Table 8-7. Associations Between Other Miscellaneous Covariates and Estimates of Herbicide or Dioxin Exposure (Continued)

Covariate	Covariate Category	Model 3					
		Comparison Mean or n (%)	Background Ranch Hand Mean or n (%)	Low Ranch Hand Mean or n (%)	High Ranch Hand Mean or n (%)	p-Value: Unadjusted	p-Value: Adjusted[a]
Current Parental Status (Child Younger than 18 Years of Age)	n	1,213	380	239	243		
	Yes	176 (14.5)	41 (10.8)	26 (10.9)	41 (16.9)	0.069	0.644
	No	1,037 (85.5)	339 (89.2)	213 (89.1)	202 (83.1)		
Worked with Vibrating Power Equipment or Tools	n	1,211	380	239	243		
	Yes	318 (26.3)	95 (25.0)	72 (30.1)	78 (32.1)	0.142	0.242
	No	893 (73.7)	285 (75.0)	167 (69.9)	165 (67.9)		
Composite Exposure to Heavy Metals	n	1,213	380	239	243		
	Yes	174 (14.3)	33 (8.7)	35 (14.6)	42 (17.3)	0.010	0.347
	No	1,039 (85.7)	347 (91.3)	204 (85.4)	201 (82.7)		

Table 8-7. Associations Between Other Miscellaneous Covariates and Estimates of Herbicide or Dioxin Exposure (Continued)

Covariate	Covariate Category	Model 4		
		1987 Dioxin (ppt) Correlation or Mean (n)	p-Value: Unadjusted	p-Value: Adjusted[a]
Current Total Household Income (dollars) (continuous)	n	854		
		r=–0.169	<0.001	0.185
(discrete)	≤ $65,000	$\bar{x}$ = 15.9 (n=434)	<0.001	0.083
	> $65,000	$\bar{x}$ = 12.3 (n=420)		
Personality Type	n	860		
	Type A	$\bar{x}$ = 13.4 (n=348)	0.314	0.671
	Type B	$\bar{x}$ = 14.5 (n=512)		
Education	n	862		
	High School	$\bar{x}$ = 18.2 (n=411)	<0.001	0.203
	College	$\bar{x}$ = 11.0 (n=451)		
Current Employment Status	n	862		
	Yes	$\bar{x}$ = 15.0 (n=559)	0.013	0.878
	No	$\bar{x}$ = 12.4 (n=303)		
Current Marital Status	n	862		
	Married	$\bar{x}$ = 13.6 (n=708)	0.119	0.794
	Not Married	$\bar{x}$ = 15.9 (n=154)		

Table 8-7. Associations Between Other Miscellaneous Covariates and Estimates of Herbicide or Dioxin Exposure (Continued)

Covariate	Covariate Category	Model 4 1987 Dioxin (ppt) Correlation or Mean (n)	Model 4 p-Value: Unadjusted	Model 4 p-Value: Adjusted[a]
Current Parental Status (Child Younger than 18 Years of Age)	n	862		
	Yes	$\bar{x}$ = 17.8 (n=108)	0.014	0.961
	No	$\bar{x}$ = 13.5 (n=754)		
Worked with Vibrating Power Equipment or Tools	n	862		
	Yes	$\bar{x}$ = 16.2 (n=245)	0.013	0.394
	No	$\bar{x}$ = 13.2 (n=617)		
Composite Exposure to Heavy Metals	n	862		
	Yes	$\bar{x}$ = 18.1 (n=110)	0.007	0.854
	No	$\bar{x}$ = 13.5 (n=752)		

[a] Adjusted for occupation.

Note: Means for discrete covariates were transformed from the logarithmic (base 2) scale for initial dioxin in Model 2 and from the ($\log_2$ (X+1)) scale for 1987 dioxin in Model 4.

dioxin were significant for categorized dioxin in Model 3 (p=0.010) and 1987 dioxin in Model 4 (p=0.007). The percentage of Ranch Hands exposed to heavy metals increased as dioxin increased in Model 3 analyses (8.7% for Ranch Hands in the background dioxin category, 14.6% for Ranch Hands in the low dioxin category, and 17.3% for Ranch Hands in the high dioxin category). After adjustment for occupation, the association was nonsignificant (p=0.347). In Model 4, average 1987 dioxin levels were greater for participants reporting exposure to heavy metals than for participants not reporting exposure to heavy metals. The association between exposure to heavy metals and 1987 dioxin was nonsignificant after adjustment for military occupation (p=0.854). All tests of association between reported exposure to heavy metals and group in Model 1 were nonsignificant (p>0.28 for both analyses). Tests of association between reported exposure to heavy metals and initial dioxin in Model 2 also were nonsignificant (p>0.40 for both analyses).

8.9 SUMMARY

The purpose of this chapter was to determine whether the covariates used throughout this report were associated with the estimates of herbicide or dioxin exposure. Military occupation, being associated with education, may have influenced the associations between covariates and dioxin estimates. Therefore, associations between covariates and the estimates of exposure in this chapter were adjusted for military occupation but not for other known or suspected confounders. Associations between covariates and dioxin estimates should be interpreted with caution and do not necessarily reflect a causal relation.

The demographic variables of age, race, and military occupation were used as matching variables in the original study design. As expected because of the matching, there were no significant differences between Ranch Hands and Comparisons for these three variables. As exhibited in previous reports, dioxin was significantly associated with military occupation. Officers had the lowest levels, followed by enlisted flyers and enlisted groundcrew. Because the Ranch Hand enlisted groundcrew tended to be younger on average than the Ranch Hand officers and enlisted flyers, a strong negative association also was seen between dioxin levels and age. When military occupation was taken into consideration, however, dioxin exposure estimates did not appear to be related to age. Race exhibited significant associations with dioxin in that Black participants appeared to have lower dioxin levels than non-Black participants. The effect of race on dioxin levels was strengthened when military occupation was considered.

Few significant associations were seen between current alcohol use or lifetime alcohol history and group or dioxin. Wine use appeared to affect dioxin exposure estimates significantly. Lower dioxin levels were associated with more wine use, both current and lifetime. As suspected in previous reports, this phenomenon appears to be related to military occupation as officers may have consumed more wine than did enlisted personnel. When adjusting for military occupation, the association between wine use and dioxin exposure was not significant.

Significant associations were observed between current cigarette smoking and lifetime cigarette smoking history and 1987 dioxin after adjustment for military occupation.

Questions posed to the participants regarding exposure to known carcinogens were intended to indicate post-SEA exposures; however, the data suggest that the participants may have included SEA exposures as well. Significant associations were seen between dioxin and both degreasing chemicals and industrial chemicals. Adjusted analysis showed that these associations were related to military occupation. It is believed that fewer officers were exposed to industrial chemicals and degreasing chemicals than enlisted personnel. The percentage of Comparisons exposed to ionizing radiation was larger than the percentage

of Ranch Hands exposed; however, a greater percentage of Ranch Hands was exposed to herbicides and insecticides and may indicate that Ranch Hands were more likely to report SEA or pre-SEA exposures as well.

The significant associations between dioxin and health measurements, such as cholesterol, HDL, the cholesterol-HDL ratio, physical activity level, and diabetic class, are likely to be explained by body fat. Higher body fat measurements are known to correspond to higher dioxin levels, lower levels of HDL cholesterol, and higher cholesterol-HDL ratios, as well as diabetes. Also, higher body fat is more likely to occur with sedentary lifestyles.

Of covariates related to sun exposure, Ranch Hands with darker hair tended to have higher levels of initial dioxin than those with lighter-colored hair. The relation between dioxin and hair color was explained by military occupation. Dioxin estimates appeared to differ with eye color in that those with brown eyes tended to have higher dioxin levels. Although eye and hair color are related, from the adjusted analysis, it did not appear that the relation between eye color and dioxin could be explained by military occupation. A larger percentage of Ranch Hands lived in latitudes farther from the equator than did Comparisons, and higher levels of dioxin were seen for those participants who live in more southerly latitudes. No significant associations were observed with the reaction to sun exposure covariates.

The relations between dioxin and current total household income, education, current employment status, current marital status, and having a child younger than 18 years old appear to be directly related to military occupation. Participants who were officers at the time of service in SEA have larger current incomes than participants who were enlisted at the time of service in SEA. Officers have the lowest dioxin levels (Table 2-8); consequently, there was a negative association between income and dioxin. A larger percentage of Ranch Hand officers tended to be college graduates than enlisted personnel, and, consequently, college graduates had lower dioxin levels than high school graduates. Differences in current employment may be due to age, income, and level of education. Current marital and parental status may be related to military occupation directly or indirectly through the relation between military occupation and socioeconomic factors.

8.10 CONCLUSION

The purpose of this chapter was to determine whether the covariates used throughout this report were associated with the estimates of dioxin exposure and, therefore, could potentially be confounding variables in subsequent statistical analyses in this report. Military occupation, being associated with education, may have influenced the associations between covariates and dioxin estimates. The associations between covariates and the estimates of dioxin exposure in this chapter were adjusted for military occupation, but not for other known or suspected confounders. Therefore, associations between covariates and dioxin estimates should be interpreted with caution.

In general, the Ranch Hand and Comparison groups were similar for the majority of the covariates; however, exceptions included reported herbicide exposure, insecticide exposure, and average lifetime latitude. A greater percentage of Ranch Hands than Comparisons reported herbicide exposure. Although the questionnaire had been structured to indicate post-SEA exposure only, a possible explanation for this association between group and herbicide exposure may have been the tendency of Ranch Hands to report their exposure to dioxin during their time of duty in SEA. A greater percentage of Ranch Hands reported exposure to insecticides than did Comparisons. More Comparisons than Ranch Hands lived in the more southerly latitudes. Ranch Hands who lived in the more southerly latitudes had a higher average initial and 1987 dioxin level than Ranch Hands living in the more northerly latitudes.

Most of the significant associations between dioxin and the covariates in the Ranch Hand group can be explained at least partially by the effects of military occupation or body fat. Of the three occupational cohorts, enlisted groundcrew had the highest levels of 1987 and initial dioxin. Adjusted analyses in the clinical chapters fully account for group, age, occupation, and other potential confounders to further investigate significant associations between covariates and dioxin. Body fat and the half-life of dioxin were known to be related, and the Models 2 and 3 analyses in the clinical chapters adjusted for body fat. In addition, body fat was used as a risk factor where appropriate. The reader is referred to these chapters for a more complete assessment of the effect of dioxin on the relevant medical endpoints.

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9 GENERAL HEALTH ASSESSMENT

9.1 INTRODUCTION

9.1.1 Background

In February 1991, in response to unanswered questions and ongoing concerns that Vietnam veterans may have been harmed by herbicide defoliants, Congress passed the Agent Orange Act of 1991. Under this legislation, Public Law 102-4, the National Academy of Sciences requested the Institute of Medicine (IOM) to conduct an independent review of all the scientific evidence relevant to the issue and to make recommendations for the directions of future research. The committee established by the IOM expanded its review beyond studies of veterans to include reports in the world literature of other populations exposed to dioxin by occupation, environmental contamination, or as a consequence of industrial accidents. The first IOM report (1), *Veterans and Agent Orange*, was published in 1994, and the first biennial update was published in 1996 (2). These references provide an inclusive resource of information on the health consequences of exposure to herbicides and, particularly, to dioxin. Among the valuable contributions was the stratification of suspect diseases into three categories—"Sufficient," "Limited/Suggestive," and "Inadequate/Insufficient"—based on the scientific evidence for and against an association with herbicide exposure.

Pertinent to the Air Force Health Study (AFHS), the IOM Committee concluded that the principal limitation of most epidemiological studies was the lack of accurate and quantitative indices of individual exposure and that studies such as the AFHS, which include tissue levels in the analyses, have limitations. Despite these concerns and caveats, the committee emphasized the merits of the model of the AFHS and proposed that a similar methodology be applied to a study of the only other veteran group with significant herbicide exposure—the Army Chemical Corps. In its first recommendation, the committee endorsed the continued follow-up of the Air Force Ranch Hand and Comparison cohorts, now in its fifteenth year.

Although the potentially lethal consequences of acute phenoxy herbicide toxication have been well defined (3, 4), the latent effects of herbicide exposure on human health remain controversial. Epidemiological studies published in the scientific literature have focused on specific clinical endpoints, particularly malignancy, and have been based on cohorts of Vietnam veterans (5-15), on civilian populations exposed to dioxins by occupation (16-28), or as a consequence of industrial accidents (29–37). These studies and others have been summarized in the comprehensive literature reviews cited above (1, 2) and those of the Veterans Health Services and Research Administration published since the last AFHS examination (38–40).

The scientific basis for these epidemiological studies in humans has been firmly established in animal studies conducted over several decades. In laboratory animals, dioxin toxicity is species- and strain-specific and appears to correlate with the presence of a stereospecific protein receptor, the aryl hydrocarbon (Ah) receptor, found in the cytosol of selected organs and capable of binding aromatic hydrocarbons (41–44). The assessment of the risk of dioxin exposure to human health is in large part based on the molecular and cellular mechanisms of dioxin toxicity in animals and has been the subject of numerous review articles (45–50). Ah receptors have been isolated in the tissue of several human organs (43, 51–54), and the comparative properties of animal and human Ah receptors have been studied (55,

56). Epidemiological studies have focused on target organ effects that have been defined in animal models including immunotoxicity, carcinogenicity, hepatotoxicity, and neurotoxicity. In the chapters that follow, these and other clinical endpoints will be considered in detail.

The lack of an accurate measure of exposure is now recognized as the principal methodological limitation common to all of the early epidemiological investigations into the effects of herbicides on human health. Assay techniques developed a decade ago (57) now permit the accurate detection and quantitative measurement of trace amounts of dioxin in blood and adipose tissue and the identification of those with significant prior exposure to dioxin. Analyses of serum dioxin data from the AFHS (58) and two other epidemiological studies (59, 60) have been published and have contributed to a better understanding of the pharmacokinetics of dioxin in man. The reliability and reproducibility of the serum dioxin assay have been established (61) and the potential effects of age, body fat, and time since exposure on the rate of dioxin elimination have been explored (58). Based on the analyses of serial serum dioxin levels taken from participants in the current study 15 to 25 years after exposure, the latest estimate of the half-life of dioxin in humans has been revised upward to 8.7 years (58). These recent analyses have confirmed an earlier report (62) that an increase in body fat is associated with prolongation of the dioxin half-life, a finding that may be relevant to the development of clinical endpoints related to obesity.

The serum dioxin assay is important to the credibility of this and other epidemiological studies. The Centers for Disease Control and Prevention study of serum dioxin levels demonstrated that all estimates of herbicide exposure employed previously in Vietnam veterans were imprecise and that there was no significant difference in the current body burden of dioxin between most Vietnam and non-Vietnam veterans of the same era (63, 64). Published reports leave no doubt that, of all veterans who served in Vietnam, the 1,300 Air Force Ranch Hand personnel were among those most highly exposed to dioxin and that, within this group, the enlisted groundcrew responsible for handling the herbicides and for maintaining the spray equipment were at greatest exposure risk (8, 9, 65).

The importance of the serum dioxin assay is reflected in the number of publications reporting serum dioxin levels in exposed populations around the world including the United States (16, 65–70), Germany (71–73), Russia (74, 75), New Zealand (76), Austria (77), Australia (78), and Italy (35, 79). Apart from the current study, only a few published reports have appeared relating clinical and laboratory indices to serum or adipose dioxin levels (16, 36, 37, 80-83). Because these studies relate health outcomes with evidence of prior exposure to dioxin, they will receive special attention in the chapters that follow.

In this and previous AFHS examinations, five variables have been included in the general health assessment: self-perception of health, appearance of illness or distress during the examination, relative age, body fat, and erythrocyte sedimentation rate. In the Serum Dioxin Analysis Report of the 1987 examination (8), positive associations were noted between measured levels of dioxin and the perception of ill health and body fat. In the 1992 examinations, these associations were again found to be significant (9).

Finally, with the exception of the 1992 examinations, a significantly higher prevalence of elevated erythrocyte sedimentation rates was noted in the Ranch Hands relative to the Comparison cohort. In a more recent study (80), one of the few to correlate laboratory indices with the current body burden of dioxin, a positive association was found between the serum dioxin level and the erythrocyte sedimentation rate. These results have raised the possibility of a subclinical dioxin-induced inflammatory process and point to the need for continued surveillance in this and the final AFHS examination in 2002.

9.1.2 Summary of Previous Analyses of the Air Force Health Study

9.1.2.1 1982 Baseline Study Summary Results

Five general health variables were included in the 1982 baseline examination: self-perception of health, appearance of illness or distress, relative age, body fat, and erythrocyte sedimentation rate. In the analysis of the baseline examination data, a statistically significant difference in self-perception of health was found between the Ranch Hand and Comparison groups, with a greater percentage of Ranch Hands reporting their health as fair or poor than Comparisons (20.6% vs. 14.2%). This was true in both the younger and older age groups (Est. RR=1.82, p=0.017 for individuals 40 or younger and Est. RR=1.35, p=0.025 for individuals older than 40). Because only 9 of 1,811 individuals were reported by the examining physician as appearing ill or distressed, this designation was apparently reserved for only very ill or distressed individuals. Nevertheless, eight of the nine individuals were Ranch Hands, the difference being of marginal significance (p=0.056). Conversely, more Ranch Hands than Comparisons were reported by the examiners as appearing younger than their actual ages (4.9% vs. 2.5%, p=0.029). No overall differences in body fat or erythrocyte sedimentation rate were found, although a significant interaction between group and age for erythrocyte sedimentation rate was noted; younger Ranch Hands had fewer erythrocyte sedimentation rate abnormalities than did Comparisons, whereas no difference was found in participants older than 40.

9.1.2.2 1985 Follow-up Study Summary Results

General physical health was evaluated by the same five measures used in the baseline examination (self-perception of health, appearance of illness or distress, relative age, body fat, and erythrocyte sedimentation rate). The Ranch Hands again rated their health as fair or poor more often than the Comparisons (9.1% vs. 7.3%, respectively), although this difference was not statistically significant. Further analysis revealed a significant group-by-occupation interaction. Differences were largely confined to the enlisted groundcrew category where the adjusted relative risk was 1.90 (p=0.003).

Ten individuals were reported as appearing acutely ill or distressed at the 1985 follow-up examination. In contrast to the baseline examination, four were Ranch Hands and six were Comparisons; thus, no group difference was suggested. Relative age, as determined by the examining physician, was not significantly different in the two groups.

The (geometric) mean erythrocyte sedimentation rates did not differ significantly, either unadjusted or after adjustment for age, race, occupation, personality score, and an age-by-personality score interaction. In the discrete analysis, 5.8 percent of the Ranch Hands had erythrocyte sedimentation rate abnormalities (>20 mm/hr), contrasted to 3.6 percent in the Comparison group. This difference was significant both unadjusted (p=0.013) and adjusted for age and personality score (p=0.011).

The mean body fat of the Ranch Hands was significantly lower than the Comparisons (21.10 percent vs. 21.54 percent, p=0.037), and the difference was of nearly the same magnitude after adjustment for age, race, and occupation.

Longitudinal differences between the 1982 baseline and the 1985 follow-up examination were assessed by analyses of two discrete variables: self-perception of health and erythrocyte sedimentation rate. Analysis of self-perception of health showed no significant group differences in the change over time, with the Ranch Hand and Comparison groups reporting symmetrical improvements in their perceptions over the 3-year period. The erythrocyte sedimentation rate analysis revealed a highly significant group difference (p=0.002), because of a reversal of findings between examinations (i.e., a significant adverse

effect in the [younger] Comparisons at the baseline examination versus a significant adverse effect in the Ranch Hands at the follow-up examination).

9.1.2.3 1987 Follow-up Study Summary Results

The general health in the Ranch Hand and Comparison groups was assessed by the same five measures used in previous AFHS examinations: self-perception of health, appearance of illness or distress, relative age, body fat, and erythrocyte sedimentation rate. There were no significant group differences, either unadjusted or adjusted for covariates (age, race, occupation, and, in the case of self-perception of health and erythrocyte sedimentation rate, personality type), nor were there any significant group-by-covariate interactions for self-perception of health, appearance of illness or distress, relative age, or percent body fat. There was little difference in the geometric mean values of erythrocyte sedimentation rate in the two groups, but Ranch Hands had a significantly higher percentage of individuals with an abnormal erythrocyte sedimentation rate (>20 mm/hr) than Comparisons. For erythrocyte sedimentation rate, there was a significant difference between groups in the change from baseline to the 1987 follow-up examination, with a relatively greater number of Ranch Hands than Comparisons shifting from normal at baseline to abnormal at the follow-up examination. Only three participants (two Ranch Hands and one Comparison) were found to have rates in excess of 100 mm/hr; one of these (a Comparison) proved to have lung cancer and died in early 1989. No diagnosis was established for either of the two Ranch Hands during the course of the 1987 examination. Longitudinal analyses revealed a similar decline in both groups over time in the percentage of individuals reporting their health as fair or poor.

9.1.2.4 Serum Dioxin Analysis of 1987 Follow-up Study Summary Results

In general, body fat and erythrocyte sedimentation rate exhibited significant positive associations with initial dioxin. The other variables exhibited positive but nonsignificant associations with initial dioxin. The unadjusted and adjusted analyses of relative age appearance exhibited significant interactions between current dioxin and time since tour of duty. For Ranch Hands with 18.6 years or less since the end of duty in Southeast Asia (SEA), the associations between relative age and current dioxin were positive and at least marginally significant for each analysis type and assumption. For the other variables, the current dioxin-by-time analyses generally displayed nonsignificant but positive associations with current dioxin.

In general, the unadjusted and adjusted analyses for the four current dioxin categories overall exhibited significant contrasts for body fat and erythrocyte sedimentation rate, and the high versus background contrast and the low versus background contrast were significant with the Ranch Hands exceeding Comparisons. The body fat results for the four current dioxin categories displayed an increasing association with dioxin within the Ranch Hands (i.e., unknown, low, and high categories); however, the background category for Comparisons exceeded the unknown category for Ranch Hands.

The longitudinal analyses of self-perception of health demonstrated significant positive associations with initial dioxin and current dioxin. The percentage of participants who reported fair or poor health decreased by more than 50 percent from 1982 to 1987. In the longitudinal analyses of erythrocyte sedimentation rate, the percentages of abnormalities in 1987 differed significantly among the current dioxin categories.

In summary, with the exception of the erythrocyte sedimentation rate, the data analyzed in the general health assessment did not reveal any adverse health effect consequent to herbicide exposure or to the current body burden of dioxin.

9.1.2.5 1992 Follow-up Study Summary Results

In the assessment of general health, significant differences between Ranch Hands and Comparisons—the enlisted groundcrew in particular—were evident for self-perception of health. Significant associations between negative self-perception of health and initial and current levels of dioxin also were evident. These results are consistent with the 1985 and 1987 follow-up examinations. In contrast to self-perception of health, no significant results were found for the appearance of illness or distress and relative age appearance, which were recorded by the examining physicians.

The analyses of body fat displayed a significant positive association with current dioxin, whether calculated on a whole-weight or lipid-adjusted basis. Erythrocyte sedimentation rate also displayed a significant positive association with current dioxin levels.

In the longitudinal analysis, the increase in the percentage of Ranch Hands who perceived their health to be poor in 1992 from those that were normal in 1982 was significantly associated with initial dioxin levels. Relative age appearance also displayed a significant positive association with initial dioxin. The change in body fat from 1982 to 1992 was significantly associated with initial dioxin, and a significant difference between Ranch Hands and Comparisons also was found, especially in enlisted groundcrew.

9.1.3 Parameters for the 1997 General Health Assessment

9.1.3.1 Dependent Variables

The general health assessment was based on data from the 1997 questionnaire, physical examination, and laboratory data.

9.1.3.1.1 Questionnaire Data

During the health interview given to each participant, the following question was asked: "Compared to other people your age, would you say your health is excellent, good, fair, or poor?" This self-reported perception was analyzed as a measure of the general health status of each participant, although it was recognized that the perception was susceptible to varying degrees of conscious and subconscious bias (most participants were aware of their serum dioxin levels). This variable was dichotomized as "excellent or good" and "fair or poor" for statistical analyses. No participants were excluded for medical reasons from the analysis of this variable.

9.1.3.1.2 Physical Examination Data

Three variables derived from the 1997 Scripps Clinic physical examination were analyzed in the assessment of general health. For the first variable, the physician at the examination recorded the appearance of illness or distress (yes, no) of the study participant. For the second variable, the physician noted the appearance of the subject as younger than, older than, or the same as his stated age. This variable was dichotomized as "older than" and "same as or younger than" for statistical analyses. To the degree that the examining physicians were kept blind to the participant's group membership, these assessments were less subject to bias than the self-perception of health.

The third variable, body fat, was a measure of the relative body mass of an individual and was calculated from height (in meters) and weight (in kilograms) recorded at the physical examination. Non-ambulatory participants were weighed on a Scale-Tronix® 6006, which allowed a participant to be weighed in a wheelchair, if necessary. Body fat was calculated from a metric body mass index (84); the formula is

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

This variable was analyzed in both the discrete and continuous forms. For purposes of discrete analyses, body fat was dichotomized as "lean or normal" (≤25 percent) and "obese" (>25 percent). Lean participants (less than 10 percent body fat) were categorized with normal participants because few of the people in this study fit this definition (nine participants: six Comparisons and three Ranch Hands). This variable did not reflect changes in weight since time of duty in SEA. No participants were excluded for medical reasons from the analyses of these three variables.

9.1.3.1.3 Laboratory Examination Data

The erythrocyte sedimentation rate (mm/hr), measured at the laboratory examination, was analyzed. Although nonspecific, a high erythrocyte sedimentation rate generally indicates an ongoing disease process. This variable was analyzed in both the discrete and continuous forms. No participants were excluded for medical reasons from the analysis of this variable.

9.1.3.2 Covariates

The effects of the covariates age, race (Black, non-Black), military occupation (officer, enlisted flyer, enlisted groundcrew), current cigarette smoking, lifetime cigarette smoking history, current alcohol use, and lifetime alcohol history were used for analyses with all dependent variables.

Age, race, and military occupation were determined from military records. Lifetime alcohol history was based on information from the 1997 questionnaire and combined with similar information gathered at the 1987 and 1992 follow-up examinations. Each participant was asked about his drinking patterns throughout his lifetime. When a participant's drinking pattern changed, he was asked to describe how his alcohol consumption differed and the duration of time that the drinking pattern lasted. The participant's average daily alcohol consumption was determined for each of the reported drinking pattern periods throughout his lifetime, and an estimate of the corresponding total number of drink-years was derived. One drink-year was the equivalent of drinking 1.5 ounces of an 80-proof alcoholic beverage, one 12-ounce beer, or one 5-ounce glass of wine per day for 1 year. Current alcohol use was defined as the average number of drinks per day during the month prior to completing the questionnaire.

Current cigarette smoking and lifetime cigarette smoking history were based on questionnaire data. For lifetime cigarette smoking history, the respondent's average smoking was estimated over his lifetime based on his responses to the 1997 questionnaire, with 1 pack-year defined as 365 packs of cigarettes smoked during a single year.

Personality type (Type A, Type B) was used as a covariate in the analysis of self-perception of health and sedimentation rate only. Personality type was determined from the Jenkins Activity Survey administered during the 1997 follow-up examination and was derived from a discriminant-function equation based on questions that best discriminate men judged to be Type A from those judged to be Type B (85). Positive scores reflect the Type A direction; negative scores reflect the Type B direction. Personality type was dichotomized as Type A or Type B for all analyses of self-perception of health and erythrocyte sedimentation rate.

9.1.4 Statistical Methods

Table 9-1 summarizes the statistical analyses performed for the general health assessment. The first part of this table describes the dependent variables and identifies the covariates, exclusions, and the statistical methods. The second part of the table further describes the covariates. A covariate was used in its continuous form whenever possible for all adjusted analyses. If the covariate was inherently discrete (e.g., military occupation), or if a categorized form was needed to develop measures of association with the dependent variables, the covariate was categorized as shown in Table 9-1.

Cutpoints for erythrocyte sedimentation rate were age-dependent. Consequently, normal and abnormal levels for erythrocyte sedimentation rate were constructed according to a participant's laboratory value and age at the physical examination. The age-specific cutpoints also are listed in Table 9-1, and the reference ages for these cutpoints are given in parentheses following the cutpoints.

Table 9-2 provides a summary of the number of participants with missing dependent variable and covariate data.

Table 9-1. Statistical Analysis for the General Health Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Covariates[a]	Exclusions	Statistical Analysis and Methods
Self-perception of Health	Q-SR	D	Fair or Poor Excellent or Good	(1)	None	U:LR A:LR L:LR
Appearance of Illness Or Distress as Assessed by Physician	PE	D	Yes No	(2)	None	U:LR A:LR L:LR,CS
Relative Age Appearance as Assessed by Physician	PE	D	Older Same or Younger	(2)	None	U:LR A:LR L:LR
Body Fat (percent)	PE	D/C	Obese: >25% Lean or Normal: ≤25%	(2)	None	U:LR,GLM A:LR,GLM L:LR,GLM
Erythrocyte Sedimentation Rate (mm/hr)	LAB	D/C	Abnormal: >15 (Age 40–49) >20 (Age ≥50) Normal: ≤15 (Age 40–49) ≤20 (Age ≥50)	(1)	None	U:LR,GLM A:LR,GLM L:LR,GLM

[a] Covariates:

(1): age, race, military occupation, current cigarette smoking, lifetime cigarette smoking history, current alcohol use, lifetime alcohol history, personality type.

(2): age, race, military occupation, current cigarette smoking, lifetime cigarette smoking history, current alcohol use, lifetime alcohol history.

Table 9-1. Statistical Analysis for the General Health Assessment (Continued)

Covariates

Variable (Units)	Data Source	Data Form	Cutpoints
Age (years)	MIL	D/C	Born ≥ 1942
			Born < 1942
Race	MIL	D	Black
			Non-Black
Occupation	MIL	D	Officer
			Enlisted Flyer
			Enlisted Groundcrew
Current Cigarette Smoking (cigarettes/day)	Q-SR	D/C	0-Never
			0-Former
			>0–20
			>20
Lifetime Cigarette Smoking History (pack-years)	Q-SR	D/C	0
			>0–10
			>10
Current Alcohol Use (drinks/day)	Q-SR	D/C	0–1
			>1–4
			>4
Lifetime Alcohol History (drink-years)	Q-SR	D/C	0
			>0–40
			>40
Personality Type	PE	D	A Direction
			B Direction

Abbreviations

Data Source: LAB: 1997 laboratory results
MIL: Air Force military records
PE: 1997 physical examination
Q-SR: 1997 health questionnaire (self-reported)

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

Statistical Analysis: U: Unadjusted analysis
A: Adjusted analysis
L: Longitudinal analysis

Statistical Methods: CS: Chi-square contingency table analysis (continuity-adjusted)
GLM: General linear models analysis
LR: Logistic regression analysis
TT: Two-sample t-test

Table 9-2. Number of Participants with Missing Data for the General Health Assessment

Variable	Variable Use	Group		Dioxin (Ranch Hands Only)		Categorized Dioxin	
		Ranch Hand	Comparison	Initial	1987	Ranch Hand	Comparison
Self-perception of Health	DEP	1	0	0	1	1	0
Erythrocyte Sedimentation Rate	DEP	0	1	0	0	0	0
Personality Type	COV	3	0	1	3	3	0
Current Cigarette Smoking	COV	1	0	0	1	1	0
Lifetime Cigarette Smoking History	COV	2	1	1	2	2	1
Current Alcohol Use	COV	1	0	0	1	1	0
Lifetime Alcohol History	COV	6	2	3	6	6	1

Note: DEP = Dependent variable.
COV = Covariate.
870 Ranch Hands and 1,251 Comparisons.
482 Ranch Hands for initial dioxin; 863 Ranch Hands for 1987 dioxin.
863 Ranch Hands and 1,213 Comparisons for categorized dioxin.

9.1.4.1 Longitudinal Analysis

Longitudinal analyses on all of the variables described above (self-perception of health, appearance of illness or distress by the physician, relative age, body fat, and erythrocyte sedimentation rate) were conducted to evaluate the changes between the 1982 baseline examination and the 1997 follow-up examination.

The erythrocyte sedimentation rate abnormal cutpoints differ by examination date and age. For the 1982 baseline examination, the cutpoint was 12 mm/hr for all participants (that is, erythrocyte sedimentation rates greater than 12 mm/hr were considered abnormal). For the 1985, 1987, 1992, and 1997 follow-up examinations, the cutpoint was 15 mm/hr for participants younger than 50 and 20 mm/hr for participants at least 50 years old at the time of the examination. A participant was considered to be normal or abnormal based on his age and the cutpoint at the given examination for discrete analyses. Methods of compensation for the change in cutpoints over time for the continuous analyses include the use of age and the measurement in 1982 as covariates.

9.2 RESULTS

9.2.1 Dependent Variable-Covariate Associations

The results of covariate associations with each dependent variable are documented in Appendix F, Table F-1. These associations are pairwise between the dependent variable and the covariate and are not adjusted for any other covariates. These results are discussed below.

Tests of associations for self-perception of health revealed significant associations with race, occupation, current cigarette smoking, and lifetime cigarette smoking history ($p=0.010$, $p=0.001$, $p=0.001$, and $p=0.001$, respectively). The percentage of Blacks who perceived their health to be fair or poor was 19.5 percent, compared to 11.5 percent for non-Blacks. Enlisted groundcrew reported their health as fair or poor most often (14.9%) among the occupation strata, followed by enlisted flyers (14.5%) and officers (7.7%). Of the participants who currently smoke and smoke 20 cigarettes or less per day, 19.9 percent reported their health as fair or poor. In contrast, 7.7 percent of participants who have never smoked reported their health as fair or poor. Participants who were the heaviest cigarette smokers across their lifetime (>10 pack-years) perceived their health as fair or poor more often than those who smoked less. The percentage for this category was 15.2 percent, whereas the percentage for participants in the moderate lifetime cigarette smoking category (>0-10 pack-years) was 10.8 percent. Of the participants who have never smoked, 7.7 percent rated their health as fair or poor.

Tests of associations for appearance of illness or distress revealed that race, current cigarette smoking, and lifetime cigarette smoking history were significant covariates ($p=0.003$, $p=0.030$, and $p=0.027$, respectively). The percentages of Blacks and non-Blacks that appeared ill or distressed were 4.7 and 1.2, respectively. Participants currently smoking more than 0, but up to 20 cigarettes per day, appeared ill or distressed most often (2.9%), followed by those in the more than 20 cigarettes per day category (2.2%), the former smoker category (1.3%), and never smoked category (0.5%). Percentages for lifetime cigarette smoking history were 2.1, 1.1, and 0.5 for the greater than 10 pack-years, the greater than 0 but no more than 10 pack-years, and the 0 pack-years categories, respectively.

For relative age appearance, significant covariate associations were found with occupation, current cigarette smoking, and lifetime cigarette smoking history ($p=0.001$ for each covariate). Enlisted flyers appearing older were 12.7 percent, while 11.0 and 5.6 percent of enlisted groundcrew and officers, respectively, appeared older. The percentage of current smokers appearing older in the greater than 20 cigarettes per day category was 25.6 percent, compared to only 3.9 percent for participants who had never smoked. The greater than 10 pack-years category of lifetime cigarette smoking history exhibited the highest percentage of participants that appeared older (13.2%). Nonsmokers exhibited the lowest percentage (3.9%).

The association tests for body fat in its continuous form revealed that current cigarette smoking, current alcohol use, and lifetime alcohol history were significant covariates ($p<0.001$, $p<0.001$, and $p=0.022$, respectively). For each analysis, each covariate was negatively associated with body fat ($r=-0.187$, $r=-0.094$, $r=-0.050$, respectively).

Significant results from the association tests for body fat in its discrete form were found among the following covariates: occupation, current cigarette smoking, lifetime cigarette smoking history, and current alcohol use ($p=0.001$, $p=0.001$, $p=0.026$, and $p=0.003$, respectively). For the occupation analysis, the percentages of participants classified as obese were 33.1 percent for enlisted groundcrew, 28.1 percent for enlisted flyers, and 25.3 percent for officers. Participants who were former smokers were classified as obese the most often (33.6%). Current smokers who smoke more than 20 cigarettes per day

exhibited the lowest percentage of obesity (19.0%). The analysis of lifetime cigarette smoking history revealed the highest proportion of obesity among participants in the greater than 0 but no more than 10 pack-years category (33.7%). Following were 28.1 percent for those in the greater than 10 pack-years category and 27.1 percent for nonsmokers. The current alcohol use analysis displayed the highest percentage of obesity (30.9%) for those participants who currently drink no more than 1 drink per day.

Analysis of erythrocyte sedimentation rate in its continuous form revealed significant associations with age, occupation, lifetime cigarette smoking history, and lifetime alcohol history ($p<0.001$, $p<0.001$, $p<0.001$, and $p=0.019$, respectively). Correlations with erythrocyte sedimentation rate were positive for age ($r=0.179$), lifetime cigarette smoking history ($r=0.155$), and lifetime alcohol history ($r=0.051$). Within the occupational strata, the mean erythrocyte sedimentation rate was 4.39 mm/hour for officers, 5.61 mm/hour for enlisted flyers, and 4.85 mm/hour for enlisted groundcrew.

Tests of association for erythrocyte sedimentation rate in its discrete form revealed that age, current cigarette smoking, and lifetime cigarette smoking history were significant covariates ($p=0.033$, $p=0.003$, and $p=0.002$, respectively). Older participants had a greater occurrence of high erythrocyte sedimentation rates (8.7%) than did younger participants (6.1%). Both current cigarette smoking and lifetime cigarette smoking history exhibited an increase in the percentage of abnormal erythrocyte sedimentation rates as the amount of cigarette smoking increased.

9.2.2 Exposure Analysis

The following section presents results of the statistical analyses of the dependent variables shown in Table 9-1. Dependent variables are grouped into three sections: (1) the Questionnaire Variable, derived from the questionnaire administered in the 1997 follow-up examination, (2) the Physical Examination Variables, obtained during the 1997 physical examination, and (3) the Laboratory Variable, derived from the laboratory portion of the 1997 follow-up examination.

Four models were examined for each dependent variable given in Table 9-1. The analyses of these models are presented below. Further details on dioxin and the modeling strategy are found in Chapters 2 and 7, respectively. These analyses were performed both unadjusted and adjusted for relevant covariates. Model 1 examined the relation between the dependent variable and group (i.e., Ranch Hand or Comparison). In this model, exposure was defined as "yes" for Ranch Hands and "no" for Comparisons without regard to the magnitude of the exposure. As an attempt to quantify exposure, three contrasts of Ranch Hands and Comparisons were performed along with the overall Ranch Hand versus Comparison contrast. These three contrasts compared Ranch Hands and Comparisons within each occupational category (i.e., officers, enlisted flyers, and enlisted groundcrew). As described in previous reports and Table 2-8, the average levels of exposure to dioxin were highest for enlisted groundcrew, followed by enlisted flyers, and then officers.

Model 2 explored the relation between the dependent variable and an extrapolated initial dioxin measure for Ranch Hands who had a 1987 dioxin measurement greater than 10 parts per trillion (ppt). If a participant did not have a 1987 dioxin level, a 1992 level was used to estimate the initial dioxin level. If a participant did not have a 1987 or a 1992 dioxin level, a 1997 level was used to estimate the initial dioxin level. A statistical adjustment for the percentage of body fat at the time of the participant's blood measurement of dioxin is included in this model to account for body-fat-related differences in elimination rate (58). This adjustment was accomplished for the unadjusted and adjusted analyses of all dependent variables except body fat in 1997. The use of body fat at the time of the participant's blood measurement of dioxin as a covariate masks the relation between body fat in 1997 and the dioxin measure.

Model 3 divided the Ranch Hands examined in Model 2 into two categories based on their initial dioxin measures. These two categories are referred to as "low Ranch Hand" and "high Ranch Hand." Two additional categories, Ranch Hands with 1987 serum dioxin levels at or below 10 ppt and Comparisons with 1987 serum dioxin levels at or below 10 ppt, were formed and included in the model. Ranch Hands with serum dioxin levels at or below 10 ppt are referred to as the "background Ranch Hand" category. Dioxin levels in 1992 were used if the 1987 levels were not available, and dioxin levels in 1997 were used if the 1987 and 1992 levels were not available. These four categories—Comparisons, background Ranch Hands, low Ranch Hands, and high Ranch Hands—were used in Model 3 analyses. The relation between the dependent variable in each of the three Ranch Hand categories and the dependent variable in the Comparison category was examined. A fourth contrast, exploring the relation of the dependent variable in the combined low and high Ranch Hand categories relative to Comparisons, also was conducted. This combination is referred to in the tables as the "low plus high Ranch Hand" category. As in Model 2, a statistical adjustment for the percentage of body fat at the time of the participant's blood measurement of dioxin was included in this model for the unadjusted and adjusted analyses of all dependent variables except body fat in 1997.

Model 4 examined the relation between the dependent variable and 1987 lipid-adjusted dioxin levels in all Ranch Hands with a dioxin measurement. If a participant did not have a 1987 dioxin measurement, the 1992 measurement was used to determine the dioxin level. If a participant did not have a 1987 or the 1992 dioxin measurement, a 1997 measurement was used to determine the dioxin level.

9.2.2.1 Questionnaire Variable

9.2.2.1.1 Self-perception of Health

The unadjusted and adjusted Model 1 analyses of self-perception of health revealed a significant difference between Ranch Hands and Comparisons across occupations (Table 9-3(a): Est. RR=1.44, p=0.007, and (b): Adj. RR=1.43, p=0.010, respectively). Unadjusted and adjusted differences within the enlisted groundcrew stratum also were significant (Table 9-3(a): Est. RR=1.50, p=0.028, and (b): Adj. RR=1.48, p=0.035, respectively). Ranch Hands perceived their health to be fair or poor more often than did Comparisons (i.e., 14.3% of Ranch Hands versus 10.4% of Comparisons overall).

Model 2 revealed a nonsignificant association between initial dioxin and self-perception of health for both the unadjusted and adjusted analyses (Table 9-3(c) and (d): p=0.859 and p=0.832, respectively).

The Model 3 unadjusted and adjusted analyses of self-perception of health revealed significant differences between Ranch Hands and Comparisons for the low Ranch Hand category (Table 9-3(e): Est. RR=1.77, p=0.005, and (f): Adj. RR=1.62, p=0.020, respectively) and the high Ranch Hand category (Table 9-3(e): Est. RR=2.14, p<0.001, and (f): Adj. RR=1.86, p=0.002, respectively). The low and high Ranch Hand categories combined were also significant in the unadjusted and adjusted analyses (Table 9-3(e): Est. RR=1.95, p<0.001, and (f): Adj. RR=1.74, p=0.001, respectively). Ranch Hands in the low and high dioxin categories perceived their health to be fair or poor more often than did Comparisons (i.e., 16.3% of Ranch Hands in the low dioxin category and 19.8% of Ranch Hands in the high dioxin category versus 9.8% of Comparisons).

The Model 4 unadjusted analysis revealed a significant relation between 1987 dioxin levels and self-perception of health (Table 9-3(g): Est. RR=1.22, p=0.002). The relation was marginally significant after adjustment for covariates (Table 9-3(h): p=0.079).

Table 9-3. Analysis of Self-perception of Health

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Fair or Poor	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***869***	***124 (14.3)***	***1.44 (1.10,1.87)***	***0.007***
	Comparison	***1,251***	***130 (10.4)***		
Officer	Ranch Hand	341	30 (8.8)	1.31 (0.78,2.18)	0.308
	Comparison	494	34 (6.9)		
Enlisted Flyer	Ranch Hand	151	26 (17.2)	1.48 (0.81,2.72)	0.203
	Comparison	187	23 (12.3)		
Enlisted Groundcrew	Ranch Hand	377	68 (18.0)	1.50 (1.05,2.15)	0.028
	Comparison	570	73 (12.8)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.43 (1.09,1.87)***	***0.010***
Officer	1.26 (0.75,2.12)	0.383
Enlisted Flyer	1.52 (0.82,2.82)	0.183
Enlisted Groundcrew	1.48 (1.03,2.14)	0.035

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Fair or Poor	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	25 (15.6)	1.02 (0.85,1.21)	0.859
Medium	162	35 (21.6)		
High	160	27 (16.9)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
477	0.98 (0.79,1.21)	0.832

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

Table 9-3. Analysis of Self-perception of Health (Continued)

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

Dioxin Category	n	Number (%) Fair or Poor	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,213	119 (9.8)		
Background RH	380	34 (9.0)	0.97 (0.65,1.45)	0.880
Low RH	239	39 (16.3)	1.77 (1.19,2.62)	0.005
High RH	243	48 (19.8)	2.14 (1.48,3.10)	<0.001
Low plus High RH	482	87 (18.1)	1.95 (1.44,2.63)	<0.001

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

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

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,211		
Background RH	376	1.13 (0.75,1.72)	0.555
Low RH	237	1.62 (1.08,2.44)	0.020
High RH	240	1.86 (1.26,2.74)	0.002
Low plus High RH	477	1.74 (1.27,2.37)	0.001

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

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Fair or Poor	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	287	23 (8.0)	1.22 (1.08,1.39)	0.002
Medium	287	41 (14.3)		
High	288	57 (19.8)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 9-3. Analysis of Self-perception of Health (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
853	1.14 (0.98,1.32)	0.079

[a] Relative risk for a twofold increase in 1987 dioxin.

9.2.2.2 Physical Examination Variables

9.2.2.2.1 Appearance of Illness or Distress as Assessed by Physician

The unadjusted and adjusted analysis of appearance of illness or distress as assessed by a physician revealed nonsignificant differences between Ranch Hands and Comparisons (p>0.24 for each contrast) in the Model 1 analyses (Table 9-4(a) and (b)). Similarly, the analyses for Model 2 (Table 9-4(c) and (d)) and Model 4 (Table 9-4(g) and (h)) each revealed a nonsignificant relation between appearance of illness or distress as assessed by a physician and dioxin (both initial and 1987 levels; p>0.11 for all analyses).

Differences between Ranch Hands with low dioxin levels and Comparisons were significant in the Model 3 unadjusted analysis of appearance of illness or distress as assessed by a physician (Table 9-4(e): Est. RR=2.78, p=0.031). A significant difference also was found when the combination of low and high Ranch Hands was contrasted with Comparisons in the unadjusted analysis (Table 9-4(e): Est. RR=2.30, p=0.041). After adjustment for covariate effects, these contrasts were marginally significant for Ranch Hands with low dioxin levels (Table 9-4(f): p=0.092) and nonsignificant for the combination of low and high Ranch Hands (p=0.118). All other contrasts examined in the unadjusted and adjusted analyses of appearance of illness or distress as assessed by physician were nonsignificant (p>0.22 for each remaining contrast).

Table 9-4. Analysis of Appearance of Illness or Distress

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***870***	***15 (1.7)***	***1.55 (0.74,3.23)***	***0.242***
	Comparison	***1,251***	***14 (1.1)***		
Officer	Ranch Hand	341	3 (0.9)	1.09 (0.24,4.89)	0.913
	Comparison	494	4 (0.8)		
Enlisted Flyer	Ranch Hand	151	3 (2.0)	1.87 (0.31,11.37)	0.494
	Comparison	187	2 (1.1)		
Enlisted Groundcrew	Ranch Hand	378	9 (2.4)	1.71 (0.66,4.48)	0.272
	Comparison	570	8 (1.4)		

Table 9-4. Analysis of Appearance of Illness or Distress (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.44 (0.67,3.06)***	***0.350***
Officer	1.13 (0.25,5.16)	0.878
Enlisted Flyer	2.12 (0.33,13.61)	0.426
Enlisted Groundcrew	1.42 (0.52,3.89)	0.496

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	7 (4.4)	0.71 (0.42,1.20)	0.178
Medium	162	3 (1.9)		
High	160	2 (1.3)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
478	0.65 (0.36,1.15)	0.117

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

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

Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,213	13 (1.1)		
Background RH	381	3 (0.8)	0.74 (0.21,2.63)	0.645
Low RH	239	7 (2.9)	2.78 (1.10,7.04)	0.031
High RH	243	5 (2.1)	1.92 (0.67,5.45)	0.223
Low plus High RH	482	12 (2.5)	2.30 (1.03,5.13)	0.041

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 9-4. Analysis of Appearance of Illness or Distress (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,211		
Background RH	378	0.76 (0.21,2.80)	0.684
Low RH	237	2.31 (0.87,6.11)	0.092
High RH	241	1.67 (0.54,5.19)	0.372
Low plus High RH	478	1.96 (0.84,4.58)	0.118

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

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	288	3 (1.0)	1.09 (0.78,1.52)	0.631
Medium	287	7 (2.4)		
High	288	5 (1.7)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED			
	Analysis Results for Log_2 (1987 Dioxin + 1)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value	
856	1.05 (0.72,1.52)	0.800	

[a] Relative risk for a twofold increase in 1987 dioxin.

9.2.2.2.2 *Relative Age Appearance as Assessed by Physician*

All unadjusted and adjusted analyses of relative age appearance as assessed by a physician were nonsignificant (Table 9-5: p>0.10 for each analysis) for Models 1 through 4.

Table 9-5. Analysis of Relative Age Appearance

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Older	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***870***	***90 (10.3)***	***1.27 (0.95,1.71)***	***0.112***
	Comparison	***1,251***	***104 (8.3)***		
Officer	Ranch Hand	341	22 (6.5)	1.29 (0.72,2.33)	0.392
	Comparison	494	25 (5.1)		
Enlisted Flyer	Ranch Hand	151	22 (14.6)	1.35 (0.71,2.56)	0.361
	Comparison	187	21 (11.2)		
Enlisted Groundcrew	Ranch Hand	378	46 (12.2)	1.22 (0.81,1.84)	0.337
	Comparison	570	58 (10.2)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.21 (0.88,1.65)***	***0.237***
Officer	1.29 (0.70,2.36)	0.410
Enlisted Flyer	1.28 (0.65,2.50)	0.476
Enlisted Groundcrew	1.14 (0.74,1.75)	0.550

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Older	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	17 (10.6)	1.05 (0.84,1.30)	0.694
Medium	162	16 (9.9)		
High	160	18 (11.3)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
478	1.01 (0.77,1.31)	0.962

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

Table 9-5. Analysis of Relative Age Appearance (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Older	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,213	102 (8.4)		
Background RH	381	39 (10.2)	1.25 (0.84,1.84)	0.271
Low RH	239	24 (10.0)	1.22 (0.76,1.94)	0.415
High RH	243	27 (11.1)	1.36 (0.87,2.13)	0.183
Low plus High RH	482	51 (10.6)	1.29 (0.90,1.83)	0.166

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,211		
Background RH	378	1.42 (0.93,2.16)	0.102
Low RH	237	1.11 (0.67,1.82)	0.691
High RH	241	1.05 (0.65,1.69)	0.857
Low plus High RH	478	1.08 (0.74,1.57)	0.706

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

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Older	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	288	33 (11.5)	0.97 (0.83,1.12)	0.654
Medium	287	25 (8.7)		
High	288	32 (11.1)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 9-5. Analysis of Relative Age Appearance (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
856	0.89 (0.75,1.05)	0.153

[a] Relative risk for a twofold increase in 1987 dioxin.

9.2.2.2.3 Body Fat (Continuous)

The Model 1 analyses of body fat in its continuous form revealed nonsignificant differences between Ranch Hands and Comparisons when examined across all occupations and within each occupation (Table 9-6(a,b): $p>0.31$ for each contrast).

The association between initial dioxin and body fat examined in the unadjusted Model 2 analyses also revealed marginally significant results (Table 9-6(c): $p=0.081$). After adjustment for covariate effects, this association became significant (Table 9-6(d): $p=0.020$). Body fat increased as initial dioxin levels increased.

Differences in mean body fat between Ranch Hands and Comparisons exhibited a dose-response relation in Model 3 analyses. As dioxin exposure increased, body fat also increased. The unadjusted and adjusted results are shown in Tables 9-6(e) and 9-6(f), respectively. Comparisons had a significantly higher body fat mean than did Background Ranch Hands ($p<0.001$ unadjusted and adjusted). The adjusted body fat mean of Ranch Hands in the low dioxin category was marginally significantly greater than Comparisons (Table 9-6(f): $p=0.052$). Ranch Hands in the high dioxin category had a significantly greater body fat mean than did Comparisons ($p=0.001$, unadjusted, and $p=0.002$, adjusted).

The Model 4 unadjusted and adjusted analyses each revealed a significant association between 1987 dioxin levels and body fat (Table 9-6(g): slope=0.046, $p<0.001$ and (h): adjusted slope=0.054, $p<0.001$). Body fat increased as dioxin levels increased. Adjusted body fat means for the low, medium, and high 1987 dioxin categories were 20.01 percent, 22.30 percent, and 23.60 percent, respectively.

Table 9-6. Analysis of Body Fat (Percent) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***870***	***22.09***	***–0.19 --***	***0.436***
	Comparison	***1,251***	***22.28***		
Officer	Ranch Hand	341	22.04	0.17 --	0.656
	Comparison	494	21.87		
Enlisted Flyer	Ranch Hand	151	21.69	–0.51 --	0.390
	Comparison	187	22.20		
Enlisted Groundcrew	Ranch Hand	378	22.30	–0.37 --	0.318
	Comparison	570	22.67		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***863***	***22.13***	***–0.17 --***	***0.481***
	Comparison	***1,248***	***22.29***		
Officer	Ranch Hand	340	21.96	0.16 --	0.674
	Comparison	493	21.81		
Enlisted Flyer	Ranch Hand	149	21.84	–0.59 --	0.319
	Comparison	186	22.43		
Enlisted Groundcrew	Ranch Hand	374	22.45	–0.31 --	0.394
	Comparison	569	22.76		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Table 9-6. Analysis of Body Fat (Percent) (Continuous) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Mean[a]	R^2	Slope (Std. Error)[b]	p-Value
Low	160	22.75	0.006	0.015 (0.009)	0.081
Medium	162	23.46			
High	160	23.71			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of body fat versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	159	22.37	0.105	0.022 (0.010)	0.020
Medium	161	23.68			
High	158	23.88			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of body fat versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

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

Dioxin Category	n	Mean[a]	Difference of Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	1,213	22.26		
Background RH	381	20.64	–1.62 --	<0.001
Low RH	239	23.04	0.78 --	0.045
High RH	243	23.57	1.31 --	0.001
Low plus High RH	482	23.30	1.04 --	0.001

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 9-6. Analysis of Body Fat (Percent) (Continuous) (Continued)

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

Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	1,211	22.25		
Background RH	378	20.73	–1.52 --	<0.001
Low RH	237	23.00	0.75 --	0.052
High RH	241	23.51	1.26 --	0.002
Low plus High RH	478	23.26	1.01 --	0.001

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	n	Mean[a]	R^2	Slope (Std. Error)[b]	p-Value
Low	288	20.35	0.072	0.046 (0.006)	<0.001
Medium	287	22.59			
High	288	23.45			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of body fat versus log_2 (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9-19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	287	20.01	0.155	0.054 (0.006)	<0.001
Medium	284	22.30			
High	285	23.60			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of body fat versus log_2 (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

9.2.2.2.4 Body Fat (Discrete)

All contrasts from the Models 1 and 2 unadjusted and adjusted analyses of body fat in its discrete form revealed nonsignificant differences between Ranch Hands and Comparisons (Table 9-7(a-d): $p>0.17$ for all contrasts).

Significantly fewer Ranch Hands in the Background category than Comparisons were obese (Table 9-7(e): Est. RR: 0.56, $p<0.001$ unadjusted, and Table 9-7(f): Adj. RR: 0.60, $p=0.001$ adjusted). Adjusted contrasts of Ranch Hands in the low dioxin category, and in the low and high dioxin categories combined, with Comparisons showed a marginally significantly higher percentage of obese Ranch Hands (Table 9-7(f): $p=0.073$ and $p=0.097$, respectively).

The Model 4 analyses revealed significant positive associations of body fat with 1987 dioxin levels, (Table 9-7(g): Est. RR=1.26, $p<0.001$, and (h): Adj. RR=1.29, $p<0.001$). Body fat increased as 1987 dioxin increased.

Table 9-7. Analysis of Body Fat (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Obese	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***870***	***244 (28.1)***	***0.91 (0.75,1.10)***	***0.316***
	Comparison	***1,251***	***376 (30.1)***		
Officer	Ranch Hand	341	88 (25.8)	1.05 (0.76,1.44)	0.767
	Comparison	494	123 (24.9)		
Enlisted Flyer	Ranch Hand	151	37 (24.5)	0.72 (0.45,1.17)	0.186
	Comparison	187	58 (31.0)		
Enlisted Groundcrew	Ranch Hand	378	119 (31.5)	0.88 (0.67,1.17)	0.382
	Comparison	570	195 (34.2)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.92 (0.75,1.11)***	***0.369***
Officer	1.05 (0.77,1.45)	0.754
Enlisted Flyer	0.71 (0.43,1.16)	0.173
Enlisted Groundcrew	0.89 (0.67,1.18)	0.431

Table 9-7. Analysis of Body Fat (Discrete) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Obese	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	160	55 (34.4)	1.00 (0.87,1.15)	0.989
Medium	162	59 (36.4)		
High	160	54 (33.8)		

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

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
478	1.00 (0.85,1.19)	0.986

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

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

Dioxin Category	n	Number (%) Obese	Est. Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,213	361 (29.8)		
Background RH	381	73 (19.2)	0.56 (0.42,0.74)	<0.001
Low RH	239	85 (35.6)	1.30 (0.97,1.74)	0.076
High RH	243	83 (34.2)	1.22 (0.91,1.64)	0.175
Low plus High RH	482	168 (34.9)	1.26 (1.01,1.58)	0.042

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

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 9-7. Analysis of Body Fat (Discrete) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,211		
Background RH	378	0.60 (0.45,0.80)	0.001
Low RH	237	1.31 (0.97,1.77)	0.073
High RH	241	1.12 (0.83,1.53)	0.451
Low plus High RH	478	1.21 (0.97,1.53)	0.097

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

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Obese	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	288	51 (17.7)	1.26 (1.14,1.40)	<0.001
Medium	287	90 (31.4)		
High	288	100 (34.7)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
856	1.29 (1.14,1.46)	<0.001

[a] Relative risk for a twofold increase in 1987 dioxin.

9.2.2.3 Laboratory Variable

9.2.2.3.1 Erythrocyte Sedimentation Rate (Continuous)

All analysis results from Models 1, 2, and 3 of erythrocyte sedimentation rate were nonsignificant (Table 9-8(a-f): p>0.17 for each analysis). The Model 4 analysis revealed a significant association between erythrocyte sedimentation rate and 1987 dioxin levels for both the unadjusted and adjusted analyses (Table 9-8(g): p=0.004, and (h): p=0.037, respectively). Erythrocyte sedimentation rate increased as

dioxin increased in these analyses. Adjusted erythrocyte sedimentation rate means for the low, medium, and high 1987 dioxin categories were 4.34 mm/hr, 4.62 mm/hr, and 5.29 mm/hr, respectively.

Table 9-8. Analysis of Erythrocyte Sedimentation Rate (mm/hr) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***870***	***4.82***	***0.09 --***	***0.680***
	Comparison	***1,251***	***4.74***		
Officer	Ranch Hand	341	4.36	–0.05 --	0.873
	Comparison	494	4.41		
Enlisted Flyer	Ranch Hand	151	5.35	–0.47 --	0.429
	Comparison	187	5.83		
Enlisted Groundcrew	Ranch Hand	378	5.06	0.35 --	0.263
	Comparison	570	4.71		

[a] Transformed from natural logarithm scale of erythrocyte sedimentation rate + 0.1.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale of erythrocyte sedimentation rate + 0.1.
[c] P-value is based on difference of means on natural logarithm scale of erythrocyte sedimentation rate + 0.1.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	Ranch Hand	860	5.12	0.04 --	0.850
	Comparison	1,248	5.08		
Officer	Ranch Hand	339	4.30	–0.08 --	0.789
	Comparison	493	4.38		
Enlisted Flyer	Ranch Hand	148	5.13	–0.60 --	0.286
	Comparison	186	5.74		
Enlisted Groundcrew	Ranch Hand	373	5.81	0.42 --	0.236
	Comparison	569	5.39		

[a] Transformed from natural logarithm scale of erythrocyte sedimentation rate + 0.1.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale of erythrocyte sedimentation rate + 0.1.
[c] P-value is based on difference of means on natural logarithm scale of erythrocyte sedimentation rate + 0.1.

Table 9-8. Analysis of Erythrocyte Sedimentation Rate (mm/hr) (Continuous) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	160	4.70	4.74	0.009	0.029 (0.034)	0.387
Medium	162	5.99	6.00			
High	160	5.04	4.99			

[a] Transformed from natural logarithm scale of erythrocyte sedimentation rate + 0.1.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of erythrocyte sedimentation rate + 0.1 versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	159	4.45	0.086	0.041 (0.039)	0.289
Medium	160	5.66			
High	158	4.83			

[a] Transformed from natural logarithm scale of erythrocyte sedimentation rate + 0.1.
[b] Slope and standard error based on natural logarithm of erythrocyte sedimentation rate + 0.1 versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

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

Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparison (95% C.I.)[c]	p-Value[d]
Comparison	1,213	4.75	4.74		
Background RH	381	4.31	4.48	–0.26 --	0.323
Low RH	239	5.12	5.06	0.32 --	0.350
High RH	243	5.32	5.12	0.38 --	0.259
Low plus High RH	482	5.22	5.09	0.35 --	0.176

[a] Transformed from natural logarithm scale of erythrocyte sedimentation rate + 0.1.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale of erythrocyte sedimentation rate + 0.1.
[d] P-value is based on difference of means on natural logarithm scale of erythrocyte sedimentation rate + 0.1.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 9-8. Analysis of Erythrocyte Sedimentation Rate (mm/hr) (Continuous) (Continued)

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

Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	1,211	5.12		
Background RH	376	4.92	–0.20 --	0.484
Low RH	237	5.12	0.00 --	0.992
High RH	240	5.48	0.36 --	0.322
Low plus High RH	477	5.29	0.17 --	0.510

[a] Transformed from natural logarithm scale of erythrocyte sedimentation rate + 0.1.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale of erythrocyte sedimentation rate + 0.1.
[c] P-value is based on difference of means on natural logarithm scale of erythrocyte sedimentation rate + 0.1.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)[b]		
1987 Dioxin	n	Mean[a]	R^2	Slope (Std. Error)[b]	p-Value
Low	288	4.20	0.009	0.063 (0.022)	0.004
Medium	287	4.81			
High	288	5.46			

[a] Transformed from natural logarithm scale of erythrocyte sedimentation rate + 0.1.
[b] Slope and standard error based on natural logarithm of erythrocyte sedimentation rate + 0.1 versus log_2 (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	285	4.34	0.088	0.052 (0.025)	0.037
Medium	284	4.62			
High	284	5.29			

[a] Transformed from natural logarithm scale of erythrocyte sedimentation rate + 0.1.
[b] Slope and standard error based on natural logarithm of erythrocyte sedimentation rate + 0.1 versus log_2 (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

9.2.2.3.2 Erythrocyte Sedimentation Rate (Discrete)

Similar to the continuous analyses, all results from the analyses of erythrocyte sedimentation rate in its discrete form in Models 1, 2, and 3 were nonsignificant (Table 9-9(a–f): p>0.13). The Model 4 unadjusted analysis revealed a significant association between erythrocyte sedimentation rate and 1987 dioxin levels (Table 9-9(g): Est. RR=1.18, p=0.040). After adjustment for covariates, this association was nonsignificant (Table 9-9(h): p=0.169).

Table 9-9. Analysis of Erythrocyte Sedimentation Rate (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***870***	***72 (8.3)***	***1.19 (0.86,1.65)***	***0.289***
	Comparison	***1,251***	***88 (7.0)***		
Officer	Ranch Hand	341	20 (5.9)	0.84 (0.48,1.49)	0.557
	Comparison	494	34 (6.9)		
Enlisted Flyer	Ranch Hand	151	17 (11.3)	1.57 (0.75,3.29)	0.235
	Comparison	187	14 (7.5)		
Enlisted Groundcrew	Ranch Hand	378	35 (9.3)	1.35 (0.84,2.17)	0.212
	Comparison	570	40 (7.0)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.17 (0.84,1.63)***	***0.356***
Officer	0.86 (0.48,1.53)	0.602
Enlisted Flyer	1.59 (0.75,3.38)	0.231
Enlisted Groundcrew	1.29 (0.79,2.10)	0.305

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	11 (6.9)	1.17 (0.93,1.46)	0.179
Medium	162	19 (11.7)		
High	160	15 (9.4)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 9-9. Analysis of Erythrocyte Sedimentation Rate (Discrete) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
477	1.23 (0.94,1.62)	0.138

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

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

Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,213	85 (7.0)		
Background RH	381	25 (6.6)	1.03 (0.65,1.64)	0.908
Low RH	239	21 (8.8)	1.25 (0.75,2.06)	0.392
High RH	243	24 (9.9)	1.34 (0.83,2.16)	0.236
Low plus High RH	482	45 (9.3)	1.29 (0.88,1.89)	0.190

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

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

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,211		
Background RH	376	1.07 (0.66,1.73)	0.777
Low RH	237	1.04 (0.61,1.75)	0.897
High RH	240	1.36 (0.82,2.26)	0.237
Low plus High RH	477	1.19 (0.80,1.77)	0.398

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

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 9-9. Analysis of Erythrocyte Sedimentation Rate (Discrete) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	288	19 (6.6)	1.18 (1.01,1.39)	0.040
Medium	287	23 (8.0)		
High	288	28 (9.7)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
Analysis Results for Log_2 (1987 Dioxin + 1)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
853	1.14 (0.94,1.38)	0.169

[a] Relative risk for a twofold increase in 1987 dioxin.

9.2.3 Longitudinal Analysis

Longitudinal analyses were conducted on five variables—self-perception of health, appearance of illness or distress, relative age, body fat, and erythrocyte sedimentation rate—to examine whether changes across time differed with respect to group membership (Model 1), initial dioxin (Model 2), and categorized dioxin (Model 3). Model 4 was not examined in longitudinal analyses because 1987 dioxin, the measure of exposure in these models, changes over time and is not available for all participants for 1982 or 1997.

Discrete analyses were performed for all variables, and continuous analyses were additionally performed for body fat and erythrocyte sedimentation rate. The longitudinal analyses for all of these variables investigated the difference between the 1982 examination and the 1997 examination. These analyses were used to investigate the temporal effects of dioxin during the 15-year period between 1982 and 1997.

The cutpoints for abnormal erythrocyte sedimentation rate differed by examination date and age. For the 1982 baseline examination, the cutpoint was 12 mm/hr for all participants. For the 1985, 1987, and 1992 follow-up examinations, the cutpoint was 15 mm/hr for participants younger than 50 and 20 mm/hr for participants at least 50 years old at the time of the examination.

Participants who were abnormal in 1982 were not included in the longitudinal analysis of discrete dependent variables. The purpose of the longitudinal analysis was to examine the effects of dioxin exposure across time. Participants who were abnormal in 1982 were not considered to be at risk for developing the condition, because the condition already existed at the time of the first collection of data for the AFHS (1982). Only participants who were normal at the 1982 examination were considered to be at risk for developing the condition; therefore, the rate of abnormalities under this restriction approximates an incidence rate between 1982 and 1997. That is, an incidence rate is a measure of the

rate at which people without a condition develop the condition during a specified period of time (86). Summary statistics are provided for reference purposes for the 1985, 1987, and 1992 examinations.

The longitudinal analyses for the discrete variables examined relative risks at the 1997 examination for participants who were classified as normal at the 1982 examination. The adjusted relative risks estimated from each of the three models were used to investigate the change in the dependent variable over time. All three models were adjusted for age; Models 2 and 3 also were adjusted for the percentage of body fat at the time of the blood measurement of dioxin. This was accomplished for all dependent variables except body fat in 1997. As described previously, the use of body fat at the time of the participant's blood measurement of dioxin as a covariate masks the relation between body fat in 1997 and the dioxin measure.

The longitudinal analysis for the two continuous variables examined the paired difference between the measurements from 1982 and 1997. These paired differences measured the change in body fat or erythrocyte sedimentation rate over time. Each of the three models used in the longitudinal analysis was adjusted for age and the dependent variable as measured in 1982 (see Chapter 7, Statistical Methods). The analyses of Models 2 and 3 for erythrocyte sedimentation rate also were adjusted for percent body fat at the time of the blood measurement of dioxin. A logarithmic transformation was applied to both of these variables for analytic purposes.

9.2.3.1 Questionnaire Variable

9.2.3.1.1 Self-perception of Health

Longitudinal analyses were conducted for the examination of participant's self-perception of health in 1997. Only participants who reported their health as excellent or good in 1982 were included in the analysis. Results from analyses of all three models are found in Table 9-10 and indicate no significant associations between self-perception of health and any of the three measures of dioxin exposure (group status, initial dioxin, or categorized dioxin: $p>0.11$ for each contrast).

Table 9-10. Longitudinal Analysis of Self-perception of Health

(a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Number (%) Fair or Poor/(n) Examination				
		1982	1985	1987	1992	1997
All	***Ranch Hand***	***152 (18.7)***	***62 (7.8)***	***43 (5.5)***	***67 (8.5)***	***117 (14.4)***
		(813)	***(795)***	***(788)***	***(792)***	***(813)***
	Comparison	***129 (13.2)***	***53 (5.5)***	***42 (4.4)***	***59 (6.2)***	***103 (10.6)***
		(974)	***(956)***	***(949)***	***(952)***	***(974)***
Officer	Ranch Hand	33 (10.7)	11 (3.6)	12 (4.0)	14 (4.6)	28 (9.1)
		(309)	(305)	(302)	(305)	(309)
	Comparison	35 (9.2)	13 (3.5)	7 (1.9)	16 (4.3)	26 (6.9)
		(379)	(373)	(367)	(374)	(379)
Enlisted Flyer	Ranch Hand	31 (21.1)	6 (4.2)	6 (4.2)	13 (9.0)	24 (16.3)
		(147)	(144)	(142)	(144)	(147)
	Comparison	22 (15.2)	9 (6.3)	4 (2.8)	10 (7.0)	16 (11.0)
		(145)	(144)	(143)	(143)	(145)
Enlisted Groundcrew	Ranch Hand	88 (24.7)	45 (13.0)	25 (7.3)	40 (11.7)	65 (18.2)
		(357)	(346)	(344)	(343)	(357)
	Comparison	72 (16.0)	31 (7.1)	31 (7.1)	33 (7.6)	61 (13.6)
		(450)	(439)	(439)	(435)	(450)

Occupational Category	Group	Excellent or Good in 1982			
		n in 1997	Number (%) Fair or Poor in 1997	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	***Ranch Hand***	***661***	***49 (7.4)***	***1.07 (0.72,1.58)***	***0.746***
	Comparison	***845***	***59 (7.0)***		
Officer	Ranch Hand	276	13 (4.7)	1.01 (0.48,2.14)	0.978
	Comparison	344	16 (4.7)		
Enlisted Flyer	Ranch Hand	116	10 (8.6)	1.37 (0.52,3.60)	0.526
	Comparison	123	8 (6.5)		
Enlisted Groundcrew	Ranch Hand	269	26 (9.7)	1.08 (0.63,1.84)	0.783
	Comparison	378	35 (9.3)		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1982 and 1997 results; results adjusted for age in 1997.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had an excellent or good self-perception of health in 1982 (see Chapter 7, Statistical Methods).

Table 9-10. Longitudinal Analysis of Self-perception of Health (Continued)

(b) MODEL 2: RANCH HANDS — INITIAL DIOXIN

	Number (%) Fair or Poor/(n) Examination				
Initial Dioxin	1982	1985	1987	1992	1997
Low	25 (16.3) (153)	14 (9.3) (150)	8 (5.3) (152)	13 (8.8) (148)	24 (15.7) (153)
Medium	40 (25.3) (158)	15 (9.7) (155)	11 (7.1) (155)	20 (12.9) (155)	34 (21.5) (158)
High	27 (17.8) (152)	20 (13.4) (149)	9 (6.1) (147)	16 (10.7) (149)	25 (16.5) (152)

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
	Excellent or Good in 1982			
Initial Dioxin	n in 1997	Number (%) Fair or Poor in 1997	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	128	9 (7.0)	0.89 (0.66,1.20)	0.440
Medium	118	17 (14.4)		
High	125	9 (7.2)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had an excellent or good self-perception of health in 1982 (see Chapter 7, Statistical Methods).

(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY

	Number (%) Fair or Poor/(n) Examination				
Dioxin Category	1982	1985	1987	1992	1997
Comparison	122 (12.9) (946)	51 (5.5) (931)	40 (4.3) (923)	54 (5.8) (925)	93 (9.8) (946)
Background RH	57 (16.6) (344)	13 (3.9) (336)	14 (4.3) (329)	17 (5.1) (335)	31 (9.0) (344)
Low RH	44 (19.2) (229)	22 (9.9) (223)	15 (6.6) (226)	20 (9.0) (222)	38 (16.6) (229)
High RH	48 (20.5) (234)	27 (11.7) (231)	13 (5.7) (228)	29 (12.6) (230)	45 (19.2) (234)
Low plus High RH	92 (19.9) (463)	49 (10.8) (454)	28 (6.2) (454)	49 (10.8) (452)	83 (17.9) (463)

Table 9-10. Longitudinal Analysis of Self-perception of Health (Continued)

Dioxin Category	Excellent or Good in 1982: n in 1997	Number (%) Fair or Poor in 1997	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
Comparison	824	53 (6.4)		
Background RH	287	13 (4.5)	0.74 (0.39,1.38)	0.339
Low RH	185	16 (8.7)	1.32 (0.74,2.38)	0.349
High RH	186	19 (10.2)	1.56 (0.89,2.75)	0.119
Low plus High RH	371	35 (9.4)	1.44 (0.92,2.26)	0.113

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin >10 ppt, Initial Dioxin > 94 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had an excellent or good self-perception of health in 1982 (see Chapter 7, Statistical Methods).

9.2.3.2 Physical Examination Variables

9.2.3.2.1 Appearance of Illness or Distress

Longitudinal analyses were conducted on participants in the 1997 follow-up who did not appear ill or distressed in 1982. The results revealed no significant differences between Ranch Hands and Comparisons in the percentage of participants that appeared ill or distressed, either when examined across all occupations or within each occupational category (Table 9-11(a): $p>0.19$ for each contrast). Analyses that examined the effect of initial dioxin on appearance of illness or distress also were nonsignificant (Table 9-11(b): $p=0.132$). A statistically significant difference in the appearance of illness or distress between Ranch Hands in the low dioxin category and Comparisons was found, with a greater percentage of Ranch Hands appearing ill or distressed (Table 9-11(c): Adj. RR=3.07, $p=0.029$). The relative risk estimate remained significant when Ranch Hands from the low and high dioxin categories were combined (Adj. RR=2.50, $p=0.049$). Other contrasts of Ranch Hands and Comparisons were nonsignificant ($p>0.24$ for each remaining contrast).

Table 9-11. Longitudinal Analysis of Appearance of Illness or Distress

(a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Number (%) Yes/(n) Examination				
		1982	1985	1987	1992	1997
All	***Ranch Hand***	***5 (0.6)***	***2 (0.3)***	***2 (0.3)***	***16 (2.0)***	***14 (1.7)***
		(817)	***(797)***	***(791)***	***(795)***	***(817)***
	Comparison	***1 (0.1)***	***3 (0.3)***	***2 (0.2)***	***13 (1.4)***	***9 (0.9)***
		(974)	***(956)***	***(948)***	***(954)***	***(974)***
Officer	Ranch Hand	3 (1.0)	1 (0.3)	1 (0.3)	8 (2.6)	3 (1.0)
		(312)	(308)	(305)	(307)	(312)
	Comparison	0 (0.0)	0 (0.0)	0 (0.0)	4 (1.1)	3 (0.8)
		(380)	(374)	(368)	(375)	(380)
Enlisted Flyer	Ranch Hand	0 (0.0)	1 (0.7)	0 (0.0)	3 (2.1)	3 (2.0)
		(148)	(145)	(143)	(145)	(148)
	Comparison	1 (0.7)	2 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)
		(144)	(143)	(142)	(142)	(144)
Enlisted Groundcrew	Ranch Hand	2 (0.6)	0 (0.0)	1 (0.3)	5 (1.5)	8 (2.2)
		(357)	(344)	(343)	(343)	(357)
	Comparison	0 (0.0)	1 (0.2)	2 (0.5)	9 (2.1)	6 (1.3)
		(450)	(439)	(438)	(437)	(450)

Occupational Category	Group	No in 1982		Adj. Relative Risk (95% C.I.)[a]	p-Value[b]
		n in 1997	Number (%) Yes in 1997		
All	***Ranch Hand***	***812***	***13 (1.6)***	***1.75 (0.74,4.11)***	***0.196***
	Comparison	***973***	***9 (0.9)***		
Officer	Ranch Hand	309	2 (0.7)	0.82 (0.14,4.95)	0.829
	Comparison	380	3 (0.8)		
Enlisted Flyer	Ranch Hand	148	3 (2.0)	--	0.258[b]
	Comparison	143	0 (0.0)		
Enlisted Groundcrew	Ranch Hand	355	8 (2.3)	1.81 (0.62,5.28)	0.280
	Comparison	450	6 (1.3)		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1982 and 1997 results; results adjusted for age in 1997.

[b] P-value determined using a chi-square test with continuity correction because of the sparse number of participants appearing ill or distressed.

--: Results not presented because of the sparse number of participants appearing ill or distressed.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who did not appear ill or distressed in 1982 (see Chapter 7, Statistical Methods).

Table 9-11. Longitudinal Analysis of Appearance of Illness or Distress (Continued)

(b) MODEL 2: RANCH HANDS — INITIAL DIOXIN

	Number (%) Yes/(n) Examination				
Initial Dioxin	1982	1985	1987	1992	1997
Low	0 (0.0)	0 (0.0)	0 (0.0)	3 (2.0)	7 (4.6)
	(154)	(151)	(153)	(149)	(154)
Medium	0 (0.0)	1 (0.7)	0 (0.0)	4 (2.6)	3 (1.9)
	(158)	(154)	(155)	(155)	(158)
High	2 (1.3)	0 (0.0)	1 (0.7)	1 (0.7)	1 (0.7)
	(152)	(148)	(147)	(149)	(152)

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
	No in 1982			
Initial Dioxin	n in 1997	Number (%) Yes in 1997	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	154	7 (4.6)	0.65 (0.35,1.20)	0.132
Medium	158	3 (1.9)		
High	150	1 (0.7)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who did not appear ill or distressed in 1982 (see Chapter 7, Statistical Methods).

(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY

	Number (%) Yes/(n) Examination				
Dioxin Category	1982	1985	1987	1992	1997
Comparison	1 (0.1)	3 (0.3)	2 (0.2)	12 (1.3)	9 (1.0)
	(946)	(931)	(922)	(927)	(946)
Background RH	3 (0.9)	1 (0.3)	1 (0.3)	7 (2.1)	3 (0.9)
	(347)	(339)	(331)	(337)	(347)
Low RH	0 (0.0)	1 (0.5)	0 (0.0)	5 (2.3)	7 (3.1)
	(229)	(223)	(226)	(222)	(229)
High RH	2 (0.9)	0 (0.0)	1 (0.4)	3 (1.3)	4 (1.7)
	(235)	(230)	(229)	(231)	(235)
Low plus High RH	2 (0.4)	1 (0.2)	1 (0.2)	8 (1.8)	11 (2.4)
	(464)	(453)	(455)	(453)	(464)

Table 9-11. Longitudinal Analysis of Appearance of Illness or Distress (Continued)

Dioxin Category	No in 1982: n in 1997	No in 1982: Number (%) Yes in 1997	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
Comparison	945	9 (1.0)		
Background RH	344	2 (0.6)	0.59 (0.13,2.77)	0.507
Low RH	229	7 (3.1)	3.07 (1.12,8.36)	0.029
High RH	233	4 (1.7)	2.04 (0.61,6.83)	0.246
Low plus High RH	462	11 (2.4)	2.50 (1.00,6.22)	0.049

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin >10 ppt, Initial Dioxin > 94 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who did not appear ill or distressed in 1982 (see Chapter 7, Statistical Methods).

9.2.3.2.2 Relative Age Appearance

The 1997 longitudinal analyses of relative age appearance were conducted among participants who appeared the same or younger than their chronological age in 1982. The associations from all analyses of relative age appearance and dioxin exposure were nonsignificant (Table 9-12: p>0.26 for each analysis).

Table 9-12. Longitudinal Analysis of Relative Age Appearance

(a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Number (%) Older/(n) Examination				
		1982	1985	1987	1992	1997
All	***Ranch Hand***	***15 (1.8)***	***25 (3.1)***	***39 (4.9)***	***40 (5.0)***	***82 (10.0)***
		(819)	***(800)***	***(793)***	***(797)***	***(819)***
	Comparison	***19 (2.0)***	***35 (3.7)***	***40 (4.2)***	***54 (5.7)***	***82 (8.4)***
		(974)	***(956)***	***(949)***	***(954)***	***(974)***
Officer	Ranch Hand	2 (0.6)	4 (1.3)	8 (2.6)	7 (2.3)	19 (6.1)
		(312)	(308)	(305)	(307)	(312)
	Comparison	3 (0.8)	1 (0.3)	8 (2.2)	13 (3.5)	19 (5.0)
		(379)	(373)	(367)	(374)	(379)
Enlisted Flyer	Ranch Hand	0 (0.0)	3 (2.1)	11 (7.7)	13 (9.0)	22 (14.9)
		(148)	(145)	(143)	(145)	(148)
	Comparison	4 (2.8)	12 (8.3)	11 (7.7)	8 (5.6)	17 (11.7)
		(145)	(144)	(143)	(143)	(145)
Enlisted Groundcrew	Ranch Hand	13 (3.6)	18 (5.2)	20 (5.8)	20 (5.8)	41 (11.4)
		(359)	(347)	(345)	(345)	(359)
	Comparison	12 (2.7)	22 (5.0)	21 (4.8)	33 (7.6)	46 (10.2)
		(450)	(439)	(439)	(437)	(450)

Occupational Category	Group	As Old As or Younger in 1982: n in 1997	Number (%) Older in 1997	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	***Ranch Hand***	***804***	***76 (9.5)***	***1.21 (0.87,1.69)***	***0.265***
	Comparison	***955***	***76 (8.0)***		
Officer	Ranch Hand	310	19 (6.1)	1.22 (0.63,2.35)	0.554
	Comparison	376	19 (5.1)		
Enlisted Flyer	Ranch Hand	148	22 (14.9)	1.35 (0.68,2.70)	0.390
	Comparison	141	16 (11.4)		
Enlisted Groundcrew	Ranch Hand	346	35 (10.1)	1.12 (0.70,1.81)	0.637
	Comparison	438	41 (9.4)		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1982 and 1997 results; results adjusted for age in 1997.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who appeared as old as or younger than their age in 1982 (see Chapter 7, Statistical Methods).

Table 9-12. Longitudinal Analysis of Relative Age Appearance (Continued)

(b) MODEL 2: RANCH HANDS — INITIAL DIOXIN

	Number (%) Older in Examination				
Initial Dioxin	1982	1985	1987	1992	1997
Low	2 (1.3)	5 (3.3)	8 (5.2)	6 (4.0)	16 (10.4)
	(154)	(151)	(153)	(149)	(154)
Medium	2 (1.3)	5 (3.2)	6 (3.9)	9 (5.8)	16 (10.1)
	(159)	(156)	(156)	(156)	(159)
High	5 (3.3)	9 (6.0)	7 (4.7)	9 (6.0)	15 (9.8)
	(153)	(149)	(148)	(150)	(153)

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
	As Old As or Younger in 1982			
Initial Dioxin	n in 1997	Number (%) Older in 1997	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	152	15 (9.9)	1.04 (0.81,1.33)	0.765
Medium	157	16 (10.2)		
High	148	13 (8.8)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who appeared as old as or younger than their age in 1982 (see Chapter 7, Statistical Methods).

(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY

	Number (%) Older in Examination				
Dioxin Category	1982	1985	1987	1992	1997
Comparison	19 (2.0)	35 (3.8)	40 (4.3)	53 (5.7)	81 (8.6)
	(946)	(931)	(923)	(927)	(946)
Background RH	6 (1.7)	6 (1.8)	18 (5.4)	15 (4.5)	35 (10.1)
	(347)	(339)	(331)	(337)	(347)
Low RH	2 (0.9)	7 (3.1)	8 (3.5)	7 (3.1)	23 (10.0)
	(230)	(224)	(227)	(223)	(230)
High RH	7 (3.0)	12 (5.2)	13 (5.7)	17 (7.3)	24 (10.2)
	(236)	(232)	(230)	(232)	(236)
Low plus High RH	9 (1.9)	19 (4.2)	21 (4.6)	24 (5.3)	47 (10.1)
	(466)	(456)	(457)	(455)	(466)