorders (Table 9-55: p=0.34 and p=0.004). The adjusted analyses of anxiety and other neuroses displayed nonsignificant positive associations with initial dioxin under both assumptions.

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

The association between current dioxin and the verified psychological disorder variables did not differ significantly between the time since tour strata for any of the unadjusted analyses. However, for other neuroses, the unadjusted maximal analysis detected a marginally significant current dioxin-by-time interaction. Also, under the maximal assumption, there was a significant positive association between current dioxin and anxiety and between current dioxin and other neuroses in the unadjusted analysis of Ranch Hands with less than or equal to 18.6 years since tour (Table 9-56: p=0.034 and p=0.003, respectively).

TABLE 9-55.

Summary of Initial Dioxin Analyses for Psychology Variables Based on Minimal and Maximal Assumptions (Ranch Hands Only)

	Unadjusted		Adjusted	
Variable	Minimal	Maximal	Minimal	Maximal
Questionnaire: Verified				
Psychoses (D)	ns*	NS	-0.042	ns
Alcohol Dependence (D)	NS	NS	ns	NS
Anxiety (D)	NS	+0.034	NS	NS
Other Neuroses (D)	NS	+0.004	NS	NS
Questionnaire: Sleep Disorders				
Trouble Falling Asleep (D)	ns	NS	ns*	ns
Waking Up During the Night (D)	ns	ns	ns	ns
Waking Up Too Early and Can't Go Back to Sleep (D)	ns	NS	** (ns)	ns
Waking Up Unrefreshed (D)	NS	+0.027	NS	NS
Involuntarily Falling Asleep During the Day (D)	ns	NS	** (ns)	** (NS)
Great or Disabling Fatigue During the Day (D)	ns	NS	ns	ns
Frightening Dreams (D)	NS	+0.025	** (NS)	NS*
Talking in Sleep (D)	NS	NS	NS	NS
Sleepwalking (D)	NS	NS	****	NS
Abnormal Movement/ Activity During the Night (D)	NS	NS	ns	NS
Sleep Problems Requiring Medication (D)	ns	ns	-0.023	-0.032
Snore Loudly in All Sleeping Positions (D)	ns	NS	** (ns)	NS

TABLE 9-55. (Continued)

Summary of Initial Dioxin Analyses for Psychology Variables
Based on Minimal and Maximal Assumptions
(Ranch Hands Only)

	Unadjusted		Adjusted	
Variable	Minimal	Maximal	Minimal	Maximal
Questionnaire: Sleep Disorders (continued)				
Insomnia (D)	ns	ns	ns	ns
Overall Sleep Disorder Index (D)	ns	NS	ns	ns
Average Sleep Each Night[a](C)	ns	ns	ns	ns
Physical Examination: SCL-90-R				
Anxiety (D)	NS	+0.022	NS	NS
Depression (D)	NS*	+0.029	NS	NS
Hostility (D)	NS	NS	ns	NS
Interpersonal Sensitivity (D)	NS	NS*	** (NS)	NS
Obsessive-Compulsive Behavior (D)	NS*	+0.002	NS	NS*
Paranoid Ideation (D)	ns	ns	ns	ns
Phobic Anxiety (D)	NS	NS	ns	NS
Psychoticism (D)	NS	+0.022	NS	NS*
Somatization (D)	NS	NS*	NS	NS
Global Severity Index (D)	NS*	+0.013	NS	NS
Positive Symptom Total (D)	NS*	+0.043	NS	NS
Positive Symptom Distress Index (D)	NS	NS	NS	NS
Physical Examination: MCMI				
Basic Personality Patterns				
Schizoid Score (C)	+<0.001	+<0.001	+0.002	+0.002
Avoidant Score (C)	+<0.001	+<0.001	** (+0.003)	+0.038
Dependent Score (C)	+0.027	+0.009	+0.018	+0.037
Histrionic Score (C)	-0.003	-0.002	-0.011	-0.037
Narcissistic Score (C)	-0.007	-0.003	ns*	-0.012
Antisocial Score (C)	ns	ns	** (ns)	****
Compulsive Score (C)	ns	ns	NS	NS

TABLE 9-55. (Continued)

Summary of Initial Dioxin Analyses for Psychology Variables
Based on Minimal and Maximal Assumptions
(Ranch Hands Only)

Variable	Unadjusted Minimal	Unadjusted Maximal	Adjusted Minimal	Adjusted Maximal
Physical Examination: MCMI (continued)				
Basic Personality Patterns (continued)				
Passive-Aggressive Score (C)	+0.046	+<0.001	NS	NS
Pathological Personality Disorders				
Schizotypal Score (C)	+<0.001	+<0.001	+<0.001	+0.001
Borderline Score (C)	NS	+0.028	NS	** (NS)
Paranoid Score (C)	NS	NS	NS	ns
Clinical Symptom Syndromes				
Anxiety Score (C)	+0.046	+<0.001	** (NS*)	****
Somatoform Score (C)	NS	+0.033	NS	+0.011
Hypomania Score (C)	ns*	ns	** (ns*)	** (ns)
Dysthymia Score (C)	NS	+0.031	****	****
Alcohol Abuse Score (C)	NS	NS	ns	ns
Drug Abuse Score (C)	ns	NS	ns	ns
Psychotic Thinking Score (C)	+<0.001	+<0.001	+0.001	+0.021
Psychotic Depression Score (C)	+0.005	+<0.001	+0.035	NS*
Psychotic Delusion Score (C)	NS	NS*	NS	NS

[a]Negative slope considered adverse for this variable.
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk 1.00 or greater for discrete analysis; slope nonnegative for continuous analysis.
-: Relative risk less than 1.00 for discrete analysis; slope negative for continuous analysis.
NS/ns: Not significant ($p>0.10$).
NS*/ns*: Marginally significant ($0.05<p\leq0.10$).
** (NS)/** (ns): Log_2 (initial dioxin)-by-covariate interaction ($0.01<p\leq0.05$); not significant when interaction is deleted; refer to Appendix Table H-1 for a detailed description of this interaction.
** (NS*)/** (ns*): Log_2 (initial dioxin)-by-covariate interaction ($0.01<p\leq0.05$); marginally significant when interaction is deleted; refer to Appendix Table H-1 for a detailed description of this interaction.
** (...): Log_2 (initial dioxin)-by-covariate interaction ($0.01<p\leq0.05$); significant when interaction is deleted and p-value is given in parentheses; refer to Appendix Table H-1 for a detailed description of this interaction.
****: Log_2 (initial dioxin)-by-covariate interaction ($p\leq0.01$); refer to Appendix Table H-1 for a detailed description of this interaction.
Note: P-value given if $p\leq0.05$.
A capital "NS" denotes relative risk 1.00 or greater for discrete analysis or slope nonnegative for continuous analysis; a lowercase "ns" denotes relative risk less than 1.00 for discrete analysis or slope negative for continuous analysis.

TABLE 9-56.

Summary of Current Dioxin and Time Analyses for Psychology Variables Based on Minimal and Maximal Assumptions (Ranch Hands Only)

	Unadjusted					
	Minimal			Maximal		
Variable	C*T	≤18.6	>18.6	C*T	≤18.6	>18.6
Questionnaire: Verified						
Psychoses (D)	ns	ns	ns	ns	NS	ns
Alcohol Dependence (D)	ns	NS	ns	ns	NS	ns
Anxiety (D)	NS	NS	NS	ns	+0.034	NS
Other Neuroses (D)	ns	NS	NS	ns*	+0.003	NS
Questionnaire: Sleep Disorders						
Trouble Falling Asleep (D)	NS	ns	NS	ns	NS	ns
Waking Up During the Night (D)	ns	ns	ns	ns	NS	ns
Waking Up Too Early and Can't Go Back to Sleep (D)	ns	NS	ns	ns	NS	ns
Waking Up Unrefreshed (D)	NS	ns	NS	NS	NS	+0.030
Involuntarily Falling Asleep During the Day (D)	ns	NS	ns	ns*	NS	ns
Great or Disabling Fatigue During the Day (D)	NS	ns	ns	ns	NS	ns
Frightening Dreams (D)	ns	NS	NS	ns	+0.011	NS
Talking in Sleep (D)	ns	NS	NS	ns	NS	NS
Sleepwalking (D)	NS	ns	NS	NS	NS	NS
Abnormal Movement/ Activity During the Night (D)	ns	NS	NS	NS	NS	NS
Sleep Problems Requiring Medication (D)	NS	ns	ns	ns	ns	ns
Snore Loudly in All Sleeping Positions (D)	ns	ns	ns	ns	NS	NS
Insomnia (D)	ns	NS	ns	ns*	NS	ns
Overall Sleep Disorder Index (D)	ns	NS	ns	ns	NS	ns
Average Sleep Each Night[a](C)	ns	ns	ns	NS	ns	ns

TABLE 9-56. (Continued)

Summary of Current Dioxin and Time Analyses for Psychology Variables Based on Minimal and Maximal Assumptions (Ranch Hands Only)

	Unadjusted					
	Minimal			Maximal		
Variable	C*T	≤18.6	>18.6	C*T	≤18.6	>18.6
Physical Examination: SCL-90-R						
Anxiety (D)	NS	NS	+0.031	NS	NS	NS*
Depression (D)	NS	NS	+0.017	ns	NS	NS*
Hostility (D)	ns	NS	NS	ns	NS	NS
Interpersonal Sensitivity (D)	ns	NS*	NS	ns	+0.018	NS
Obsessive-Compulsive Behavior (D)	NS	NS	+0.031	NS	+0.043	+0.018
Paranoid Ideation (D)	ns	ns	ns	ns	NS	ns
Phobic Anxiety (D)	NS	ns	NS	ns	NS	NS
Psychoticism (D)	NS	NS	NS	ns	NS	NS
Somatization (D)	+0.015	ns	NS*	NS	NS	NS
Global Severity Index (D)	NS	NS	+0.026	ns	NS*	NS*
Positive Symptom Total (D)	NS	NS	NS	ns	+0.041	NS
Positive Symptom Distress Index (D)	NS	ns	NS	ns	NS	NS
Physical Examination: MCMI						
Basic Personality Patterns						
Schizoid Score (C)	NS*	NS	+<0.001	NS*	NS	+<0.001
Avoidant Score (C)	+0.028	NS	+<0.001	NS*	NS	+<0.001
Dependent Score (C)	NS	NS	+0.033	NS	NS	+0.023
Histrionic Score (C)	ns*	ns	-0.001	ns*	ns	-<0.001
Narcissistic Score (C)	ns	ns	-0.015	ns	ns	-0.005
Antisocial Score (C)	ns	NS	ns	ns	NS	ns
Compulsive Score (C)	ns	ns	ns	ns	ns	ns
Passive-Aggressive Score (C)	NS	NS	+0.037	NS	+0.044	+0.007

TABLE 9-56. (Continued)

Summary of Current Dioxin and Time Analyses for Psychology Variables Based on Minimal and Maximal Assumptions (Ranch Hands Only)

	Unadjusted					
	Minimal			Maximal		
Variable	C*T	≤18.6	>18.6	C*T	≤18.6	>18.6
Physical Examination: MCMI (continued)						
Pathological Personality Disorders						
Schizotypal Score (C)	NS	NS	+<0.001	NS	+0.037	+<0.001
Borderline Score (C)	NS	ns	NS	NS	NS	NS*
Paranoid Score (C)	NS	NS	NS	ns	NS	NS
Clinical Symptom Syndromes						
Anxiety Score (C)	NS	ns	+0.026	ns	+0.038	+0.028
Somatoform Score (C)	NS	NS	NS	ns	NS*	NS
Hypomania Score (C)	ns	ns	ns*	ns	ns	-0.050
Dysthymia Score (C)	NS	NS	NS	NS	NS	NS*
Alcohol Abuse Score (C)	NS	ns	NS	NS	ns	NS
Drug Abuse Score (C)	ns	NS	ns	ns	NS	ns
Psychotic Thinking Score (C)	NS*	NS	+<0.001	NS*	NS	+<0.001
Psychotic Depression Score (C)	NS	NS	+0.006	NS	NS	+<0.001
Psychotic Delusion Score (C)	NS	NS	+0.041	NS	NS	+0.020

[a]Negative slope considered adverse for this variable.
C: Continuous analysis.
D: Discrete analysis.
+: C*T: Relative risk/slope for ≤18.6 category less than relative risk/slope for >18.6 category.
≤18.6 and >18.6: Relative risk 1.00 or greater for discrete analysis; slope nonnegative for continuous analysis.
-: C*T: Relative risk/slope for ≤18.6 category greater than relative risk/slope for >18.6 category.
≤18.6 and >18.6: Relative risk less than 1.00 for discrete analysis; slope negative for continuous analysis.
NS/ns: Not significant (p>0.10).
NS*/ns*: Marginally significant (0.05<p≤0.10).
Note: P-value given if p≤0.05.
C*T: Log_2 (current dioxin)-by-time interaction hypothesis test.
≤18.6: Log_2 (current dioxin) hypothesis test for Ranch Hands with time since end of tour of 18.6 years or less.
>18.6: Log_2 (current dioxin) hypothesis test for Ranch Hands with time since end of tour greater than 18.6 years.
A capital "NS" denotes relative risk/slope for ≤18.6 category less than relative risk/slope for >18.6 category, relative risk 1.00 or greater for discrete analysis, or slope nonnegative for continuous analysis; a lowercase "ns" denotes relative risk/slope for ≤18.6 category greater than relative risk/slope for >18.6 category, relative risk less than 1.00 for discrete analysis, or slope negative for continuous analysis.

TABLE 9-56. (Continued)

Summary of Current Dioxin and Time Analyses for Psychology Variables Based on Minimal and Maximal Assumptions (Ranch Hands Only)

	Adjusted					
	Minimal			Maximal		
Variable	C*T	≤18.6	>18.6	C*T	≤18.6	>18.6
Questionnaire: Verified						
Psychoses (D)	ns	ns	ns	ns	NS	ns
Alcohol Dependence (D)	ns	NS	ns	ns	NS	ns
Anxiety (D)	NS	NS	NS	ns	NS	NS
Other Neuroses (D)	ns	NS	ns	ns	NS*	ns
Questionnaire: Sleep Disorders						
Trouble Falling Asleep (D)	NS	ns	ns	ns	ns	ns
Waking Up During the Night (D)	****	****	****	****	****	****
Waking Up Too Early and Can't Go Back to Sleep (D)	ns	NS	ns	ns	NS	ns
Waking Up Unrefreshed (D)	** (NS)	** (ns)	** (NS)	NS	ns	NS
Involuntarily Falling Asleep During the Day (D)	ns	NS	ns	ns*	NS	ns
Great or Disabling Fatigue During the Day (D)	****	****	****	ns	NS	ns
Frightening Dreams (D)	****	****	****	** (ns)	** (+0.033)	** (NS)
Talking in Sleep (D)	ns	NS	NS	ns	NS	NS
Sleepwalking (D)	NS	ns	NS	NS	NS	NS
Abnormal Movement/ Activity During the Night (D)	ns	NS	ns	NS	NS	NS
Sleep Problems Requiring Medication (D)	NS	ns*	ns*	NS	ns	ns*
Snore Loudly in All Sleeping Positions (D)	ns	ns	ns	ns	NS	NS
Insomnia (D)	ns	NS	ns	ns*	NS	ns*
Overall Sleep Disorder Index (D)	ns	ns	ns*	ns	NS	ns
Average Sleep Each Night[a] (C)	****	****	****	** (NS)	** (ns)	** (ns)

TABLE 9-56. (Continued)

Summary of Current Dioxin and Time Analyses for Psychology Variables Based on Minimal and Maximal Assumptions (Ranch Hands Only)

	Adjusted					
	Minimal			Maximal		
Variable	C*T	≤18.6	>18.6	C*T	≤18.6	>18.6
Physical Examination: SCL-90-R						
Anxiety (D)	NS*	ns	+0.028	NS	NS	NS
Depression (D)	NS	ns	NS	ns	NS	NS
Hostility (D)	NS	ns	ns	ns	NS	ns
Interpersonal Sensitivity (D)	ns	NS	NS	ns	NS*	NS
Obsessive-Compulsive Behavior (D)	NS	ns	NS	ns	NS	NS
Paranoid Ideation (D)	ns	ns	ns	ns	NS	ns
Phobic Anxiety (D)	** (NS)	** (ns)	** (NS)	** (ns)	** (NS)	** (NS)
Psychoticism (D)	NS	NS	NS	ns	NS	NS
Somatization (D)	+0.025	ns	NS*	** (NS)	** (NS)	** (NS)
Global Severity Index (D)	** (NS)	** (NS)	** (NS)	ns	NS	NS
Positive Symptom Total (D)	NS	NS	NS	ns	NS	NS
Positive Symptom Distress Index (D)	NS	ns	NS	ns	NS	NS
Physical Examination: MCMI						
Basic Personality Patterns						
Schizoid Score (C)	NS*	NS	+0.001	** (+0.044)	** (NS)	** (+<0.001)
Avoidant Score (C)	+0.029	NS	+<0.001	+0.045	ns	+0.006
Dependent Score (C)	NS	NS	+0.020	NS	NS	+0.026
Histrionic Score (C)	ns	ns	-0.006	****	****	****
Narcissistic Score (C)	ns	NS	ns*	ns*	ns	-0.009
Antisocial Score (C)	ns	NS	ns	ns	NS	ns
Compulsive Score (C)	ns	NS	NS	ns	NS	NS
Passive-Aggressive Score (C)	NS	ns	NS	NS	NS	NS
Pathological Personality Disorders						
Schizotypal Score (C)	NS	NS	+ 0.002	NS	NS	+0.002
Borderline Score (C)	NS	ns	NS	NS	NS	NS
Paranoid Score (C)	NS	NS	NS	ns	NS	NS

TABLE 9-56. (Continued)

Summary of Current Dioxin and Time Analyses for Psychology Variables Based on Minimal and Maximal Assumptions (Ranch Hands Only)

	Adjusted					
	Minimal			Maximal		
Variable	C*T	≤18.6	>18.6	C*T	≤18.6	>18.6
Physical Examination: MCMI (continued)						
Clinical Symptom Syndromes						
Anxiety Score (C)	NS	ns	NS*	ns	NS	NS
Somatoform Score (C)	NS	NS	NS	ns	+0.030	NS
Hypomania Score (C)	ns	ns	ns*	ns	NS	-0.045
Dysthymia Score (C)	NS	NS	NS	NS	NS	NS*
Alcohol Abuse Score (C)	NS	ns	NS	NS	ns	ns
Drug Abuse Score (C)	ns	NS	ns	ns	NS	ns
Psychotic Thinking Score (C)	NS*	NS	+<0.001	NS*	NS	+0.001
Psychotic Depression Score (C)	NS	NS	+0.034	NS	NS	+0.017
Psychotic Delusion Score (C)	NS	ns	NS	NS	ns	NS*

[a]Negative slope considered adverse for this variable.
C: Continuous analysis.
D: Discrete analysis.
+: C*T: Relative risk/slope for ≤18.6 category less than relative risk/slope for >18.6 category.
≤18.6 and >18.6: Relative risk 1.00 or greater for discrete analysis; slope nonnegative for continuous analysis.
-: C*T: Relative risk/slope for ≤18.6 category greater than relative risk/slope for >18.6 category.
≤18.6 and >18.6: Relative risk less than 1.00 for discrete analysis; slope negative for continuous analysis.
NS/ns: Not significant (p>0.10).
NS*/ns*: Marginally significant (0.05<p≤0.10).
** (NS)/** (ns): Log_2 (current dioxin)-by-time-by-covariate interaction (0.01<p≤0.05); not significant when interaction is deleted; refer to Appendix Table H-1 for a detailed description of this interaction.
** (...): Categorized current dioxin-by-covariate interaction (0.01<p≤0.05); significant when interaction is deleted and p-value is given in parentheses; refer to Appendix Table H-1 for a detailed description of this interaction.
****: Log_2 (current dioxin)-by-time-by-covariate interaction (p≤0.01); refer to Appendix Table H-1 for a detailed description of this interaction.
Note: P-value given if p≤0.05.
C*T: Log_2 (current dioxin)-by-time interaction hypothesis test.
≤18.6: Log_2 (current dioxin) hypothesis test for Ranch Hands with time since end of tour of 18.6 years or less.
>18.6 Log_2 (current dioxin) hypothesis test for Ranch Hands with time since end of tour greater than 18.6 years.
A capital "NS" denotes relative risk/slope for ≤18.6 category less than relative risk/slope for >18.6 category, relative risk 1.00 or greater for discrete analysis, or slope nonnegative for continuous analysis; a lowercase "ns" denotes relative risk/slope for ≤18.6 category greater than relative risk/slope for >18.6 category, relative risk less than 1.00 for discrete analysis, or slope negative for continuous analysis.

TABLE 9-57.

Summary of Categorized Current Dioxin Analyses for Psychology Variables (Ranch Hands and Comparisons)

Variable	All	Unadjusted: Unknown versus Background	Unadjusted: Low versus Background	Unadjusted: High versus Background
Questionnaire: Verified				
Psychoses (D)	NS	ns	ns	ns
Alcohol Dependence (D)	NS	NS	ns	NS
Anxiety (D)	NS	ns	NS	NS
Other Neuroses (D)	0.008	ns	+0.003	NS
Questionnaire: Sleep Disorders				
Trouble Falling Asleep (D)	NS	ns	ns*	ns
Waking Up During the Night (D)	NS	ns	ns	ns
Waking Up Too Early and Can't Go Back to Sleep (D)	NS	ns	ns	ns
Waking Up Unrefreshed (D)	NS*	ns*	ns	NS
Involuntarily Falling Asleep During the Day (D)	NS	NS	ns	NS
Great or Disabling Fatigue During the Day (D)	NS	ns	NS	NS
Frightening Dreams (D)	0.010	ns	ns	+0.002
Talking in Sleep (D)	NS	ns	ns	+0.038
Sleepwalking (D)	NS	NS	ns	NS
Abnormal Movement/ Activity During the Night (D)	NS	ns	NS	ns
Sleep Problems Requiring Medication (D)	NS	NS	NS	ns
Snore Loudly in All Sleeping Positions (D)	NS	ns	NS	NS
Insomnia (D)	NS	ns	ns	ns
Overall Sleep Disorder Index (D)	NS	ns	NS	NS
Average Sleep Each Night[a] (C)	NS	NS	NS	ns

TABLE 9-57. (Continued)

Summary of Categorized Current Dioxin Analyses for Psychology Variables
(Ranch Hands and Comparisons)

Variable	All	Unadjusted: Unknown versus Background	Unadjusted: Low versus Background	Unadjusted: High versus Background
Physical Examination: SCL-90-R				
Anxiety (D)	0.043	ns	NS	+0.012
Depression (D)	NS*	ns	NS	+0.015
Hostility (D)	NS	ns	NS	NS
Interpersonal Sensitivity (D)	NS	ns	ns	NS
Obsessive-Compulsive Behavior (D)	NS*	ns	NS	NS*
Paranoid Ideation (D)	NS	ns	NS	ns
Phobic Anxiety (D)	0.042	-0.024	NS	NS
Psychoticism (D)	NS	ns	ns	NS
Somatization (D)	NS	ns	NS	NS*
Global Severity Index (D)	0.025	ns	NS	+0.005
Positive Symptom Total (D)	NS*	ns	NS	+0.019
Positive Symptom Distress Index (D)	NS*	ns	NS	NS
Physical Examination: MCMI				
Basic Personality Patterns				
Schizoid Score (C)	<0.001	ns	NS	+<0.001
Avoidant Score (C)	0.035	ns	NS	+0.032
Dependent Score (C)	0.033	-0.032	ns*	NS
Histrionic Score (C)	0.014	NS	ns	-0.003
Narcissistic Score (C)	0.025	+0.048	NS	ns
Antisocial Score (C)	NS*	NS	+0.016	NS
Compulsive Score (C)	NS	NS	NS	ns
Passive-Aggressive Score (C)	NS*	ns	NS.	NS
Pathological Personality Disorders				
Schizotypal Score (C)	0.003	ns	NS	+0.004
Borderline Score (C)	NS	-0.033	ns	NS
Paranoid Score (C)	NS	NS	NS	NS

TABLE 9-57. (Continued)

Summary of Categorized Current Dioxin Analyses for Psychology Variables (Ranch Hands and Comparisons)

Variable	All	Unadjusted: Unknown versus Background	Unadjusted: Low versus Background	Unadjusted: High versus Background
Physical Examination: MCMI (continued)				
Clinical Symptom Syndromes				
Anxiety Score (C)	0.038	-0.023	ns	NS
Somatoform Score (C)	NS	ns	ns	NS
Hypomania Score (C)	NS	NS	NS	ns*
Dysthymia Score (C)	NS	ns*	ns	NS
Alcohol Abuse Score (C)	NS	ns	ns	ns
Drug Abuse Score (C)	NS	ns	NS	ns
Psychotic Thinking Score (C)	0.004	ns*	ns	+0.012
Psychotic Depression Score (C)	NS*	ns*	ns	NS
Psychotic Delusion Score (C)	NS*	NS	NS*	+0.026

[a]Negative difference considered adverse for this variable.
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk 1.00 or greater for discrete analysis; difference in means nonnegative for continuous analysis.
-: Relative risk less than 1.00 for discrete analysis; difference in means negative for continuous analysis.
NS/ns: Not significant ($p>0.10$).
NS*/ns*: Marginally significant ($0.05<p\leq0.10$).
Note: P-value given if $p<0.05$.
A capital "NS" denotes relative risk 1.00 or greater for discrete analysis or difference of means nonnegative for continuous analysis; a lowercase "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis; a capital "NS" in the first column does not imply directionality.

TABLE 9-57. (Continued)

Summary of Categorized Current Dioxin Analyses for Psychology Variables
(Ranch Hands and Comparisons)

Variable	All	Adjusted: Unknown versus Background	Adjusted: Low versus Background	Adjusted: High versus Background
Questionnaire: Verified				
Psychoses (D)	NS	ns	ns	ns
Alcohol Dependence (D)	NS	NS	ns	NS
Anxiety (D)	NS	ns	NS	NS
Other Neuroses (D)	0.024	NS	+0.003	NS
Questionnaire: Sleep Disorders				
Trouble Falling Asleep (D)	NS*	ns	ns*	ns*
Waking Up During the Night (D)	** (NS)	** (ns)	** (ns)	** (ns)
Waking Up Too Early and Can't Go Back to Sleep (D)	NS	ns	ns	ns
Waking Up Unrefreshed (D)	NS	ns*	ns	NS
Involuntarily Falling Asleep During the Day (D)	NS	NS	ns	NS
Great or Disabling Fatigue During the Day (D)	NS	ns	NS	ns
Frightening Dreams (D)	0.035	ns	ns	+0.007
Talking in Sleep (D)	NS	NS	ns	NS
Sleepwalking (D)	NS	NS	ns	NS
Abnormal Movement/ Activity During the Night (D)	NS	ns	NS	ns
Sleep Problems Requiring Medication (D)	NS	NS	NS	ns
Snore Loudly in All Sleeping Positions (D)	0.049	-0.050	NS	NS
Insomnia (D)	NS	ns	ns	ns
Overall Sleep Disorder Index (D)	NS	ns	ns	NS
Average Sleep Each Night[d] (C)	NS	NS	NS	ns

TABLE 9-57. (Continued)

Summary of Categorized Current Dioxin Analyses for Psychology Variables
(Ranch Hands and Comparisons)

Variable	All	Adjusted: Unknown versus Background	Adjusted: Low versus Background	Adjusted: High versus Background
Physical Examination: SCL-90-R				
Anxiety (D)	NS	ns	NS	NS
Depression (D)	NS	ns	NS	NS*
Hostility (D)	NS	ns	NS	ns
Interpersonal Sensitivity (D)	NS	ns	ns	NS
Obsessive-Compulsive Behavior (D)	NS	ns	NS	NS
Paranoid Ideation (D)	NS	ns	NS	ns
Phobic Anxiety (D)	NS*	-0.033	NS	ns
Psychoticism (D)	NS	ns	ns	NS
Somatization (D)	** (NS)	** (NS)	** (NS)	** (NS)
Global Severity Index (D)	NS	ns	NS	NS*
Positive Symptom Total (D)	NS	ns	NS	NS
Positive Symptom Distress Index (D)	NS*	ns	NS	NS
Physical Examination: MCMI				
Basic Personality Patterns				
Schizoid Score (C)	0.027	ns	NS	+0.006
Avoidant Score (C)	NS	ns	NS	NS
Dependent Score (C)	NS	ns	-0.037	NS
Histrionic Score (C)	NS	ns	ns	-0.020
Narcissistic Score (C)	NS*	NS*	NS	ns
Antisocial Score (C)	** (NS*)	** (NS)	** (+0.012)	** (NS)
Compulsive Score (C)	NS	NS	NS	NS
Passive-Aggressive Score (C)	** (NS)	** (ns)	** (NS)	** (NS)
Pathological Personality Disorders				
Schizotypal Score (C)	NS*	ns	ns	+0.029
Borderline Score (C)	** (NS)	** (ns)	** (ns)	** (ns)
Paranoid Score (C)	NS	NS*	NS	NS

TABLE 9-57. (Continued)

Summary of Categorized Current Dioxin Analyses for Psychology Variables (Ranch Hands and Comparisons)

Variable	All	Adjusted: Unknown versus Background	Adjusted: Low versus Background	Adjusted: High versus Background
Physical Examination: MCMI (continued)				
Clinical Symptom Syndromes				
Anxiety Score (C)	** (NS)	** (ns)	** (ns)	** (NS)
Somatoform Score (C)	** (NS)	** (ns)	** (ns)	** (NS)
Hypomania Score (C)	****	****	****	****
Dysthymia Score (C)	** (NS)	** (ns)	** (ns)	** (NS)
Alcohol Abuse Score (C)	****	****	****	****
Drug Abuse Score (C)	NS	ns	NS	ns
Psychotic Thinking Score (C)	NS	ns	ns	NS
Psychotic Depression Score (C)	NS	ns	ns	NS
Psychotic Delusion Score (C)	NS	NS	NS	NS

[a]Negative difference considered adverse for this variable.
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk 1.00 or greater for discrete analysis; difference in means nonnegative for continuous analysis.
-: Relative risk less than 1.00 for discrete analysis; difference in means negative for continuous analysis.
NS/ns: Not significant ($p>0.10$).
NS*/ns*: Marginally significant ($0.05<p\leq0.10$).
** (NS)/** (ns): Categorized current dioxin-by-covariate interaction ($0.01<p\leq0.05$); not significant when interaction is deleted; refer to Appendix Table H-1 for a detailed description of this interaction.
** (NS*): Categorized current dioxin-by-covariate interaction ($0.01<p\leq0.05$), marginally significant when interaction is deleted; refer to Appendix Table H-1 for a detailed description of this interaction.
** (...): Categorized current dioxin-by-covariate interaction ($0.01<p\leq0.05$); significant when interaction is deleted and p-value is given in parentheses; refer to Appendix Table H-1 for a detailed description of this interaction.
****: Log_2 (current dioxin)-by-time-by-covariate interaction ($p\leq0.01$); refer to Appendix Table H-1 for a detailed description of this interaction.
Note: P-value given if $p\leq0.05$.
A capital "NS" denotes relative risk 1.00 or greater for discrete analysis or difference of means nonnegative for continuous analysis; a lowercase "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis; a capital "NS" in the first column does not imply directionality.

The adjusted analyses of the verified psychological disorder variables did not detect any significant interactions between current dioxin and time since tour or any significant associations with current dioxin within the time strata. There was a marginally significant positive association exhibited between other neuroses and current dioxin for Ranch Hands in the maximal cohort with 18.6 years or less since the end of their tour.

Model 3: Ranch Hand and Comparisons by Current Dioxin Category

In the unadjusted analyses of the verified psychological variables, other neuroses was the only variable with a significant overall contrast of the four current dioxin categories (Table 9-57: p=0.008). For this variable, the percentage of verified cases was significantly higher for the Ranch Hands in the low current dioxin category than for the Comparisons in the background category (p=0.003).

The adjusted analyses showed results similar to those of the unadjusted analyses. Other neuroses was the only verified psychological variable to have a significant overall contrast (Table 9-57: p=0.024), and the contrast of the low versus background category was again significant (p=0.003) with the percentage of verified cases higher for the low category.

Questionnaire: Sleep Disorders

Based on participants' responses to a series of questions regarding sleep problems, 12 disorders were analyzed. In addition, insomnia (defined using 3 of the 12 disorders), are overall sleep disorder index, and average sleep each night were analyzed. Ranch Hands and Comparisons with PTSD based on the 1985 MMPI were excluded from the analyses of the sleep disorder variables.

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Unadjusted analyses found that none of the sleep disorders was significantly associated with initial dioxin under the minimal assumption. However, under the maximal assumption, the sleep disorders of waking up unrefreshed and frightening dreams were significantly related to an increase in initial dioxin (Table 9-55: p=0.027 and p=0.025, respectively).

Under both assumptions, the adjusted analysis found significant negative relationships between initial dioxin and the disorder of sleep problems that required medication (Table 9-55: p= .023 for the minimal assumption and p=0.032 for the maximal assumption). Also, under the maximal assumption, there was a marginally significant positive association between initial dioxin and the percentage of Ranch Hands who reported having trouble falling asleep. Similarly, under the maximal assumption, there was a marginally significant positive association between initial dioxin and the frequency of Ranch Hands who experienced frightening dreams.

Table 9-58 lists several significant initial dioxin-by-covariate interactions in the adjusted analyses. Stratified results showed older Ranch Hands and Ranch Hands with a college education generally had a positive association between initial dioxin and the sleep disorders while younger Ranch Hands and Ranch Hands with a high school education had a

TABLE 9-58.

Summary of Dioxin-by-Covariate Interactions from Adjusted Analyses of Psychology Variables

Variable	Assumption	Covariate
Model 1: Ranch Hands - Log_2 (Initial Dioxin)		
Waking Up Too Early and Can't Go Back to Sleep	Minimal	AGE
Involuntarily Falling Asleep During the Day	Minimal	RACE
Involuntarily Falling Asleep During the Day	Maximal	RACE
Frightening Dreams	Minimal	EDUC
Sleepwalking	Minimal	EDUC
Snore Loudly in All Sleeping Positions	Minimal	AGE
Interpersonal Sensitivity (SCL-90-R)	Minimal	EDUC
Avoidant Score (MCMI)	Minimal	EDUC
Antisocial Score (MCMI)	Minimal	ALC
Antisocial Score (MCMI)	Maximal	ALC
Borderline Score (MCMI)	Maximal	EDUC
Anxiety Score (MCMI)	Minimal	RACE
Anxiety Score (MCMI)	Maximal	RACE
Hypomania Score (MCMI)	Minimal	RACE
Hypomania Score (MCMI)	Maximal	RACE
Dysthymia Score (MCMI)	Minimal	RACE
Dysthymia Score (MCMI)	Maximal	RACE
Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time		
Waking Up During the Night	Minimal	AGE
Waking Up During the Night	Maximal	ALC
Waking Up Unrefreshed	Minimal	AGE
Great or Disabling Fatigue During the Day	Minimal	AGE
Frightening Dreams	Minimal	RACE
Frightening Dreams	Maximal	RACE
Average Sleep Each Night	Minimal	RACE
Average Sleep Each Night	Maximal	RACE
Phobic Anxiety (SCL-90-R)	Minimal	RACE
Phobic Anxiety (SCL-90-R)	Maximal	RACE
Somatization (SCL-90-R)	Maximal	ALC
Global Severity Index (SCL-90-R)	Minimal	RACE
Schizoid Score (MCMI)	Maximal	DRKYR

TABLE 9-58. (Continued)

Summary of Dioxin-by-Covariate Interactions from
Adjusted Analyses of Psychology Variables

Variable	Assumption	Covariate
Model 3: Ranch Hands and Comparisons by Current Dioxin Category		
Histrionic Score (MCMI)	--	RACE
Waking Up During the Night	--	RACE
Somatization (SCL-90-R)	--	RACE
Antisocial Score (MCMI)	--	ALC
Passive-Aggressive Score (MCMI)	--	AGE
Borderline Score (MCMI)	--	EDUC
Anxiety Score (MCMI)	--	RACE
Somatoform Score (MCMI)	--	ALC, DRKYR
Hypomania Score (MCMI)	--	RACE
Dysthymia Score (MCMI)	--	RACE
Alcohol Abuse Score (MCMI)	--	RACE

corresponding negative association. After deletion of these interactions from the adjusted models, none of the variables exhibited a significant association with initial dioxin.

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

The unadjusted current dioxin and time since tour analyses of the sleep disorder variables did not exhibit any significant results under the minimal assumption. The maximal unadjusted analyses detected a marginally significant current dioxin-by-time interaction for the variables involuntarily falling asleep during the day and insomnia. However, the associations within the time strata were nonsignificant for both of these variables.

Also under the maximal assumption, the unadjusted analysis displayed a significant positive association between current dioxin and waking up unrefreshed for the time greater than 18.6 years stratum and between current dioxin and frightening dreams for the less than or equal to 18.6 years time stratum (Table 9-56: p=0.030 and p=0.011, respectively).

The adjusted analysis of the minimal cohort was similar to the corresponding unadjusted analysis. There were no significant current dioxin-by-time since tour interactions for the minimal cohort, but there were marginally significant negative associations between current dioxin and sleep problems requiring medication for both time strata and between current dioxin and the overall sleep disorder index for Ranch Hands with early tours. Under the maximal assumption, the current dioxin-by-time since tour interaction was marginally significant for both involuntarily falling asleep during the day and insomnia. Also, after the deletion of a current dioxin-by-time-by-race interaction, the maximal analysis detected a significant positive association between current dioxin and frightening dreams for the less than or equal to 18.6 years time stratum (Table 9-56: p=0.033). For Ranch Hands with early tours, there were marginally significant negative associations with current dioxin for sleep problems requiring medication and insomnia.

For several of the sleep disorder variables, there was a significant interaction among current dioxin, time since tour, and one of the covariates (listed in Table 9-58). Four of these interactions were with the race covariate and were mainly caused by the sparse number of Blacks with sleep disorders in the analyses.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The unadjusted and adjusted analyses of the sleep disorder variables and categorized current dioxin were generally not significant. In the unadjusted analysis of trouble falling asleep, the contrast of the low versus background current dioxin category was marginally significant with the prevalence of trouble falling asleep lower for the Ranch Hands in the low category than for the Comparisons in the background category. The unadjusted analysis of waking up unrefreshed found a marginally significant overall difference among the current dioxin categories, with the percentage of cases of the sleep disorder lower for the Ranch Hands in the unknown category than for the Comparisons in the background category.

In the unadjusted analysis of the sleep disorder variables and categorized current dioxin, frightening dreams was the only variable with a significant overall contrast of the four

current dioxin categories (Table 9-57: p=0.010). The percentage of Ranch Hands in the high category who reported frightening dreams was significantly higher than the corresponding percentage of Comparisons in the background category (p=0.002). Similarly, the unadjusted analysis of talking in sleep displayed a significantly higher prevalence of the sleep disorder for Ranch Hands in the high current dioxin category than for Comparisons in the background category (p=0.038).

The adjusted analysis of trouble falling asleep detected a marginally significant overall contrast of the four current dioxin categories. The contrasts of low versus background and high versus background were also marginally significant with the prevalence of trouble falling asleep higher for Comparisons in the background category than for Ranch Hands in the low and high categories. The unknown versus background contrast for waking up unrefreshed was also marginally significant with the unknown category having a lower percentage of participants with the sleep disorder.

In the adjusted analysis, the only sleep disorders with a significant overall contrast of the four current dioxin categories were frightening dreams and snore loudly in all sleeping positions (Table 9-57: p=0.035 and p=0.049, respectively). The analysis of frightening dreams found the percentage of Ranch Hands in the high category who reported frightening dreams was significantly higher than the percentage of Comparisons in the background category (p=0.007). In contrast, the percentage of Ranch Hands in the unknown category who snored loudly in all sleeping positions was significantly lower than the corresponding percentage of Comparisons in the background category (p=0.050).

Only one significant categorized current dioxin-by-covariate interaction was detected (listed in Table 9-58). The analysis was of waking up during the night, and the covariate was race. This interaction was also most likely caused by the sparse number of Blacks who reported waking up during the night.

Physical Examination: SCL-90-R Variables

The SCL-90-R, a multidimensional self-reported symptom inventory designed to measure symptomatic psychological distress, presented nine primary symptom measures and three global indices of distress for evaluation. Participants with PTSD based on the 1985 MMPI were excluded from the analysis of these variables.

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

In the unadjusted analysis of the minimal cohort, there was a marginally significant positive association between initial dioxin and the following SCL-90-R variables: depression, obsessive-compulsive behavior, global severity index, and positive symptom total. Under the maximal assumption, the positive association with initial dioxin became significant for each of the aforementioned variables. The maximal unadjusted analysis also detected significant positive associations with initial dioxin for anxiety and psychoticism and marginally significant positive associations for interpersonal sensitivity and somatization.

After adjusting for covariate information, the minimal analysis of the SCL-90-R variables did not detect a significant association with initial dioxin for any of the variables. The maximal adjusted analysis did detect a marginally significant positive association between initial dioxin and obsessive-compulsive behavior and psychoticism.

The adjusted analysis of the SCL-90-R variables and initial dioxin only detected one significant initial dioxin-by-covariate interaction. Under the minimal assumption, the analysis of interpersonal sensitivity displayed a significant interaction between initial dioxin and education (listed in Table 9-58), but stratified results did not show a significant initial dioxin effect for Ranch Hands with either a high school or college education level. After deletion of this interaction from the model, the analysis of interpersonal sensitivity remained nonsignificant.

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

The association between current dioxin and the SCL-90-R variables did not differ significantly between time since tour strata for any of the unadjusted analyses except the minimal analysis of somatization (Table 9-56: p=0.015). The minimal unadjusted analysis of this variable also detected a marginally significant positive association with current dioxin for Ranch Hands with more than 18.6 years since tour.

For anxiety and depression, the unadjusted analysis under the minimal assumption detected significant positive associations with current dioxin for Ranch Hands with greater than 18.6 years since tour (Table 9-56: p=0.031 and p=0.017, respectively). Similar marginally significant associations existed for the corresponding analyses under the maximal assumption. The unadjusted analysis of interpersonal sensitivity displayed a marginally significant positive association with current dioxin for Ranch Hands with less than or equal to 18.6 years since tour under the minimal assumption. A significant positive association existed for the same analysis under the maximal assumption (p=0.018).

For the SCL-90-R obsessive-compulsive behavior symptom, the minimal unadjusted analysis detected a significant positive association with current dioxin for Ranch Hands with more than 18.6 years since tour (Table 9-56: p=0.031). The maximal analysis of this same variable displayed a significant positive associations with current dioxin for both time strata ($\leq$18.6: p=0.043; >18.6: p=0.018). The unadjusted analysis of the global severity index also found a significant positive association with current dioxin for Ranch Hands in the greater than 18.6 years time stratum of the minimal cohort (p=0.026). The maximal analysis of the global severity index detected a positive association with current dioxin of borderline significance for both time strata. Under the maximal assumption, the unadjusted analysis of the positive symptom total exhibited a significant positive association with current dioxin for Ranch Hands with 18.6 years or less since tour (p=0.041).

The adjusted minimal analyses found a marginally significant current dioxin-by-time since tour interaction for anxiety and significant current dioxin-by-time interaction for somatization (Table 9-56: p=0.025). In contrast, the same analyses restricted to Ranch Hands with more than 18.6 years since tour found a significant positive association between anxiety and current dioxin (p=0.028) and marginally significant positive association between

current dioxin and somatization. Under the maximal assumption, the interaction between current dioxin and time was not significant for any SCL-90-R variables. However, for Ranch Hands with less than or equal to 18.6 years since tour, there was a marginally significant positive association between current dioxin and interpersonal sensitivity.

Table 9-58 lists four current dioxin-by-time-by-covariate interactions for the SCL-90-R analyses. Three of these interactions were with the covariate race and were consequently caused by the sparse number of Blacks with abnormal scores. After deletion of these interactions from the models, the analyses were all nonsignificant.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The unadjusted analyses of categorized current dioxin found significant overall differences among the four current dioxin categories for anxiety, phobic anxiety, and the global severity index (Table 9-57: p=0.043, p=0.042, and p=0.025) and marginally significant overall differences significant overall differences for depression, obsessive-compulsive behavior, the positive symptom total, and the positive symptom distress index. Specifically, Ranch Hands in the high current dioxin category had a significantly higher prevalence of anxiety and depression (p=0.012 and p=0.015, respectively), and a significantly greater percentage of participants classified as abnormal on the global severity index and positive symptom total (p=0.005 and p=0.019) than the Comparisons in the background category. These Ranch Hands also had a marginally higher risk of obsessive-compulsive behavior and somatization. In contrast, Ranch Hands in the unknown current dioxin category had a significantly lower prevalence of phobic anxiety than the Comparisons in the background category (p=0.042). The Ranch Hands in the low current dioxin category did not differ from the Comparisons for any of the 12 SCL-90-R variables.

The Ranch Hands in the unknown current dioxin category had a lower risk of all the SCL-90-R symptoms than the Comparisons in the background category. However, the Ranch Hands in the low category had a higher risk for all but two of the SCL-90-R variables (interpersonal sensitivity and psychoticism) and those in the high current dioxin category had a higher risk for all of the SCL-90-R symptoms (except paranoid ideation) than the Comparisons in the background category.

In the adjusted analyses of categorized current dioxin, the overall contrasts of the four current dioxin categories were marginally significant for phobic anxiety and the positive symptom distress index. Also, in the adjusted analysis of depression and the global severity index, the contrast of the background versus high category was marginally significant with the Ranch Hands in the high category having a higher risk than the Comparisons in the background category. Similar to the unadjusted analysis, the Ranch Hands in the unknown current dioxin category had a significantly lower prevalence of phobic anxiety than the Comparisons in the background category (Table 9-57: p=0.033).

The adjusted analyses of categorized current dioxin with the SCL-90-R variables only detected one significant interaction between categorized current dioxin and a covariate (listed in Table 9-58). The interaction was with race in the analysis of somatization and was caused

by the sparse number of Blacks with abnormal somatization scores in the analysis. After deletion of this interaction, the analysis was nonsignificant.

Physical Examination: MCMI Variables

The MCMI, a self-administered test, presented scores for eight basic personality patterns, three pathological personality disorders, and nine clinical symptom syndromes to be evaluated. Participants with PTSD based on the 1985 MMPI were excluded from the analyses.

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Unadjusted analyses found that initial dioxin was positively associated with the MCMI schizoid, avoidant, dependent, passive-aggressive, schizotypal, anxiety, psychotic thinking, and psychotic depression scores under both the minimal and the maximal assumptions (Table 9-55: $p<0.03$ for all analyses). For the histrionic and narcissistic scores, there were a significant negative associations with initial dioxin under both assumptions ($p<0.01$ for all analyses). The unadjusted analyses of the borderline, somatoform, and dysthymia scores detected significant positive associations with initial dioxin for the maximal cohort ($p<0.04$ for all analyses). For the hypomania score, there was a negative association with initial dioxin of borderline significance under the minimal assumption. The unadjusted analysis of the psychotic delusion score found a marginally significant positive association with initial dioxin under the maximal assumption. For the remaining five MCMI variables (antisocial, compulsive, paranoid, alcohol abuse, and drug abuse scores), the unadjusted results were nonsignificant under both assumptions.

The adjusted analyses of the MCMI variables were similar to the unadjusted analyses. Significant positive associations with initial dioxin were displayed for the schizoid, avoidant (after deletion of an initial dioxin-by-education interaction), dependent, schizotypal, and psychotic thinking scores under both assumptions (Table 9-55: $p<0.04$ for all analyses). The adjusted analysis of the MCMI histrionic score detected a significant negative association with initial dioxin for both the maximal and the minimal cohorts ($p<0.04$ for both analyses). The minimal analysis of the narcissistic score detected a marginally significant negative association with initial dioxin while the maximal analysis displayed a similar significant association.

After the deletion of an initial dioxin-by-race interaction, the minimal analysis detected a marginally significant positive relationship between initial dioxin and the anxiety score and a marginally significant negative association between initial dioxin and the hypomania score. Under the maximal assumption, there was a significant positive association between initial dioxin and the somatoform score (Table 9-55: $p=0.011$). The minimal analysis of the psychotic depression score exhibited a significant positive association with initial dioxin ($p=0.035$), and there was a similar marginally significant association under the maximal assumption.

Table 9-58 lists several initial dioxin-by-covariate interactions for the MCMI variables. Stratified analyses of the interactions between initial dioxin and education indicated a

stronger positive relationship for Ranch Hands with a college education than for those with a high school education. Also, the interactions involving current alcohol use showed a stronger negative association with initial dioxin for Ranch Hands with increased current alcohol levels. In the stratified analyses of the initial dioxin-by-race interactions for the anxiety and dysthymia scores, Blacks had a negative association with initial dioxin while non-Blacks displayed a positive association. In contrast, the stratified analysis of the initial dioxin-by-race interaction for the hypomania score exhibited a positive association with initial dioxin for Blacks and a negative association for non-Blacks. However, the results of the stratified analyses of the initial dioxin-by-race interactions may have been distorted by the small number of Blacks in the analyses.

Model 2: Ranch Hands - Log_2 (Current Dioxin) and Time

In the unadjusted analysis of the MCMI variables, the avoidant score was the only variable with a significant current dioxin-by-time since tour interaction under the minimal assumption (Table 9-56: $p=0.028$). Marginally significant interactions between current dioxin and time were exhibited for the schizoid, histrionic, and psychotic thinking scores. There were no significant results for the time less than or equal to 18.6 years stratum for the MCMI variables under the minimal assumption. However, for Ranch Hands with greater than 18.6 years since tour, there were significant positive associations with current dioxin for the schizoid, avoidant, dependent, passive-aggressive, schizotypal, anxiety, psychotic thinking, psychotic depression, and psychotic delusion scores ($p<0.05$ for each analysis). Also, the analyses of the histrionic and narcissistic scores detected significant negative associations with current dioxin for this same time stratum under the minimal assumption, and a similar marginally significant negative relationship for the hypomania score.

Under the maximal assumption, the unadjusted analyses did not detect any significant current dioxin-by-time since tour interactions for the MCMI variables. However, the interaction between current dioxin and time since tour was marginally significant for the schizoid, avoidant, histrionic, and psychotic thinking scores. The maximal unadjusted analyses of the passive-aggressive, schizotypal, and anxiety scores detected significant positive associations with current dioxin for both time strata. (Table 9-56: $p<0.05$ for all analyses).

Similar to the minimal unadjusted analyses, the maximal analyses of the schizoid, avoidant, dependent, psychotic thinking, psychotic depression, and psychotic delusion scores exhibited significant positive associations with current dioxin for Ranch Hands with greater than 18.6 years since tour. Also, the same analyses of the histrionic, narcissistic, and hypomania scores displayed significant negative associations with current dioxin. For Ranch Hands in the time less than or equal to 18.6 years stratum, the maximal unadjusted analysis detected a marginally significant positive association between the somatoform score and current dioxin. The analysis of the borderline and dysthymia scores displayed a marginally significant positive association with current dioxin for the greater than 18.6 years stratum.

Similar to the minimal unadjusted analyses, the minimal adjusted analyses of the MCMI variables detected a significant current dioxin-by-time since tour interaction for only the avoidant score under the minimal assumption (Table 9-56: $p=0.029$). There were also marginally significant current dioxin-by-time interactions for the schizoid and psychotic

thinking scores. As in the unadjusted analyses, there were no significant results for the time less than or equal to 18.6 years stratum under the minimal assumption.

For Ranch Hands in the greater than 18.6 years since tour time stratum of the minimal cohort, there were significant positive associations with current dioxin for the schizoid, avoidant, dependent, schizotypal, psychotic thinking, and psychotic depression scores (Table 9-56: $p<0.035$ for each analysis). For this same time stratum, there was a significant negative association between current dioxin and the histrionic score ($p=0.006$) and a similar marginally significant negative relationship between current dioxin and the narcissistic and hypomania scores. Also, there was a marginally significant positive association between current dioxin and the anxiety score.

Under the maximal assumption, the current dioxin-by-time since tour interaction was significant only for the schizoid score (after deletion of a current dioxin-by-time-by-lifetime alcohol history interaction) and the avoidant score (Table 9-56: $p=0.044$ and $p=0.045$). There were also marginally significant current dioxin-by-time interactions for the narcissistic and psychotic thinking scores.

The adjusted maximal analysis detected a significant positive association between current dioxin and the somatoform score for Ranch Hands with less than or equal to 18.6 years since tour (Table 9-56: $p=0.030$). This was the only significant result found for the maximal adjusted analyses of this time stratum.

For the greater than 18.6 years time stratum, several of the maximal adjusted analyses were significant. A significant positive association was detected with current dioxin for the following MCMI variables: schizoid score (after deletion of the current dioxin-by-time-by-lifetime alcohol history interaction), avoidant score, dependent score, schizotypal score, psychotic thinking score, and psychotic depression score (Table 9-56: $p<0.30$ for each analysis). There were also significant negative associations with current dioxin for the narcissistic and hypomania scores. The positive associations between current dioxin and the dysthymia score and between current dioxin and the psychotic delusion score were marginally significant.

Only two current dioxin-by-time-by-covariate interactions were detected in the maximal adjusted analysis (Table 9-58).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In the unadjusted analysis of the four current dioxin categories, 8 out of 20 of the MCMI variables displayed a significant overall contrast of the four categories: schizoid, avoidant, dependent, histrionic, narcissistic, schizotypal, anxiety, and psychotic thinking scores (Table 9-57: $p<0.04$ for all analyses). The unadjusted analyses also exhibited marginally significant overall simultaneous contrasts of the four current dioxin categories for the antisocial, passive-aggressive, psychotic depression, and psychotic delusion scores.

The unadjusted analyses found that Ranch Hands in the unknown current dioxin category had significantly lower mean dependent, borderline, and anxiety scores than the

Comparisons in the background category (Table 9-57: $p<0.04$ for all analyses). These Ranch Hands also had marginally lower average dysthymia, psychotic thinking, and psychotic depression scores than the Comparisons. In contrast, the unadjusted analyses showed the Ranch Hands in the unknown category had a significantly higher mean narcissistic score than the Comparisons in the background category ($p=0.048$).

Very few differences were found between the mean MCMI scores of the Ranch Hands in the low current dioxin category and the Comparisons in the background category in the unadjusted analyses. These Ranch Hands did have a significantly higher mean antisocial score than the Comparisons (Table 9-57: $p=0.016$) and a marginally higher mean psychotic delusion score. The contrast of the mean dependent score of the Ranch Hands in the low category versus the mean score of the Comparisons in the background category was of borderline significance with the Ranch Hands having a lower mean dependent score than the Comparisons.

The unadjusted analyses detected significantly higher mean schizoid, avoidant, schizotypal, psychotic thinking, and psychotic delusion scores for the Ranch Hands in the high current dioxin category than the Comparisons in the background category (Table 9-57: $p<0.04$ for all analyses). These Ranch Hands also had a significantly lower mean histrionic score ($p=0.003$) and a marginally lower hypomania score than the Comparisons in the background category.

Only 7 of the 20 MCMI variables had significant or marginally significant results after adjusting for covariate information. The overall contrast of the four current dioxin categories was significant for only the schizoid score (Table 9-57: $p=0.027$). Marginally significant overall differences among the four current dioxin categories were also found for the narcissistic, antisocial (after deletion of a categorized current dioxin-by-current alcohol use interaction), and schizotypal scores.

In the adjusted analysis, the contrast of the Ranch Hands in the unknown category and the Comparisons in the background category was of borderline significance for the narcissistic score and the paranoid score with Ranch Hands having higher mean scores than the Comparisons. The adjusted analyses also found Ranch Hands in the low current dioxin category had a significantly lower mean dependent score than Comparisons in the background category (Table 9-57: $p=0.037$). In addition, after the deletion of a categorized current dioxin-by-current alcohol use interaction, the adjusted analysis found that the Ranch Hands in the low category had a significantly higher mean antisocial score than the Comparisons ($p=0.012$). The adjusted analyses also showed that Ranch Hands in the high current dioxin category had significantly higher mean schizoid and schizotypal scores ($p=0.006$ and $p=0.029$) and a significantly lower histrionic score ($p=0.020$) than the Comparisons in the background category.

The adjusted analyses of the MCMI variables detected several categorized current dioxin-by-covariate interactions (listed in Table 9-58). After deletion of these interactions, the adjusted analyses were nonsignificant except as stated above for the antisocial score. The stratified analyses of these interactions did not detect any overlying dioxin effects or patterns for the individual strata.

CONCLUSION

In general, the results of the analyses of the verified psychological disorders, reported sleep disorders, and the SCL-90-R variables did not reveal significant associations with initial dioxin or current dioxin and time since tour or find significant differences among the four current dioxin categories. In contrast, several of the analyses of the MCMI variables displayed significant results. However, there was a lack of consistency across similar variables included in the SCL-90-R, MCMI, and reported information. Additionally, the continuous scale of the MCMI variables allowed for a greater ability to detect small differences in the mean MCMI scores than the capability of the discrete analyses of the other three psychological abnormalities. In conclusion, the body burden of dioxin does not appear to be related to psychological or psychophysiological disorders.

CHAPTER 9

REFERENCES

1. Peterson, R.E., M.D. Seefeld, B.J. Christian, C.L. Potter, C.K. Kelling, and R.E. Keesey. 1984. The wasting syndrome in 2,3,7,8-tetrachlorodibenzo-p-dioxin toxicity: Basic features and their interpretation. In *Banbury Report 18: Biological mechanisms of dioxin action*, eds. A. Poland and R.D. Kimbrough. Cold Spring Harbor, New York: Cold Spring Harbor Laboratory.

2. Schantz, S.L., and R.E. Bowman. 1989. Learning in monkeys exposed perinatally to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). *Neurotoxicology Teratol.* 11:13-19.

3. Ashe, W.F., and R.R. Suskind. 1949, 1950. Reports on chloracne cases. In *Report of the Kettering Laboratory*. Nitro, West Virginia: Monsanto Chemical Company.

4. Suskind, R.R. 1953. A clinical and environmental survey. In *Report of the Kettering Laboratory*. Nitro, West Virginia: Monsanto Chemical Company.

5. Moses, M., R. Lilis, K.D. Crow, J. Thornton, A. Fischbein, H.A. Anderson, and I.J. Selikoff. 1984. Health status of workers with past exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin in the manufacture of 2,4,5-trichlorophenoxyacetic acid: Comparison of findings with and without chloracne. *Am. J. Ind. Med.* 5:161-82.

6. Suskind, R.R., and V.S. Hertzberg. 1984. Human health effects of 2,4,5-T and its toxic contaminants. *JAMA* 251:2372-80.

7. Baader, E.W., and A.J. Bauer. 1951. Industrial intoxication due to pentachlorophenol. *Ind. Med. Surg.* 20:289-90.

8. Suskind, R.R. 1977. Chloracne and associated health problems in the manufacture of 2,4,5-T. Report to the Joint Conference, National Institute of Environmental Health Sciences and International Agency for Research on Cancer, World Health Organization, January, at Lyon, France.

9. Goldman, P.J. 1973. Schweist akute Chlorakne, eine Massenintoxikation durch 2,3,7,8-tetrachlorodibenzodioxin (severe, acute chloracne, a mass intoxication due to 2,3,7,8-tetrachlorodibenzo-dioxin). *Der Hautarzt.* 24:149-52.

10. Vos, J.G., T.J. Sterringa, D. Zellenrath, H.J. Docter, and L.M. Daldkerup. 1977. TCDD accident at a chemical factory in the Netherlands. Report to the Joint Conference, National Institute of Environmental Health Sciences and International Agency for Research on Cancer, World Health Organization, January, at Lyon, France.

11. Telegina, K.A., and L.J. Bikbulatova. 1970. Affection of the follicular apparatus of the skin in workers employed in the production of the butyl ester of 2,4,5-T. *Vestnik. Derm. Ven.* 44:35-39.

12. Jirasek, L., J. Kalensky, K. Kubec, J. Pazderova, and E. Lucas. 1974. Part 2, Acne chlorina, porphyria cutanea tarda and other manifestations of general intoxication during the manufacture of herbicides. *Czech. Dermatol.* 49:145-57.

13. Pazderova-Vejlupkova, J., M. Nemcova, J. Pickova, L. Jirasek, and E. Lukas. 1981. The development and prognosis of chronic intoxication by tetrachlorodibenzo-p-dioxin in men. *Arch. Environ. Health* 36:5-11.

14. Poland, A.P., D. Smith, G. Metter, and P. Possick. 1971. A health survey of workers in a 2,4,-D and 2,4,5-T plant, with special attention to chloracne, porphyria cutanea tardas, and psychologic parameters. *Arch. Environ. Health* 22:316-27.

15. Oliver, R.M. 1975. Toxic effects of 2,3,7,8-tetrachlorodibenzo-1,4-dioxin in laboratory workers. *Br. J. Ind. Med.* 32:46-53.

16. Hoffman, R.E., P.A. Stehr-Green, K.B. Webb, G. Evans, A.P. Knutsen, W.F. Schramm, J.L. Staake, B.B. Gibson, and K.K. Steinberg. 1986. Health effects of long-term exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *JAMA* 225:2031-38.

17. Robinowitz, R., W.R. Roberts, M.P. Dolan, E.T. Patterson, H.L. Charles, H.G. Atkins, and W.E. Penk. 1989. Carcinogenicity and teratogenicity vs. psychogenicity: Psychological characteristics associated with self-reported Agent Orange exposure among Vietnam combat veterans who seek treatment for substance abuse. *J. Clin. Psychol.* 45:718-28.

18. American Psychiatry Association. 1980. *Diagnostic and statistical manual of mental disorders*. 3d ed. Washington, DC.

19. Faltus, F.J., A.D. Sirota, J. Parsons, M. Daamen, and M.L. Schare. 1986. Exacerbation of post-traumatic stress disorder symptomatology in Vietnam veterans. *Military Med.* 151:648-49.

20. Van Putten, T., and J. Yager. 1984. Post-traumatic stress disorder. *Arch. Gen. Psychiatry* 41:411-13.

21. Atkinson, R.M., R.G. Henderson, L.F. Sparr, and S. Deale. 1982. Assessment of Vietnam veterans for post-traumatic stress disorder in veterans disability claims. *Am. J. Psychiatry* 129:1118-21.

22. Flicker, M.R., and A.L. Young. 1983. Evaluation of veterans for Agent Orange exposure. Presented at the Symposium on Chlorinated Dioxins and Dibenzofurans in the Total Environment, September, before the Division of Environmental Chemistry, American Chemical Society, Washington, DC.

23. Blackburn, A.B. 1983. Review of the effects of Agent Orange: A psychiatric perspective on the controversy. *Military Med.* 148:333-40.

24. True, W.R., J. Goldberg, and S.A. Eisen. 1988. Stress symptomatology among Vietnam veterans. In Part 2, Analysis of the Veterans Administration survey of veterans. *Am. J. Epidemiol.* 128:85-92.

25. Krogeski, G.P., and G.R. Leon. 1983. Correlates of self-reported and objectively determined exposure to Agent Orange. *Am. J. Psychiatry* 140:1443-49.

26. Levy, C.J. 1988. Agent Orange exposure and post-traumatic stress disorder. *J. Nerv. Ment. Dis.* 176:242-45.

27. Stellman, S.D., J.D. Stellman, and J.F. Sommer, Jr. 1988. Combat and herbicide exposures in Vietnam among a sample of American Legionnaires. *Environ. Res.* 47:112-28.

28. Stellman, J.D., S.D. Stellman, and J.F. Sommer, Jr. 1988. Social and behavioral consequences of the Vietnam experience among American Legionnaires. *Environ. Res.* 47:129-49.

29. U.S. Centers for Disease Control. 1988. Health status of Vietnam veterans. In Part 1, Psychosocial characteristics. *JAMA* 259:2701-02.

30. Thomas, W.F., W.D. Grubbs, T.G. Karrison, M.B. Lustik, R.H. Roegner, D.E. Williams, W.H. Wolfe, J.E. Michalek, J.C. Miner, and R.W. Ogershok. 1990. Epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: 1987 followup examination results, NTIS: AD A 222 573. USAF School of Aerospace Medicine, Human Systems Division, Brooks Air Force Base, Texas.

31. Bixler, E.O., A. Kales, C.R. Soldatos, J.D. Kales, and S. Healy. 1979. Prevalence of sleep disorders in the Los Angeles metropolitan area. *Am. J. Psychiatry* 136:1257-62.

32. Keane, T.M., R.F. Malloy, and J.A. Fairbank. 1984. Empirical development of an MMPI subscale for the assessment of combat-related post-traumatic stress disorder. *J. Consulting and Clinical Psychology* 52:888-91.

33. Derogatis, L.R. 1975. *The SCL-90-R*. Baltimore, Maryland: Clinical Psychometrics Research.

34. Millon, T. 1983. *Millon Clinical Multiaxial Inventory Manual*. 3rd ed. Minneapolis: Interpretive Scoring Systems, National Computer Systems, Inc.

35. Choca, J.P., C.A. Peterson, and L.A. Shanley. 1986. Factor analysis of the Millon Clinical Multiaxial Inventory. *Journal of Consulting and Clinical Psychology* 54:253-55.

36. Goldberg, J., W.R. Hines, III, and S.A. True. 1990. A twin study of the effects of the Vietnam war on post-traumatic stress disorder. *JAMA* 263:1227-32.