

## Table of Contents

---

<b>16 ENDOCRINE ASSESSMENT .....</b>	<b>16-1</b>
16.1 INTRODUCTION.....	16-1
16.1.1 Background.....	16-1
16.1.2 Summary of Previous Analyses of the Air Force Health Study.....	16-3
16.1.2.1 1982 Baseline Study Summary Results.....	16-3
16.1.2.2 1985 Follow-up Study Summary Results.....	16-3
16.1.2.3 1987 Follow-up Study Summary Results.....	16-4
16.1.2.4 Serum Dioxin Analysis of 1987 Follow-up Study Summary Results.....	16-4
16.1.2.5 1992 Follow-up Study Summary Results.....	16-4
16.1.3 Parameters for the 1997 Endocrine Assessment.....	16-5
16.1.3.1 Dependent Variables.....	16-5
16.1.3.2 Medical Records Data.....	16-5
16.1.3.2.1 Physical Examination Data.....	16-6
16.1.3.2.2 Laboratory Examination Data.....	16-6
16.1.3.3 Covariates.....	16-7
16.1.4 Statistical Methods.....	16-7
16.2 RESULTS.....	16-11
16.2.1 Dependent Variable-Covariate Associations.....	16-11
16.2.2 Exposure Analysis.....	16-15
16.2.2.1 Medical Records Variables.....	16-16
16.2.2.1.1 Past Thyroid Disease.....	16-16
16.2.2.1.2 Composite Diabetes Indicator.....	16-18
16.2.2.1.3 Diabetic Severity.....	16-21
16.2.2.1.4 Time to Diabetes Onset.....	16-29
16.2.2.2 Physical Examination Variables.....	16-32
16.2.2.2.1 Thyroid Gland.....	16-32
16.2.2.2.2 Testicular Examination.....	16-34
16.2.2.3 Laboratory Examination Variables.....	16-37
16.2.2.3.1 TSH (Continuous).....	16-37
16.2.2.3.2 TSH (Discrete).....	16-40
16.2.2.3.3 Thyroxine (Continuous).....	16-46
16.2.2.3.4 Thyroxine (Discrete).....	16-49
16.2.2.3.5 Anti-Thyroid Antibodies.....	16-51
16.2.2.3.6 Fasting Glucose (Continuous).....	16-53
16.2.2.3.7 Fasting Glucose (Discrete).....	16-57
16.2.2.3.8 2-Hour Postprandial Glucose (Continuous).....	16-59
16.2.2.3.9 2-Hour Postprandial Glucose (Discrete).....	16-63
16.2.2.3.10 Fasting Urinary Glucose.....	16-65
16.2.2.3.11 2-Hour Postprandial Urinary Glucose.....	16-67
16.2.2.3.12 Serum Insulin (Continuous).....	16-70
16.2.2.3.13 Serum Insulin (Discrete).....	16-74
16.2.2.3.14 $\alpha$ -1-C Hemoglobin (Continuous).....	16-80
16.2.2.3.15 $\alpha$ -1-C Hemoglobin (Discrete).....	16-83
16.2.2.3.16 Total Testosterone (Continuous).....	16-86
16.2.2.3.17 Total Testosterone (Discrete).....	16-89
16.2.2.3.18 Free Testosterone (Continuous).....	16-91

16.2.2.3.19	Free Testosterone (Discrete) .....	16-94
16.2.2.3.20	Estradiol (Continuous) .....	16-97
16.2.2.3.21	Estradiol (Discrete) .....	16-100
16.2.2.3.22	LH (Continuous) .....	16-102
16.2.2.3.23	LH (Discrete) .....	16-106
16.2.2.3.24	FSH (Continuous) .....	16-108
16.2.2.3.25	FSH (Discrete) .....	16-111
16.2.3	Longitudinal Analysis .....	16-114
16.2.3.1	Medical Records Variables .....	16-115
16.2.3.1.1	Composite Diabetes Indicator .....	16-115
16.2.3.2	Laboratory Examination Variables .....	16-118
16.2.3.2.1	TSH (Continuous) .....	16-118
16.2.3.2.2	TSH (Discrete) .....	16-120
16.2.3.2.3	Fasting Glucose (Continuous) .....	16-122
16.2.3.2.4	Fasting Glucose (Discrete) .....	16-124
16.2.3.2.5	2-Hour Postprandial Glucose (Continuous) .....	16-127
16.2.3.2.6	2-Hour Postprandial Glucose (Discrete) .....	16-130
16.2.3.2.7	Total Testosterone (Continuous) .....	16-133
16.2.3.2.8	Total Testosterone (Discrete) .....	16-136
16.3	DISCUSSION .....	16-139
16.4	SUMMARY .....	16-141
16.4.1	Model 1: Group Analysis .....	16-141
16.4.2	Model 2: Initial Dioxin Analysis.....	16-144
16.4.3	Model 3: Categorized Dioxin Analysis.....	16-145
16.4.4	Model 4: 1987 Dioxin Level Analysis .....	16-148
16.5	CONCLUSION .....	16-150
<b>REFERENCES .....</b>		<b>16-151</b>

## List of Tables

---

Table 16-1. Statistical Analysis for the Endocrine Assessment.....	16-8
Table 16-2. Number of Participants Excluded or with Missing Data for the Endocrine Assessment .....	16-11
Table 16-3. Analysis of Past Thyroid Disease .....	16-16
Table 16-4. Analysis of Composite Diabetes Indicator .....	16-19
Table 16-5. Analysis of Diabetic Severity .....	16-23
Table 16-6. Analysis of Time to Diabetes Onset (years) .....	16-29
Table 16-7. Analysis of Thyroid Gland .....	16-32
Table 16-8. Analysis of Testicular Examination.....	16-35
Table 16-9. Analysis of TSH ( $\mu$ IU/ml) (Continuous).....	16-37
Table 16-10. Analysis of TSH (Discrete) .....	16-41
Table 16-11. Analysis of Thyroxine ( $\mu$ g/dl) (Continuous) .....	16-46
Table 16-12. Analysis of Thyroxine (Discrete) .....	16-49
Table 16-13. Analysis of Anti-Thyroid Antibodies .....	16-51
Table 16-14. Analysis of Fasting Glucose (mg/dl) (Continuous) .....	16-54
Table 16-15. Analysis of Fasting Glucose (Discrete) .....	16-57
Table 16-16. Analysis of 2-Hour Postprandial Glucose (mg/dl) (Continuous) .....	16-60
Table 16-17. Analysis of 2-Hour Postprandial Glucose (Discrete).....	16-63
Table 16-18. Analysis of Fasting Urinary Glucose.....	16-65
Table 16-19. Analysis of 2-Hour Postprandial Urinary Glucose .....	16-68
Table 16-20. Analysis of Serum Insulin ( $\mu$ IU/ml) (Continuous).....	16-71
Table 16-21. Analysis of Serum Insulin (Discrete).....	16-75
Table 16-22. Analysis of $\alpha$ -1-C Hemoglobin (percent) (Continuous).....	16-80
Table 16-23. Analysis of $\alpha$ -1-C Hemoglobin (Discrete) .....	16-83
Table 16-24. Analysis of Total Testosterone (ng/dl) (Continuous) .....	16-86
Table 16-25. Analysis of Total Testosterone (Discrete) .....	16-89
Table 16-26. Analysis of Free Testosterone (pg/ml) (Continuous).....	16-92
Table 16-27. Analysis of Free Testosterone (Discrete).....	16-95
Table 16-28. Analysis of Estradiol (pg/ml) (Continuous).....	16-97
Table 16-29. Analysis of Estradiol (Discrete).....	16-100
Table 16-30. Analysis of LH (mIU/ml) (Continuous) .....	16-103
Table 16-31. Analysis of LH (Discrete).....	16-106
Table 16-32. Analysis of FSH (mIU/ml) (Continuous) .....	16-108

Table 16-33. Analysis of FSH (Discrete).....	16-112
Table 16-34. Normal Ranges from Air Force Health Study Examinations for Dependent Variables Used in Endocrine Longitudinal Analysis.....	16-115
Table 16-35. Longitudinal Analysis of Composite Diabetes Indicator.....	16-115
Table 16-36. Longitudinal Analysis of TSH ( $\mu$ IU/ml) (Continuous) .....	16-118
Table 16-37. Longitudinal Analysis of TSH (Discrete).....	16-120
Table 16-38. Longitudinal Analysis of Fasting Glucose (mg/dl) (Continuous).....	16-122
Table 16-39. Longitudinal Analysis of Fasting Glucose (Discrete).....	16-125
Table 16-40. Longitudinal Analysis of 2-Hour Postprandial Glucose (mg/dl) (Continuous).....	16-128
Table 16-41. Longitudinal Analysis of 2-Hour Postprandial Glucose (Discrete).....	16-131
Table 16-42. Longitudinal Analysis of Total Testosterone (ng/dl) (Continuous).....	16-134
Table 16-43. Longitudinal Analysis of Total Testosterone (Discrete).....	16-137
Table 16-44. Summary of Group Analysis (Model 1) for Endocrine Variables (Ranch Hands vs. Comparisons) .....	16-141
Table 16-45. Summary of Initial Dioxin Analysis (Model 2) for Endocrine Variables (Ranch Hands Only).....	16-144
Table 16-46. Summary of Categorized Dioxin Analysis (Model 3) for Endocrine Variables (Ranch Hands vs. Comparisons) .....	16-146
Table 16-47. Summary of 1987 Dioxin Analysis (Model 4) for Endocrine Variables (Ranch Hands Only).....	16-148

## 16 ENDOCRINE ASSESSMENT

---

### 16.1 INTRODUCTION

#### 16.1.1 Background

The essential role of membrane and intracellular receptors in human endocrine function has been firmly established and extensively studied (1). In animal models, much of the basic research into the mechanism of dioxin endocrine toxicity has focused on the dioxin-binding aryl hydrocarbon (Ah) receptor, which has similarities to the endocrine receptors that mediate function of the thyroid, adrenal, and gonadal hormones (2-5).

Animal research has documented that the thyroid is a target organ for dioxin toxicity, although the mechanism has not been defined clearly (6-11). In other studies, dioxin-induced changes in thyroid indices (serum thyroxine [ $T_4$ ], triiodothyronine [ $T_3$ ], and thyroid stimulating hormone [TSH]) were directionally different with species and strain specificity (12, 13). The mechanism by which dioxin interacts with or regulates thyroid function in experimental animals remains under investigation. In competing for thyroid hormone binding sites in target organs (14) or by accelerating the metabolism of thyroid hormones by hepatic enzyme induction (15), dioxin administration can induce a mildly hypothyroid state associated with elevated levels of TSH.

How these experimental studies relate to the effect of dioxin on human thyroid function has not been established. The most recently published morbidity reports on the workers exposed to dioxin during a chemical factory explosion in Germany in 1953 included thyroid disorders in the analyses. Across all exposure categories, an increased incidence of thyroid disease was found in workers relative to referents (16). Thyroid disease occurred in 11 of 158 in the exposed cohort but in only two of 161 referents. The heterogeneous mix of thyroid disorders—four cases of thyrotoxicosis, four cases of goiter, two cases of hypothyroidism, and one other unspecified disorder—weighs against a possible relation with dioxin exposure. In the analyses of laboratory measurements from the same exposed population, the authors found positive associations between each of the exposure indices and selected tests of thyroid function,  $T_4$ , and thyroxine binding globulin (17). Unfortunately, the most widely used measure of thyroid function—serum TSH—was not included in the analyses.

The finding in laboratory animals of physicochemical similarities between the dioxin-binding Ah and glucocorticoid receptors (5, 18) has prompted further investigation into the interaction of dioxin with other steroid hormones. A review by Couture, et al. (19) provided a comprehensive summary of the research into the developmental toxicity and teratogenicity of dioxin in experimental animals.

Experimental studies have documented numerous adverse male reproductive effects in laboratory animals exposed to dioxin, including reduced testicular weight, impaired spermatogenesis, decreased testicular testosterone secretion, and atrophy of the androgen-sensitive seminal vesicles and epididymis (20-24). Although dioxin administration is associated with diminished testosterone secretion in rats (23, 25, 26), the mechanism is unknown and may involve the hypothalamic-pituitary axis. In rats, dioxin inhibits the secretion of luteinizing hormone (LH) by the pituitary gland, an effect associated with androgen deficiency (27, 28). In other experiments, dioxin inhibited the response of the pituitary to gonadotropin-releasing hormone secreted by the hypothalamus (29).

Additional experiments have explored the effects of dioxin on the pituitary and hypothalamus (30, 31). The use of microsurgical techniques in female rats revealed that dioxin toxicity is aggravated by hypophysectomy, with a sparing effect noted upon administering either corticosterone or thyroid hormone (30). Another study defined a biochemical basis for the effect of dioxin on prolactin levels controlled by the adenohypophysis in female rats (32). Studies on the effects of dioxin on the pituitary-adrenal axis have documented significant suppression of corticosterone production by the adrenal gland (33) and defined a biochemical basis for the apparent reduction in bioactivity of adrenocorticotrophic hormone secreted by the pituitary (34).

The National Institute for Occupational Safety and Health (NIOSH) has conducted several long-term epidemiological studies of factory workers who experienced significant occupational exposure to dioxin in chemical production plants (35, 36). In their most recently published report (37), serum levels of three endocrine indices—testosterone, LH, and follicle stimulating hormone (FSH)—were examined in relation to current and calculated initial serum dioxin levels in 248 participants. Current serum dioxin levels were positively and significantly related to both LH and FSH and inversely related to testosterone. In contrast to the NIOSH results, a recent report of the Air Force Health Study (AFHS) population found no relation between the body burden of dioxin and reproductive or endocrine indices, including serum testosterone, FSH, LH, sperm counts and morphology, and anatomic abnormalities of the testes (38).

The possibility that dioxin might affect glucose metabolism in humans was first raised in 1981 with the publication of an occupational study that reported an unusually high prevalence of abnormal glucose tolerance tests (40%) and a 20-percent incidence of diabetes in chemical production workers exposed to dioxin (39). The results of analyses pertinent to glucose metabolism based on serum dioxin data collected during the 1987 and 1992 AFHS examinations recently have been published (40). In the 1987 examination, Ranch Hand participants with the highest serum dioxin levels were nearly three times as likely to have elevations in fasting blood sugar than were Comparisons (41). In the 1992 examination, Ranch Hand participants with high levels of serum dioxin had significantly higher fasting and 2-hour postprandial glucose results than those with lower levels of serum dioxin (42), an effect that was shown to be independent of the serum triglyceride level (43). In nondiabetic Ranch Hands, serum insulin, like the 2-hour postprandial glucose, was positively and significantly associated with current serum dioxin levels. In contrast, in diabetic participants, a consistent inverse dose-response effect was found in all models relating serum insulin to current serum dioxin. Although cause and effect have not been established, these results provide further evidence for an association between glucose intolerance and dioxin levels and raise the possibility that, in a subset of those predisposed to diabetes, dioxin may impair insulin production.

Whether dioxin exposure is in fact a risk factor for the development of diabetes remains controversial. Recent reports from NIOSH noted statistically significant associations between the prevalence of diabetes and elevated fasting blood sugar with increasing serum dioxin levels (44), although the authors could not exclude confounding by the traditional diabetic risk factors of age, obesity, and family history of diabetes. Other epidemiological studies, some of which have included serum dioxin levels in the analyses, have failed to find an association between glucose intolerance and exposure to dioxin (16, 17, 45).

In the most recent publication by the Institute of Medicine, a special section is devoted to the subject of dioxin exposure as a risk factor for the development of diabetes (46). Based on its comprehensive review of the literature, the committee concluded that “at this time, there is inadequate/insufficient evidence to determine whether an association exists between herbicide or dioxin exposure and increased risk of diabetes.”

## 16.1.2 Summary of Previous Analyses of the Air Force Health Study

### *16.1.2.1 1982 Baseline Study Summary Results*

A laboratory evaluation of the endocrine system was used for analysis in the baseline examination in 1982. Five measures of endocrine status were assessed: T<sub>3</sub> percent uptake, T<sub>4</sub>, free thyroxine index (FTI), testosterone, and 2-hour postprandial glucose.

Results showed significant group differences for T<sub>3</sub> percent uptake (abnormally low), predominantly in Ranch Hands 40 years old or younger. The highest percentage of abnormalities was in participants with high body fat. No group difference was noted for elevated 2-hour postprandial glucose values and, as expected, the prevalence of abnormal values was associated with increased age and higher body fat. Lower testosterone values also were associated with increased age and higher body fat. Higher mean testosterone values were significantly more prevalent in the Ranch Hand group. Significant mean shifts were not noted for the T<sub>3</sub> percent uptake, T<sub>4</sub>, and the FTI.

These data, coupled with the animal literature on the profound influence of the endocrine system on lethality and body fat metabolism following dioxin exposure, clearly underscored the importance of a more comprehensive evaluation of the endocrine system.

### *16.1.2.2 1985 Follow-up Study Summary Results*

Questionnaire and review-of-systems data for past thyroid disease were similar in both the Ranch Hand and Comparison groups. These historical data were confirmed by a medical records review. Physical examination findings were necessarily limited to data from palpation of the thyroid gland and testicles; the unadjusted results showed no significant group differences.

Evaluation of the endocrine system was conducted primarily by laboratory testing. The thyroid test battery consisted of T<sub>3</sub> percent uptake and TSH, as determined by radioimmunoassay techniques. Testosterone, initial cortisol, differential cortisol (the difference between the initial and 2-hour cortisol levels), and 2-hour postprandial glucose levels also were analyzed. The T<sub>3</sub> percent uptake data showed no group differences for either mean values or frequency of abnormally low or high values. TSH results revealed a significantly higher mean level in the Ranch Hand group, but this difference was not detected by discrete analysis of the proportions of abnormally high TSH results.

The mean level of testosterone remained significantly elevated for Ranch Hands, as contrasted with Comparisons, in the 10 to 25 percent body fat category, but this difference was not reflected in the discrete analyses. For the few participants with less than 10 percent body fat (six Ranch Hands, four Comparisons), mean testosterone levels were lower for Ranch Hands than for Comparisons.

Two timed cortisol specimens showed no significant group differences in mean values or the percentage of participants with abnormalities. The difference between the timed cortisol results, termed the "differential cortisol," showed no significant group differences for non-Blacks or Blacks born before 1942, but Black Ranch Hands born in or after 1942 had a lower mean differential cortisol level than did their Comparisons.

Group means of 2-hour postprandial glucose levels were not statistically different, but discrete analyses revealed that there was a significantly higher frequency of glucose-impaired (at least 140 mg/dl, but less than 200 mg/dl) Comparisons than Ranch Hands. A variable comprising known diabetics and individuals classified as diabetic by the glucose tolerance test showed no difference between the Ranch Hand and

Comparison groups. The covariates age, race, and body fat were significantly associated with diabetes in this analysis.

#### *16.1.2.3 1987 Follow-up Study Summary Results*

The endocrine assessment did not disclose any statistically significant differences between the Ranch Hand and Comparison groups. The percentage of participants who indicated problems with current thyroid disease was similar between groups, as were the percentages with thyroid and testicular abnormalities determined by palpation at the physical examination. The Ranch Hand TSH mean was marginally significantly higher than the Comparison TSH mean. Ranch Hand and Comparison mean levels were similar for T<sub>3</sub> percent uptake, FSH, testosterone, and 2-hour postprandial glucose. The percentage of Ranch Hands with abnormal values for these five laboratory variables was higher than the percentage of Comparisons with abnormal values; however, the difference in the percentage of abnormal values between Ranch Hands and Comparisons was not statistically significant for these five laboratory variables. In addition, analyses were performed on a composite diabetes indicator. A participant was considered diabetic for this indicator if he had a verified history of diabetes or had a 2-hour postprandial glucose level of at least 200 mg/dl. The difference in the percentage of Ranch Hands and Comparisons considered diabetic, as determined through this composite diabetes indicator, was not significant.

#### *16.1.2.4 Serum Dioxin Analysis of 1987 Follow-up Study Summary Results*

The endocrine assessment found a strong positive association between initial dioxin and diabetes prevalence and testes abnormalities; however, the analyses of current dioxin levels in Ranch Hands and Comparisons indicated that the increased risk was apparent only for Ranch Hands in the high current dioxin category (>33.3 parts per trillion [ppt]). These Ranch Hands also had significantly higher mean levels of TSH, fasting glucose, and 2-hour postprandial glucose than background Comparisons, as well as lower mean levels of T<sub>3</sub> percent uptake and testosterone. The discrete analyses of these variables found a significant increase in abnormally elevated fasting glucose levels and diabetic 2-hour postprandial glucose levels as both initial dioxin and current dioxin increased.

#### *16.1.2.5 1992 Follow-up Study Summary Results*

The assessment of the endocrine system included an extensive evaluation of thyroid, pancreatic, and gonadal functions and their relation to dioxin exposure. Analyses of thyroid functions did not identify significant differences between Ranch Hands and Comparisons. Similarly, the prevalence of diabetes in the two populations was not significantly different, although significant positive associations were found between time to the onset of diabetes and both lipid-adjusted and whole weight dioxin levels, as measured in 1987.

Significant glucose metabolism results were confined to the current serum dioxin analyses. These results suggested a possible mechanism for dioxin effect on glucose metabolism and the development of diabetes. Diabetic Ranch Hands with high levels of current serum dioxin had significantly higher fasting glucose levels than those with lower levels of dioxin. Nondiabetic Ranch Hands, on the other hand, exhibited an inverse association between fasting glucose and current serum dioxin and a positive association between 2-hour postprandial glucose and current serum dioxin. Serum dioxin levels were significantly related to elevated insulin levels in nondiabetic, but not in diabetic Ranch Hands. This was suggestive of a dioxin effect on glucose metabolism with a heightened release of insulin in Ranch Hands with a fully responsive pancreas. When this pancreatic response is no longer effective, elevated glucose levels lead to the clinical diagnosis of diabetes and loss of the dose-response between dioxin and insulin.

Analyses of gonadal functions detected a significant inverse dose-response relation between current serum dioxin and total serum testosterone in Ranch Hands. These results supported those described in the Serum Dioxin Analysis of the 1987 Follow-up Examination, but the clinical meaning was uncertain.

In conclusion, although the existence of endocrine disorders was comparable in Ranch Hands and Comparisons, the assessment of glucose metabolism showed the possibility of adverse effects from dioxin in relation to glucose intolerance and insulin production.

### 16.1.3 Parameters for the 1997 Endocrine Assessment

#### *16.1.3.1 Dependent Variables*

Questionnaire, physical examination, and laboratory data collected at the AFHS 1997 follow-up examination were used in the endocrine assessment. The self-reported information collected from the 1997 questionnaire was subsequently verified and analyses were based on the verified data.

#### *16.1.3.2 Medical Records Data*

The 1997 questionnaire posed a general screening question on thyroid function and disease. Each participant was asked the following question during the in-person health interview: "Since the date of the last interview, has a doctor told you for the first time that you had thyroid problems?" All affirmative responses were verified by a medical records review and added to previously reported and verified information on the thyroid function from the 1982 baseline examination and the 1985, 1987, and 1992 follow-up examinations for each participant. Thyroid disease was classified according to the International Classification of Diseases, 9<sup>th</sup> Revision, Clinical Modification (ICD-9-CM) diagnostic codes. The ICD-9-CM codes for thyroid disease encompassed 240.0-246.9. Based on the verified data, history of thyroid disease was classified as "yes" or "no." Participants with a pre-Southeast Asia (SEA) history of thyroid disease were excluded from the analysis of thyroid disease history.

Similar information was asked of each participant regarding diabetes. This information also was verified and combined with previous information. ICD-9-CM codes 250.00-250.93 were used to classify diabetes. Participants with a verified history of diabetes were combined with those participants with a 2-hour postprandial glucose level of 200 mg/dl or greater at the 1997 physical examination and classified as "yes" for a composite diabetes indicator variable. Those participants without a verified history of diabetes and with a 2-hour postprandial glucose level of less than 200 mg/dl at the 1997 physical examination were classified as "no." This composite diabetes indicator, derived from a medical records review and laboratory results, was analyzed as part of the endocrine assessment. Participants classified as "yes" were designated as diabetics and participants classified as "no" were designated as nondiabetics.

After the data were analyzed, medical records of all participants designated as diabetic, based on medical records, were reviewed to determine diabetic type (1 or 2). One participant (a Ranch Hand veteran) was diagnosed as having type 1 (insulin-dependent) diabetes and the remainder were diagnosed as having type 2 (adult onset) diabetes. A reanalysis with the single Ranch Hand with type 1 diabetes excluded yielded the same results as those already presented.

As part of the 1997 questionnaire, questions were asked of diabetics regarding the use of insulin, oral diabetes medication, and diet. This self-reported information was verified and a diabetic severity index was constructed and analyzed for all participants. This index was categorized as "requiring insulin," "oral hypoglycemic," "diet only," or "no treatment" for diabetics and "no diabetes" for nondiabetics.

The date on which a participant was first diagnosed with diabetes was used to measure a time to diabetes onset by determining the number of years between the date of diagnosis and the end date of the last tour of duty in SEA. Time to diabetes onset for those participants who have not been diagnosed with diabetes was the number of years between the 1997 examination date and the end date of the last tour of duty in SEA. This method of determining time to diabetes onset also was used for participants with a 2-hour postprandial glucose level of 200 mg/dl or greater at the 1997 physical examination but not yet diagnosed with diabetes.

Participants with a pre-SEA history of diabetes were excluded from the analyses of the composite diabetes indicator, diabetic severity, and time to diabetes onset.

#### *16.1.3.2.1 Physical Examination Data*

The physical examination of endocrine function included manual palpation of the thyroid gland and testes. Thyroid abnormalities consisted of enlarged gland, tenderness, presence of nodules, or thyroidectomies. Testicular abnormalities consisted of atrophied or absent testes. Participants with a pre-SEA history of thyroid disease and participants who are currently taking thyroid medication were excluded from the analysis of the thyroid gland. For the analysis of testicular abnormalities, participants with pre-SEA orchiectomies or participants with a missing testicle because of an undescended testicle or a congenital absence were excluded.

#### *16.1.3.2.2 Laboratory Examination Data*

For the 1997 follow-up examination, 14 laboratory variables were analyzed statistically in the endocrine assessment for all participants. TSH ( $\mu$ IU/ml), thyroxine ( $\mu$ g/dl), LH (mIU/ml), FSH (mIU/ml), and total testosterone (ng/dl) were conducted using Ciba Corning ACS 180<sup>®</sup> equipment. Abbott IMX<sup>®</sup> equipment was used to measure  $\alpha$ -1-C hemoglobin (percent) and estradiol (pg/ml). Measurements for fasting glucose (mg/dl) were taken using Dade RxL<sup>®</sup> equipment. Fasting urinary glucose analyses were conducted by dipstick methods using Bayer Atlas<sup>®</sup> equipment. Anti-thyroid antibodies were analyzed using passive hemagglutination assay. Free testosterone (pg/ml) was conducted by radioimmunoassay.

In addition, the analyses of 2-hour postprandial glucose (mg/dl), serum insulin ( $\mu$ IU/ml), and the presence of 2-hour postprandial urinary glucose were restricted to nondiabetics only. Measurements for 2-hour postprandial glucose (mg/dl) were taken using Dade RxL<sup>®</sup> equipment. Analyses for 2-hour postprandial urinary glucose were conducted by dipstick methods using Bayer Atlas<sup>®</sup> equipment. Abbott IMX<sup>®</sup> equipment was used to measure serum insulin. The 100-gram glucose load for the postprandial assays was standardized by the use of Glucola<sup>®</sup> and was not given to diabetics unless requested by the participant.

All laboratory variables were analyzed in both discrete and continuous forms except for anti-thyroid antibodies, fasting urinary glucose, and 2-hour postprandial urinary glucose. These variables were analyzed as discrete variables only and categorized as “present” or “absent.”

TSH and serum insulin were categorized as “abnormally low,” “normal,” and “abnormally high.” The results for 2-hour postprandial glucose were coded as “normal” and “impaired.” All other laboratory results were dichotomized as “normal” or “abnormal” (abnormally high for all variables, except for thyroxine, total testosterone, and free testosterone, which were classified according to abnormally low values).

Participants with thyroidectomies, a pre-SEA history of thyroid disease, or who are taking thyroid medication were excluded from the analyses of TSH, thyroxine, and anti-thyroid antibodies. For total and free testosterone, participants with orchiectomies (pre-SEA or post-SEA), participants with a missing testicle because of an undescended testicle or a congenital absence, and participants currently taking testosterone medication were excluded. Participants with pre-SEA diabetes were excluded from the analysis of fasting glucose, fasting urinary glucose, and  $\alpha$ -1-C hemoglobin. Participants who were diabetic (pre-SEA and post-SEA) or participants with a 2-hour postprandial glucose level greater than or equal to 200 mg/dl were excluded from the analyses of 2-hour postprandial glucose, 2-hour postprandial urinary glucose, and serum insulin.

As described above, a 100-gram glucose load for the postprandial assays was standardized by the use of Glucola<sup>®</sup>. Some participants were not given Glucola<sup>®</sup> by request. A subset of these participants was not classified as diabetic through a medical records review; their 2-hour postprandial glucose was less than 200 mg/dl without consuming the Glucola<sup>®</sup>. Consequently, these participants could not be classified as diabetic or nondiabetic for the composite diabetes indicator and were considered to have an unknown diabetic status. These participants were excluded from analyses of 2-hour postprandial glucose, 2-hour postprandial urinary glucose, and serum insulin.

### 16.1.3.3 Covariates

The endocrine assessment included the effects of age, race, and military occupation in the adjusted analyses of all variables. To adjust for the effects of stress on endocrinologic measures, personality type was used as an additional covariate for past thyroid disease, thyroid gland abnormalities, TSH, thyroxine, and anti-thyroid antibodies. Age, race, occupation, personality type, and body fat were included in the adjusted analyses of the testes-related variables (testicular examination, total testosterone, and free testosterone). A covariate characterizing family history of diabetes was included for the diabetes-related variables, along with age, race, military occupation, personality type, and body fat. These dependent variables included the composite diabetes indicator, diabetic severity, time to diabetes onset, fasting and 2-hour postprandial glucose, fasting and 2-hour postprandial urinary glucose, serum insulin, and  $\alpha$ -1-C hemoglobin.

Age, race, and military occupation were determined from military records. 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 (47). Positive scores reflected the type A direction; negative scores reflected the type B direction. Personality type was dichotomized as type A or type B.

Body fat was calculated from a metric body mass index (48); the formula is

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

Each participant was asked in the 1997 questionnaire whether anyone in his immediate family ever had diabetes or sugar diabetes. A family history of diabetes covariate was constructed from this question and used in adjusted analyses of all diabetic-related dependent variables.

### 16.1.4 Statistical Methods

Table 16-1 summarizes the statistical analysis that was performed for the endocrine assessment. The first part of this table describes the dependent variables and identifies the covariates and the statistical

methods. The second part of this 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, the covariate was categorized as shown in Table 16-1. Table 16-2 provides a summary of the number of participants with missing dependent variable and covariate data. In addition, the number of participants excluded because of medical conditions is given.

**Table 16-1. Statistical Analysis for the Endocrine Assessment**

**Dependent Variables**

Variable (Units)	Data Source	Data Form	Cutpoints	Covariates <sup>a</sup>	Exclusions <sup>b</sup>	Statistical Analysis and Methods
Past Thyroid Disease	MR-V	D	Yes No	(1)	(a)	U:LR A:LR
Composite Diabetes Indicator	MR-V/ LAB	D	<ul style="list-style-type: none"> <li>• Diabetic: Verified History or <math>\geq 200</math> mg/dl 2-hr. post-prandial glucose</li> <li>• Nondiabetic: Otherwise</li> </ul>	(2)	(b)	U:LR A:LR L:LR
Diabetic Severity	MR-V	D	Requiring Insulin Oral Hypoglycemics Diet Only No Treatment No Diabetes	(2)	(b)	U:PR A:PR
Time to Diabetes Onset (years)	MR-V/ LAB/ MIL	C	--	(2)	(b)	U:ST A:ST
Thyroid Gland	PE	D	Abnormal Normal	(1)	(c)	U:LR A:LR
Testicular Examination	PE	D	Abnormal Normal	(3)	(d)	U:LR A:LR
TSH ( $\mu$ IU/ml)	LAB	D/C	Abnormal Low: $<0.35$ Normal: 0.35-5.5 Abnormal High: $>5.5$	(1)	(e)	U:PR,GLM A:PR,GLM L:PR,GLM
Thyroxine ( $T_4$ ) ( $\mu$ g/dl)	LAB	D/C	Low: $<4.8$ Normal: $\geq 4.8$	(1)	(e)	U:LR,GLM A:LR,GLM
Anti-Thyroid Antibodies	LAB	D	Present Absent	(1)	(e)	U:LR A:LR
Fasting Glucose (mg/dl)	LAB	D/C	High: $>110$ Normal: $\leq 110$	(2)	(b)	U:LR,GLM A:LR,GLM L:LR,GLM
2-Hour Postprandial Glucose (mg/dl)	LAB	D/C	Impaired: 140- $<200$ Normal: $<140$	(2)	(f)	U:LR,GLM A:LR,GLM L:LR,GLM

**Table 16-1. Statistical Analysis for the Endocrine Assessment (Continued)**

Variable (Units)	Data Source	Data Form	Cutpoints	Covariates <sup>a</sup>	Exclusions <sup>b</sup>	Statistical Analysis and Methods
Fasting Urinary Glucose	LAB	D	Present Absent	(2)	(b)	U:LR A:LR
2-Hour Postprandial Urinary Glucose	LAB	D	Present Absent	(2)	(f)	U:LR A:LR
Serum Insulin (μIU/ml)	LAB	D/C	Abnormal Low: <18 Normal: 18-56 Abnormal High: >56	(2)	(f)	U:PR,GLM A:PR,GLM
α-1-C Hemoglobin (percent)	LAB	D/C	High: >7.7 Normal: ≤7.7	(2)	(b)	U:LR,GLM A:LR,GLM
Total Testosterone (ng/dl)	LAB	D/C	Low: <241 (Ages 45-49) <230 (Age ≥50) Normal: ≥241 (Ages 45-49) ≥230 (Age ≥50)	(3)	(g)	U:LR,GLM A:LR,GLM L:LR,GLM
Free Testosterone (pg/ml)	LAB	D/C	Low: <6 Normal: ≥6	(3)	(g)	U:LR,GLM A:LR,GLM
Estradiol (pg/ml)	LAB	D/C	High: >50 Normal: ≤50	(4)	None	U:LR,GLM A:LR,GLM
LH (mIU/ml)	LAB	D/C	High: >9.3 Normal: ≤9.3	(4)	None	U:LR,GLM A:LR,GLM
FSH (mIU/ml)	LAB	D/C	High: >15 Normal: ≤15	(4)	None	U:LR,GLM A:LR,GLM

<sup>a</sup>Covariates:

- (1): age, race, military occupation, personality type.
- (2): age, race, military occupation, personality type, body fat, family history of diabetes.
- (3): age, race, military occupation, personality type, body fat.
- (4): age, race, military occupation.

<sup>b</sup>Exclusions:

- (a): participants with a pre-SEA history of thyroid disease.
- (b): participants with a pre-SEA history of diabetes.
- (c): participants with a pre-SEA history of thyroid disease, participants currently taking thyroid medication.
- (d): participants with a pre-SEA orchiectomy, participants with a testicle absent (undescended or congenital absence).
- (e): participants with a pre-SEA history of thyroid disease, participants with a thyroidectomy, participants currently taking thyroid medication.
- (f): all diabetics (pre- and post-SEA), participants whose diabetic status was unknown at the 1997 physical examination.
- (g): participants with an orchiectomy (pre-SEA or post-SEA), participants with a testicle absent (undescended or congenital absence), participants currently taking testosterone medication.

**Table 16-1. Statistical Analysis for the Endocrine Assessment (Continued)**

**Covariates**

Variable (Units)	Data Source	Data Form	Cutpoints
Age (years)	MIL	D/C	Born $\geq$ 1942 Born <1942
Race	MIL	D	Black Non-Black
Occupation	MIL	D	Officer Enlisted Flyer Enlisted Groundcrew
Personality Type	PE	D	A direction B direction
Body Fat (percent)	PE	D/C	Obese: >25% Lean or Normal: $\leq$ 25%
Family History of Diabetes	Q-SR	D	Yes No

**Abbreviations**

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

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

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

Statistical Methods: GLM: General linear models analysis  
LR: Logistic regression analysis  
PR: Polytomous logistic regression analysis  
ST: Survival time analysis

Cutpoints for total testosterone were age-dependent. Consequently, normal and abnormal levels for total testosterone were constructed according to a participant's laboratory value and age at the physical examination. The age-specific cutpoints are listed in Table 16-1; the reference ages for these cutpoints are given in parentheses following the cutpoints.

The analysis of time to diabetes onset was based on a regression analysis of time to onset in which time to onset was modeled as a linear combination of exposure variables and covariates. Further details on the statistical procedures used for the analysis of time to onset are discussed in Chapter 7, Statistical Methods.

**Table 16-2. Number of Participants Excluded or with Missing Data for the Endocrine Assessment**

Variable	Variable Use	Group		Dioxin (Ranch Hands Only)		Categorized Dioxin	
		Ranch Hand	Comparison	Initial	1987	Ranch Hand	Comparison
Composite Diabetes Indicator	DEP	9	18	5	7	7	17
Diabetic Severity	DEP	9	18	5	7	7	17
Time to Diabetes Onset	DEP	9	18	5	7	7	17
Testicular Examination	DEP	1	0	0	1	1	0
2-hour Postprandial Glucose	DEP	1	2	1	1	1	2
2-hour Postprandial Urinary Glucose	DEP	3	5	2	3	3	5
Serum Insulin	DEP	1	2	1	1	1	2
Personality Type	COV	3	0	1	3	3	0
Family History of Diabetes	COV	7	12	4	7	7	12
Pre-SEA Thyroid Disease	EXC	7	5	4	7	7	5
Pre-SEA Diabetes	EXC	2	1	2	2	2	1
Taking Thyroid Medication	EXC	24	44	13	24	24	44
Diabetic or Diabetic Status Unknown	EXC	156	228	113	152	152	217
Pre-SEA Orchiectomy	EXC	2	2	1	2	2	2
Thyroidectomy	EXC	12	15	5	12	12	15
Pre- or Post-SEA Orchiectomy	EXC	8	5	4	8	8	5
Testicle Undescended or Congenitally Absent	EXC	6	13	3	6	6	13
Taking Testosterone Medication	EXC	6	7	3	5	5	7

Note: DEP = Dependent variable.

COV = Covariate.

EXC = Exclusion.

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.

## 16.2 RESULTS

### 16.2.1 Dependent Variable-Covariate Associations

The associations between the dependent variables examined in the endocrine assessment and the covariates used in the adjusted analysis were investigated. The results are presented in Appendix F, Table F-8. These associations are pairwise between the dependent variable and the covariate and are not adjusted for any other covariates. Participants were excluded from each of the analyses as given in Table 16-1. Statistically significant associations are discussed below.

The covariate tests of association for past thyroid disease revealed a significant positive association with age ( $p=0.020$ ).

A participant with a verified history of diabetes or a 2-hour postprandial glucose level of greater than or equal to 200 mg/dl was considered diabetic in the composite diabetes indicator variable. The covariate

tests of association revealed age ( $p=0.001$ ), race ( $p=0.011$ ), personality type ( $p=0.001$ ), body fat ( $p=0.001$ ), and family history of diabetes ( $p=0.001$ ) to be associated significantly with the composite diabetes indicator. The percentage of diabetic participants increased with age. A higher percentage of Black participants than non-Black participants were diabetic (25.6% versus 16.4%). The percentage of diabetic participants was higher for participants with type B personalities than participants with type A personalities (19.5% versus 13.0%). A higher percentage of obese participants were diabetic than lean and normal participants (28.6% versus 12.1%). A greater percentage of participants with a family history of diabetes were diabetic, relative to participants with no family history of diabetes (24.9% versus 14.1%).

Tests of covariate association revealed age ( $p=0.001$ ), race ( $p=0.023$ ), personality type ( $p=0.001$ ), body fat ( $p=0.001$ ), and family history of diabetes ( $p=0.001$ ) to be significantly associated with diabetic severity. The percentage of nondiabetic participants was greater for younger participants, non-Blacks, those with a type A personality, lean participants, and participants with no family history of diabetes. The percentages of older participants who used no treatment, diet, oral hypoglycemics, and insulin to treat diabetes were 6.2, 2.5, 7.5, and 2.6, respectively. Percentages for younger participants were smaller than for older participants for all forms of treatment. The analysis of race showed that for Black participants, 7.2 percent used no treatment, 2.4 percent used diet only as a form of treatment, 11.2 percent used oral hypoglycemics, and 3.2 percent used insulin. For all forms of treatment, the percentages of non-Black participants were smaller than for Black participants. Covariate analyses revealed that 4.3 percent, 1.1 percent, 3.5 percent, and 2.1 percent of participants with type A personalities used no treatment, diet, oral hypoglycemics, and insulin, respectively, to treat their disorder. For participants with type B personalities, 6.3 percent, 2.1 percent, 6.8 percent, and 1.9 percent, respectively, used these methods in the treatment of diabetes. Of the obese participants, 9.9 percent used no treatment, 2.1 percent used diet as a form of treatment, 10.2 percent used oral hypoglycemics, and 2.1 percent used insulin. The percentages of lean or normal participants using these methods were less for each form of treatment. Of the participants with a family history of diabetes, 7.5 percent used no treatment, 2.2 percent used diet to treat their disorder, 9.1 percent used hypoglycemics, and 3.5 percent used insulin. The percentages of participants with no family history of diabetes using these methods were less for each form of treatment.

Time to diabetes onset was associated significantly with age ( $p<0.001$ ), race ( $p=0.007$ ), personality type ( $p<0.001$ ), body fat ( $p<0.001$ ), and family history of diabetes ( $p<0.001$ ). Time to diabetes onset decreased significantly with increases in age and body fat. Black participants had a shorter time to diabetes onset than did non-Black participants. Participants with type A personalities had a significantly longer time to diabetes onset than did participants with type B personalities. Participants with a family history of diabetes had a significantly shorter time to diabetes onset than did participants with no family history of diabetes.

Abnormalities of the thyroid gland were significantly associated with occupation ( $p=0.019$ ). Officers had the highest percentage of participants with abnormal thyroid glands (1.9%), followed by enlisted flyers (0.6%), then enlisted groundcrew (0.5%).

Tests of covariate association showed the percentage of abnormal testicular examinations to be significantly associated with age ( $p=0.001$ ) and occupation ( $p=0.021$ ). Older participants had a higher percentage of abnormal testicular examinations than did younger participants (6.2% versus 1.4%). Officers had the highest percentage of abnormal testicular examinations (5.2%), followed by enlisted flyers (5.1%), then enlisted groundcrew (2.8%).

TSH in its continuous form increased significantly with age ( $p<0.001$ ). Race and occupation also were significant ( $p<0.001$  and  $p=0.007$ ). Non-Black participants had a higher mean TSH level than did Black

participants (1.87  $\mu$ IU/ml versus 1.38  $\mu$ IU/ml). Officers had the highest mean TSH level (1.94  $\mu$ IU/ml), followed by enlisted groundcrew (1.78  $\mu$ IU/ml), then enlisted flyers (1.77  $\mu$ IU/ml). No significant covariate associations were seen with TSH in its discrete form.

Thyroxine in its continuous form was significantly associated with occupation ( $p < 0.001$ ). Enlisted flyers had the highest mean thyroxine level (7.26  $\mu$ g/dl), followed by enlisted groundcrew (7.20  $\mu$ g/dl), then officers (6.81  $\mu$ g/dl). Tests of covariate associations with thyroxine in its discrete form revealed no significant associations.

Fasting glucose in its continuous form increased with age ( $p < 0.001$ ) and body fat ( $p < 0.001$ ). Occupation ( $p = 0.039$ ), personality type ( $p = 0.001$ ), and family history of diabetes ( $p < 0.001$ ) also were associated significantly with fasting glucose. Enlisted flyers had the highest mean fasting glucose level (104.1 mg/dl), followed by enlisted groundcrew (101.8 mg/dl), then officers (100.4 mg/dl). Participants with type B personalities had a higher mean fasting glucose level than did participants with type A personalities (102.9 mg/dl versus 99.6 mg/dl). Participants with a family history of diabetes had a higher mean fasting glucose level (107.1 mg/dl) than did those participants with no family history of diabetes (99.8 mg/dl).

Fasting glucose in its discrete form increased with age ( $p = 0.001$ ) and body fat ( $p = 0.001$ ). Race ( $p = 0.040$ ), personality type ( $p = 0.001$ ), and family history of diabetes ( $p = 0.001$ ) also were significant in the tests of covariate association. Black participants had a greater percentage of high fasting glucose levels than did non-Black participants (24.2% versus 16.7%). A greater percentage of high fasting glucose values was seen for participants with personality type B (19.4%) versus personality type A (13.6%). Participants with a family history of diabetes had a higher prevalence of high fasting glucose levels (25.2% versus 14.4%).

Two-hour postprandial glucose was analyzed only for nondiabetics. Two-hour postprandial glucose in its continuous form increased with age ( $p < 0.001$ ) and body fat ( $p < 0.001$ ). Occupation ( $p = 0.014$ ), personality type ( $p = 0.035$ ), and family history of diabetes ( $p = 0.003$ ) also were significant. Enlisted flyers had the highest mean 2-hour postprandial glucose level (109.7 mg/dl), followed by enlisted groundcrew (104.8 mg/dl), then officers (103.5 mg/dl). Participants with type B personalities had a higher mean 2-hour postprandial glucose level than did participants with type A personalities (106.3 mg/dl versus 103.3 mg/dl). Participants with a family history of diabetes had a higher mean 2-hour postprandial glucose level (108.9 mg/dl) than those with no family history of diabetes (104.0 mg/dl).

Tests of covariate association for 2-hour postprandial glucose in its dichotomous form showed age ( $p = 0.001$ ), race ( $p = 0.007$ ), body fat ( $p = 0.001$ ), and family history of diabetes ( $p = 0.024$ ) to be significant. The percentage of participants with 2-hour postprandial glucose results classified as impaired increased with age and body fat. Non-Black participants had a higher percentage of impaired values than did Black participants (16.4% versus 5.4%). Participants with a family history of diabetes had a higher prevalence of impaired values than did participants with no family history of diabetes (19.5% versus 14.7%).

The presence of fasting urinary glucose was significantly associated with occupation ( $p = 0.029$ ), personality type ( $p = 0.004$ ), body fat ( $p = 0.001$ ), and family history of diabetes ( $p = 0.012$ ). The prevalence of participants with fasting urinary glucose present increased with body fat. Enlisted groundcrew had the highest percentage of positive fasting urinary glucose results (5.2%), followed by enlisted flyers (5.0%), then officers (2.8%). A greater prevalence of participants with fasting urinary glucose present was seen for participants with personality type B (5.2%) versus personality type A (2.6%). Participants with a family history of diabetes had a higher prevalence of positive fasting urinary glucose results than did participants with no family history of diabetes (6.1% versus 3.5%).

Two-hour postprandial urinary glucose was analyzed only for nondiabetics. The presence of 2-hour postprandial urinary glucose was significantly associated with occupation ( $p=0.033$ ). Enlisted flyers had the highest prevalence of positive 2-hour postprandial urinary glucose results (26.7%), followed by enlisted groundcrew (24.9%), then officers (20.1%).

Serum insulin was analyzed only for nondiabetics. Serum insulin in its continuous form increased significantly with age ( $p<0.001$ ) and body fat ( $p<0.001$ ). Occupation ( $p=0.001$ ), personality type ( $p=0.006$ ), and family history of diabetes ( $p=0.001$ ) also were significant. Enlisted flyers had the highest mean serum insulin level (52.55  $\mu\text{IU/ml}$ ), followed by enlisted groundcrew (50.58  $\mu\text{IU/ml}$ ), then officers (43.67  $\mu\text{IU/ml}$ ). Participants with type B personalities had a higher mean serum insulin level than participants with type A personalities (50.42  $\mu\text{IU/ml}$  versus 44.72  $\mu\text{IU/ml}$ ). Participants with a family history of diabetes had a higher mean insulin level (54.32  $\mu\text{IU/ml}$ ) than those with no family history of diabetes (46.28  $\mu\text{IU/ml}$ ).

Serum insulin in its discrete form was significantly associated with age ( $p=0.003$ ), occupation ( $p=0.024$ ), personality type ( $p=0.018$ ), body fat ( $p=0.001$ ), and family history of diabetes ( $p=0.001$ ). Younger participants had a higher percentage of abnormally low and a lower percentage of abnormally high serum insulin levels than did older participants. Officers had the highest percentage of abnormally low serum insulin levels (14.9%) and the lowest percentage of abnormally high serum insulin levels (37.4%). Participants with personality type A had a higher percentage of abnormally low serum insulin levels (14.9%) and a lower percentage of abnormally high serum insulin levels (38.4%) than did participants with personality type B. Obese participants had a lower percentage of abnormally low serum insulin levels (2.5%) than did lean or normal participants (16.4%). Lean or normal participants had a lower percentage of abnormally high serum insulin levels (32.0%) than obese participants (71.0%). Participants with no family history of diabetes had a higher prevalence of abnormally low serum insulin levels (14.2%) than did participants with a history of diabetes (8.5%). The prevalence of abnormally high serum insulin values was greater for participants with a family history of diabetes than for participants with no history of diabetes (49.6% versus 39.4%).

Age and body fat significantly increased with  $\alpha$ -1-C hemoglobin in its continuous form ( $p<0.001$  for each). Race, occupation, personality type, and family history of diabetes also were significant ( $p<0.001$  for each). Black participants had a significantly higher mean  $\alpha$ -1-C hemoglobin level than did non-Black participants (7.07 percent versus 6.45 percent). Enlisted flyers had the highest mean  $\alpha$ -1-C hemoglobin level (6.61 percent), followed by enlisted groundcrew (6.58 percent), then officers (6.33 percent). Participants with personality type B had a higher mean  $\alpha$ -1-C hemoglobin level than did participants with personality type A (6.57 percent versus 6.36 percent). Participants with a family history of diabetes had a higher mean  $\alpha$ -1-C hemoglobin level than did participants with no family history of diabetes (6.73 percent versus 6.40 percent).

The discrete form of  $\alpha$ -1-C hemoglobin paralleled the continuous analysis. Age ( $p=0.001$ ), race ( $p=0.001$ ), occupation ( $p=0.002$ ), personality type ( $p=0.001$ ), body fat ( $p=0.001$ ), and family history of diabetes ( $p=0.001$ ) were all significantly associated with  $\alpha$ -1-C hemoglobin in the tests of covariate association. The covariate categories with the highest mean levels also had the greatest percentage of abnormal high  $\alpha$ -1-C hemoglobin levels.

Total testosterone in its continuous form decreased with age and body fat ( $p<0.001$  each). Occupation also was significant ( $p=0.043$ ). Officers had the lowest mean total testosterone level (410.7 ng/dl), followed by enlisted groundcrew (429.7 ng/dl), then enlisted flyers (433.4 ng/dl).

Tests of covariate association for total testosterone in its dichotomous form showed body fat to be significant ( $p=0.001$ ). Obese participants had a higher percentage of low testosterone levels than did lean or normal participants (15.3% versus 4.7%).

Free testosterone in its continuous form decreased with age and body fat ( $p<0.001$  each). Occupation ( $p<0.001$ ) and personality type ( $p=0.001$ ) also were significant. Officers had the lowest mean free testosterone level (13.12 pg/ml), followed by enlisted flyers (13.99 pg/ml), then enlisted groundcrew (14.65 pg/ml). Participants with type B personalities had a lower mean free testosterone level than did participants with type A personalities (13.68 pg/ml versus 14.37 pg/ml). Free testosterone in its discrete form decreased significantly with age ( $p=0.001$ ) and body fat ( $p=0.002$ ).

Both the continuous and discrete forms of estradiol were significantly associated with race ( $p=0.008$  and  $p=0.013$ , respectively). Black participants had a higher mean estradiol level as well as a higher percentage of high estradiol values than non-Blacks. The mean estradiol level was 44.26 pg/ml for Blacks and 40.15 pg/ml for non-Blacks. For Blacks, 37.5 percent had high estradiol levels, whereas 27.0 percent of non-Blacks had high estradiol levels.

LH in both its continuous and discrete forms increased significantly with age ( $p<0.001$  and  $p=0.001$ , respectively).

FSH in its continuous form increased significantly with age ( $p<0.001$ ). Occupation was also significantly associated with FSH ( $p=0.008$ ). Officers had the highest mean FSH level (6.31 mIU/ml), followed by enlisted flyers (6.00 mIU/ml), then enlisted groundcrew (5.75 mIU/ml).

Similarly, FSH in its dichotomous form was significantly associated with age ( $p=0.001$ ) and occupation ( $p=0.001$ ). Older participants had a greater percentage of high FSH values (11.2%) than did younger participants (4.0%). Officers had the highest percentage of high FSH results (10.4%), followed by enlisted flyers (9.2%), then enlisted groundcrew (5.5%).

### 16.2.2 Exposure Analysis

The following section presents results of the statistical analysis of the dependent variables shown in Table 16-1. Four models were examined for each dependent variable. 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 in Table 2-8, the average levels of exposure to dioxin were highest for enlisted groundcrew, followed by enlisted flyers, 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 ppt. If a participant did not have a 1987 dioxin level, the 1992 level was used to estimate the initial dioxin level. If a participant did not have a 1987 or a 1992 dioxin level, the 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 was included in this model to account for body-fat-related differences in elimination rate (49).

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 1987 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 level was not available, and dioxin levels in 1997 were used if the 1987 and 1992 levels were not available. The 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.

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 a 1992 dioxin measurement, the 1997 measurement was used to determine the dioxin level.

16.2.2.1 Medical Records Variables

16.2.2.1.1 Past Thyroid Disease

All unadjusted and adjusted analyses for Models 1 through 4 were nonsignificant (Table 16-3(a–h):  $p > 0.17$  for each analysis).

**Table 16-3. Analysis of Past Thyroid Disease**

<b>(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED</b>					
Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
<i>All</i>	<i>Ranch Hand</i>	863	65 (7.5)	<i>0.89 (0.64,1.22)</i>	<i>0.456</i>
	<i>Comparison</i>	1,246	105 (8.4)		
Officer	Ranch Hand	338	29 (8.6)	0.91 (0.56,1.48)	0.704
	Comparison	492	46 (9.3)		
Enlisted Flyer	Ranch Hand	150	15 (10.0)	1.37 (0.64,2.94)	0.415
	Comparison	187	14 (7.5)		
Enlisted Groundcrew	Ranch Hand	375	21 (5.6)	0.69 (0.40,1.18)	0.171
	Comparison	567	45 (7.9)		

  

<b>(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED</b>		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
<i>All</i>	<i>0.89 (0.64,1.22)</i>	<i>0.459</i>
Officer	0.91 (0.56,1.48)	0.701
Enlisted Flyer	1.37 (0.64,2.94)	0.419
Enlisted Groundcrew	0.70 (0.41,1.19)	0.189

**Table 16-3. Analysis of Past Thyroid Disease (Continued)**

<b>(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED</b>				
<b>Initial Dioxin Category Summary Statistics</b>			<b>Analysis Results for Log<sub>2</sub> (Initial Dioxin)<sup>a</sup></b>	
<b>Initial Dioxin</b>	<b>n</b>	<b>Number (%) Yes</b>	<b>Estimated Relative Risk (95% C.I.)<sup>b</sup></b>	<b>p-Value</b>
Low	160	12 (7.5)	1.13 (0.88,1.45)	0.360
Medium	160	9 (5.6)		
High	158	14 (8.9)		

<sup>a</sup> Adjusted for percent body fat at the time of the blood measurement of dioxin.

<sup>b</sup> Relative risk for a twofold increase in initial dioxin.

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

<b>(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED</b>			
<b>Analysis Results for Log<sub>2</sub> (Initial Dioxin)</b>			
<b>n</b>	<b>Adjusted Relative Risk (95% C.I.)<sup>a</sup></b>		<b>p-Value</b>
477	1.20 (0.88,1.64)		0.245

<sup>a</sup> Relative risk for a twofold increase in initial dioxin.

<b>(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED</b>				
<b>Dioxin Category</b>	<b>n</b>	<b>Number (%) Yes</b>	<b>Est. Relative Risk (95% C.I.)<sup>ab</sup></b>	<b>p-Value</b>
Comparison	1,208	102 (8.4)		
Background RH	378	30 (7.9)	0.97 (0.64,1.49)	0.906
Low RH	237	15 (6.3)	0.73 (0.41,1.27)	0.263
High RH	241	20 (8.3)	0.94 (0.57,1.56)	0.825
Low plus High RH	478	35 (7.3)	0.83 (0.55,1.24)	0.362

<sup>a</sup> Relative risk and confidence interval relative to Comparisons.

<sup>b</sup> 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 16-3. Analysis of Past Thyroid Disease (Continued)**

<b>(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED</b>			
<b>Dioxin Category</b>	<b>n</b>	<b>Adjusted Relative Risk (95% C.I.)<sup>a</sup></b>	<b>p-Value</b>
Comparison	1,208		
Background RH	376	0.92 (0.60,1.42)	0.707
Low RH	237	0.70 (0.40,1.22)	0.209
High RH	240	1.07 (0.64,1.81)	0.792
Low plus High RH	477	0.87 (0.57,1.30)	0.490

<sup>a</sup> 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.

<b>(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED</b>			
<b>1987 Dioxin Category Summary Statistics</b>			<b>Analysis Results for Log<sub>2</sub> (1987 Dioxin + 1)</b>
<b>1987 Dioxin</b>	<b>n</b>	<b>Number (%) Yes</b>	<b>Estimated Relative Risk (95% C.I.)<sup>a</sup></b>
Low	287	25 (8.7)	1.01 (0.85,1.20)
Medium	285	19 (6.7)	0.892
High	284	21 (7.4)	

<sup>a</sup> Relative risk for a twofold increase in 1987 dioxin.

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

<b>(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED</b>			
<b>Analysis Results for Log<sub>2</sub> (1987 Dioxin + 1)</b>			
<b>n</b>	<b>Adjusted Relative Risk (95% C.I.)<sup>a</sup></b>		<b>p-Value</b>
853	1.10 (0.89,1.36)		0.358

<sup>a</sup> Relative risk for a twofold increase in 1987 dioxin.

#### 16.2.2.1.2 Composite Diabetes Indicator

The composite diabetes indicator variable was a dichotomous classification of whether a participant was considered diabetic or not. A participant with a verified history of diabetes or a postprandial glucose level of greater than or equal to 200 mg/dl was considered diabetic for these analyses.

The Model 1 unadjusted and adjusted analyses did not show a significant difference in the number of diabetic participants between Ranch Hands and Comparisons across all occupations or within each occupational stratum (Table 16-4(a,b): p>0.49 for each analysis).

**Table 16-4. Analysis of Composite Diabetes Indicator**

<b>(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED</b>					
Occupational Category	Group	n	Number (%) Diabetic	Est. Relative Risk (95% C.I.)	p-Value
<i>All</i>	<i>Ranch Hand</i>	859	145 (16.9)	0.99 (0.79,1.25)	0.960
	<i>Comparison</i>	1,232	209 (17.0)		
Officer	Ranch Hand	337	52 (15.4)	1.08 (0.73,1.59)	0.709
	Comparison	490	71 (14.5)		
Enlisted Flyer	Ranch Hand	148	27 (18.2)	0.86 (0.50,1.48)	0.583
	Comparison	184	38 (20.7)		
Enlisted Groundcrew	Ranch Hand	374	66 (17.6)	0.98 (0.70,1.38)	0.915
	Comparison	558	100 (17.9)		

<b>(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED</b>		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
<i>All</i>	1.04 (0.81,1.33)	0.755
Officer	1.08 (0.72,1.63)	0.711
Enlisted Flyer	0.82 (0.45,1.47)	0.498
Enlisted Groundcrew	1.11 (0.77,1.61)	0.572

<b>(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED</b>				
Initial Dioxin Category Summary Statistics			Analysis Results for Log <sub>2</sub> (Initial Dioxin) <sup>a</sup>	
Initial Dioxin	n	Number (%) Diabetic	Estimated Relative Risk (95% C.I.) <sup>b</sup>	p-Value
Low	157	32 (20.4)	1.11 (0.94,1.32)	0.231
Medium	158	35 (22.2)		
High	160	39 (24.4)		

<sup>a</sup> Adjusted for percent body fat at the time of the blood measurement of dioxin.

<sup>b</sup> Relative risk for a twofold increase in initial dioxin.

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

<b>(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED</b>		
Analysis Results for Log <sub>2</sub> (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.) <sup>a</sup>	p-Value
470	1.36 (1.09,1.69)	0.005

<sup>a</sup> Relative risk for a twofold increase in initial dioxin.

**Table 16-4. Analysis of Composite Diabetes Indicator (Continued)**

<b>(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED</b>				
Dioxin Category	n	Number (%) Diabetic	Est. Relative Risk (95% C.I.) <sup>ab</sup>	p-Value
Comparison	1,195	199 (16.7)		
Background RH	379	37 (9.8)	0.67 (0.45,0.98)	0.041
Low RH	235	49 (20.9)	1.27 (0.88,1.84)	0.202
High RH	240	57 (23.8)	1.33 (0.94,1.90)	0.111
Low plus High RH	475	106 (22.3)	1.30 (0.99,1.72)	0.064

<sup>a</sup> Relative risk and confidence interval relative to Comparisons.

<sup>b</sup> 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.

<b>(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED</b>			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.) <sup>a</sup>	p-Value
Comparison	1,183		
Background RH	375	0.69 (0.46,1.02)	0.065
Low RH	232	1.22 (0.83,1.79)	0.311
High RH	238	1.47 (1.00,2.17)	0.048
Low plus High RH	470	1.34 (1.00,1.80)	0.049

<sup>a</sup> 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.

<b>(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED</b>				
1987 Dioxin Category Summary Statistics			Analysis Results for Log <sub>2</sub> (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Diabetic	Estimated Relative Risk (95% C.I.) <sup>a</sup>	p-Value
Low	286	22 (7.7)	1.35 (1.20,1.52)	<0.001
Medium	284	54 (19.0)		
High	284	67 (23.6)		

<sup>a</sup> 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 16-4. Analysis of Composite Diabetes Indicator (Continued)**

<b>(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED</b>		
<b>Analysis Results for Log<sub>2</sub> (1987 Dioxin + 1)</b>		
<b>n</b>	<b>Adjusted Relative Risk (95% C.I.)<sup>a</sup></b>	<b>p-Value</b>
845	1.43 (1.21,1.68)	<0.001

<sup>a</sup> Relative risk for a twofold increase in 1987 dioxin.

The unadjusted Model 2 analysis did not reveal a significant relation between initial dioxin and the percentage of diabetic participants (Table 16-4(c):  $p=0.231$ ). After adjusting for covariates, the results became significant (Table 16-4(d): Adj. RR=1.36,  $p=0.005$ ). The percentages of diabetic participants in the low, medium, and high initial dioxin categories were 20.4, 22.2, and 24.4, respectively.

The unadjusted Model 3 analysis of the composite diabetes indicator revealed significant differences between Ranch Hands in the background dioxin category and Comparisons, as well as between Ranch Hands in the low plus high dioxin category and Comparisons (Table 16-4(e): Est. RR=0.67,  $p=0.041$ ; Est. RR=1.30,  $p=0.064$ , respectively). After adjusting for covariates, three significant contrasts were revealed: Ranch Hands in the background dioxin category versus Comparisons (Table 16-4(f): Adj. RR=0.69,  $p=0.065$ ), Ranch Hands in the high dioxin category versus Comparisons (Table 16-4(f): Adj. RR=1.47,  $p=0.048$ ), and Ranch Hands in the low plus high dioxin category versus Comparisons (Table 16-4(f): Adj. RR=1.34,  $p=0.049$ ). The percentage of diabetic Comparisons was 16.7, versus 9.8 percent for Ranch Hands in the background dioxin category, 23.8 percent of Ranch Hands in the high dioxin category, and 22.3 percent for Ranch Hands in the low plus high dioxin category.

The unadjusted and adjusted Model 4 analyses each revealed a significant positive association between 1987 dioxin and the percentage of diabetic participants (Table 16-4(g,h): Est. RR=1.35,  $p<0.001$ ; Adj. RR=1.43,  $p<0.001$ , respectively). The percentages of diabetic participants in the low, medium, and high 1987 dioxin categories were 7.7, 19.0, and 23.6, respectively.

#### 16.2.2.1.3 Diabetic Severity

The unadjusted Model 1 analysis of diabetic severity revealed marginally significant or significant differences between the percentage of Ranch Hands and Comparisons taking oral hypoglycemics (Table 16-5(a): Est. RR=0.71,  $p=0.097$ ) and requiring insulin (Table 16-5(a): Est. RR=2.04,  $p=0.026$ ). The percentage of participants taking oral hypoglycemics was 4.4 for Ranch Hands versus 6.3 for Comparisons. The percentage of participants requiring insulin in the Ranch Hand group was 2.8 versus 1.4 in the Comparison group. Stratifying by occupation revealed a marginally significant difference between the percentage of Ranch Hand and Comparison officers requiring insulin (Table 16-5(a): Est. RR=2.53,  $p=0.054$ ). For Ranch Hand officers, 3.6 percent required insulin versus 1.4 percent for Comparison officers. After adjusting for covariates, a significant difference in the percentage of Ranch Hands and Comparisons requiring insulin was observed (Table 16-5(b): Adj. RR=2.20,  $p=0.017$ ). In addition, marginally significant differences were seen between the percentage of Ranch Hands and Comparisons requiring insulin in both the officer stratum and the enlisted groundcrew stratum (Table 16-5(b): Adj. RR=2.39,  $p=0.074$ ; Adj. RR=2.52,  $p=0.084$ , respectively).

The unadjusted Model 2 analysis of diabetic severity did not reveal a significant relation between initial dioxin and the severity of diabetes (Table 16-5(c):  $p\geq 0.25$  for each contrast). After adjusting for covariates, the percentage of Ranch Hands taking oral hypoglycemic and requiring insulin was associated

significantly with initial dioxin (Table 16-5(d): Adj. RR=1.41, p=0.062 for oral hypoglycemics; Adj. RR=2.47, p=0.001 for requiring insulin). The percentages of Ranch Hands taking oral hypoglycemics in the low, medium, and high initial dioxin categories were 5.1, 6.3, and 8.8, respectively. The percentages of participants requiring insulin in the low, medium, and high initial dioxin categories were 2.5, 3.8, and 3.8, respectively.

The Model 3 unadjusted analysis revealed a significant difference between the percentage of Ranch Hands in the background dioxin category and Comparisons who took oral hypoglycemics to control diabetes (Table 16-5(e): Est. RR=0.27, p=0.006). For Ranch Hands in the background dioxin category, 1.3 percent used oral hypoglycemics versus 6.0 percent of Comparisons. Three Ranch Hand dioxin categories were significantly different from the Comparisons in the percentage of participants requiring insulin: Ranch Hands in the low dioxin category versus Comparisons (Table 16-5(e): Est. RR=2.43, p=0.042), Ranch Hands in the high dioxin category versus Comparisons (Table 16-5(e): Est. RR=2.40, p=0.046), and Ranch Hands in the low plus high dioxin category versus Comparisons (Table 16-5(e): Est. RR=2.41, p=0.013). The percentages of requiring insulin Ranch Hands in the low dioxin category, high dioxin category, and low plus high dioxin category were 3.4, 3.3, and 3.4, respectively, versus 1.4 percent for Comparisons.

The adjusted Model 3 analysis revealed a marginally significant difference between the percentage of Ranch Hands in the high dioxin category and Comparisons who used diet only to control diabetes (Table 16-5(f): Adj. RR=2.32, p=0.089). For Ranch Hands in the high dioxin category, 2.9 percent used diet alone to treat their diabetes versus 1.4 percent of Comparisons. A significant difference between the percentage of Ranch Hands in the background dioxin category and Comparisons who took oral hypoglycemics was observed (Table 16-5(f): Adj. RR=0.28, p=0.008). Three Ranch Hand dioxin categories were significantly different from the Comparisons in the percentage of participants that required insulin: Ranch Hands in the low dioxin category (Table 16-5(f): Adj. RR=2.41, p=0.050), Ranch Hands in the high dioxin category (Table 16-5(f): Adj. RR=3.46, p=0.009), and Ranch Hands in the low plus high dioxin category (Table 16-5(f): Adj. RR=2.90, p=0.004).

The unadjusted Model 4 analysis of diabetic severity revealed a significant positive association between 1987 dioxin and the percentage of diabetics who used no treatment for diabetes (Table 16-5(g): Est. RR=1.28, p=0.010). A positive association between 1987 dioxin and the percentage of diabetics using oral hypoglycemics also was observed (Table 16-5(g): Est. RR=1.58, p<0.001). Adjusting for covariates revealed significant or marginally significant positive associations with 1987 dioxin for all four contrasts: no treatment (Table 16-5(h): Adj. RR=1.23, p=0.097), diet only (Table 16-5(h): Adj. RR=1.49, p=0.048), oral hypoglycemic (Table 16-5(h): Adj. RR=1.85, p<0.001), and requiring insulin (Table 16-5(h): Adj. RR=1.38, p=0.084).

Table 16-5. Analysis of Diabetic Severity

<b>(a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED</b>										
Occupational Category	Group	n	Number (%)					Contrast vs. Nondiabetic	Est. Relative Risk (95% C.I.)	p-Value
			Nondiabetic	No Treatment	Diet Only	Oral Hypo-glycemic	Requiring Insulin			
<i>All</i>	<i>Ranch Hand Comparison</i>	<i>859</i>	<i>730 (85.0)</i>	<i>49 (5.7)</i>	<i>18 (2.1)</i>	<i>38 (4.4)</i>	<i>24 (2.8)</i>	<i>No Treatment</i>	<i>1.07 (0.73,1.57)</i>	<i>0.721</i>
		<i>1,232</i>	<i>1,054 (85.6)</i>	<i>66 (5.4)</i>	<i>18 (1.5)</i>	<i>77 (6.3)</i>	<i>17 (1.4)</i>	<i>Diet Only</i>	<i>1.44 (0.75,2.79)</i>	<i>0.275</i>
								<i>Oral Hypo-glycemic</i>	<i>0.71 (0.48,1.06)</i>	<i>0.097</i>
								<i>Requiring Insulin</i>	<i>2.04 (1.09,3.82)</i>	<i>0.026</i>
Officer	Ranch Hand Comparison	337	289 (85.8)	16 (4.7)	8 (2.4)	12 (3.6)	12 (3.6)	No Treatment	0.94 (0.49,1.80)	0.859
		490	426 (86.9)	25 (5.1)	6 (1.2)	26 (5.3)	7 (1.4)	Diet Only	1.97 (0.67,5.72)	0.215
								Oral Hypo-glycemic	0.68 (0.34,1.37)	0.281
								Requiring Insulin	2.53 (0.98,6.50)	0.054
Enlisted Flyer	Ranch Hand Comparison	148	125 (84.5)	9 (6.1)	2 (1.4)	9 (6.1)	3 (2.0)	No Treatment	0.78 (0.33,1.87)	0.579
		184	152 (82.6)	14 (7.6)	2 (1.1)	12 (6.5)	4 (2.2)	Diet Only	1.22 (0.17,8.76)	0.846
								Oral Hypo-glycemic	0.91 (0.37,2.23)	0.840
								Requiring Insulin	0.91 (0.20,4.15)	0.905
Enlisted Groundcrew	Ranch Hand Comparison	374	316 (84.5)	24 (6.4)	8 (2.1)	17 (4.5)	9 (2.4)	No Treatment	1.34 (0.76,2.36)	0.314
		558	476 (85.3)	27 (4.8)	10 (1.8)	39 (7.0)	6 (1.1)	Diet Only	1.21 (0.47,3.09)	0.697
								Oral Hypo-glycemic	0.66 (0.37,1.18)	0.160
								Requiring Insulin	2.26 (0.80,6.41)	0.125

**Table 16-5. Analysis of Diabetic Severity (Continued)**

<b>(b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED</b>			
<b>Occupational Category</b>	<b>Contrast vs. Nondiabetic</b>	<b>Adj. Relative Risk (95% C.I.)</b>	<b>p-Value</b>
<i>All</i>	<i>No Treatment</i>	<i>1.10 (0.74,1.62)</i>	<i>0.642</i>
	<i>Diet Only</i>	<i>1.52 (0.78,2.96)</i>	<i>0.219</i>
	<i>Oral Hypoglycemic</i>	<i>0.73 (0.48,1.11)</i>	<i>0.137</i>
	<i>Requiring Insulin</i>	<i>2.20 (1.15,4.20)</i>	<i>0.017</i>
Officer	No Treatment	0.96 (0.50,1.86)	0.902
	Diet Only	2.04 (0.69,5.99)	0.195
	Oral Hypoglycemic	0.68 (0.33,1.39)	0.288
	Requiring Insulin	2.39 (0.92,6.20)	0.074
Enlisted Flyer	No Treatment	0.71 (0.29,1.72)	0.445
	Diet Only	1.09 (0.15,7.93)	0.931
	Oral Hypoglycemic	0.75 (0.29,1.91)	0.544
	Requiring Insulin	1.22 (0.24,6.24)	0.811
Enlisted Groundcrew	No Treatment	1.48 (0.83,2.66)	0.185
	Diet Only	1.32 (0.51,3.41)	0.572
	Oral Hypoglycemic	0.76 (0.41,1.41)	0.384
	Requiring Insulin	2.52 (0.88,7.23)	0.084

**Table 16-5. Analysis of Diabetic Severity (Continued)**

<b>(c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED</b>										
<b>Initial Dioxin Category Summary Statistics</b>							<b>Analysis Results for Log<sub>2</sub> (Initial Dioxin)<sup>a</sup></b>			
<b>Initial Dioxin Category</b>	<b>n</b>	<b>Number (%)</b>					<b>Requiring Insulin</b>	<b>Contrast vs. Nondiabetic</b>	<b>Est. Relative Risk (95% C.I.)<sup>b</sup></b>	<b>p-Value</b>
		<b>Nondiabetic</b>	<b>No Treatment</b>	<b>Diet Only</b>	<b>Oral Hypoglycemic</b>					
Low	157	131 (83.4)	11 (7.0)	3 (1.9)	8 (5.1)	4 (2.5)	No Treatment	1.14 (0.87,1.49)	0.332	
Medium	158	128 (81.0)	9 (5.7)	5 (3.2)	10 (6.3)	6 (3.8)	Diet Only	1.12 (0.74,1.71)	0.584	
High	160	124 (77.5)	12 (7.5)	4 (2.5)	14 (8.8)	6 (3.8)	Oral Hypoglycemic	1.13 (0.87,1.48)	0.358	
							Requiring Insulin	1.23 (0.86,1.76)	0.250	

<sup>a</sup> Adjusted for percent body fat at the time of the blood measurement of dioxin.

<sup>b</sup> Relative risk for a twofold increase in initial dioxin.

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

<b>(d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED</b>				
<b>n</b>	<b>Analysis Results for Log<sub>2</sub> (Initial Dioxin)</b>			
	<b>Contrast vs. Nondiabetic</b>	<b>Adjusted Relative Risk (95% C.I.)<sup>a</sup></b>		<b>p-Value</b>
470	No Treatment	1.29 (0.93,1.78)		0.121
	Diet Only	1.25 (0.74,2.11)		0.411
	Oral Hypoglycemic	1.41 (0.98,2.01)		0.062
	Requiring Insulin	2.47 (1.43,4.25)		0.001

<sup>a</sup> Relative risk for a twofold increase in initial dioxin.

**Table 16-5. Analysis of Diabetic Severity (Continued)**

<b>(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED</b>						
<b>Dioxin Category</b>	<b>n</b>	<b>Number (%)</b>				
		<b>Nondiabetic</b>	<b>No Treatment</b>	<b>Diet Only</b>	<b>Oral Hypoglycemic</b>	<b>Requiring Insulin</b>
Comparison	1,195	1,026 (85.9)	63 (5.3)	17 (1.4)	72 (6.0)	17 (1.4)
Background RH	379	344 (90.8)	16 (4.2)	6 (1.6)	5 (1.3)	8 (2.1)
Low RH	235	195 (83.0)	13 (5.5)	5 (2.1)	14 (6.0)	8 (3.4)
High RH	240	188 (78.3)	19 (7.9)	7 (2.9)	18 (7.5)	8 (3.3)
Low plus High RH	475	383 (80.6)	32 (6.7)	12 (2.5)	32 (6.7)	16 (3.4)

  

<b>Contrast vs. Nondiabetic</b>								
<b>Dioxin Category</b>	<b>No Treatment</b>		<b>Diet Only</b>		<b>Oral Hypoglycemic</b>		<b>Requiring Insulin</b>	
	<b>Est. Relative Risk (95% C.I.)<sup>ab</sup></b>	<b>p-Value</b>						
Comparison								
Background RH	0.91 (0.51,1.61)	0.749	1.23 (0.48,3.17)	0.668	0.27 (0.11,0.69)	0.006	1.55 (0.66,3.63)	0.318
Low RH	1.04 (0.55,1.94)	0.912	1.49 (0.54,4.11)	0.437	0.92 (0.49,1.72)	0.795	2.43 (1.03,5.72)	0.042
High RH	1.43 (0.83,2.47)	0.202	2.00 (0.81,4.92)	0.131	1.08 (0.61,1.91)	0.799	2.40 (1.02,5.65)	0.046
Low plus High RH	1.22 (0.77,1.92)	0.394	1.73 (0.81,3.70)	0.156	1.00 (0.63,1.58)	0.988	2.41 (1.20,4.83)	0.013

<sup>a</sup> Relative risk and confidence interval relative to Comparisons.

<sup>b</sup> 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 16-5. Analysis of Diabetic Severity (Continued)**

<b>(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED</b>					
<b>Dioxin Category</b>	<b>n</b>	<b>No Treatment vs. Nondiabetic</b>		<b>Diet Only vs. Nondiabetic</b>	
		<b>Adj. Relative Risk (95% C.I.)<sup>a</sup></b>	<b>p-Value</b>	<b>Adj. Relative Risk (95% C.I.)<sup>a</sup></b>	<b>p-Value</b>
Comparison	1,183				
Background RH	375	0.92 (0.51,1.65)	0.771	1.24 (0.47,3.30)	0.661
Low RH	232	0.95 (0.50,1.80)	0.878	1.55 (0.55,4.34)	0.408
High RH	238	1.58 (0.89,2.81)	0.122	2.32 (0.88,6.12)	0.089
Low plus High RH	470	1.23 (0.77,1.95)	0.385	1.90 (0.87,4.15)	0.108

  

<b>Dioxin Category</b>	<b>n</b>	<b>Oral Hypoglycemic vs. Nondiabetic</b>		<b>Requiring Insulin vs. Nondiabetic</b>	
		<b>Adj. Relative Risk (95% C.I.)<sup>a</sup></b>	<b>p-Value</b>	<b>Adj. Relative Risk (95% C.I.)<sup>a</sup></b>	<b>p-Value</b>
Comparison	1,183				
Background RH	375	0.28 (0.11,0.71)	0.008	1.42 (0.59,3.45)	0.435
Low RH	232	0.89 (0.46,1.71)	0.726	2.41 (1.00,5.82)	0.050
High RH	238	1.17 (0.63,2.18)	0.624	3.46 (1.36,8.81)	0.009
Low plus High RH	470	1.02 (0.63,1.65)	0.931	2.90 (1.40,5.99)	0.004

<sup>a</sup> 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 16-5. Analysis of Diabetic Severity (Continued)**

<b>(g) MODEL 4: RANCH HANDS — 1987 DIOXIN — UNADJUSTED</b>									
1987 Dioxin Category Summary Statistics							Analysis Results for Log <sub>2</sub> (1987 Dioxin +1) <sup>a</sup>		
Initial Dioxin Category	n	Number (%)					Contrast vs. Nondiabetic	Est. Relative Risk (95% C.I.) <sup>a</sup>	p-Value
		Nondiabetic	No Treatment	Diet Only	Oral Hypoglycemic	Requiring Insulin			
Low	286	264 (92.3)	11 (3.8)	2 (0.7)	3 (1.1)	6 (2.1)	No Treatment	1.28 (1.06,1.55)	0.010
Medium	284	239 (84.2)	17 (6.0)	8 (2.8)	12 (4.2)	8 (2.8)	Diet Only	1.27 (0.94,1.72)	0.120
High	284	224 (78.9)	20 (7.0)	8 (2.8)	22 (7.7)	10 (3.5)	Oral Hypoglycemic	1.58 (1.28,1.94)	<0.001
							Requiring Insulin	1.15 (0.87,1.50)	0.323

<sup>a</sup> Relative risk for a twofold increase in 1987 dioxin.

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

<b>(h) MODEL 4: RANCH HANDS — 1987 DIOXIN — ADJUSTED</b>			
Analysis Results for Log <sub>2</sub> (1987 Dioxin + 1)			
n	Contrast vs. Nondiabetic	Adjusted Relative Risk (95% C.I.) <sup>a</sup>	p-Value
845	No Treatment	1.23 (0.96,1.58)	0.097
	Diet Only	1.49 (1.00,2.20)	0.048
	Oral Hypoglycemic	1.85 (1.37,2.49)	<0.001
	Requiring Insulin	1.38 (0.96,2.00)	0.084

<sup>a</sup> Relative risk for a twofold increase in 1987 dioxin.

16.2.2.1.4 Time to Diabetes Onset

The time to diabetes onset from time of duty in SEA did not differ significantly between Ranch Hands and Comparisons in the Model 1 unadjusted and adjusted analyses (Table 16-6(a,b):  $p \geq 0.39$  for each analysis).

**Table 16-6. Analysis of Time to Diabetes Onset (years)**

<b>(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED</b>				
<b>Occupational Category</b>	<b>Group</b>	<b>n</b>	<b>Coefficient (Std. Error)<sup>a</sup></b>	<b>p-Value<sup>b</sup></b>
<i>All</i>	<i>Ranch Hand</i>	<i>859</i>	<i>0.018 (0.035)</i>	<i>0.603</i>
	<i>Comparison</i>	<i>1,232</i>		
Officer	Ranch Hand	337	-0.008 (0.077)	0.916
	Comparison	490		
Enlisted Flyer	Ranch Hand	148	0.064 (0.075)	0.390
	Comparison	184		
Enlisted Groundcrew	Ranch Hand	374	0.015 (0.041)	0.715
	Comparison	558		

<sup>a</sup> Coefficient and standard error for group in a survival time analysis model, using a censored Weibull distribution. A negative coefficient implies that the time to diabetes onset is shorter for Ranch Hands than for Comparisons.

<sup>b</sup> P-value based on the group coefficient in a survival time analysis model, using a censored Weibull distribution.

<b>(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED</b>				
<b>Occupational Category</b>	<b>Group</b>	<b>n</b>	<b>Adj. Coefficient (Std. Error)<sup>a</sup></b>	<b>p-Value<sup>b</sup></b>
<i>All</i>	<i>Ranch Hand</i>	<i>850</i>	<i>0.006 (0.035)</i>	<i>0.871</i>
	<i>Comparison</i>	<i>1,220</i>		
Officer	Ranch Hand	335	-0.001 (0.079)	0.993
	Comparison	488		
Enlisted Flyer	Ranch Hand	145	0.066 (0.077)	0.390
	Comparison	178		
Enlisted Groundcrew	Ranch Hand	370	-0.018 (0.043)	0.666
	Comparison	554		

<sup>a</sup> Coefficient and standard error for group in a survival time analysis model, using a censored Weibull distribution. A negative coefficient implies that the time to diabetes onset is shorter for Ranch Hands than for Comparisons.

<sup>b</sup> P-value based on the group coefficient in a survival time analysis model, using a censored Weibull distribution.

**Table 16-6. Analysis of Time to Diabetes Onset (years) (Continued)**

<b>(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED</b>			
<b>Initial Dioxin Category Summary Statistics</b>		<b>Analysis Results for Log<sub>2</sub> (Initial Dioxin)<sup>a</sup></b>	
<b>Initial Dioxin</b>	<b>n</b>	<b>Slope (Std. Error)<sup>b</sup></b>	<b>p-Value</b>
Low	157	-0.0214 (0.023)	0.356
Medium	158		
High	160		

<sup>a</sup> Adjusted for percent body fat at the time of the blood measurement of dioxin.

<sup>b</sup> Slope and standard error based on time to diabetes onset versus log<sub>2</sub> (initial dioxin) in a survival time analysis model, using a censored Weibull distribution. A negative slope implies that the time to diabetes onset is shorter as initial dioxin increases.

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

<b>(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED</b>			
<b>Initial Dioxin Category Summary Statistics</b>		<b>Analysis Results for Log<sub>2</sub> (Initial Dioxin)</b>	
<b>Initial Dioxin</b>	<b>n</b>	<b>Adjusted Slope (Std. Error)<sup>a</sup></b>	<b>p-Value</b>
Low	156	-0.074 (0.030)	0.013
Medium	154		
High	160		

<sup>a</sup> Slope and standard error based on time to diabetes onset versus log<sub>2</sub> (initial dioxin) in a survival time analysis model, using a censored Weibull distribution. A negative slope implies that the time to diabetes onset is shorter as initial dioxin increases.

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

<b>(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED</b>			
<b>Dioxin Category</b>	<b>n</b>	<b>Coefficient (Std. Error)<sup>ab</sup></b>	<b>p-Value<sup>c</sup></b>
Comparison	1,195		
Background RH	379	0.143 (0.058)	0.013
Low RH	235	-0.058 (0.051)	0.254
High RH	240	-0.058 (0.048)	0.233
Low plus High RH	475	-0.058 (0.039)	0.134

<sup>a</sup> Adjusted for percent body fat at the time of the blood measurement of dioxin.

<sup>b</sup> Coefficient and standard error for Ranch Hand versus Comparison contrast in a survival time analysis model, using a censored Weibull distribution. A negative coefficient implies that the time to diabetes onset is shorter for the Ranch Hand category than for Comparisons.

<sup>c</sup> P-value based on the Ranch Hand versus Comparison contrast in a survival time analysis model, using a censored Weibull distribution.

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 16-6. Analysis of Time to Diabetes Onset (years) (Continued)**

<b>(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED</b>			
<b>Dioxin Category</b>	<b>n</b>	<b>Adj. Coefficient (Std. Error)<sup>a</sup></b>	<b>p-Value<sup>b</sup></b>
Comparison	1,183		
Background RH	375	0.134 (0.059)	0.024
Low RH	232	-0.065 (0.052)	0.214
High RH	238	-0.085 (0.051)	0.100
Low plus High RH	470	-0.075 (0.040)	0.061

<sup>a</sup> Coefficient and standard error for Ranch Hand versus Comparison contrast in a survival time analysis model, using a censored Weibull distribution. A negative coefficient implies that the time to diabetes onset is shorter for the Ranch Hand category than for Comparisons.

<sup>b</sup> P-value based on the Ranch Hand versus Comparison contrast in a survival time analysis model, using a censored Weibull distribution.

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.

<b>(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED</b>			
<b>1987 Dioxin Category Summary Statistics</b>		<b>Analysis Results for Log<sub>2</sub> (1987 Dioxin +1)</b>	
<b>1987 Dioxin</b>	<b>n</b>	<b>Slope (Std. Error)<sup>a</sup></b>	<b>p-Value</b>
Low	286	-0.098 (0.021)	<0.001
Medium	284		
High	284		

<sup>a</sup> Slope and standard error based on time to diabetes onset versus log<sub>2</sub> (1987 dioxin + 1) in a survival time analysis model, using a censored Weibull distribution. A negative slope implies that the time to diabetes onset is shorter as 1987 dioxin increases.

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

<b>(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED</b>			
<b>1987 Dioxin Category Summary Statistics</b>		<b>Analysis Results for Log<sub>2</sub> (1987 Dioxin +1)</b>	
<b>1987 Dioxin</b>	<b>n</b>	<b>Adjusted Slope (Std. Error)<sup>a</sup></b>	<b>p-Value</b>
Low	282	-0.118 (0.027)	<0.001
Medium	283		
High	280		

<sup>a</sup> Slope and standard error based on time to diabetes onset versus log<sub>2</sub> (1987 dioxin + 1) in a survival time analysis model, using a censored Weibull distribution. A negative slope implies that the time to diabetes onset is shorter as 1987 dioxin increases.

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

The Model 2 unadjusted analysis did not reveal a significant relation between initial dioxin and time to diabetes onset (Table 16-6(c):  $p=0.356$ ). After adjusting for covariates, the results became significant (Table 16-6(d): adjusted slope= $-0.074$ ,  $p=0.013$ ). The time to diabetes onset was shorter for Ranch Hands with higher initial dioxin levels.

The Model 3 unadjusted and adjusted analyses each revealed a significant difference in time to diabetes onset between Ranch Hands in the background dioxin category and Comparisons (Table 16-6(e,f):  $p=0.013$ , unadjusted;  $p=0.024$ , adjusted). The time to diabetes onset was significantly longer for Ranch Hands in the background dioxin category than for Comparisons. The adjusted Model 3 analysis also revealed two other marginally significant contrasts: Ranch Hands in the high dioxin category versus Comparisons (Table 16-6(f):  $p=0.100$ ) and Ranch Hands in the low plus high dioxin category versus Comparisons (Table 16-6(f):  $p=0.061$ ). In each of these two contrasts, the time to diabetes onset from time of duty in SEA was shorter for the Ranch Hand category than for the Comparison category.

The unadjusted and adjusted Model 4 analyses each revealed a significant association between time to diabetes onset and 1987 dioxin (Table 16-6(g,h): slope= $-0.098$ ,  $p<0.001$ ; adjusted slope= $-0.118$ ,  $p<0.001$ , respectively). In each analysis, the time to diabetes onset was shorter for Ranch Hands with higher 1987 dioxin levels.

### 16.2.2.2 Physical Examination Variables

#### 16.2.2.2.1 Thyroid Gland

All unadjusted and adjusted analyses in Models 1 through 4 showed no significant associations with dioxin (Table 16-7(a-h):  $p>0.11$  for each analysis).

**Table 16-7. Analysis of Thyroid Gland**

<b>(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED</b>					
Occupational Category	Group	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)	p-Value
<i>All</i>	<i>Ranch Hand</i>	<i>843</i>	<i>6 (0.7)</i>	<i>0.53 (0.21,1.36)</i>	<i>0.171</i>
	<i>Comparison</i>	<i>1,203</i>	<i>16 (1.3)</i>		
Officer	Ranch Hand	328	4 (1.2)	0.52 (0.16,1.63)	0.260
	Comparison	470	11 (2.3)		
Enlisted Flyer	Ranch Hand	144	1 (0.7)	1.27 (0.08,20.41)	0.868
	Comparison	182	1 (0.5)		
Enlisted Groundcrew	Ranch Hand	371	1 (0.3)	0.37 (0.04,3.32)	0.374
	Comparison	551	4 (0.7)		

  

<b>(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED</b>		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
<i>All</i>	<i>0.54 (0.21,1.39)</i>	<i>0.183</i>
Officer	0.53 (0.17,1.67)	0.276
Enlisted Flyer	1.23 (0.08,19.88)	0.883
Enlisted Groundcrew	0.38 (0.04,3.39)	0.384

Note: Results are not adjusted for race because of the sparse number of participants with an abnormal thyroid gland.

**Table 16-7. Analysis of Thyroid Gland (Continued)**

<b>(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED</b>				
<b>Initial Dioxin Category Summary Statistics</b>			<b>Analysis Results for Log<sub>2</sub> (Initial Dioxin)<sup>a</sup></b>	
<b>Initial Dioxin</b>	<b>n</b>	<b>Number (%) Abnormal</b>	<b>Estimated Relative Risk (95% C.I.)<sup>b</sup></b>	<b>p-Value</b>
Low	157	1 (0.6)	0.95 (0.32,2.81)	0.923
Medium	158	0 (0.0)		
High	152	1 (0.7)		

<sup>a</sup> Adjusted for percent body fat at the time of the blood measurement of dioxin.

<sup>b</sup> Relative risk for a twofold increase in initial dioxin.

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

<b>(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED</b>		
<b>Analysis Results for Log<sub>2</sub> (Initial Dioxin)</b>		
<b>n</b>	<b>Adjusted Relative Risk (95% C.I.)<sup>a</sup></b>	<b>p-Value</b>
466	1.01 (0.32,3.17)	0.981

<sup>a</sup> Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race and occupation because of the sparse number of Ranch Hands with an abnormal thyroid gland.

<b>(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED</b>				
<b>Dioxin Category</b>	<b>n</b>	<b>Number (%) Abnormal</b>	<b>Est. Relative Risk (95% C.I.)<sup>ab</sup></b>	<b>p-Value</b>
Comparison	1,165	16 (1.4)		
Background RH	369	4 (1.1)	0.82 (0.27,2.47)	0.718
Low RH	233	1 (0.4)	0.31 (0.04,2.32)	0.253
High RH	234	1 (0.4)	0.30 (0.04,2.27)	0.242
Low plus High RH	467	2 (0.4)	0.30 (0.07,1.32)	0.112

<sup>a</sup> Relative risk and confidence interval relative to Comparisons.

<sup>b</sup> 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 16-7. Analysis of Thyroid Gland (Continued)**

<b>(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED</b>			
<b>Dioxin Category</b>	<b>n</b>	<b>Adjusted Relative Risk (95% C.I.)<sup>a</sup></b>	<b>p-Value</b>
Comparison	1,165		
Background RH	367	0.65 (0.21,2.01)	0.457
Low RH	233	0.29 (0.04,2.19)	0.229
High RH	233	0.56 (0.07,4.62)	0.590
Low plus High RH	466	0.40 (0.09,1.81)	0.234

<sup>a</sup> 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.

Results are not adjusted for race because of the sparse number of participants with an abnormal thyroid gland.

<b>(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED</b>				
<b>1987 Dioxin Category Summary Statistics</b>			<b>Analysis Results for Log<sub>2</sub> (1987 Dioxin + 1)</b>	
<b>1987 Dioxin</b>	<b>n</b>	<b>Number (%) Abnormal</b>	<b>Estimated Relative Risk (95% C.I.)<sup>a</sup></b>	<b>p-Value</b>
Low	279	3 (1.1)	0.85 (0.47,1.51)	0.562
Medium	280	2 (0.7)		
High	277	1 (0.4)		

<sup>a</sup> Relative risk for a twofold increase in 1987 dioxin.

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

<b>(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED</b>			
<b>Analysis Results for Log<sub>2</sub> (1987 Dioxin + 1)</b>			
<b>n</b>	<b>Adjusted Relative Risk (95% C.I.)<sup>a</sup></b>		<b>p-Value</b>
833	1.09 (0.50,2.36)		0.825

<sup>a</sup> Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for race because of the sparse number of Ranch Hands with an abnormal thyroid gland.

#### 16.2.2.2.2 Testicular Examination

The unadjusted and adjusted Model 1 and 2 analyses of testicular examination were nonsignificant (Table 16-8(a–d): p>0.10 for each analysis).

**Table 16-8. Analysis of Testicular Examination**

<b>(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED</b>					
Occupational Category	Group	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)	p-Value
<i>All</i>	<i>Ranch Hand</i>	<i>861</i>	<i>39 (4.5)</i>	<i>1.20 (0.78,1.85)</i>	<i>0.409</i>
	<i>Comparison</i>	<i>1,237</i>	<i>47 (3.8)</i>		
Officer	Ranch Hand	336	16 (4.8)	0.86 (0.45,1.62)	0.635
	Comparison	490	27 (5.5)		
Enlisted Flyer	Ranch Hand	148	9 (6.1)	1.42 (0.54,3.79)	0.478
	Comparison	184	8 (4.3)		
Enlisted Groundcrew	Ranch Hand	377	14 (3.7)	1.77 (0.81,3.87)	0.152
	Comparison	563	12 (2.1)		

<b>(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED</b>		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
<i>All</i>	<i>1.20 (0.77,1.87)</i>	<i>0.427</i>
Officer	0.84 (0.44,1.62)	0.611
Enlisted Flyer	1.31 (0.48,3.55)	0.595
Enlisted Groundcrew	1.96 (0.88,4.39)	0.101

<b>(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED</b>				
Initial Dioxin Category Summary Statistics			Analysis Results for Log <sub>2</sub> (Initial Dioxin) <sup>a</sup>	
Initial Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.) <sup>b</sup>	p-Value
Low	158	10 (6.3)	0.93 (0.66,1.29)	0.653
Medium	162	8 (4.9)		
High	158	6 (3.8)		

<sup>a</sup> Adjusted for percent body fat at the time of the blood measurement of dioxin.

<sup>b</sup> Relative risk for a twofold increase in initial dioxin.

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

<b>(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED</b>		
Analysis Results for Log <sub>2</sub> (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.) <sup>a</sup>	p-Value
477	1.08 (0.72,1.61)	0.714

<sup>a</sup> Relative risk for a twofold increase in initial dioxin.

**Table 16-8. Analysis of Testicular Examination (Continued)**

<b>(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED</b>				
<b>Dioxin Category</b>	<b>n</b>	<b>Number (%) Abnormal</b>	<b>Est. Relative Risk (95% C.I.)<sup>ab</sup></b>	<b>p-Value</b>
Comparison	1,199	47 (3.9)		
Background RH	376	14 (3.7)	0.89 (0.49,1.65)	0.722
Low RH	237	15 (6.3)	1.68 (0.92,3.06)	0.091
High RH	241	9 (3.7)	1.00 (0.48,2.07)	0.994
Low plus High RH	478	24 (5.0)	1.29 (0.77,2.16)	0.333

<sup>a</sup> Relative risk and confidence interval relative to Comparisons.

<sup>b</sup> 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.

<b>(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED</b>			
<b>Dioxin Category</b>	<b>n</b>	<b>Adjusted Relative Risk (95% C.I.)<sup>a</sup></b>	<b>p-Value</b>
Comparison	1,199		
Background RH	374	0.84 (0.45,1.58)	0.594
Low RH	237	1.46 (0.78,2.71)	0.236
High RH	240	1.39 (0.63,3.03)	0.415
Low plus High RH	477	1.42 (0.82,2.45)	0.207

<sup>a</sup> 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.

<b>(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED</b>				
<b>1987 Dioxin Category Summary Statistics</b>			<b>Analysis Results for Log<sub>2</sub> (1987 Dioxin + 1)</b>	
<b>1987 Dioxin</b>	<b>n</b>	<b>Number (%) Abnormal</b>	<b>Estimated Relative Risk (95% C.I.)<sup>a</sup></b>	<b>p-Value</b>
Low	284	9 (3.2)	1.01 (0.81,1.26)	0.903
Medium	284	17 (6.0)		
High	286	12 (4.2)		

<sup>a</sup> 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 16-8. Analysis of Testicular Examination (Continued)**

<b>(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED</b>		
Analysis Results for Log <sub>2</sub> (1987 Dioxin + 1)		
n	Adjusted Relative Risk (95% C.I.) <sup>a</sup>	p-Value
851	1.09 (0.82,1.44)	0.545

<sup>a</sup> Relative risk for a twofold increase in 1987 dioxin.

The unadjusted Model 3 analysis revealed a marginally significant difference in the percentage of abnormal testicular examination results between Ranch Hands in the low dioxin category and Comparisons (Table 16-8(e): Est. RR=1.68, p=0.091). The percentage of participants with abnormal testicular examination results for Ranch Hands in the low dioxin category was 6.3 versus 3.9 percent for the Comparisons. After covariate adjustment, the results were not significant (Table 16-8(f): p>0.20 for each contrast).

The unadjusted and adjusted Model 4 analyses of testicular examination were not significant (Table 16-8(g,h): p>0.54 for each analysis).

### 16.2.2.3 Laboratory Examination Variables

#### 16.2.2.3.1 TSH (Continuous)

The unadjusted Model 1 analysis of TSH in its continuous form did not reveal any significant mean differences between Ranch Hands and Comparisons across all occupations or within each occupational stratum (Table 16-9(a): p≥0.13 for each contrast). The adjusted analysis showed no significant overall group difference between Ranch Hands and Comparisons (Table 16-9(b): p=0.105). Stratifying the adjusted analysis by occupation revealed a marginally significant difference between Ranch Hands and Comparisons in the enlisted groundcrew stratum (Table 16-9(b): difference of adjusted means=0.11 μIU/ml, p=0.088). The adjusted mean TSH level for Ranch Hand enlisted groundcrew was 1.71 μIU/ml versus 1.60 μIU/ml for Comparison enlisted groundcrew.

**Table 16-9. Analysis of TSH (μIU/ml) (Continuous)**

<b>(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED</b>					
Occupational Category	Group	n	Mean <sup>a</sup>	Difference of Means (95% C.I.) <sup>b</sup>	p-Value <sup>c</sup>
<i>All</i>	<i>Ranch Hand</i>	<i>841</i>	<i>1.88</i>	<i>0.08 --</i>	<i>0.130</i>
	<i>Comparison</i>	<i>1,199</i>	<i>1.81</i>		
Officer	Ranch Hand	326	2.01	0.12 --	0.170
	Comparison	468	1.89		
Enlisted Flyer	Ranch Hand	144	1.72	-0.10 --	0.428
	Comparison	182	1.82		
Enlisted Groundcrew	Ranch Hand	371	1.84	0.11 --	0.139
	Comparison	549	1.73		

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

<sup>c</sup> P-value is based on difference of means on natural logarithm scale.

**Table 16-9. Analysis of TSH ( $\mu\text{IU/ml}$ ) (Continuous)**

<b>(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED</b>					
Occupational Category	Group	n	Adjusted Mean <sup>a</sup>	Difference of Adj. Means (95% C.I.) <sup>b</sup>	p-Value <sup>c</sup>
<i>All</i>	<i>Ranch Hand</i>	838	1.64	0.07 --	0.105
	<i>Comparison</i>	1,199	1.57		
Officer	Ranch Hand	325	1.69	0.10 --	0.178
	Comparison	468	1.59		
Enlisted Flyer	Ranch Hand	143	1.48	-0.09 --	0.370
	Comparison	182	1.58		
Enlisted Groundcrew	Ranch Hand	370	1.71	0.11 --	0.088
	Comparison	549	1.60		

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

<sup>c</sup> P-value is based on difference of means on natural logarithm scale.

<b>(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED</b>				<b>Analysis Results for Log<sub>2</sub> (Initial Dioxin)<sup>b</sup></b>		
<b>Initial Dioxin Category Summary Statistics</b>				<b>R<sup>2</sup></b>	<b>Slope (Std. Error)<sup>c</sup></b>	<b>p-Value</b>
<b>Initial Dioxin</b>	<b>n</b>	<b>Mean<sup>a</sup></b>	<b>Adj. Mean<sup>ab</sup></b>			
Low	157	1.94	1.94	0.002	-0.015 (0.021)	0.475
Medium	158	1.85	1.85			
High	152	1.78	1.78			

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Adjusted for percent body fat at the time of the blood measurement of dioxin.

<sup>c</sup> Slope and standard error based on natural logarithm of TSH versus log<sub>2</sub> (initial dioxin).

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

<b>(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED</b>				<b>Analysis Results for Log<sub>2</sub> (Initial Dioxin)</b>		
<b>Initial Dioxin Category Summary Statistics</b>			<b>R<sup>2</sup></b>	<b>Adj. Slope (Std. Error)<sup>b</sup></b>	<b>p-Value</b>	
<b>Initial Dioxin</b>	<b>n</b>	<b>Adj. Mean<sup>a</sup></b>				
Low	157	1.53	0.071	-0.019 (0.024)	0.433	
Medium	157	1.45				
High	152	1.39				

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Slope and standard error based on natural logarithm of TSH versus log<sub>2</sub> (initial dioxin).

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

**Table 16-9. Analysis of TSH ( $\mu\text{IU/ml}$ ) (Continuous)**

<b>(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED</b>					
Dioxin Category	n	Mean <sup>a</sup>	Adj. Mean <sup>ab</sup>	Difference of Adj. Mean vs. Comparisons (95% C.I.) <sup>c</sup>	p-Value <sup>d</sup>
Comparison	1,161	1.80	1.80		
Background RH	367	1.90	1.91	0.11 --	0.129
Low RH	233	1.90	1.89	0.09 --	0.273
High RH	234	1.82	1.81	0.01 --	0.942
Low plus High RH	467	1.86	1.85	0.05 --	0.446

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Adjusted for percent body fat at the time of the blood measurement of dioxin.

<sup>c</sup> Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

<sup>d</sup> P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin  $\leq$  10 ppt.

Background (Ranch Hand): 1987 Dioxin  $\leq$  10 ppt.

Low (Ranch Hand): 1987 Dioxin  $>$  10 ppt, 10 ppt  $<$  Initial Dioxin  $\leq$  94 ppt.

High (Ranch Hand): 1987 Dioxin  $>$  10 ppt, Initial Dioxin  $>$  94 ppt.

<b>(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED</b>				
Dioxin Category	n	Adj. Mean <sup>a</sup>	Difference of Adj. Mean vs. Comparisons (95% C.I.) <sup>b</sup>	p-Value <sup>c</sup>
Comparison	1,161	1.57		
Background RH	365	1.64	0.07 --	0.250
Low RH	233	1.64	0.07 --	0.292
High RH	233	1.62	0.05 --	0.454
Low plus High RH	466	1.63	0.06 --	0.237

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

<sup>c</sup> P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin  $\leq$  10 ppt.

Background (Ranch Hand): 1987 Dioxin  $\leq$  10 ppt.

Low (Ranch Hand): 1987 Dioxin  $>$  10 ppt, 10 ppt  $<$  Initial Dioxin  $\leq$  94 ppt.

High (Ranch Hand): 1987 Dioxin  $>$  10 ppt, Initial Dioxin  $>$  94 ppt.

**Table 16-9. Analysis of TSH ( $\mu\text{IU/ml}$ ) (Continuous)**

<b>(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED</b>					
1987 Dioxin Category Summary Statistics			Analysis Results for $\text{Log}_2$ (1987 Dioxin + 1)		
1987 Dioxin	n	Mean <sup>a</sup>	R <sup>2</sup>	Adjusted Slope (Std. Error) <sup>b</sup>	p-Value
Low	278	1.88	<0.001	-0.000 (0.015)	0.977
Medium	279	1.98			
High	277	1.77			

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Slope and standard error based on natural logarithm of TSH versus  $\text{log}_2$  (1987 dioxin + 1).

Note: Low =  $\leq 7.9$  ppt; Medium =  $> 7.9$ – $19.6$  ppt; High =  $> 19.6$  ppt.

<b>(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED</b>					
1987 Dioxin Category Summary Statistics			Analysis Results for $\text{Log}_2$ (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean <sup>a</sup>	R <sup>2</sup>	Adjusted Slope (Std. Error) <sup>b</sup>	p-Value
Low	276	1.53	0.046	0.008 (0.017)	0.624
Medium	279	1.62			
High	276	1.48			

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Slope and standard error based on natural logarithm of TSH versus  $\text{log}_2$  (1987 dioxin + 1).

Note: Low =  $\leq 7.9$  ppt; Medium =  $> 7.9$ – $19.6$  ppt; High =  $> 19.6$  ppt.

Unadjusted and adjusted analyses for Models 2, 3, and 4 showed no significant relations between TSH in its continuous form and dioxin (Table 16-9(c–h):  $p > 0.12$  for each analysis).

#### 16.2.2.3.2 TSH (Discrete)

The unadjusted and adjusted Model 1 analyses of TSH in its discrete form did not reveal significant differences across all occupations (Table 16-10(a,b):  $p \geq 0.14$  for each analysis). After stratifying by occupation, both the unadjusted and adjusted analyses revealed significant differences in the percentage of abnormal high TSH values between Ranch Hand and Comparison enlisted groundcrew (Table 16-10(a,b): Est. RR=2.06,  $p=0.044$ ; Adj. RR=2.11,  $p=0.037$ , respectively). Of the Ranch Hand enlisted groundcrew, 5.1 percent had abnormally high TSH values versus 2.6 percent of the Comparison enlisted groundcrew.

Unadjusted and adjusted analyses in Models 2, 3, and 4 did not show significant associations between dioxin and TSH in its discrete form (Table 16-10(c–h):  $p > 0.12$  for each analysis).

**Table 16-10. Analysis of TSH (Discrete)**

<b>(a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED</b>									
Occupational Category	Group	n	Number (%)			Abnormal Low vs. Normal		Abnormal High vs. Normal	
			Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)	p-Value	Est. Relative Risk (95% C.I.)	p-Value
<i>All</i>	<i>Ranch Hand Comparison</i>	<i>841</i> <i>1,199</i>	<i>10 (1.2)</i> <i>9 (0.8)</i>	<i>795 (94.5)</i> <i>1,153 (96.2)</i>	<i>36 (4.3)</i> <i>37 (3.1)</i>	<i>1.61 (0.65,3.98)</i>	<i>0.301</i>	<i>1.41 (0.88,2.25)</i>	<i>0.149</i>
Officer	Ranch Hand Comparison	326 468	4 (1.2) 2 (0.4)	308 (94.5) 449 (95.9)	14 (4.3) 17 (3.6)	2.92 (0.53,16.01)	0.218	1.20 (0.58,2.47)	0.620
Enlisted Flyer	Ranch Hand Comparison	144 182	3 (2.1) 2 (1.1)	138 (95.8) 174 (95.6)	3 (2.1) 6 (3.3)	1.89 (0.31,11.48)	0.488	0.63 (0.15,2.57)	0.519
Enlisted Groundcrew	Ranch Hand Comparison	371 549	3 (0.8) 5 (0.9)	349 (94.1) 530 (96.5)	19 (5.1) 14 (2.6)	0.91 (0.22,3.84)	0.899	2.06 (1.02,4.16)	0.044

  

<b>(b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED</b>				
Occupational Category	Abnormal Low vs. Normal		Abnormal High vs. Normal	
	Adj. Relative Risk (95% C.I.)	p-Value	Adj. Relative Risk (95% C.I.)	p-Value
<i>All</i>	<i>1.57 (0.63,3.88)</i>	<i>0.332</i>	<i>1.42 (0.89,2.28)</i>	<i>0.140</i>
Officer	2.78 (0.50,15.33)	0.241	1.18 (0.57,2.44)	0.648
Enlisted Flyer	2.01 (0.33,12.28)	0.448	0.63 (0.15,2.55)	0.513
Enlisted Groundcrew	0.88 (0.21,3.71)	0.859	2.11 (1.04,4.28)	0.037

**Table 16-10. Analysis of TSH (Discrete) (Continued)**

<b>(c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED</b>								
<b>Initial Dioxin Category Summary Statistics</b>				<b>Analysis Results for Log<sub>2</sub> (Initial Dioxin)<sup>a</sup></b>				
<b>Initial Dioxin Category</b>	<b>n</b>	<b>Number (%)</b>			<b>Abnormal Low vs. Normal</b>		<b>Abnormal High vs. Normal</b>	
		<b>Abnormal Low</b>	<b>Normal</b>	<b>Abnormal High</b>	<b>Est. Relative Risk (95% C.I.)<sup>b</sup></b>	<b>p-Value</b>	<b>Est. Relative Risk (95% C.I.)<sup>b</sup></b>	<b>p-Value</b>
Low	157	1 (0.6)	150 (95.5)	6 (3.8)	1.40 (0.73,2.71)	0.311	1.27 (0.89,1.79)	0.183
Medium	158	0 (0.0)	154 (97.5)	4 (2.5)				
High	152	3 (2.0)	142 (93.4)	7 (4.6)				

<sup>a</sup> Adjusted for percent body fat at the time of the blood measurement of dioxin.

<sup>b</sup> Relative risk for a twofold increase in initial dioxin.

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

<b>(d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED</b>				
<b>Analysis Results for Log<sub>2</sub> (Initial Dioxin)</b>				
<b>n</b>	<b>Abnormal Low vs. Normal</b>		<b>Abnormal High vs. Normal</b>	
	<b>Adj. Relative Risk (95% C.I.)<sup>a</sup></b>	<b>p-Value</b>	<b>Adj. Relative Risk (95% C.I.)<sup>a</sup></b>	<b>p-Value</b>
467	1.62 (0.82,3.20)	0.161	1.29 (0.90,1.85)	0.169

<sup>a</sup> Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for occupation and personality type because of the sparse number of Ranch Hands with an abnormally low TSH level.

**Table 16-10. Analysis of TSH (Discrete) (Continued)**

<b>(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED</b>								
<b>Dioxin Category</b>	<b>n</b>	<b>Number (%)</b>			<b>Abnormal Low vs. Normal</b>		<b>Abnormal High vs. Normal</b>	
		<b>Abnormal Low</b>	<b>Normal</b>	<b>Abnormal High</b>	<b>Est. Relative Risk (95% C.I.)<sup>ab</sup></b>	<b>p-Value</b>	<b>Est. Relative Risk (95% C.I.)<sup>ab</sup></b>	<b>p-Value</b>
Comparison	1,161	9 (0.8)	1,116 (96.1)	36 (3.1)				
Background RH	367	6 (1.6)	344 (93.7)	17 (4.6)	2.27 (0.80,6.50)	0.125	1.46 (0.80,2.64)	0.214
Low RH	233	1 (0.4)	225 (96.6)	7 (3.0)	0.54 (0.07,4.31)	0.564	0.97 (0.43,2.22)	0.951
High RH	234	3 (1.3)	221 (94.4)	10 (4.3)	1.60 (0.43,6.02)	0.485	1.47 (0.72,3.02)	0.294
Low plus High RH	467	4 (0.9)	446 (95.5)	17 (3.6)	0.93 (0.25,3.48)	0.919	1.20 (0.66,2.17)	0.553

<sup>a</sup> Relative risk and confidence interval relative to Comparisons.

<sup>b</sup> 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 16-10. Analysis of TSH (Discrete) (Continued)**

<b>(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED</b>					
Dioxin Category	n	Abnormal Low vs. Normal		Abnormal High vs. Normal	
		Adj. Relative Risk (95% C.I.) <sup>a</sup>	p-Value	Adj. Relative Risk (95% C.I.) <sup>a</sup>	p-Value
Comparison	1,161				
Background RH	365	2.33 (0.79,6.87)	0.125	1.43 (0.78,2.62)	0.244
Low RH	233	0.52 (0.06,4.15)	0.536	0.98 (0.43,2.24)	0.963
High RH	233	1.51 (0.39,5.91)	0.550	1.58 (0.74,3.35)	0.236
Low plus High RH	466	0.89 (0.24,3.33)	0.858	1.24 (0.68,2.28)	0.481

<sup>a</sup> 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.

<b>(g) MODEL 4: RANCH HANDS — 1987 DIOXIN — UNADJUSTED</b>								
1987 Dioxin Category Summary Statistics					Analysis Results for Log <sub>2</sub> (1987 Dioxin + 1)			
1987 Dioxin Category	n	Number (%)			Abnormal Low vs. Normal		Abnormal High vs. Normal	
		Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.) <sup>a</sup>	p-Value	Est. Relative Risk (95% C.I.) <sup>a</sup>	p-Value
Low	278	4 (1.4)	260 (93.5)	14 (5.0)	0.97 (0.63,1.48)	0.881	0.98 (0.78,1.24)	0.894
Medium	279	3 (1.1)	266 (95.3)	10 (3.6)				
High	277	3 (1.1)	264 (95.3)	10 (3.6)				

<sup>a</sup> 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 16-10. Analysis of TSH (Discrete) (Continued)**

<b>(h) MODEL 4: RANCH HANDS — 1987 DIOXIN — ADJUSTED</b>				
<b>Analysis Results for Log<sub>2</sub> (1987 Dioxin + 1)</b>				
<b>Abnormal Low vs. Normal</b>			<b>Abnormal High vs. Normal</b>	
<b>n</b>	<b>Adj. Relative Risk (95% C.I.)<sup>a</sup></b>	<b>p-Value</b>	<b>Adj. Relative Risk (95% C.I.)<sup>a</sup></b>	<b>p-Value</b>
831	1.08 (0.64,1.83)	0.767	0.97 (0.74,1.27)	0.832

<sup>a</sup> Relative risk for a twofold increase in 1987 dioxin.

16.2.2.3.3 Thyroxine (Continuous)

The unadjusted and adjusted Models 1 and 2 analyses of thyroxine in its continuous form were not significant (Table 16-11(a,b):  $p > 0.12$  for each analysis).

**Table 16-11. Analysis of Thyroxine (µg/dl) (Continuous)**

<b>(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED</b>					
Occupational Category	Group	n	Mean <sup>a</sup>	Difference of Means (95% C.I.) <sup>b</sup>	p-Value <sup>c</sup>
<i>All</i>	<i>Ranch Hand</i>	<i>841</i>	<i>7.07</i>	<i>0.03 --</i>	<i>0.601</i>
	<i>Comparison</i>	<i>1,199</i>	<i>7.04</i>		
Officer	Ranch Hand	326	6.76	-0.08 --	0.373
	Comparison	468	6.84		
Enlisted Flyer	Ranch Hand	144	7.28	0.03 --	0.818
	Comparison	182	7.24		
Enlisted Groundcrew	Ranch Hand	371	7.27	0.12 --	0.154
	Comparison	549	7.15		

<sup>a</sup> Transformed from square root scale.

<sup>b</sup> Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.

<sup>c</sup> P-value is based on difference of means on square root scale.

<b>(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED</b>					
Occupational Category	Group	n	Adjusted Mean <sup>a</sup>	Difference of Adj. Means (95% C.I.) <sup>b</sup>	p-Value <sup>c</sup>
<i>All</i>	<i>Ranch Hand</i>	<i>838</i>	<i>6.96</i>	<i>0.03 --</i>	<i>0.565</i>
	<i>Comparison</i>	<i>1,199</i>	<i>6.93</i>		
Officer	Ranch Hand	325	6.58	-0.08 --	0.370
	Comparison	468	6.66		
Enlisted Flyer	Ranch Hand	143	7.12	0.04 --	0.774
	Comparison	182	7.08		
Enlisted Groundcrew	Ranch Hand	370	7.19	0.13 --	0.129
	Comparison	549	7.06		

<sup>a</sup> Transformed from square root scale.

<sup>b</sup> Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.

<sup>c</sup> P-value is based on difference of means on square root scale.

**Table 16-11. Analysis of Thyroxine ( $\mu\text{g/dl}$ ) (Continuous) (Continued)**

<b>(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED</b>						
Initial Dioxin Category Summary Statistics				Analysis Results for $\text{Log}_2$ (Initial Dioxin) <sup>b</sup>		
Initial Dioxin	n	Mean <sup>a</sup>	Adj. Mean <sup>ab</sup>	R <sup>2</sup>	Slope (Std. Error) <sup>c</sup>	p-Value
Low	157	7.11	7.12	0.012	0.010 (0.008)	0.250
Medium	158	7.15	7.16			
High	152	7.28	7.26			

<sup>a</sup> Transformed from square root scale.

<sup>b</sup> Adjusted for percent body fat at the time of the blood measurement of dioxin.

<sup>c</sup> Slope and standard error based on square root of thyroxine versus  $\text{log}_2$  (initial dioxin).

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

<b>(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED</b>						
Initial Dioxin Category Summary Statistics				Analysis Results for $\text{Log}_2$ (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean <sup>a</sup>		R <sup>2</sup>	Adj. Slope (Std. Error) <sup>b</sup>	p-Value
Low	157	6.99		0.045	–0.004 (0.010)	0.682
Medium	157	6.89				
High	152	6.89				

<sup>a</sup> Transformed from square root scale.

<sup>b</sup> Slope and standard error based on square root of thyroxine versus  $\text{log}_2$  (initial dioxin).

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

<b>(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED</b>						
Dioxin Category	n	Mean <sup>a</sup>	Adj. Mean <sup>ab</sup>	Difference of Adj. Mean vs. Comparisons (95% C.I.) <sup>c</sup>		p-Value <sup>d</sup>
Comparison	1,161	7.04	7.04			
Background RH	367	6.95	6.95	–0.09	--	0.221
Low RH	233	7.13	7.13	0.09	--	0.344
High RH	234	7.23	7.23	0.19	--	0.053
Low plus High RH	467	7.18	7.18	0.14	--	0.059

<sup>a</sup> Transformed from square root scale.

<sup>b</sup> Adjusted for percent body fat at the time of the blood measurement of dioxin.

<sup>c</sup> Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.

<sup>d</sup> P-value is based on difference of means on square root scale.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin  $\leq$  10 ppt.

Background (Ranch Hand): 1987 Dioxin  $\leq$  10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin  $\leq$  94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

**Table 16-11. Analysis of Thyroxine ( $\mu\text{g/dl}$ ) (Continuous) (Continued)**

<b>(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED</b>				
Dioxin Category	n	Adj. Mean <sup>a</sup>	Difference of Adj. Mean vs. Comparisons (95% C.I.) <sup>b</sup>	p-Value <sup>c</sup>
Comparison	1,161	6.93		
Background RH	365	6.93	0.00 --	0.969
Low RH	233	7.02	0.09 --	0.344
High RH	233	6.98	0.05 --	0.646
Low plus High RH	466	7.00	0.07 --	0.357

<sup>a</sup> Transformed from square root scale.

<sup>b</sup> Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.

<sup>c</sup> P-value is based on difference of means on square root scale.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin  $\leq$  10 ppt.

Background (Ranch Hand): 1987 Dioxin  $\leq$  10 ppt.

Low (Ranch Hand): 1987 Dioxin  $>$  10 ppt, 10 ppt  $<$  Initial Dioxin  $\leq$  94 ppt.

High (Ranch Hand): 1987 Dioxin  $>$  10 ppt, Initial Dioxin  $>$  94 ppt.

<b>(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED</b>					
1987 Dioxin Category Summary Statistics			Analysis Results for $\text{Log}_2$ (1987 Dioxin + 1)		
1987 Dioxin	n	Mean <sup>a</sup>	R <sup>2</sup>	Slope (Std. Error) <sup>b</sup>	p-Value
Low	278	6.95	0.008	0.015 (0.006)	0.009
Medium	279	7.03			
High	277	7.25			

<sup>a</sup> Transformed from square root scale.

<sup>b</sup> Slope and standard error based on square root of thyroxine versus  $\text{log}_2$  (1987 dioxin + 1).

Note: Low =  $\leq$ 7.9 ppt; Medium =  $>$ 7.9–19.6 ppt; High =  $>$ 19.6 ppt.

<b>(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED</b>					
1987 Dioxin Category Summary Statistics			Analysis Results for $\text{Log}_2$ (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean <sup>a</sup>	R <sup>2</sup>	Adjusted Slope (Std. Error) <sup>b</sup>	p-Value
Low	276	6.92	0.047	-0.001 (0.007)	0.862
Medium	279	6.91			
High	276	6.91			

<sup>a</sup> Transformed from square root scale.

<sup>b</sup> Slope and standard error based on square root of thyroxine versus  $\text{log}_2$  (1987 dioxin + 1).

Note: Low =  $\leq$ 7.9 ppt; Medium =  $>$ 7.9–19.6 ppt; High =  $>$ 19.6 ppt.

The unadjusted Model 3 analysis of thyroxine in its continuous form revealed two marginally significant contrasts: Ranch Hands in the high dioxin category versus Comparisons and Ranch Hands in the low plus high dioxin category versus Comparisons (Table 16-11(e): difference of means=0.19 µg/dl, p=0.053; difference of means=0.14 µg/dl, p=0.059, respectively). The adjusted analysis did not reveal any significant contrasts (Table 16-11(f): p>0.34 for each contrast).

The Model 4 unadjusted analysis revealed a significant positive association between thyroxine and 1987 dioxin (Table 16-11(g): adjusted slope=0.015, p=0.009). After covariate adjustment, the results became nonsignificant (Table 16-11(h): p=0.862).

#### 16.2.2.3.4 Thyroxine (Discrete)

All unadjusted and adjusted analyses for Models 1 through 4 showed no significant relations between dioxin and thyroxine in its discrete form (Table 16-12(a-h): p>0.14 for each analysis).

**Table 16-12. Analysis of Thyroxine (Discrete)**

<b>(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED</b>					
Occupational Category	Group	n	Number (%) Low	Est. Relative Risk (95% C.I.)	p-Value
<i>All</i>	<i>Ranch Hand</i>	841	23 (2.7)	<i>1.03 (0.60,1.77)</i>	<i>0.928</i>
	<i>Comparison</i>	1,199	32 (2.7)		
Officer	Ranch Hand	326	13 (4.0)	1.17 (0.56,2.47)	0.674
	Comparison	468	16 (3.4)		
Enlisted Flyer	Ranch Hand	144	3 (2.1)	1.27 (0.25,6.39)	0.772
	Comparison	182	3 (1.6)		
Enlisted Groundcrew	Ranch Hand	371	7 (1.9)	0.79 (0.31,2.01)	0.624
	Comparison	549	13 (2.4)		

  

<b>(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED</b>			
Occupational Category	Adjusted Relative Risk (95% C.I.)		p-Value
<i>All</i>	<i>1.04 (0.61,1.80)</i>		<i>0.875</i>
Officer	1.21 (0.57,2.55)		0.622
Enlisted Flyer	1.24 (0.25,6.24)		0.796
Enlisted Groundcrew	0.80 (0.32,2.02)		0.636

  

<b>(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED</b>				
Initial Dioxin Category Summary Statistics			Analysis Results for Log <sub>2</sub> (Initial Dioxin) <sup>a</sup>	
Initial Dioxin	n	Number (%) Low	Estimated Relative Risk (95% C.I.) <sup>b</sup>	p-Value
Low	157	3 (1.9)	1.22 (0.79,1.89)	0.375
Medium	158	1 (0.6)		
High	152	6 (3.9)		

<sup>a</sup> Adjusted for percent body fat at the time of the blood measurement of dioxin.

<sup>b</sup> Relative risk for a twofold increase in initial dioxin.

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

**Table 16-12. Analysis of Thyroxine (Discrete) (Continued)**

<b>(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED</b>		
Analysis Results for Log <sub>2</sub> (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.) <sup>a</sup>	p-Value
466	1.51 (0.87,2.62)	0.143

<sup>a</sup> Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race because of the sparse number of Ranch Hands with a low thyroxine level.

<b>(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED</b>				
Dioxin Category	n	Number (%) Low	Est. Relative Risk (95% C.I.) <sup>ab</sup>	p-Value
Comparison	1,161	31 (2.7)		
Background RH	367	13 (3.5)	1.40 (0.72,2.71)	0.325
Low RH	233	3 (1.3)	0.47 (0.14,1.55)	0.215
High RH	234	7 (3.0)	1.08 (0.47,2.49)	0.858
Low plus High RH	467	10 (2.1)	0.71 (0.33,1.54)	0.390

<sup>a</sup> Relative risk and confidence interval relative to Comparisons.

<sup>b</sup> 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.

<b>(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED</b>			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.) <sup>a</sup>	p-Value
Comparison	1,161		
Background RH	365	1.23 (0.63,2.42)	0.545
Low RH	233	0.45 (0.14,1.49)	0.192
High RH	233	1.53 (0.62,3.73)	0.354
Low plus High RH	466	0.83 (0.38,1.82)	0.641

<sup>a</sup> 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 16-12. Analysis of Thyroxine (Discrete) (Continued)**

<b>(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED</b>					
1987 Dioxin Category Summary Statistics			Analysis Results for Log <sub>2</sub> (1987 Dioxin + 1)		
1987 Dioxin	n	Number (%) Low	Estimated Relative Risk (95% C.I.) <sup>a</sup>		p-Value
Low	278	8 (2.9)	0.97 (0.73,1.29)		0.825
Medium	279	8 (2.9)			
High	277	7 (2.5)			

<sup>a</sup> Relative risk for a twofold increase in 1987 dioxin.

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

<b>(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED</b>			
Analysis Results for Log <sub>2</sub> (1987 Dioxin + 1)			
n	Adjusted Relative Risk (95% C.I.) <sup>a</sup>		p-Value
831	1.14 (0.79,1.64)		0.487

<sup>a</sup> Relative risk for a twofold increase in 1987 dioxin.

#### 16.2.2.3.5 Anti-Thyroid Antibodies

All unadjusted and adjusted analyses for Models 1 through 4 were nonsignificant (Table 16-13(a–h): p>0.43 for each analysis).

**Table 16-13. Analysis of Anti-Thyroid Antibodies**

<b>(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED</b>					
Occupational Category	Group	n	Number (%) Present	Est. Relative Risk (95% C.I.)	p-Value
<i>All</i>	<i>Ranch Hand</i>	<i>841</i>	<i>5 (0.6)</i>	<i>1.02 (0.32,3.22)</i>	<i>0.975</i>
	<i>Comparison</i>	<i>1,199</i>	<i>7 (0.6)</i>		
Officer	Ranch Hand	326	2 (0.6)	0.72 (0.13,3.93)	0.701
	Comparison	468	4 (0.9)		
Enlisted Flyer	Ranch Hand	144	2 (1.4)	2.55 (0.23,28.40)	0.447
	Comparison	182	1 (0.5)		
Enlisted Groundcrew	Ranch Hand	371	1 (0.3)	0.74 (0.07,8.18)	0.805
	Comparison	549	2 (0.4)		

**Table 16-13. Analysis of Anti-Thyroid Antibodies (Continued)**

<b>(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED</b>		
<b>Occupational Category</b>	<b>Adjusted Relative Risk (95% C.I.)</b>	<b>p-Value</b>
<i>All</i>	<i>1.01 (0.32,3.21)</i>	<i>0.981</i>
Officer	0.73 (0.13,4.02)	0.717
Enlisted Flyer	2.62 (0.24,29.23)	0.434
Enlisted Groundcrew	0.73 (0.07,8.06)	0.796

Note: Results are not adjusted for race because of the sparse number of participants with anti-thyroid antibodies present.

<b>(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED</b>				
<b>Initial Dioxin Category Summary Statistics</b>			<b>Analysis Results for Log<sub>2</sub> (Initial Dioxin)<sup>a</sup></b>	
<b>Initial Dioxin</b>	<b>n</b>	<b>Number (%) Present</b>	<b>Estimated Relative Risk (95% C.I.)<sup>b</sup></b>	<b>p-Value</b>
Low	157	0 (0.0)	0.93 (0.30,2.89)	0.905
Medium	158	2 (1.3)		
High	152	0 (0.0)		

<sup>a</sup> Adjusted for percent body fat at the time of the blood measurement of dioxin.

<sup>b</sup> Relative risk for a twofold increase in initial dioxin.

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

<b>(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED</b>			
<b>Analysis Results for Log<sub>2</sub> (Initial Dioxin)</b>			
<b>n</b>	<b>Adjusted Relative Risk (95% C.I.)<sup>a</sup></b>		<b>p-Value</b>
466	1.01 (0.31,3.23)		0.990

<sup>a</sup> Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race and occupation because of the sparse number of Ranch Hands with anti-thyroid antibodies present.

<b>(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED</b>				
<b>Dioxin Category</b>	<b>n</b>	<b>Number (%) Present</b>	<b>Est. Relative Risk (95% C.I.)<sup>ab</sup></b>	<b>p-Value</b>
Comparison	1,161	7 (0.6)		
Background RH	367	3 (0.8)	1.20 (0.30,4.69)	0.798
Low RH	233	1 (0.4)	0.73 (0.09,5.96)	0.768
High RH	234	1 (0.4)	0.80 (0.10,6.56)	0.834
Low plus High RH	467	2 (0.4)	0.76 (0.16,3.70)	0.736

<sup>a</sup> Relative risk and confidence interval relative to Comparisons.

<sup>b</sup> 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 16-13. Analysis of Anti-Thyroid Antibodies (Continued)**

<b>(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED</b>			
<b>Dioxin Category</b>	<b>n</b>	<b>Adjusted Relative Risk (95% C.I.)<sup>a</sup></b>	<b>p-Value</b>
Comparison	1,161		
Background RH	365	1.07 (0.27,4.26)	0.921
Low RH	233	0.73 (0.09,5.99)	0.765
High RH	233	1.07 (0.12,9.66)	0.951
Low plus High RH	466	0.88 (0.17,4.46)	0.879

<sup>a</sup> 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.

Results are not adjusted for race because of the sparse number of participants with anti-thyroid antibodies present.

<b>(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED</b>				
<b>1987 Dioxin Category Summary Statistics</b>			<b>Analysis Results for Log<sub>2</sub> (1987 Dioxin + 1)</b>	
<b>1987 Dioxin</b>	<b>n</b>	<b>Number (%) Present</b>	<b>Estimated Relative Risk (95% C.I.)<sup>a</sup></b>	<b>p-Value</b>
Low	278	2 (0.7)	0.82 (0.43,1.55)	0.535
Medium	279	2 (0.7)		
High	277	1 (0.4)		

<sup>a</sup> Relative risk for a twofold increase in 1987 dioxin.

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

<b>(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED</b>			
<b>Analysis Results for Log<sub>2</sub> (1987 Dioxin + 1)</b>			
<b>n</b>	<b>Adjusted Relative Risk (95% C.I.)<sup>a</sup></b>		<b>p-Value</b>
831	0.86 (0.41,1.80)		0.689

<sup>a</sup> Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for race because of the sparse number of Ranch Hands with anti-thyroid antibodies present.

#### 16.2.2.3.6 Fasting Glucose (Continuous)

The unadjusted and adjusted Model 1 analyses did not reveal a significant difference in mean fasting glucose levels between all Ranch Hands and Comparisons or after stratifying by occupation (Table 16-14(a,b): p>0.38 for each analysis).

Fasting glucose in its continuous form was not significantly associated with initial dioxin in the unadjusted Model 2 analysis (Table 16-14(c):  $p=0.174$ ). After adjusting for covariates, the results became significant (Table 16-14(d): adjusted slope=0.023,  $p=0.014$ ). The adjusted mean fasting glucose levels in the low, medium, and high initial dioxin categories were 104.5 mg/dl, 109.2 mg/dl, and 109.5 mg/dl, respectively.

The unadjusted and adjusted Model 3 analyses of fasting glucose showed no significant mean differences between any of the Ranch Hand dioxin categories and Comparisons (Table 16-14(e,f):  $p>0.10$  for each contrast).

**Table 16-14. Analysis of Fasting Glucose (mg/dl) (Continuous)**

<b>(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED</b>					
Occupational Category	Group	n	Mean <sup>a</sup>	Difference of Means (95% C.I.) <sup>b</sup>	p-Value <sup>c</sup>
<i>All</i>	<i>Ranch Hand</i>	<i>868</i>	<i>101.4</i>	-0.3 --	<i>0.745</i>
	<i>Comparison</i>	<i>1,250</i>	<i>101.8</i>		
Officer	Ranch Hand	339	101.1	1.1 --	0.468
	Comparison	494	100.0		
Enlisted Flyer	Ranch Hand	151	103.2	-1.7 --	0.507
	Comparison	187	104.9		
Enlisted Groundcrew	Ranch Hand	378	101.0	-1.3 --	0.388
	Comparison	569	102.3		

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

<sup>c</sup> P-value is based on difference of means on natural logarithm scale.

<b>(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED</b>					
Occupational Category	Group	n	Adjusted Mean <sup>a</sup>	Difference of Adj. Means (95% C.I.) <sup>b</sup>	p-Value <sup>c</sup>
<i>All</i>	<i>Ranch Hand</i>	<i>859</i>	<i>103.7</i>	<i>0.0</i> --	<i>0.970</i>
	<i>Comparison</i>	<i>1,238</i>	<i>103.8</i>		
Officer	Ranch Hand	337	101.9	0.9 --	0.550
	Comparison	492	101.0		
Enlisted Flyer	Ranch Hand	148	104.1	-1.6 --	0.516
	Comparison	181	105.7		
Enlisted Groundcrew	Ranch Hand	374	104.7	-0.3 --	0.819
	Comparison	565	105.1		

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

<sup>c</sup> P-value is based on difference of means on natural logarithm scale.

**Table 16-14. Analysis of Fasting Glucose (mg/dl) (Continuous) (Continued)**

<b>(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED</b>						
Initial Dioxin Category Summary Statistics				Analysis Results for Log <sub>2</sub> (Initial Dioxin) <sup>b</sup>		
Initial Dioxin	n	Mean <sup>a</sup>	Adj. Mean <sup>ab</sup>	R <sup>2</sup>	Slope (Std. Error) <sup>c</sup>	p-Value
Low	159	101.4	102.2	0.102	0.011 (0.008)	0.174
Medium	161	104.5	104.7			
High	160	104.9	103.9			

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Adjusted for percent body fat at the time of the blood measurement of dioxin.

<sup>c</sup> Slope and standard error based on natural logarithm of fasting glucose versus log<sub>2</sub> (initial dioxin).

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

<b>(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED</b>					
Initial Dioxin Category Summary Statistics			Analysis Results for Log <sub>2</sub> (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean <sup>a</sup>	R <sup>2</sup>	Adj. Slope (Std. Error) <sup>b</sup>	p-Value
Low	158	104.5	0.160	0.023 (0.009)	0.014
Medium	157	109.2			
High	160	109.5			

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Slope and standard error based on natural logarithm of fasting glucose versus log<sub>2</sub> (initial dioxin).

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

<b>(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED</b>					
Dioxin Category	n	Mean <sup>a</sup>	Adj. Mean <sup>ab</sup>	Difference of Adj. Mean vs. Comparisons (95% C.I.) <sup>c</sup>	p-Value <sup>d</sup>
Comparison	1,212	101.7	101.6		
Background RH	381	98.4	100.3	–1.3 --	0.298
Low RH	238	101.4	100.8	–0.8 --	0.618
High RH	242	105.8	103.9	2.3 --	0.121
Low plus High RH	480	103.6	102.4	0.8 --	0.485

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Adjusted for percent body fat at the time of the blood measurement of dioxin.

<sup>c</sup> Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

<sup>d</sup> 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 16-14. Analysis of Fasting Glucose (mg/dl) (Continuous) (Continued)**

<b>(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED</b>				
Dioxin Category	n	Adj. Mean <sup>a</sup>	Difference of Adj. Mean vs. Comparisons (95% C.I.) <sup>b</sup>	p-Value <sup>c</sup>
Comparison	1,200	103.8		
Background RH	377	102.8	-1.0 --	0.418
Low RH	235	102.9	-0.9 --	0.551
High RH	240	106.3	2.5 --	0.106
Low plus High RH	475	104.6	0.8 --	0.482

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

<sup>c</sup> 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.

<b>(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED</b>					
1987 Dioxin Category Summary Statistics			Analysis Results for Log <sub>2</sub> (1987 Dioxin + 1)		
1987 Dioxin	n	Mean <sup>a</sup>	R <sup>2</sup>	Slope (Std. Error) <sup>b</sup>	p-Value
Low	288	97.8	0.019	0.020 (0.005)	<0.001
Medium	286	101.6			
High	287	104.6			

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Slope and standard error based on natural logarithm of fasting glucose versus log<sub>2</sub> (1987 dioxin + 1).

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

<b>(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED</b>					
1987 Dioxin Category Summary Statistics			Analysis Results for Log <sub>2</sub> (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean <sup>a</sup>	R <sup>2</sup>	Adjusted Slope (Std. Error) <sup>b</sup>	p-Value
Low	284	101.0	0.082	0.018 (0.006)	0.002
Medium	285	102.7			
High	283	107.2			

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Slope and standard error based on natural logarithm of fasting glucose versus log<sub>2</sub> (1987 dioxin + 1).

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

Both the unadjusted and adjusted Model 4 analyses showed significant positive associations between fasting glucose in its continuous form and 1987 dioxin (Table 16-14(g,h): slope=0.020, p<0.001, for the

unadjusted analysis; adjusted slope=0.018, p=0.002, for the adjusted analysis). The adjusted mean fasting glucose values in the low, medium, and high 1987 dioxin categories were 101.0 mg/dl, 102.7 mg/dl, and 107.2 mg/dl, respectively.

#### 16.2.2.3.7 Fasting Glucose (Discrete)

The percentage of participants with high fasting glucose levels did not significantly differ between Ranch Hands and Comparisons across all occupations or within each occupational stratum in the Model 1 analysis (Table 16-15(a,b): p>0.52 for each analysis).

**Table 16-15. Analysis of Fasting Glucose (Discrete)**

<b>(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED</b>					
Occupational Category	Group	n	Number (%) High	Est. Relative Risk (95% C.I.)	p-Value
<i>All</i>	<i>Ranch Hand</i>	868	152 (17.5)	1.04 (0.83,1.31)	0.741
	<i>Comparison</i>	1,250	212 (17.0)		
Officer	Ranch Hand	339	56 (16.5)	1.11 (0.76,1.61)	0.603
	Comparison	494	75 (15.2)		
Enlisted Flyer	Ranch Hand	151	29 (19.2)	1.00 (0.58,1.72)	0.991
	Comparison	187	36 (19.3)		
Enlisted Groundcrew	Ranch Hand	378	67 (17.7)	1.00 (0.71,1.40)	0.992
	Comparison	569	101 (17.8)		

  

<b>(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED</b>		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
<i>All</i>	1.07 (0.84,1.37)	0.562
Officer	1.11 (0.75,1.64)	0.611
Enlisted Flyer	0.90 (0.50,1.60)	0.712
Enlisted Groundcrew	1.12 (0.78,1.61)	0.526

  

<b>(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED</b>				
Initial Dioxin Category Summary Statistics			Analysis Results for Log <sub>2</sub> (Initial Dioxin) <sup>a</sup>	
Initial Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.) <sup>b</sup>	p-Value
Low	159	29 (18.2)	1.13 (0.95,1.34)	0.172
Medium	161	35 (21.7)		
High	160	38 (23.8)		

<sup>a</sup> Adjusted for percent body fat at the time of the blood measurement of dioxin.

<sup>b</sup> Relative risk for a twofold increase in initial dioxin.

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

**Table 16-15. Analysis of Fasting Glucose (Discrete) (Continued)**

<b>(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED</b>		
Analysis Results for Log <sub>2</sub> (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.) <sup>a</sup>	p-Value
475	1.31 (1.06,1.62)	0.013

<sup>a</sup> Relative risk for a twofold increase in initial dioxin.

<b>(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED</b>				
Dioxin Category	n	Number (%) High	Est. Relative Risk (95% C.I.) <sup>ab</sup>	p-Value
Comparison	1,212	203 (16.7)		
Background RH	381	48 (12.6)	0.89 (0.63,1.26)	0.517
Low RH	238	44 (18.5)	1.07 (0.73,1.56)	0.721
High RH	242	58 (24.0)	1.35 (0.95,1.91)	0.097
Low plus High RH	480	102 (21.3)	1.20 (0.91,1.59)	0.200

<sup>a</sup> Relative risk and confidence interval relative to Comparisons.

<sup>b</sup> 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.

<b>(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED</b>			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.) <sup>a</sup>	p-Value
Comparison	1,200		
Background RH	377	0.91 (0.63,1.31)	0.609
Low RH	235	1.03 (0.70,1.53)	0.877
High RH	240	1.44 (0.99,2.11)	0.056
Low plus High RH	475	1.22 (0.91,1.64)	0.178

<sup>a</sup> 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 16-15. Analysis of Fasting Glucose (Discrete) (Continued)**

<b>(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED</b>			
<b>1987 Dioxin Category Summary Statistics</b>			<b>Analysis Results for Log<sub>2</sub> (1987 Dioxin + 1)</b>
<b>1987 Dioxin</b>	<b>n</b>	<b>Number (%) High</b>	<b>Estimated Relative Risk (95% C.I.)<sup>a</sup></b>
Low	288	34 (11.8)	1.25 (1.11,1.41)
Medium	286	51 (17.8)	
High	287	65 (22.6)	<b>p-Value</b> <0.001

<sup>a</sup> Relative risk for a twofold increase in 1987 dioxin.

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

<b>(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED</b>			
<b>Analysis Results for Log<sub>2</sub> (1987 Dioxin + 1)</b>			
<b>n</b>	<b>Adjusted Relative Risk (95% C.I.)<sup>a</sup></b>		<b>p-Value</b>
852	1.25 (1.08,1.46)		0.003

<sup>a</sup> Relative risk for a twofold increase in 1987 dioxin.

The unadjusted Model 2 analysis did not show a significant relation between initial dioxin and the percentage of participants with high fasting glucose levels (Table 16-15(c):  $p=0.172$ ). After adjusting for covariates, the results became significant (Table 16-15(b): Adj. RR=1.31,  $p=0.013$ ). The percentages of participants with high fasting glucose values in the low, medium, and high initial dioxin categories were 18.2, 21.7, and 23.8, respectively.

Both the unadjusted and adjusted Model 3 analyses revealed a marginally significant difference in the percentage of high fasting glucose levels between Ranch Hands in the high dioxin category and Comparisons (Table 16-15(e,f): Est. RR=1.35,  $p=0.097$ ; Adj. RR=1.44,  $p=0.056$ , respectively). The percentage of abnormal fasting glucose values for Ranch Hands in the high dioxin category was 24.0 versus 16.7 percent for Comparisons.

The unadjusted and adjusted Model 4 analyses each revealed significant positive associations between high fasting glucose levels and 1987 dioxin (Table 16-15(g,h): Est. RR=1.25,  $p<0.001$ ; Adj. RR=1.25,  $p=0.003$ , respectively). The percentages of participants with high fasting glucose values in the low, medium, and high 1987 dioxin categories were 11.8, 17.8, and 22.6, respectively.

#### 16.2.2.3.8 2-Hour Postprandial Glucose (Continuous)

The unadjusted and adjusted Model 1 analyses of 2-hour postprandial glucose in its continuous form did not show a significant difference between all Ranch Hands and Comparisons (Table 16-16(a,b):  $p>0.70$  for each analysis). Stratifying by occupation revealed significant differences between Ranch Hand and Comparison officers in both the unadjusted and adjusted analyses (Table 16-16(a,b): difference of means=4.3 mg/dl,  $p=0.053$ , for the unadjusted analysis; difference of adjusted means=3.5 mg/dl,  $p=0.086$ , for the adjusted analysis). The adjusted mean 2-hour postprandial glucose level for Ranch Hand officers was 103.0 mg/dl versus 99.5 mg/dl for Comparison officers.

**Table 16-16. Analysis of 2-Hour Postprandial Glucose (mg/dl) (Continuous)**

<b>(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED</b>					
Occupational Category	Group	n	Mean <sup>a</sup>	Difference of Means (95% C.I.) <sup>b</sup>	p-Value <sup>c</sup>
<i>All</i>	<i>Ranch Hand</i>	<i>714</i>	<i>105.2</i>	<i>0.3 --</i>	<i>0.818</i>
	<i>Comparison</i>	<i>1,023</i>	<i>104.9</i>		
Officer	Ranch Hand	285	106.1	4.3 --	0.053
	Comparison	419	101.8		
Enlisted Flyer	Ranch Hand	121	107.8	-3.5 --	0.342
	Comparison	146	111.3		
Enlisted Groundcrew	Ranch Hand	308	103.4	-2.3 --	0.274
	Comparison	458	105.8		

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

<sup>c</sup> P-value is based on difference of means on natural logarithm scale.

<b>(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED</b>					
Occupational Category	Group	n	Adjusted Mean <sup>a</sup>	Difference of Adj. Means (95% C.I.) <sup>b</sup>	p-Value <sup>c</sup>
<i>All</i>	<i>Ranch Hand</i>	<i>705</i>	<i>105.5</i>	<i>0.5 --</i>	<i>0.702</i>
	<i>Comparison</i>	<i>1,014</i>	<i>105.0</i>		
Officer	Ranch Hand	283	103.0	3.5 --	0.086
	Comparison	418	99.5		
Enlisted Flyer	Ranch Hand	118	106.4	-2.9 --	0.405
	Comparison	142	109.3		
Enlisted Groundcrew	Ranch Hand	304	106.0	-1.2 --	0.563
	Comparison	454	107.2		

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

<sup>c</sup> P-value is based on difference of means on natural logarithm scale.

<b>(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED</b>				<b>Analysis Results for Log<sub>2</sub> (Initial Dioxin)<sup>b</sup></b>		
<b>Initial Dioxin Category Summary Statistics</b>				<b>R<sup>2</sup></b>	<b>Slope (Std. Error)<sup>c</sup></b>	<b>p-Value</b>
<b>Initial Dioxin</b>	<b>n</b>	<b>Mean<sup>a</sup></b>	<b>Adj. Mean<sup>ab</sup></b>			
Low	125	107.4	108.3	0.076	-0.010 (0.011)	0.363
Medium	123	105.9	106.2			
High	121	107.4	106.2			

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Adjusted for percent body fat at the time of the blood measurement of dioxin.

<sup>c</sup> Slope and standard error based on natural logarithm of 2-hour postprandial glucose versus log<sub>2</sub> (initial dioxin).

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

**Table 16-16. Analysis of 2-Hour Postprandial Glucose (mg/dl) (Continuous) (Continued)**

<b>(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED</b>					
<b>Initial Dioxin Category Summary Statistics</b>			<b>Analysis Results for Log<sub>2</sub> (Initial Dioxin)</b>		
<b>Initial Dioxin</b>	<b>n</b>	<b>Adj. Mean<sup>a</sup></b>	<b>R<sup>2</sup></b>	<b>Adj. Slope (Std. Error)<sup>b</sup></b>	<b>p-Value</b>
Low	124	108.1	0.139	0.003 (0.013)	0.832
Medium	119	106.7			
High	121	110.3			

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Slope and standard error based on natural logarithm of 2-hour postprandial glucose versus log<sub>2</sub> (initial dioxin).

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

<b>(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED</b>					
<b>Dioxin Category</b>	<b>n</b>	<b>Mean<sup>a</sup></b>	<b>Adj. Mean<sup>ab</sup></b>	<b>Difference of Adj. Mean vs. Comparisons (95% C.I.)<sup>c</sup></b>	<b>p-Value<sup>d</sup></b>
Comparison	996	104.9	104.7		
Background RH	342	103.6	105.3	0.6 --	0.718
Low RH	186	107.3	107.1	2.4 --	0.296
High RH	183	106.5	104.5	-0.2 --	0.942
Low plus High RH	369	106.9	105.8	1.1 --	0.521

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Adjusted for percent body fat at the time of the blood measurement of dioxin.

<sup>c</sup> Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

<sup>d</sup> 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 16-16. Analysis of 2-Hour Postprandial Glucose (mg/dl) (Continuous) (Continued)**

<b>(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED</b>				
Dioxin Category	n	Adj. Mean <sup>a</sup>	Difference of Adj. Mean vs. Comparisons (95% C.I.) <sup>b</sup>	p-Value <sup>c</sup>
Comparison	987	105.1		
Background RH	338	106.1	1.0 --	0.585
Low RH	183	106.1	1.0 --	0.655
High RH	181	104.6	-0.5 --	0.804
Low plus High RH	364	105.4	0.3 --	0.900

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

<sup>c</sup> 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.

<b>(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED</b>					
1987 Dioxin Category Summary Statistics			Analysis Results for Log <sub>2</sub> (1987 Dioxin + 1)		
1987 Dioxin	n	Mean <sup>a</sup>	R <sup>2</sup>	Slope (Std. Error) <sup>b</sup>	p-Value
Low	264	103.7	0.003	0.011 (0.007)	0.115
Medium	230	106.0			
High	217	106.5			

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Slope and standard error based on natural logarithm of 2-hour postprandial glucose versus log<sub>2</sub> (1987 dioxin + 1).

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

<b>(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED</b>					
1987 Dioxin Category Summary Statistics			Analysis Results for Log <sub>2</sub> (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean <sup>a</sup>	R <sup>2</sup>	Adjusted Slope (Std. Error) <sup>b</sup>	p-Value
Low	260	105.1	0.137	0.002 (0.008)	0.850
Medium	229	103.7			
High	213	105.3			

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Slope and standard error based on natural logarithm of 2-hour postprandial glucose versus log<sub>2</sub> (1987 dioxin + 1).

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

The unadjusted and adjusted analyses of 2-hour postprandial glucose in Models 2 through 4 were nonsignificant (Table 16-16(c–h): p>0.11 for each analysis).

16.2.2.3.9 2-Hour Postprandial Glucose (Discrete)

The percentage of participants with impaired 2-hour postprandial glucose levels did not significantly differ between Ranch Hands and Comparisons across all occupations (Table 16-17(a,b):  $p > 0.91$  for both unadjusted and adjusted analyses). Stratifying the unadjusted analysis by occupation revealed a marginally significant difference between Ranch Hand and Comparison officers (Table 16-17(a): Est. RR=1.51,  $p=0.052$ ). The percentage of 2-hour postprandial glucose values classified as impaired for Ranch Hand officers was 18.2 versus 12.9 percent for Comparison officers. No significant contrasts were revealed after stratifying the adjusted analysis by occupation (Table 16-17(b):  $p \geq 0.11$  for each contrast).

**Table 16-17. Analysis of 2-Hour Postprandial Glucose (Discrete)**

<b>(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED</b>					
Occupational Category	Group	n	Number (%) Impaired	Est. Relative Risk (95% C.I.)	p-Value
<i>All</i>	<i>Ranch Hand</i>	<i>714</i>	<i>113 (15.8)</i>	<i>1.01 (0.77,1.31)</i>	<i>0.960</i>
	<i>Comparison</i>	<i>1,023</i>	<i>161 (15.7)</i>		
Officer	Ranch Hand	285	52 (18.2)	1.51 (1.00,2.28)	0.052
	Comparison	419	54 (12.9)		
Enlisted Flyer	Ranch Hand	121	22 (18.2)	0.82 (0.45,1.52)	0.534
	Comparison	146	31 (21.2)		
Enlisted Groundcrew	Ranch Hand	308	39 (12.7)	0.73 (0.48,1.11)	0.136
	Comparison	458	76 (16.6)		

  

<b>(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED</b>		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
<i>All</i>	<i>0.98 (0.75,1.30)</i>	<i>0.912</i>
Officer	1.42 (0.92,2.20)	0.110
Enlisted Flyer	0.81 (0.43,1.54)	0.526
Enlisted Groundcrew	0.75 (0.48,1.16)	0.191

  

<b>(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED</b>				
Initial Dioxin Category Summary Statistics			Analysis Results for Log <sub>2</sub> (Initial Dioxin) <sup>a</sup>	
Initial Dioxin	n	Number (%) Impaired	Estimated Relative Risk (95% C.I.) <sup>b</sup>	p-Value
Low	125	23 (18.4)	0.88 (0.71,1.10)	0.267
Medium	123	23 (18.7)		
High	121	20 (16.5)		

<sup>a</sup> Adjusted for percent body fat at the time of the blood measurement of dioxin.

<sup>b</sup> Relative risk for a twofold increase in initial dioxin.

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

**Table 16-17. Analysis of 2-Hour Postprandial Glucose (Discrete) (Continued)**

<b>(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED</b>		
Analysis Results for Log <sub>2</sub> (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.) <sup>a</sup>	p-Value
364	0.99 (0.76,1.29)	0.940

<sup>a</sup> Relative risk for a twofold increase in initial dioxin.

<b>(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED</b>				
Dioxin Category	n	Number (%) Impaired	Est. Relative Risk (95% C.I.) <sup>ab</sup>	p-Value
Comparison	996	155 (15.6)		
Background RH	342	47 (13.7)	0.98 (0.68,1.40)	0.906
Low RH	186	35 (18.8)	1.27 (0.84,1.92)	0.260
High RH	183	31 (16.9)	1.00 (0.65,1.54)	0.999
Low plus High RH	369	66 (17.9)	1.13 (0.82,1.56)	0.468

<sup>a</sup> Relative risk and confidence interval relative to Comparisons.

<sup>b</sup> 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.

<b>(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED</b>			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.) <sup>a</sup>	p-Value
Comparison	987		
Background RH	338	0.94 (0.64,1.37)	0.729
Low RH	183	1.12 (0.73,1.72)	0.616
High RH	181	1.01 (0.64,1.60)	0.960
Low plus High RH	364	1.06 (0.76,1.49)	0.722

<sup>a</sup> 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 16-17. Analysis of 2-Hour Postprandial Glucose (Discrete) (Continued)**

<b>(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED</b>					
<b>1987 Dioxin Category Summary Statistics</b>			<b>Analysis Results for Log<sub>2</sub> (1987 Dioxin + 1)</b>		
<b>1987 Dioxin</b>	<b>n</b>	<b>Number (%) Impaired</b>	<b>Estimated Relative Risk (95% C.I.)<sup>a</sup></b>		<b>p-Value</b>
Low	264	38 (14.4)	1.06 (0.92,1.22)		0.394
Medium	230	40 (17.4)			
High	217	35 (16.1)			

<sup>a</sup> Relative risk for a twofold increase in 1987 dioxin.

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

<b>(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED</b>			
<b>Analysis Results for Log<sub>2</sub> (1987 Dioxin + 1)</b>			
<b>n</b>	<b>Adjusted Relative Risk (95% C.I.)<sup>a</sup></b>		<b>p-Value</b>
702	1.10 (0.91,1.33)		0.332

<sup>a</sup> Relative risk for a twofold increase in 1987 dioxin.

All unadjusted and adjusted Models 2 through 4 analyses were nonsignificant (Table 16-17(c–h): p>0.26 for each analysis).

#### 16.2.2.3.10 Fasting Urinary Glucose

The unadjusted and adjusted Models 1 through 3 analyses of fasting urinary glucose were nonsignificant (Table 16-18(a–f): p>0.12 for each analysis).

**Table 16-18. Analysis of Fasting Urinary Glucose**

<b>(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED</b>					
<b>Occupational Category</b>	<b>Group</b>	<b>n</b>	<b>Number (%) Present</b>	<b>Est. Relative Risk (95% C.I.)</b>	<b>p-Value</b>
<i>All</i>	<i>Ranch Hand</i>	868	35 (4.0)	0.93 (0.60,1.44)	0.745
	<i>Comparison</i>	1,250	54 (4.3)		
Officer	Ranch Hand	339	11 (3.2)	1.35 (0.59,3.09)	0.482
	Comparison	494	12 (2.4)		
Enlisted Flyer	Ranch Hand	151	8 (5.3)	1.11 (0.42,2.94)	0.839
	Comparison	187	9 (4.8)		
Enlisted Groundcrew	Ranch Hand	378	16 (4.2)	0.72 (0.39,1.32)	0.288
	Comparison	569	33 (5.8)		

**Table 16-18. Analysis of Fasting Urinary Glucose (Continued)**

<b>(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED</b>		
<b>Occupational Category</b>	<b>Adjusted Relative Risk (95% C.I.)</b>	<b>p-Value</b>
<i>All</i>	<i>0.98 (0.63,1.52)</i>	<i>0.924</i>
Officer	1.40 (0.61,3.22)	0.432
Enlisted Flyer	1.13 (0.41,3.11)	0.816
Enlisted Groundcrew	0.77 (0.42,1.43)	0.412

<b>(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED</b>				
<b>Initial Dioxin Category Summary Statistics</b>			<b>Analysis Results for Log<sub>2</sub> (Initial Dioxin)<sup>a</sup></b>	
<b>Initial Dioxin</b>	<b>n</b>	<b>Number (%) Present</b>	<b>Estimated Relative Risk (95% C.I.)<sup>b</sup></b>	<b>p-Value</b>
Low	159	5 (3.1)	1.19 (0.90,1.57)	0.220
Medium	161	13 (8.1)		
High	160	9 (5.6)		

<sup>a</sup> Adjusted for percent body fat at the time of the blood measurement of dioxin.

<sup>b</sup> Relative risk for a twofold increase in initial dioxin.

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

<b>(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED</b>			
<b>Analysis Results for Log<sub>2</sub> (Initial Dioxin)</b>			
<b>n</b>	<b>Adjusted Relative Risk (95% C.I.)<sup>a</sup></b>		<b>p-Value</b>
475	1.27 (0.90,1.79)		0.173

<sup>a</sup> Relative risk for a twofold increase in initial dioxin.

<b>(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED</b>				
<b>Dioxin Category</b>	<b>n</b>	<b>Number (%) Present</b>	<b>Est. Relative Risk (95% C.I.)<sup>ab</sup></b>	<b>p-Value</b>
Comparison	1,212	51 (4.2)		
Background RH	381	7 (1.8)	0.53 (0.24,1.19)	0.124
Low RH	238	9 (3.8)	0.81 (0.38,1.70)	0.571
High RH	242	18 (7.4)	1.51 (0.85,2.69)	0.160
Low plus High RH	480	27 (5.6)	1.11 (0.66,1.85)	0.696

<sup>a</sup> Relative risk and confidence interval relative to Comparisons.

<sup>b</sup> 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 16-18. Analysis of Fasting Urinary Glucose (Continued)**

<b>(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED</b>			
<b>Dioxin Category</b>	<b>n</b>	<b>Adjusted Relative Risk (95% C.I.)<sup>a</sup></b>	<b>p-Value</b>
Comparison	1,200		
Background RH	377	0.63 (0.27,1.43)	0.265
Low RH	235	0.92 (0.43,1.97)	0.827
High RH	240	1.33 (0.71,2.49)	0.369
Low plus High RH	475	1.11 (0.65,1.89)	0.704

<sup>a</sup> 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.

<b>(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED</b>				
<b>1987 Dioxin Category Summary Statistics</b>			<b>Analysis Results for Log<sub>2</sub> (1987 Dioxin + 1)</b>	
<b>1987 Dioxin</b>	<b>n</b>	<b>Number (%) Present</b>	<b>Estimated Relative Risk (95% C.I.)<sup>a</sup></b>	<b>p-Value</b>
Low	288	3 (1.0)	1.38 (1.12,1.71)	0.004
Medium	286	11 (3.8)		
High	287	20 (7.0)		

<sup>a</sup> Relative risk for a twofold increase in 1987 dioxin.

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

<b>(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED</b>			
<b>Analysis Results for Log<sub>2</sub> (1987 Dioxin + 1)</b>			
<b>n</b>	<b>Adjusted Relative Risk (95% C.I.)<sup>a</sup></b>		<b>p-Value</b>
852	1.47 (1.11,1.94)		0.006

<sup>a</sup> Relative risk for a twofold increase in 1987 dioxin.

Both the unadjusted and adjusted Model 4 analyses revealed significant positive relations between fasting urinary glucose and 1987 dioxin (Table 16-18(g,h): Est. RR=1.38, p=0.004; Adj. RR=1.47, p=0.006, respectively). The percentages of participants with fasting urinary glucose in the low, medium, and high 1987 dioxin categories were 1.0, 3.8, and 7.0, respectively.

#### 16.2.2.3.11 2-Hour Postprandial Urinary Glucose

The unadjusted Model 1 analysis of 2-hour postprandial urinary glucose did not reveal a significant overall group difference between Ranch Hands and Comparisons (Table 16-19(a): p=0.122). Stratifying the unadjusted analysis by occupation revealed a significant difference between Ranch Hand and Comparison officers (Table 16-19(a): Est. RR=1.49, p=0.034). The prevalence of 2-hour postprandial

urinary glucose was greater for Ranch Hand officers (24.0%) than for Comparison officers (17.5%). The adjusted Model 1 analysis revealed a significant difference between Ranch Hands and Comparisons across all occupations and within the officer stratum (Table 16-19(b): Adj. RR=1.22, p=0.094; Adj. RR=1.47, p=0.044, respectively). The presence of 2-hour postprandial urinary glucose for Ranch Hands was 25.1 percent versus 21.9 percent for Comparisons. For the officers, 24.0 percent of the Ranch Hands had 2-hour postprandial urinary glucose present versus 17.5 percent of the Comparisons.

**Table 16-19. Analysis of 2-Hour Postprandial Urinary Glucose**

<b>(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED</b>					
Occupational Category	Group	n	Number (%) Present	Est. Relative Risk (95% C.I.)	p-Value
<i>All</i>	<i>Ranch Hand</i>	<i>712</i>	<i>179 (25.1)</i>	<i>1.19 (0.95,1.50)</i>	<i>0.122</i>
	<i>Comparison</i>	<i>1,021</i>	<i>224 (21.9)</i>		
Officer	Ranch Hand	283	68 (24.0)	1.49 (1.03,2.17)	0.034
	Comparison	418	73 (17.5)		
Enlisted Flyer	Ranch Hand	121	28 (23.1)	0.71 (0.41,1.24)	0.233
	Comparison	145	43 (29.7)		
Enlisted Groundcrew	Ranch Hand	308	83 (26.9)	1.20 (0.86,1.67)	0.291
	Comparison	458	108 (23.6)		

  

<b>(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED</b>		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
<i>All</i>	<i>1.22 (0.97,1.53)</i>	<i>0.094</i>
Officer	1.47 (1.01,2.14)	0.044
Enlisted Flyer	0.73 (0.42,1.28)	0.276
Enlisted Groundcrew	1.26 (0.90,1.76)	0.180

  

<b>(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED</b>				
Initial Dioxin Category Summary Statistics			Analysis Results for Log <sub>2</sub> (Initial Dioxin) <sup>a</sup>	
Initial Dioxin	n	Number (%) Present	Estimated Relative Risk (95% C.I.) <sup>b</sup>	p-Value
Low	124	34 (27.4)	0.94 (0.78,1.14)	0.535
Medium	123	30 (24.4)		
High	121	30 (24.8)		

<sup>a</sup> Adjusted for percent body fat at the time of the blood measurement of dioxin.

<sup>b</sup> Relative risk for a twofold increase in initial dioxin.

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

**Table 16-19. Analysis of 2-Hour Postprandial Urinary Glucose (Continued)**

<b>(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED</b>		
Analysis Results for Log <sub>2</sub> (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.) <sup>a</sup>	p-Value
363	0.94 (0.75,1.17)	0.585

<sup>a</sup> Relative risk for a twofold increase in initial dioxin.

<b>(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED</b>				
Dioxin Category	n	Number (%) Present	Est. Relative Risk (95% C.I.) <sup>ab</sup>	p-Value
Comparison	994	214 (21.5)		
Background RH	341	85 (24.9)	1.20 (0.90,1.60)	0.222
Low RH	185	52 (28.1)	1.43 (1.00,2.03)	0.050
High RH	183	42 (23.0)	1.10 (0.75,1.60)	0.636
Low plus High RH	368	94 (25.5)	1.25 (0.95,1.65)	0.118

<sup>a</sup> Relative risk and confidence interval relative to Comparisons.

<sup>b</sup> 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.

<b>(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED</b>			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.) <sup>a</sup>	p-Value
Comparison	985		
Background RH	337	1.32 (0.98,1.78)	0.072
Low RH	182	1.41 (0.98,2.02)	0.064
High RH	181	0.97 (0.66,1.44)	0.885
Low plus High RH	363	1.17 (0.88,1.56)	0.283

<sup>a</sup> 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 16-19. Analysis of 2-Hour Postprandial Urinary Glucose (Continued)**

<b>(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED</b>			
<b>1987 Dioxin Category Summary Statistics</b>			<b>Analysis Results for Log<sub>2</sub> (1987 Dioxin + 1)</b>
<b>1987 Dioxin</b>	<b>n</b>	<b>Number (%) Present</b>	<b>Estimated Relative Risk (95% C.I.)<sup>a</sup></b>
Low	264	70 (26.5)	0.97 (0.86,1.10)
Medium	228	54 (23.7)	
High	217	55 (25.3)	0.664

<sup>a</sup> Relative risk for a twofold increase in 1987 dioxin.

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

<b>(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED</b>			
<b>Analysis Results for Log<sub>2</sub> (1987 Dioxin + 1)</b>			
<b>n</b>	<b>Adjusted Relative Risk (95% C.I.)<sup>a</sup></b>		<b>p-Value</b>
700	0.90 (0.78,1.03)		0.129

<sup>a</sup> Relative risk for a twofold increase in 1987 dioxin.

Both the unadjusted and adjusted Model 2 analyses were nonsignificant (Table 16-19(c,d):  $p > 0.53$  for each analysis).

A significant difference between Ranch Hands in the low dioxin category and Comparisons was seen in the unadjusted Model 3 analysis of 2-hour postprandial urinary glucose (Table 16-19(e): Est. RR=1.43,  $p=0.050$ ). After adjusting for covariates, two marginally significant contrasts were seen: Ranch Hands in the background dioxin category versus Comparisons (Table 16-19(f): Adj. RR=1.32,  $p=0.072$ ) and Ranch Hands in the low dioxin category versus Comparisons (Table 16-19(f): Adj. RR=1.41,  $p=0.064$ ). The presence of 2-hour postprandial urinary glucose for Ranch Hands in the background dioxin category, Ranch Hands in the low dioxin category, and Comparisons was 24.9 percent, 28.1 percent, and 21.5 percent, respectively.

The unadjusted and adjusted Model 4 analyses did not reveal a significant association between 2-hour postprandial urinary glucose and 1987 dioxin (Table 16-19(g,h):  $p > 0.12$  for each analysis).

#### 16.2.2.3.12 Serum Insulin (Continuous)

The unadjusted and adjusted Models 1 and 2 analyses of serum insulin in its continuous form were nonsignificant (Table 16-20(a–d):  $p \geq 0.17$  for each analysis).

The unadjusted Model 3 analysis revealed a significant difference in mean serum insulin levels between Ranch Hands in the low plus high dioxin category and Comparisons (Table 16-20(e): difference of means=5.00  $\mu\text{IU/ml}$ ,  $p=0.046$ ). The mean serum insulin level for Ranch Hands in the low plus high dioxin category was 52.35  $\mu\text{IU/ml}$  versus 47.35  $\mu\text{IU/ml}$  for Comparisons. After adjusting for covariates, the results became nonsignificant (Table 16-20(f):  $p > 0.19$  for each contrast).

**Table 16-20. Analysis of Serum Insulin ( $\mu\text{U/ml}$ ) (Continuous)**

<b>(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED</b>					
Occupational Category	Group	n	Mean <sup>a</sup>	Difference of Means (95% C.I.) <sup>b</sup>	p-Value <sup>c</sup>
<i>All</i>	<i>Ranch Hand</i>	<i>714</i>	<i>47.95</i>	<i>0.03 --</i>	<i>0.990</i>
	<i>Comparison</i>	<i>1,023</i>	<i>47.92</i>		
Officer	Ranch Hand	285	45.60	3.20 --	0.283
	Comparison	419	42.40		
Enlisted Flyer	Ranch Hand	121	49.81	-5.11 --	0.369
	Comparison	146	54.92		
Enlisted Groundcrew	Ranch Hand	308	49.49	-1.84 --	0.574
	Comparison	458	51.33		

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

<sup>c</sup> P-value is based on difference of means on natural logarithm scale.

<b>(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED</b>					
Occupational Category	Group	n	Adjusted Mean <sup>a</sup>	Difference of Adj. Means (95% C.I.) <sup>b</sup>	p-Value <sup>c</sup>
<i>All</i>	<i>Ranch Hand</i>	<i>705</i>	<i>49.07</i>	<i>1.09 --</i>	<i>0.562</i>
	<i>Comparison</i>	<i>1,014</i>	<i>47.99</i>		
Officer	Ranch Hand	283	43.72	2.40 --	0.353
	Comparison	418	41.32		
Enlisted Flyer	Ranch Hand	118	49.21	-2.99 --	0.548
	Comparison	142	52.20		
Enlisted Groundcrew	Ranch Hand	304	53.35	1.05 --	0.735
	Comparison	454	52.31		

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

<sup>c</sup> P-value is based on difference of means on natural logarithm scale.

<b>(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED</b>				<b>Analysis Results for Log<sub>2</sub> (Initial Dioxin)<sup>b</sup></b>		
<b>Initial Dioxin Category Summary Statistics</b>				<b>R<sup>2</sup></b>	<b>Slope (Std. Error)<sup>c</sup></b>	<b>p-Value</b>
<b>Initial Dioxin</b>	<b>n</b>	<b>Mean<sup>a</sup></b>	<b>Adj. Mean<sup>ab</sup></b>			
Low	125	52.55	54.14	0.092	0.020 (0.036)	0.571
Medium	123	52.18	52.70			
High	121	59.81	57.42			

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Adjusted for percent body fat at the time of the blood measurement of dioxin.

<sup>c</sup> Slope and standard error based on natural logarithm of serum insulin versus log<sub>2</sub> (initial dioxin).

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

**Table 16-20. Analysis of Serum Insulin ( $\mu\text{IU/ml}$ ) (Continuous) (Continued)**

<b>(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED</b>					
<b>Initial Dioxin Category Summary Statistics</b>			<b>Analysis Results for <math>\text{Log}_2</math> (Initial Dioxin)</b>		
<b>Initial Dioxin</b>	<b>n</b>	<b>Adj. Mean<sup>a</sup></b>	<b>R<sup>2</sup></b>	<b>Adj. Slope (Std. Error)<sup>b</sup></b>	<b>p-Value</b>
Low	124	57.88	0.195	0.054 (0.040)	0.170
Medium	119	56.68			
High	121	67.03			

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Slope and standard error based on natural logarithm of serum insulin versus  $\text{log}_2$  (initial dioxin).

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

<b>(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED</b>					
<b>Dioxin Category</b>	<b>n</b>	<b>Mean<sup>a</sup></b>	<b>Adj. Mean<sup>ab</sup></b>	<b>Difference of Adj. Mean vs. Comparisons (95% C.I.)<sup>c</sup></b>	<b>p-Value<sup>d</sup></b>
Comparison	996	47.73	47.35		
Background RH	342	42.18	45.29	–2.06 --	0.393
Low RH	186	52.51	51.97	4.62 --	0.157
High RH	183	57.01	52.74	5.39 --	0.105
Low plus High RH	369	54.70	52.35	5.00 --	0.046

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Adjusted for percent body fat at the time of the blood measurement of dioxin.

<sup>c</sup> Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

<sup>d</sup> P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin  $\leq$  10 ppt.

Background (Ranch Hand): 1987 Dioxin  $\leq$  10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin  $\leq$  94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

**Table 16-20. Analysis of Serum Insulin ( $\mu\text{IU/ml}$ ) (Continuous) (Continued)**

<b>(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED</b>				
Dioxin Category	n	Adj. Mean <sup>a</sup>	Difference of Adj. Mean vs. Comparisons (95% C.I.) <sup>b</sup>	p-Value <sup>c</sup>
Comparison	987	47.57		
Background RH	338	47.31	-0.26 --	0.914
Low RH	183	49.87	2.30 --	0.455
High RH	181	51.51	3.94 --	0.226
Low plus High RH	364	50.68	3.11 --	0.195

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

<sup>c</sup> P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin  $\leq$  10 ppt.

Background (Ranch Hand): 1987 Dioxin  $\leq$  10 ppt.

Low (Ranch Hand): 1987 Dioxin  $>$  10 ppt, 10 ppt  $<$  Initial Dioxin  $\leq$  94 ppt.

High (Ranch Hand): 1987 Dioxin  $>$  10 ppt, Initial Dioxin  $>$  94 ppt.

<b>(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED</b>					
1987 Dioxin Category Summary Statistics			Analysis Results for $\text{Log}_2$ (1987 Dioxin + 1)		
1987 Dioxin	n	Mean <sup>a</sup>	R <sup>2</sup>	Slope (Std. Error) <sup>b</sup>	p-Value
Low	264	41.18	0.025	0.100 (0.023)	$<$ 0.001
Medium	230	49.71			
High	217	56.76			

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Slope and standard error based on natural logarithm of serum insulin versus  $\text{log}_2$  (1987 dioxin + 1).

Note: Low =  $\leq$ 7.9 ppt; Medium =  $>$ 7.9–19.6 ppt; High =  $>$ 19.6 ppt.

<b>(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED</b>					
1987 Dioxin Category Summary Statistics			Analysis Results for $\text{Log}_2$ (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean <sup>a</sup>	R <sup>2</sup>	Adjusted Slope (Std. Error) <sup>b</sup>	p-Value
Low	260	46.56	0.235	0.026 (0.025)	0.305
Medium	229	47.08			
High	213	53.05			

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Slope and standard error based on natural logarithm of serum insulin versus  $\text{log}_2$  (1987 dioxin + 1).

Note: Low =  $\leq$ 7.9 ppt; Medium =  $>$ 7.9–19.6 ppt; High =  $>$ 19.6 ppt.

The unadjusted Model 4 analysis revealed a significant relation between serum insulin in its continuous form and 1987 dioxin (Table 16-20(g): slope=0.100,  $p<0.001$ ). The mean serum insulin levels in the low, medium, and high 1987 dioxin categories were 41.18  $\mu\text{IU/ml}$ , 49.71  $\mu\text{IU/ml}$ , and 56.76  $\mu\text{IU/ml}$ , respectively. After adjustment for covariates, the association was nonsignificant (Table 16-20(h):  $p=0.305$ ).

#### 16.2.2.3.13 Serum Insulin (Discrete)

Unadjusted and adjusted analyses in Models 1 and 2 did not show significant associations between dioxin and serum insulin in its discrete form (Table 16-21(a–d):  $p>0.14$  for each analysis).

The unadjusted Model 3 analysis revealed a marginally significant difference between the percentage of Ranch Hands in the high dioxin category and Comparisons with abnormally low serum insulin levels (Table 16-21(e): Est. RR=0.58,  $p=0.082$ ). The adjusted Model 3 analysis of abnormally low serum insulin levels revealed two marginally significant contrasts: Ranch Hands in the high dioxin category versus Comparisons (Table 16-21(f): Adj. RR=0.55,  $p=0.081$ ) and Ranch Hands in the low plus high dioxin category versus Comparisons (Table 16-21(f): Adj. RR=0.68,  $p=0.093$ ). The percentages of abnormally low serum insulin values for Ranch Hands in the high dioxin category, Ranch Hands in the low plus high dioxin category, and Comparisons were 7.1, 8.9, and 13.2, respectively.

The unadjusted Model 4 analysis revealed a significant association between 1987 dioxin and both abnormally low serum insulin levels (Table 16-21(g): Est. RR=0.83,  $p=0.050$ ) and abnormally high serum insulin levels (Table 16-21(g): Est. RR=1.16,  $p=0.008$ ). The percentage of participants with abnormally low serum insulin levels decreased with 1987 dioxin while the percentage of participants with abnormally high serum insulin levels increased with 1987 dioxin. The percentages of participants with abnormally low serum insulin levels in the low, medium, and high 1987 dioxin categories were 15.2, 11.7, and 7.8, respectively. The percentages of participants with abnormally high serum insulin levels in the low, medium, and high 1987 dioxin categories were 34.1, 41.7, and 49.8, respectively. Model 4 adjusted analyses showed no significant association between abnormal serum insulin levels and 1987 dioxin ( $p>0.58$  for both contrasts).

Table 16-21. Analysis of Serum Insulin (Discrete)

<b>(a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED</b>									
Occupational Category	Group	n	Number (%)			Abnormal Low vs. Normal		Abnormal High vs. Normal	
			Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)	p-Value	Est. Relative Risk (95% C.I.)	p-Value
<i>All</i>	<i>Ranch Hand</i>	<i>714</i>	<i>86 (12.0)</i>	<i>334 (46.8)</i>	<i>294 (41.2)</i>	<i>0.85 (0.62,1.15)</i>	<i>0.278</i>	<i>0.92 (0.75,1.13)</i>	<i>0.443</i>
	<i>Comparison</i>	<i>1,023</i>	<i>138 (13.5)</i>	<i>453 (44.3)</i>	<i>432 (42.2)</i>				
Officer	Ranch Hand	285	36 (12.6)	137 (48.1)	112 (39.3)	0.76 (0.48,1.20)	0.235	1.08 (0.78,1.49)	0.655
	Comparison	419	69 (16.5)	199 (47.5)	151 (36.0)				
Enlisted Flyer	Ranch Hand	121	15 (12.4)	56 (46.3)	50 (41.3)	1.11 (0.49,2.51)	0.803	0.70 (0.42,1.17)	0.173
	Comparison	146	14 (9.6)	58 (39.7)	74 (50.7)				
Enlisted Groundcrew	Ranch Hand	308	35 (11.4)	141 (45.8)	132 (42.9)	0.88 (0.55,1.42)	0.613	0.89 (0.65,1.21)	0.442
	Comparison	458	55 (12.0)	196 (42.8)	207 (45.2)				

  

<b>(b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED</b>				
Occupational Category	Abnormal Low vs. Normal		Abnormal High vs. Normal	
	Adj. Relative Risk (95% C.I.)	p-Value	Adj. Relative Risk (95% C.I.)	p-Value
<i>All</i>	<i>0.79 (0.58,1.08)</i>	<i>0.143</i>	<i>0.96 (0.77,1.21)</i>	<i>0.749</i>
Officer	0.76 (0.48,1.22)	0.256	1.08 (0.75,1.53)	0.688
Enlisted Flyer	0.83 (0.35,1.95)	0.671	0.72 (0.41,1.27)	0.257
Enlisted Groundcrew	0.81 (0.50,1.33)	0.412	0.97 (0.69,1.36)	0.870

**Table 16-21. Analysis of Serum Insulin (Discrete) (Continued)**

<b>(c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED</b>									
Initial Dioxin Category Summary Statistics					Analysis Results for Log <sub>2</sub> (Initial Dioxin) <sup>a</sup>				
Initial Dioxin Category	n	Number (%)			Abnormal Low vs. Normal		Abnormal High vs. Normal		
		Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.) <sup>b</sup>	p-Value	Est. Relative Risk (95% C.I.) <sup>b</sup>	p-Value	
Low	125	12 (9.6)	61 (48.8)	52 (41.6)	0.96 (0.70,1.32)	0.815	1.07 (0.90,1.28)	0.447	
Medium	123	13 (10.6)	51 (41.5)	59 (48.0)					
High	121	8 (6.6)	52 (43.0)	61 (50.4)					

<sup>a</sup> Adjusted for percent body fat at the time of the blood measurement of dioxin.

<sup>b</sup> Relative risk for a twofold increase in initial dioxin.

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

<b>(d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED</b>				
Analysis Results for Log <sub>2</sub> (Initial Dioxin)				
n	Abnormal Low vs. Normal		Abnormal High vs. Normal	
	Adj. Relative Risk (95% C.I.) <sup>a</sup>	p-Value	Adj. Relative Risk (95% C.I.) <sup>a</sup>	p-Value
364	0.97 (0.65,1.47)	0.901	1.15 (0.93,1.43)	0.182

<sup>a</sup> Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race because of the sparse number of Ranch Hands with an abnormally low serum insulin level.

**Table 16-21. Analysis of Serum Insulin (Discrete) (Continued)**

<b>(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED</b>								
<b>Dioxin Category</b>	<b>n</b>	<b>Number (%)</b>			<b>Abnormal Low vs. Normal</b>		<b>Abnormal High vs. Normal</b>	
		<b>Abnormal Low</b>	<b>Normal</b>	<b>Abnormal High</b>	<b>Est. Relative Risk (95% C.I.)<sup>ab</sup></b>	<b>p-Value</b>	<b>Est. Relative Risk (95% C.I.)<sup>ab</sup></b>	<b>p-Value</b>
Comparison	996	131 (13.2)	447 (44.9)	418 (42.0)				
Background RH	342	51 (14.9)	169 (49.4)	122 (35.7)	0.96 (0.66,1.39)	0.820	0.91 (0.69,1.20)	0.507
Low RH	186	20 (10.8)	81 (43.5)	85 (45.7)	0.84 (0.50,1.43)	0.527	1.14 (0.81,1.61)	0.460
High RH	183	13 (7.1)	83 (45.4)	87 (47.5)	0.58 (0.31,1.07)	0.082	0.99 (0.70,1.40)	0.968
Low plus High RH	369	33 (8.9)	164 (44.4)	172 (46.6)	0.70 (0.45,1.07)	0.102	1.06 (0.82,1.39)	0.643

<sup>a</sup> Relative risk and confidence interval relative to Comparisons.

<sup>b</sup> 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 16-21. Analysis of Serum Insulin (Discrete) (Continued)**

<b>(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED</b>					
Dioxin Category	n	Abnormal Low vs. Normal		Abnormal High vs. Normal	
		Adj. Relative Risk (95% C.I.) <sup>a</sup>	p-Value	Adj. Relative Risk (95% C.I.) <sup>a</sup>	p-Value
Comparison	987				
Background RH	338	0.90 (0.61,1.31)	0.573	0.99 (0.74,1.34)	0.971
Low RH	183	0.82 (0.47,1.44)	0.496	1.00 (0.70,1.44)	0.994
High RH	181	0.55 (0.29,1.08)	0.081	0.94 (0.65,1.37)	0.759
Low plus High RH	364	0.68 (0.43,1.07)	0.093	0.97 (0.74,1.28)	0.843

<sup>a</sup> Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin  $\leq$  10 ppt.

Background (Ranch Hand): 1987 Dioxin  $\leq$  10 ppt.

Low (Ranch Hand): 1987 Dioxin  $>$  10 ppt, 10 ppt  $<$  Initial Dioxin  $\leq$  94 ppt.

High (Ranch Hand): 1987 Dioxin  $>$  10 ppt, Initial Dioxin  $>$  94 ppt.

<b>(g) MODEL 4: RANCH HANDS — 1987 DIOXIN — UNADJUSTED</b>								
1987 Dioxin Category Summary Statistics				Analysis Results for Log <sub>2</sub> (1987 Dioxin + 1)				
1987 Dioxin Category	n	Number (%)			Abnormal Low vs. Normal		Abnormal High vs. Normal	
		Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.) <sup>a</sup>	p-Value	Est. Relative Risk (95% C.I.) <sup>a</sup>	p-Value
Low	264	40 (15.2)	134 (50.8)	90 (34.1)	0.83 (0.69,1.00)	0.050	1.16 (1.04,1.30)	0.008
Medium	230	27 (11.7)	107 (46.5)	96 (41.7)				
High	217	17 (7.8)	92 (42.4)	108 (49.8)				

<sup>a</sup> Relative risk for a twofold increase in 1987 dioxin.

Note: Low =  $\leq$ 7.9 ppt; Medium =  $>$ 7.9–19.6 ppt; High =  $>$ 19.6 ppt.

**Table 16-21. Analysis of Serum Insulin (Discrete) (Continued)**

<b>(h) MODEL 4: RANCH HANDS — 1987 DIOXIN — ADJUSTED</b>				
<b>Analysis Results for Log<sub>2</sub> (1987 Dioxin + 1)</b>				
<b>Abnormal Low vs. Normal</b>			<b>Abnormal High vs. Normal</b>	
<b>n</b>	<b>Adj. Relative Risk (95% C.I.)<sup>a</sup></b>	<b>p-Value</b>	<b>Adj. Relative Risk (95% C.I.)<sup>a</sup></b>	<b>p-Value</b>
702	0.94 (0.76,1.17)	0.589	1.03 (0.89,1.19)	0.685

<sup>a</sup> Relative risk for a twofold increase in 1987 dioxin.

16.2.2.3.14  $\alpha$ -1-C Hemoglobin (Continuous)

The unadjusted and adjusted Model 1 analyses did not reveal a significant difference in mean  $\alpha$ -1-C hemoglobin levels between all Ranch Hands and Comparisons or after stratifying by occupation (Table 16-22(a,b):  $p \geq 0.28$  for each analysis).

**Table 16-22. Analysis of  $\alpha$ -1-C Hemoglobin (percent) (Continuous)**

<b>(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED</b>					
Occupational Category	Group	n	Mean <sup>a</sup>	Difference of Means (95% C.I.) <sup>b</sup>	p-Value <sup>c</sup>
<i>All</i>	<i>Ranch Hand</i>	<i>868</i>	<i>6.48</i>	<i>-0.01 --</i>	<i>0.919</i>
	<i>Comparison</i>	<i>1,250</i>	<i>6.49</i>		
Officer	Ranch Hand	339	6.37	0.07 --	0.387
	Comparison	494	6.31		
Enlisted Flyer	Ranch Hand	151	6.53	-0.14 --	0.280
	Comparison	187	6.67		
Enlisted Groundcrew	Ranch Hand	378	6.57	-0.03 --	0.714
	Comparison	569	6.59		

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

<sup>c</sup> P-value is based on difference of means on natural logarithm scale.

<b>(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED</b>					
Occupational Category	Group	n	Adjusted Mean <sup>a</sup>	Difference of Adj. Means (95% C.I.) <sup>b</sup>	p-Value <sup>c</sup>
<i>All</i>	<i>Ranch Hand</i>	<i>859</i>	<i>6.77</i>	<i>0.01 --</i>	<i>0.882</i>
	<i>Comparison</i>	<i>1,238</i>	<i>6.76</i>		
Officer	Ranch Hand	337	6.61	0.06 --	0.427
	Comparison	492	6.55		
Enlisted Flyer	Ranch Hand	148	6.74	-0.14 --	0.284
	Comparison	181	6.88		
Enlisted Groundcrew	Ranch Hand	374	6.91	0.01 --	0.905
	Comparison	565	6.90		

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

<sup>c</sup> P-value is based on difference of means on natural logarithm scale.

**Table 16-22. Analysis of  $\alpha$ -1-C Hemoglobin (percent) (Continuous) (Continued)**

<b>(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED</b>						
Initial Dioxin Category Summary Statistics				Analysis Results for Log <sub>2</sub> (Initial Dioxin) <sup>b</sup>		
Initial Dioxin	n	Mean <sup>a</sup>	Adj. Mean <sup>ab</sup>	R <sup>2</sup>	Slope (Std. Error) <sup>c</sup>	p-Value
Low	159	6.43	6.47	0.107	0.017 (0.006)	0.009
Medium	161	6.70	6.71			
High	160	6.77	6.72			

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Adjusted for percent body fat at the time of the blood measurement of dioxin.

<sup>c</sup> Slope and standard error based on natural logarithm of  $\alpha$ -1-C hemoglobin versus log<sub>2</sub> (initial dioxin).

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

<b>(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED</b>						
Initial Dioxin Category Summary Statistics				Analysis Results for Log <sub>2</sub> (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean <sup>a</sup>		R <sup>2</sup>	Adj. Slope (Std. Error) <sup>b</sup>	p-Value
Low	158	6.68		0.163	0.024 (0.007)	0.001
Medium	157	7.01				
High	160	7.05				

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Slope and standard error based on natural logarithm of  $\alpha$ -1-C hemoglobin versus log<sub>2</sub> (initial dioxin).

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

<b>(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED</b>						
Dioxin Category	n	Mean <sup>a</sup>	Adj. Mean <sup>ab</sup>	Difference of Adj. Mean vs. Comparisons (95% C.I.) <sup>c</sup>		p-Value <sup>d</sup>
Comparison	1,212	6.49	6.48			
Background RH	381	6.29	6.38	–0.10	--	0.116
Low RH	238	6.47	6.44	–0.04	--	0.588
High RH	242	6.79	6.70	0.22	--	0.005
Low plus High RH	480	6.63	6.57	0.09	--	0.138

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Adjusted for percent body fat at the time of the blood measurement of dioxin.

<sup>c</sup> Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

<sup>d</sup> 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 16-22. Analysis of  $\alpha$ -1-C Hemoglobin (percent) (Continuous) (Continued)**

<b>(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED</b>				
Dioxin Category	n	Adj. Mean <sup>a</sup>	Difference of Adj. Mean vs. Comparisons (95% C.I.) <sup>b</sup>	p-Value <sup>c</sup>
Comparison	1,200	6.78		
Background RH	377	6.72	-0.06 --	0.412
Low RH	235	6.70	-0.08 --	0.330
High RH	240	6.97	0.19 --	0.022
Low plus High RH	475	6.83	0.05 --	0.363

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

<sup>c</sup> P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin  $\leq$  10 ppt.

Background (Ranch Hand): 1987 Dioxin  $\leq$  10 ppt.

Low (Ranch Hand): 1987 Dioxin  $>$  10 ppt, 10 ppt  $<$  Initial Dioxin  $\leq$  94 ppt.

High (Ranch Hand): 1987 Dioxin  $>$  10 ppt, Initial Dioxin  $>$  94 ppt.

<b>(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED</b>					
1987 Dioxin Category Summary Statistics			Analysis Results for Log <sub>2</sub> (1987 Dioxin + 1)		
1987 Dioxin	n	Mean <sup>a</sup>	R <sup>2</sup>	Slope (Std. Error) <sup>b</sup>	p-Value
Low	288	6.24	0.033	0.021 (0.004)	<0.001
Medium	286	6.46			
High	287	6.74			

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Slope and standard error based on natural logarithm of  $\alpha$ -1-C hemoglobin versus log<sub>2</sub> (1987 dioxin + 1).

Note: Low =  $\leq$ 7.9 ppt; Medium =  $>$ 7.9–19.6 ppt; High =  $>$ 19.6 ppt.

<b>(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED</b>					
1987 Dioxin Category Summary Statistics			Analysis Results for Log <sub>2</sub> (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean <sup>a</sup>	R <sup>2</sup>	Adjusted Slope (Std. Error) <sup>b</sup>	p-Value
Low	284	6.63	0.119	0.016 (0.005)	<0.001
Medium	285	6.68			
High	283	7.02			

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Slope and standard error based on natural logarithm of  $\alpha$ -1-C hemoglobin versus log<sub>2</sub> (1987 dioxin + 1).

Note: Low =  $\leq$ 7.9 ppt; Medium =  $>$ 7.9–19.6 ppt; High =  $>$ 19.6 ppt.

Both the unadjusted and adjusted Model 2 analyses revealed significant relations between  $\alpha$ -1-C hemoglobin and initial dioxin (Table 16-22(c,d): slope=0.017, p=0.009, for the unadjusted analysis;

adjusted slope=0.024, p=0.001, for the adjusted analysis). The adjusted mean  $\alpha$ -1-C hemoglobin levels in the low, medium, and high initial dioxin categories were 6.68, 7.01, and 7.05 percent, respectively.

The unadjusted and adjusted Model 3 analyses each revealed a significant difference between Ranch Hands in the high dioxin category and Comparisons (Table 16-22(e,f): difference of means=0.22 percent, p=0.005, for the unadjusted analysis; difference of adjusted means=0.19 percent, p=0.022, for the adjusted analysis). The adjusted mean  $\alpha$ -1-C hemoglobin level for Ranch Hands in the high dioxin category was 6.97 percent versus 6.78 percent for the Comparisons.

A significant relation was seen between  $\alpha$ -1-C hemoglobin in its continuous form and 1987 dioxin in each of the unadjusted and adjusted Model 4 analyses (Table 16-22(g,h): slope=0.021, p<0.001; adjusted slope=0.016, p<0.001, respectively). The adjusted mean  $\alpha$ -1-C hemoglobin levels in the low, medium, and high initial dioxin categories were 6.63 percent, 6.68 percent, and 7.02 percent, respectively.

#### 16.2.2.3.15 $\alpha$ -1-C Hemoglobin (Discrete)

The unadjusted Model 1 analysis of  $\alpha$ -1-C hemoglobin in its discrete form did not reveal any significant differences between Ranch Hands and Comparisons across all occupations or within each occupational stratum (Table 16-23(a): p $\geq$ 0.25 for each contrast). The adjusted analysis did not reveal a significant overall group difference between Ranch Hands and Comparisons (Table 16-23(b): p=0.373). After stratifying by occupation, a marginally significant difference was seen between Ranch Hand and Comparison enlisted groundcrew (Table 16-23(b): Adj. RR=1.43, p=0.087). The percentage of Ranch Hand enlisted groundcrew with high  $\alpha$ -1-C hemoglobin values was 13.8 percent versus 11.2 percent for Comparison enlisted groundcrew.

**Table 16-23. Analysis of  $\alpha$ -1-C Hemoglobin (Discrete)**

<b>(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED</b>					
<b>Occupational Category</b>	<b>Group</b>	<b>n</b>	<b>Number (%) High</b>	<b>Est. Relative Risk (95% C.I.)</b>	<b>p-Value</b>
<i>All</i>	<i>Ranch Hand</i>	<i>868</i>	<i>97 (11.2)</i>	<i>1.08 (0.82,1.43)</i>	<i>0.571</i>
	<i>Comparison</i>	<i>1,250</i>	<i>130 (10.4)</i>		
Officer	Ranch Hand	339	28 (8.3)	1.11 (0.67,1.85)	0.684
	Comparison	494	37 (7.5)		
Enlisted Flyer	Ranch Hand	151	17 (11.3)	0.69 (0.36,1.31)	0.259
	Comparison	187	29 (15.5)		
Enlisted Groundcrew	Ranch Hand	378	52 (13.8)	1.26 (0.85,1.86)	0.250
	Comparison	569	64 (11.2)		

**Table 16-23. Analysis of  $\alpha$ -1-C Hemoglobin (Discrete) (Continued)**

<b>(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED</b>		
<b>Occupational Category</b>	<b>Adjusted Relative Risk (95% C.I.)</b>	<b>p-Value</b>
<i>All</i>	<i>1.14 (0.85,1.53)</i>	<i>0.373</i>
Officer	1.13 (0.67,1.90)	0.652
Enlisted Flyer	0.65 (0.33,1.28)	0.210
Enlisted Groundcrew	1.43 (0.95,2.16)	0.087

<b>(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED</b>				
<b>Initial Dioxin Category Summary Statistics</b>			<b>Analysis Results for Log<sub>2</sub> (Initial Dioxin)<sup>a</sup></b>	
<b>Initial Dioxin</b>	<b>n</b>	<b>Number (%) High</b>	<b>Estimated Relative Risk (95% C.I.)<sup>b</sup></b>	<b>p-Value</b>
Low	159	16 (10.1)	1.28 (1.05,1.56)	0.013
Medium	161	23 (14.3)		
High	160	31 (19.4)		

<sup>a</sup> Adjusted for percent body fat at the time of the blood measurement of dioxin.

<sup>b</sup> Relative risk for a twofold increase in initial dioxin.

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

<b>(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED</b>		
<b>Analysis Results for Log<sub>2</sub> (Initial Dioxin)</b>		
<b>n</b>	<b>Adjusted Relative Risk (95% C.I.)<sup>a</sup></b>	<b>p-Value</b>
475	1.53 (1.19,1.96)	0.001

<sup>a</sup> Relative risk for a twofold increase in initial dioxin.

<b>(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED</b>				
<b>Dioxin Category</b>	<b>n</b>	<b>Number (%) High</b>	<b>Est. Relative Risk (95% C.I.)<sup>ab</sup></b>	<b>p-Value</b>
Comparison	1,212	125 (10.3)		
Background RH	381	25 (6.6)	0.75 (0.47,1.18)	0.210
Low RH	238	25 (10.5)	0.95 (0.60,1.53)	0.841
High RH	242	45 (18.6)	1.73 (1.17,2.55)	0.006
Low plus High RH	480	70 (14.6)	1.29 (0.92,1.80)	0.138

<sup>a</sup> Relative risk and confidence interval relative to Comparisons.

<sup>b</sup> 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 16-23. Analysis of  $\alpha$ -1-C Hemoglobin (Discrete) (Continued)**

<b>(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED</b>			
<b>Dioxin Category</b>	<b>n</b>	<b>Adjusted Relative Risk (95% C.I.)<sup>a</sup></b>	<b>p-Value</b>
Comparison	1,200		
Background RH	377	0.84 (0.53,1.35)	0.474
Low RH	235	0.94 (0.58,1.52)	0.799
High RH	240	1.76 (1.16,2.67)	0.008
Low plus High RH	475	1.29 (0.91,1.82)	0.148

<sup>a</sup> Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin  $\leq$  10 ppt.

Background (Ranch Hand): 1987 Dioxin  $\leq$  10 ppt.

Low (Ranch Hand): 1987 Dioxin  $>$  10 ppt, 10 ppt  $<$  Initial Dioxin  $\leq$  94 ppt.

High (Ranch Hand): 1987 Dioxin  $>$  10 ppt, Initial Dioxin  $>$  94 ppt.

<b>(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED</b>				
<b>1987 Dioxin Category Summary Statistics</b>			<b>Analysis Results for Log<sub>2</sub> (1987 Dioxin + 1)</b>	
<b>1987 Dioxin</b>	<b>n</b>	<b>Number (%) High</b>	<b>Estimated Relative Risk (95% C.I.)<sup>a</sup></b>	<b>p-Value</b>
Low	288	16 (5.6)	1.39 (1.21,1.60)	$<$ 0.001
Medium	286	28 (9.8)		
High	287	51 (17.8)		

<sup>a</sup> Relative risk for a twofold increase in 1987 dioxin.

Note: Low =  $\leq$ 7.9 ppt; Medium =  $>$ 7.9–19.6 ppt; High =  $>$ 19.6 ppt.

<b>(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED</b>			
<b>Analysis Results for Log<sub>2</sub> (1987 Dioxin + 1)</b>			
<b>n</b>	<b>Adjusted Relative Risk (95% C.I.)<sup>a</sup></b>		<b>p-Value</b>
852	1.37 (1.15,1.64)		$<$ 0.001

<sup>a</sup> Relative risk for a twofold increase in 1987 dioxin.

The unadjusted and adjusted Model 2 analyses each revealed significant associations between initial dioxin and  $\alpha$ -1-C hemoglobin in its dichotomous form (Table 16-23(c,d): Est. RR=1.28,  $p=0.013$ ; Adj. RR=1.53,  $p=0.001$ , respectively). The percentages of Ranch Hands with high  $\alpha$ -1-C hemoglobin values in the low, medium, and high initial dioxin categories were 10.1, 14.3, and 19.4, respectively.

The Model 3 unadjusted and adjusted analyses each revealed a significant difference in the percentage of high  $\alpha$ -1-C hemoglobin values between Ranch Hands in the high dioxin category and Comparisons (Table 16-23(e,f): Est. RR=1.73,  $p=0.006$ ; Adj. RR=1.76,  $p=0.008$ , respectively). The percentage of high  $\alpha$ -1-C hemoglobin values for Ranch Hands in the high dioxin category was 18.6 versus 10.3 percent for Comparisons.

A significant relation was seen between  $\alpha$ -1-C hemoglobin and 1987 dioxin in each of the Model 4 unadjusted and adjusted analyses (Table 16-23(g,h): Est. RR=1.39,  $p<0.001$ ; Adj. RR=1.37,  $p<0.001$ , respectively). The percentages of participants with high  $\alpha$ -1-C hemoglobin values in the low, medium, and high 1987 dioxin categories were 5.6, 9.8, and 17.8, respectively.

16.2.2.3.16 Total Testosterone (Continuous)

The unadjusted and adjusted Model 1 analyses did not reveal any significant differences in mean total testosterone levels between Ranch Hands and Comparisons across all occupations or within each occupational stratum (Table 16-24(a,b):  $p>0.57$  for each contrast).

**Table 16-24. Analysis of Total Testosterone (ng/dl) (Continuous)**

<b>(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED</b>					
Occupational Category	Group	n	Mean <sup>a</sup>	Difference of Means (95% C.I.) <sup>b</sup>	p-Value <sup>c</sup>
<i>All</i>	<i>Ranch Hand</i>	<i>850</i>	<i>423.1</i>	<i>0.5 --</i>	<i>0.945</i>
	<i>Comparison</i>	<i>1,227</i>	<i>422.6</i>		
Officer	Ranch Hand	330	406.9	-6.4 --	0.606
	Comparison	485	413.4		
Enlisted Flyer	Ranch Hand	146	439.6	11.2 --	0.577
	Comparison	182	428.4		
Enlisted Groundcrew	Ranch Hand	374	431.2	2.5 --	0.835
	Comparison	560	428.7		

<sup>a</sup> Transformed from square root scale.

<sup>b</sup> Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.

<sup>c</sup> P-value is based on difference of means on square root scale.

<b>(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED</b>					
Occupational Category	Group	n	Adjusted Mean <sup>a</sup>	Difference of Adj. Means (95% C.I.) <sup>b</sup>	p-Value <sup>c</sup>
<i>All</i>	<i>Ranch Hand</i>	<i>847</i>	<i>422.3</i>	<i>-1.1 --</i>	<i>0.883</i>
	<i>Comparison</i>	<i>1,227</i>	<i>423.4</i>		
Officer	Ranch Hand	329	412.5	-2.2 --	0.848
	Comparison	485	414.7		
Enlisted Flyer	Ranch Hand	145	439.6	9.2 --	0.618
	Comparison	182	430.4		
Enlisted Groundcrew	Ranch Hand	373	418.5	-3.7 --	0.733
	Comparison	560	422.2		

<sup>a</sup> Transformed from square root scale.

<sup>b</sup> Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.

<sup>c</sup> P-value is based on difference of means on square root scale.

**Table 16-24. Analysis of Total Testosterone (ng/dl) (Continuous) (Continued)**

<b>(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED</b>						
Initial Dioxin Category Summary Statistics				Analysis Results for Log <sub>2</sub> (Initial Dioxin) <sup>b</sup>		
Initial Dioxin	n	Mean <sup>a</sup>	Adj. Mean <sup>ab</sup>	R <sup>2</sup>	Slope (Std. Error) <sup>c</sup>	p-Value
Low	156	404.1	397.7	0.118	0.287 (0.144)	0.047
Medium	160	392.3	392.0			
High	156	421.1	428.0			

<sup>a</sup> Transformed from square root scale.

<sup>b</sup> Adjusted for percent body fat at the time of the blood measurement of dioxin.

<sup>c</sup> Slope and standard error based on square root of total testosterone versus log<sub>2</sub> (initial dioxin).

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

<b>(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED</b>						
Initial Dioxin Category Summary Statistics				Analysis Results for Log <sub>2</sub> (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean <sup>a</sup>		R <sup>2</sup>	Adj. Slope (Std. Error) <sup>b</sup>	p-Value
Low	156	415.1		0.206	-0.015 (0.161)	0.927
Medium	159	395.2				
High	156	404.7				

<sup>a</sup> Transformed from square root scale.

<sup>b</sup> Slope and standard error based on square root of total testosterone versus log<sub>2</sub> (initial dioxin).

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

<b>(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED</b>						
Dioxin Category	n	Mean <sup>a</sup>	Adj. Mean <sup>ab</sup>	Difference of Adj. Mean vs. Comparisons (95% C.I.) <sup>c</sup>		p-Value <sup>d</sup>
Comparison	1,189	422.0	423.0			
Background RH	372	448.1	429.8	6.8 --		0.499
Low RH	234	399.1	404.6	-18.4 --		0.118
High RH	238	412.1	429.4	6.4 --		0.592
Low plus High RH	472	405.6	417.0	-6.0 --		0.508

<sup>a</sup> Transformed from square root scale.

<sup>b</sup> Adjusted for percent body fat at the time of the blood measurement of dioxin.

<sup>c</sup> Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.

<sup>d</sup> P-value is based on difference of means on square root 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 16-24. Analysis of Total Testosterone (ng/dl) (Continuous) (Continued)**

<b>(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED</b>				
<b>Dioxin Category</b>	<b>n</b>	<b>Adj. Mean<sup>a</sup></b>	<b>Difference of Adj. Mean vs. Comparisons (95% C.I.)<sup>b</sup></b>	<b>p-Value<sup>c</sup></b>
Comparison	1,189	422.9		
Background RH	370	434.4	11.5 --	0.248
Low RH	234	414.5	-8.4 --	0.470
High RH	237	416.8	-6.1 --	0.613
Low plus High RH	471	415.7	-7.2 --	0.420

<sup>a</sup> Transformed from square root scale.

<sup>b</sup> Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.

<sup>c</sup> P-value is based on difference of means on square root 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.

<b>(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED</b>					
<b>1987 Dioxin Category Summary Statistics</b>			<b>Analysis Results for Log<sub>2</sub> (1987 Dioxin + 1)</b>		
<b>1987 Dioxin</b>	<b>n</b>	<b>Mean<sup>a</sup></b>	<b>R<sup>2</sup></b>	<b>Slope (Std. Error)<sup>b</sup></b>	<b>p-Value</b>
Low	281	455.3	0.010	-0.296 (0.101)	0.003
Medium	281	408.2			
High	282	409.7			

<sup>a</sup> Transformed from square root scale.

<sup>b</sup> Slope and standard error based on square root of total testosterone versus log<sub>2</sub> (1987 dioxin + 1).

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

<b>(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED</b>					
<b>1987 Dioxin Category Summary Statistics</b>			<b>Analysis Results for Log<sub>2</sub> (1987 Dioxin + 1)</b>		
<b>1987 Dioxin</b>	<b>n</b>	<b>Adj. Mean<sup>a</sup></b>	<b>R<sup>2</sup></b>	<b>Adjusted Slope (Std. Error)<sup>b</sup></b>	<b>p-Value</b>
Low	279	439.1	0.193	-0.149 (0.109)	0.172
Medium	281	418.6			
High	281	409.3			

<sup>a</sup> Transformed from square root scale.

<sup>b</sup> Slope and standard error based on square root of total testosterone versus log<sub>2</sub> (1987 dioxin + 1).

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

The unadjusted Model 2 analysis revealed a significant relation between initial dioxin and total testosterone in its continuous form (Table 16-24(c): slope=0.287, p=0.047). After adjusting for covariates, the results became nonsignificant (Table 16-24(d): p=0.927).

The unadjusted and adjusted Model 3 analyses of total testosterone showed no significant mean differences between any of the Ranch Hand dioxin categories and the Comparison group (Table 16-24(e,f): p>0.11 for each contrast).

A significant relation between 1987 dioxin and total testosterone was revealed in the unadjusted Model 4 analysis (Table 16-24(g): slope=-0.296, p=0.003). After covariate adjustment, the results became nonsignificant (Table 16-24(h): p=0.172).

#### 16.2.2.3.17 Total Testosterone (Discrete)

The unadjusted and adjusted Models 1 and 2 analyses of total testosterone in its dichotomous form were not significant (Table 16-25(a-d): p>0.30 for each analysis).

**Table 16-25. Analysis of Total Testosterone (Discrete)**

<b>(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED</b>					
Occupational Category	Group	n	Number (%) Low	Est. Relative Risk (95% C.I.)	p-Value
<i>All</i>	<i>Ranch Hand</i>	850	72 (8.5)	<i>1.17 (0.85,1.61)</i>	<i>0.344</i>
	<i>Comparison</i>	1,227	90 (7.3)		
Officer	Ranch Hand	330	29 (8.8)	1.28 (0.76,2.14)	0.352
	Comparison	485	34 (7.0)		
Enlisted Flyer	Ranch Hand	146	12 (8.2)	1.39 (0.60,3.25)	0.445
	Comparison	182	11 (6.0)		
Enlisted Groundcrew	Ranch Hand	374	31 (8.3)	1.03 (0.64,1.67)	0.890
	Comparison	560	45 (8.0)		

  

<b>(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED</b>		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
<i>All</i>	<i>1.16 (0.83,1.63)</i>	<i>0.378</i>
Officer	1.22 (0.71,2.07)	0.475
Enlisted Flyer	1.21 (0.50,2.96)	0.673
Enlisted Groundcrew	1.11 (0.67,1.83)	0.688

  

<b>(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED</b>				
Initial Dioxin Category Summary Statistics			Analysis Results for Log <sub>2</sub> (Initial Dioxin) <sup>a</sup>	
Initial Dioxin	n	Number (%) Low	Estimated Relative Risk (95% C.I.) <sup>b</sup>	p-Value
Low	156	13 (8.3)	1.00 (0.80,1.26)	0.973
Medium	160	19 (11.9)		
High	156	16 (10.3)		

<sup>a</sup> Adjusted for percent body fat at the time of the blood measurement of dioxin.

<sup>b</sup> Relative risk for a twofold increase in initial dioxin.

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

**Table 16-25. Analysis of Total Testosterone (Discrete) (Continued)**

<b>(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED</b>		
Analysis Results for Log <sub>2</sub> (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.) <sup>a</sup>	p-Value
471	1.16 (0.87,1.55)	0.307

<sup>a</sup> Relative risk for a twofold increase in initial dioxin.

<b>(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED</b>				
Dioxin Category	n	Number (%) Low	Est. Relative Risk (95% C.I.) <sup>ab</sup>	p-Value
Comparison	1,189	88 (7.4)		
Background RH	372	23 (6.2)	1.04 (0.64,1.69)	0.878
Low RH	234	20 (8.6)	1.08 (0.64,1.84)	0.767
High RH	238	28 (11.8)	1.40 (0.88,2.25)	0.156
Low plus High RH	472	48 (10.2)	1.23 (0.84,1.82)	0.285

<sup>a</sup> Relative risk and confidence interval relative to Comparisons.

<sup>b</sup> 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.

<b>(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED</b>			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.) <sup>a</sup>	p-Value
Comparison	1,189		
Background RH	370	0.98 (0.59,1.62)	0.934
Low RH	234	0.95 (0.55,1.62)	0.841
High RH	237	1.55 (0.94,2.55)	0.085
Low plus High RH	471	1.21 (0.82,1.80)	0.340

<sup>a</sup> 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 16-25. Analysis of Total Testosterone (Discrete) (Continued)**

<b>(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED</b>			
<b>1987 Dioxin Category Summary Statistics</b>			<b>Analysis Results for Log<sub>2</sub> (1987 Dioxin + 1)</b>
<b>1987 Dioxin</b>	<b>n</b>	<b>Number (%) Low</b>	<b>Estimated Relative Risk (95% C.I.)<sup>a</sup></b>
Low	281	17 (6.0)	1.22 (1.05,1.43)
Medium	281	21 (7.5)	
High	282	33 (11.7)	<b>p-Value</b> 0.013

<sup>a</sup> Relative risk for a twofold increase in 1987 dioxin.

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

<b>(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED</b>		
<b>Analysis Results for Log<sub>2</sub> (1987 Dioxin + 1)</b>		
<b>n</b>	<b>Adjusted Relative Risk (95% C.I.)<sup>a</sup></b>	<b>p-Value</b>
841	1.20 (0.96,1.49)	0.106

<sup>a</sup> Relative risk for a twofold increase in 1987 dioxin.

The unadjusted Model 3 analysis did not reveal any significant differences between any of the Ranch Hand dioxin categories and the Comparison group (Table 16-25(e):  $p > 0.15$  for each contrast). Adjusting for covariates revealed a marginally significant difference in the percentage of low total testosterone values between Ranch Hands in the high dioxin category and Comparisons (Table 16-25(f): Adj. RR=1.55,  $p=0.085$ ). The percentage of low total testosterone values for Ranch Hands in the high dioxin category was 11.8 versus 7.4 percent for Comparisons.

The unadjusted Model 4 analysis revealed a significant relation between 1987 dioxin and total testosterone in its discrete form (Table 16-25(g): Est. RR=1.22,  $p=0.013$ ). After adjusting for covariates, the results became nonsignificant (Table 16-25(h):  $p=0.106$ ).

#### 16.2.2.3.18 Free Testosterone (Continuous)

The unadjusted and adjusted Model 1 analyses did not reveal a significant difference in mean free testosterone levels between all Ranch Hands and Comparisons or after stratifying by occupation (Table 16-26(a,b):  $p > 0.20$  for each analysis).

**Table 16-26. Analysis of Free Testosterone (pg/ml) (Continuous)**

<b>(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED</b>					
Occupational Category	Group	n	Mean <sup>a</sup>	Difference of Means (95% C.I.) <sup>b</sup>	p-Value <sup>c</sup>
<i>All</i>	<i>Ranch Hand</i>	<i>850</i>	<i>13.96</i>	<i>0.04 --</i>	<i>0.852</i>
	<i>Comparison</i>	<i>1,227</i>	<i>13.92</i>		
Officer	Ranch Hand	330	12.91	-0.36 --	0.269
	Comparison	485	13.26		
Enlisted Flyer	Ranch Hand	146	14.03	0.08 --	0.878
	Comparison	182	13.95		
Enlisted Groundcrew	Ranch Hand	374	14.89	0.40 --	0.209
	Comparison	560	14.49		

<sup>a</sup> Transformed from square root scale.

<sup>b</sup> Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.

<sup>c</sup> P-value is based on difference of means on square root scale.

<b>(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED</b>					
Occupational Category	Group	n	Adjusted Mean <sup>a</sup>	Difference of Adj. Means (95% C.I.) <sup>b</sup>	p-Value <sup>c</sup>
<i>All</i>	<i>Ranch Hand</i>	<i>847</i>	<i>13.80</i>	<i>0.01 --</i>	<i>0.941</i>
	<i>Comparison</i>	<i>1,227</i>	<i>13.79</i>		
Officer	Ranch Hand	329	13.39	-0.21 --	0.464
	Comparison	485	13.61		
Enlisted Flyer	Ranch Hand	145	14.23	0.13 --	0.783
	Comparison	182	14.10		
Enlisted Groundcrew	Ranch Hand	373	13.81	0.17 --	0.528
	Comparison	560	13.64		

<sup>a</sup> Transformed from square root scale.

<sup>b</sup> Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.

<sup>c</sup> P-value is based on difference of means on square root scale.

<b>(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED</b>						
Initial Dioxin Category Summary Statistics				Analysis Results for Log <sub>2</sub> (Initial Dioxin) <sup>b</sup>		
Initial Dioxin	n	Mean <sup>a</sup>	Adj. Mean <sup>ab</sup>	R <sup>2</sup>	Slope (Std. Error) <sup>c</sup>	p-Value
Low	156	13.08	12.94	0.084	0.066 (0.022)	0.003
Medium	160	13.69	13.68			
High	156	14.59	14.75			

<sup>a</sup> Transformed from square root scale.

<sup>b</sup> Adjusted for percent body fat at the time of the blood measurement of dioxin.

<sup>c</sup> Slope and standard error based on square root of free testosterone versus log<sub>2</sub> (initial dioxin).

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

**Table 16-26. Analysis of Free Testosterone (pg/ml) (Continuous) (Continued)**

<b>(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED</b>					
Initial Dioxin Category Summary Statistics			Analysis Results for Log <sub>2</sub> (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean <sup>a</sup>	R <sup>2</sup>	Adj. Slope (Std. Error) <sup>b</sup>	p-Value
Low	156	13.42	0.240	-0.008 (0.024)	0.742
Medium	159	13.61			
High	156	13.61			

<sup>a</sup> Transformed from square root scale.

<sup>b</sup> Slope and standard error based on square root of free testosterone versus log<sub>2</sub> (initial dioxin).

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

<b>(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED</b>					
Dioxin Category	n	Mean <sup>a</sup>	Adj. Mean <sup>ab</sup>	Difference of Adj. Mean vs. Comparisons (95% C.I.) <sup>c</sup>	p-Value <sup>d</sup>
Comparison	1,189	13.93	13.95		
Background RH	372	14.24	13.85	-0.10 --	0.703
Low RH	234	13.11	13.23	-0.72 --	0.022
High RH	238	14.46	14.85	0.90 --	0.006
Low plus High RH	472	13.78	14.03	0.08 --	0.745

<sup>a</sup> Transformed from square root scale.

<sup>b</sup> Adjusted for percent body fat at the time of the blood measurement of dioxin.

<sup>c</sup> Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.

<sup>d</sup> P-value is based on difference of means on square root 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.

<b>(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED</b>					
Dioxin Category	n	Adj. Mean <sup>a</sup>	Difference of Adj. Mean vs. Comparisons (95% C.I.) <sup>b</sup>	p-Value <sup>c</sup>	
Comparison	1,189	13.80			
Background RH	370	13.98	0.18 --	0.459	
Low RH	234	13.50	-0.30 --	0.315	
High RH	237	13.94	0.14 --	0.643	
Low plus High RH	471	13.72	-0.08 --	0.735	

<sup>a</sup> Transformed from square root scale.

<sup>b</sup> Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.

<sup>c</sup> P-value is based on difference of means on square root 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 16-26. Analysis of Free Testosterone (pg/ml) (Continuous) (Continued)**

<b>(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED</b>					
1987 Dioxin Category Summary Statistics			Analysis Results for Log <sub>2</sub> (1987 Dioxin +1)		
1987 Dioxin	n	Mean <sup>a</sup>	R <sup>2</sup>	Slope (Std. Error) <sup>b</sup>	p-Value
Low	281	14.56	0.001	-0.010 (0.015)	0.489
Medium	281	13.17			
High	282	14.23			

<sup>a</sup> Transformed from square root scale.

<sup>b</sup> Slope and standard error based on square root of free testosterone versus log<sub>2</sub> (1987 dioxin + 1).

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

<b>(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED</b>					
1987 Dioxin Category Summary Statistics			Analysis Results for Log <sub>2</sub> (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean <sup>a</sup>	R <sup>2</sup>	Adjusted Slope (Std. Error) <sup>b</sup>	p-Value
Low	279	14.49	0.234	-0.029 (0.016)	0.066
Medium	281	13.65			
High	281	13.66			

<sup>a</sup> Transformed from square root scale.

<sup>b</sup> Slope and standard error based on square root of free testosterone versus log<sub>2</sub> (1987 dioxin + 1).

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

A significant association was seen between free testosterone and initial dioxin in the unadjusted Model 2 analysis (Table 16-26(c): slope=0.066, p=0.003). The adjusted analysis results were nonsignificant (Table 16-26(d): p=0.742).

The unadjusted Model 3 analysis of free testosterone in its continuous form revealed two significant contrasts: Ranch Hands in the low dioxin category versus Comparisons and Ranch Hands in the high dioxin category versus Comparisons (Table 16-26(e): difference of means=-0.72 pg/ml, p=0.022; difference of means=0.90 pg/ml, p=0.006, respectively). The adjusted analysis did not reveal any significant contrasts (Table 16-26(f): p>0.31 for each contrast).

The unadjusted Model 4 analysis did not reveal any significant relation between 1987 dioxin and free testosterone in its continuous form (Table 16-26(g): p=0.489). After covariate adjustment, a marginally significant inverse relation between 1987 dioxin and mean free testosterone level was seen (Table 16-26(h): adjusted slope=-0.029, p=0.066). The adjusted mean free testosterone levels in the low, medium, and high 1987 dioxin categories were 14.49 pg/ml, 13.65 pg/ml, and 13.66 pg/ml, respectively.

#### 16.2.2.3.19 Free Testosterone (Discrete)

The unadjusted and adjusted Model 1 analyses did not reveal a significant overall group difference between Ranch Hands and Comparisons (Table 16-27(a,b): p>0.81 for both analyses). In each of the unadjusted and adjusted analyses, stratifying by occupation revealed a marginally significant difference between Ranch Hands and Comparisons in the enlisted flyer stratum (Table 16-27(a,b): Est. RR=7.76,

p=0.059; Adj. RR=6.41, p=0.091, respectively). The percentage of low free testosterone values for the Ranch Hand enlisted flyers was 4.1 versus 0.5 percent for Comparison enlisted flyers.

**Table 16-27. Analysis of Free Testosterone (Discrete)**

<b>(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED</b>					
Occupational Category	Group	n	Number (%) Low	Est. Relative Risk (95% C.I.)	p-Value
<i>All</i>	<i>Ranch Hand</i>	850	15 (1.8)	1.08 (0.55,2.13)	0.815
	<i>Comparison</i>	1,227	20 (1.6)		
Officer	Ranch Hand	330	7 (2.1)	1.03 (0.39,2.73)	0.954
	Comparison	485	10 (2.1)		
Enlisted Flyer	Ranch Hand	146	6 (4.1)	7.76 (0.92,65.18)	0.059
	Comparison	182	1 (0.5)		
Enlisted Groundcrew	Ranch Hand	374	2 (0.5)	0.33 (0.07,1.53)	0.157
	Comparison	560	9 (1.6)		

<b>(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED</b>		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
<i>All</i>	1.09 (0.54,2.19)	0.812
Officer	1.06 (0.39,2.90)	0.911
Enlisted Flyer	6.41 (0.74,55.13)	0.091
Enlisted Groundcrew	0.37 (0.08,1.76)	0.210

<b>(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED</b>				
Initial Dioxin Category Summary Statistics			Analysis Results for Log <sub>2</sub> (Initial Dioxin) <sup>a</sup>	
Initial Dioxin	n	Number (%) Low	Estimated Relative Risk (95% C.I.) <sup>b</sup>	p-Value
Low	156	5 (3.2)	0.46 (0.21,0.98)	0.019
Medium	160	4 (2.5)		
High	156	0 (0.0)		

<sup>a</sup> Adjusted for percent body fat at the time of the blood measurement of dioxin.

<sup>b</sup> Relative risk for a twofold increase in initial dioxin.

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

<b>(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED</b>		
Analysis Results for Log <sub>2</sub> (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.) <sup>a</sup>	p-Value
471	0.41 (0.14,1.18)	0.051

<sup>a</sup> Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for occupation because of the sparse number of participants with a low free testosterone level.

**Table 16-27. Analysis of Free Testosterone (Discrete) (Continued)**

<b>(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED</b>				
<b>Dioxin Category</b>	<b>n</b>	<b>Number (%) Low</b>	<b>Est. Relative Risk (95% C.I.)<sup>ab</sup></b>	<b>p-Value</b>
Comparison	1,189	20 (1.7)		
Background RH	372	5 (1.3)	0.94 (0.35,2.55)	0.906
Low RH	234	8 (3.4)	1.95 (0.84,4.52)	0.120
High RH	238	1 (0.4)	0.21 (0.03,1.57)	0.128
Low plus High RH	472	9 (1.9)	0.63 (0.20,1.99)	0.431

<sup>a</sup> Relative risk and confidence interval relative to Comparisons.

<sup>b</sup> 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.

<b>(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED</b>			
<b>Dioxin Category</b>	<b>n</b>	<b>Adjusted Relative Risk (95% C.I.)<sup>a</sup></b>	<b>p-Value</b>
Comparison	1,189		
Background RH	370	0.88 (0.32,2.46)	0.811
Low RH	234	1.38 (0.57,3.35)	0.470
High RH	237	0.28 (0.04,2.21)	0.227
Low plus High RH	471	0.62 (0.19,2.01)	0.424

<sup>a</sup> 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.

<b>(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED</b>			<b>Analysis Results for Log<sub>2</sub> (1987 Dioxin + 1)</b>	
<b>1987 Dioxin Category Summary Statistics</b>			<b>Estimated Relative Risk (95% C.I.)<sup>a</sup></b>	
<b>1987 Dioxin</b>	<b>n</b>	<b>Number (%) Low</b>	<b>p-Value</b>	
Low	281	2 (0.7)	0.94 (0.65,1.36)	
Medium	281	9 (3.2)	0.744	
High	282	3 (1.1)		

<sup>a</sup> 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 16-27. Analysis of Free Testosterone (Discrete) (Continued)**

<b>(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED</b>		
<b>Analysis Results for Log<sub>2</sub> (1987 Dioxin + 1)</b>		
<b>n</b>	<b>Adjusted Relative Risk (95% C.I.)<sup>a</sup></b>	<b>p-Value</b>
841	0.94 (0.52,1.70)	0.835

<sup>a</sup> Relative risk for a twofold increase in 1987 dioxin.

Both the unadjusted and adjusted Model 2 analyses revealed significant relations between initial dioxin and free testosterone (Table 16-27(c,d): Est. RR=0.46, p=0.019; Adj. RR=0.41, p=0.051, respectively). The percentages of low free testosterone values within the low, medium, and high initial dioxin categories were 3.2, 2.5, and 0.0, respectively.

The unadjusted and adjusted Models 3 and 4 analyses were nonsignificant (Table 16-27(e–h): p≥0.12 for each analysis).

*16.2.2.3.20 Estradiol (Continuous)*

Unadjusted and adjusted Model 1 analyses of estradiol in its continuous form did not reveal significant overall group differences between Ranch Hands and Comparisons (Table 16-28(a,b): p>0.38 for each analysis). After stratifying by occupation, a significant difference was seen between Ranch Hand officers and Comparison officers in both the unadjusted and adjusted analyses (Table 16-28(a,b): difference of means=-3.43 pg/ml, p=0.003, for unadjusted; difference of adjusted means=-3.55 pg/ml, p=0.003, for adjusted). The adjusted mean estradiol value for Ranch Hand officers was 40.35 pg/ml versus a mean value of 43.90 pg/ml for Comparison officers.

**Table 16-28. Analysis of Estradiol (pg/ml) (Continuous)**

<b>(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED</b>					
<b>Occupational Category</b>	<b>Group</b>	<b>n</b>	<b>Mean<sup>a</sup></b>	<b>Difference of Means (95% C.I.)<sup>b</sup></b>	<b>p-Value<sup>c</sup></b>
<i>All</i>	<i>Ranch Hand</i>	<i>870</i>	<i>40.06</i>	<i>-0.57 --</i>	<i>0.434</i>
	<i>Comparison</i>	<i>1,251</i>	<i>40.63</i>		
Officer	Ranch Hand	341	38.38	-3.43 --	0.003
	Comparison	494	41.81		
Enlisted Flyer	Ranch Hand	151	42.87	2.17 --	0.238
	Comparison	187	40.70		
Enlisted Groundcrew	Ranch Hand	378	40.49	0.89 --	0.418
	Comparison	570	39.60		

<sup>a</sup> Transformed from square root scale.

<sup>b</sup> Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.

<sup>c</sup> P-value is based on difference of means on square root scale.

**Table 16-28. Analysis of Estradiol (pg/ml) (Continuous) (Continued)**

<b>(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED</b>					
Occupational Category	Group	n	Adjusted Mean <sup>a</sup>	Difference of Adj. Means (95% C.I.) <sup>b</sup>	p-Value <sup>c</sup>
<i>All</i>	<i>Ranch Hand</i>	<i>870</i>	<i>42.18</i>	<i>-0.65 --</i>	<i>0.384</i>
	<i>Comparison</i>	<i>1,251</i>	<i>42.83</i>		
Officer	Ranch Hand	341	40.35	-3.55 --	0.003
	Comparison	494	43.90		
Enlisted Flyer	Ranch Hand	151	44.77	2.21 --	0.241
	Comparison	187	42.56		
Enlisted Groundcrew	Ranch Hand	378	42.26	0.89 --	0.427
	Comparison	570	41.37		

<sup>a</sup> Transformed from square root scale.

<sup>b</sup> Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.

<sup>c</sup> P-value is based on difference of means on square root scale.

<b>(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED</b>						
Initial Dioxin Category Summary Statistics				Analysis Results for Log <sub>2</sub> (Initial Dioxin) <sup>b</sup>		
Initial Dioxin	n	Mean <sup>a</sup>	Adj. Mean <sup>ab</sup>	R <sup>2</sup>	Slope (Std. Error) <sup>c</sup>	p-Value
Low	160	38.37	38.41	0.007	0.084 (0.049)	0.087
Medium	162	42.23	42.24			
High	160	41.37	41.32			

<sup>a</sup> Transformed from square root scale.

<sup>b</sup> Adjusted for percent body fat at the time of the blood measurement of dioxin.

<sup>c</sup> Slope and standard error based on square root of estradiol versus log<sub>2</sub> (initial dioxin).

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

<b>(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED</b>						
Initial Dioxin Category Summary Statistics				Analysis Results for Log <sub>2</sub> (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean <sup>a</sup>		R <sup>2</sup>	Adj. Slope (Std. Error) <sup>b</sup>	p-Value
Low	160	40.16		0.019	0.046 (0.057)	0.423
Medium	162	42.95				
High	160	41.36				

<sup>a</sup> Transformed from square root scale.

<sup>b</sup> Slope and standard error based on square root of estradiol versus log<sub>2</sub> (initial dioxin).

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

**Table 16-28. Analysis of Estradiol (pg/ml) (Continuous) (Continued)**

<b>(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED</b>					
<b>Dioxin Category</b>	<b>n</b>	<b>Mean<sup>a</sup></b>	<b>Adj. Mean<sup>ab</sup></b>	<b>Difference of Adj. Mean vs. Comparisons (95% C.I.)<sup>c</sup></b>	<b>p-Value<sup>d</sup></b>
Comparison	1,213	40.69	40.68		
Background RH	381	39.50	39.71	-0.97 --	0.323
Low RH	239	39.65	39.58	-1.10 --	0.350
High RH	243	41.64	41.43	0.75 --	0.523
Low plus High RH	482	40.65	40.51	-0.17 --	0.852

<sup>a</sup> Transformed from square root scale.

<sup>b</sup> Adjusted for percent body fat at the time of the blood measurement of dioxin.

<sup>c</sup> Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.

<sup>d</sup> P-value is based on difference of means on square root 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.

<b>(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED</b>					
<b>Dioxin Category</b>	<b>n</b>	<b>Adj. Mean<sup>a</sup></b>	<b>Difference of Adj. Mean vs. Comparisons (95% C.I.)<sup>b</sup></b>	<b>p-Value<sup>c</sup></b>	
Comparison	1,213	42.96			
Background RH	381	41.76	-1.20 --	0.241	
Low RH	239	41.51	-1.45 --	0.231	
High RH	243	44.13	1.17 --	0.347	
Low plus High RH	482	42.82	-0.14 --	0.888	

<sup>a</sup> Transformed from square root scale.

<sup>b</sup> Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.

<sup>c</sup> P-value is based on difference of means on square root 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 16-28. Analysis of Estradiol (pg/ml) (Continuous) (Continued)**

<b>(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED</b>					
1987 Dioxin Category Summary Statistics			Analysis Results for Log <sub>2</sub> (1987 Dioxin +1)		
1987 Dioxin	n	Mean <sup>a</sup>	R <sup>2</sup>	Adjusted Slope (Std. Error) <sup>b</sup>	p-Value
Low	288	39.14	0.002	0.039 (0.031)	0.212
Medium	287	39.72			
High	288	41.57			

<sup>a</sup> Transformed from square root scale.

<sup>b</sup> Slope and standard error based on square root of estradiol versus log<sub>2</sub> (1987 dioxin + 1).

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

<b>(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED</b>					
1987 Dioxin Category Summary Statistics			Analysis Results for Log <sub>2</sub> (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean <sup>a</sup>	R <sup>2</sup>	Adjusted Slope (Std. Error) <sup>b</sup>	p-Value
Low	288	42.60	0.017	0.019 (0.036)	0.599
Medium	287	42.42			
High	288	44.00			

<sup>a</sup> Transformed from square root scale.

<sup>b</sup> Slope and standard error based on square root of estradiol versus log<sub>2</sub> (1987 dioxin + 1).

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

The unadjusted Model 2 analysis revealed a marginally significant positive association between estradiol in its continuous form and initial dioxin (Table 16-28(c): slope=0.084, p=0.087). After adjusting for covariates, the results became nonsignificant (Table 16-28(d): p=0.423).

Unadjusted and adjusted analyses for Models 3 and 4 were nonsignificant (Table 16-28(e–h): p>0.21 for each analysis).

#### 16.2.2.3.21 Estradiol (Discrete)

The unadjusted and adjusted Model 1 analyses of estradiol in its discrete form did not reveal a significant difference between Ranch Hands and Comparisons (Table 16-29(a,b): p≥0.12 for each contrast).

**Table 16-29. Analysis of Estradiol (Discrete)**

<b>(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED</b>					
Occupational Category	Group	n	Number (%) High	Est. Relative Risk (95% C.I.)	p-Value
<i>All</i>	<i>Ranch Hand</i>	870	236 (27.1)	0.96 (0.79,1.16)	0.666
	<i>Comparison</i>	1,251	350 (28.0)		
Officer	Ranch Hand	341	80 (23.5)	0.78 (0.57,1.08)	0.131
	Comparison	494	139 (28.1)		
Enlisted Flyer	Ranch Hand	151	44 (29.1)	0.89 (0.56,1.42)	0.632
	Comparison	187	59 (31.6)		
Enlisted Groundcrew	Ranch Hand	378	112 (29.6)	1.16 (0.87,1.55)	0.319
	Comparison	570	152 (26.7)		

**Table 16-29. Analysis of Estradiol (Discrete) (Continued)**

<b>(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED</b>		
<b>Occupational Category</b>	<b>Adjusted Relative Risk (95% C.I.)</b>	<b>p-Value</b>
<i>All</i>	<b>0.95 (0.78,1.16)</b>	<b>0.619</b>
Officer	0.78 (0.56,1.07)	0.120
Enlisted Flyer	0.89 (0.56,1.42)	0.616
Enlisted Groundcrew	1.16 (0.87,1.55)	0.312

<b>(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED</b>				
<b>Initial Dioxin Category Summary Statistics</b>			<b>Analysis Results for Log<sub>2</sub> (Initial Dioxin)<sup>a</sup></b>	
<b>Initial Dioxin</b>	<b>n</b>	<b>Number (%) High</b>	<b>Estimated Relative Risk (95% C.I.)<sup>b</sup></b>	<b>p-Value</b>
Low	160	33 (20.6)	1.17 (1.00,1.36)	0.045
Medium	162	52 (32.1)		
High	160	47 (29.4)		

<sup>a</sup> Adjusted for percent body fat at the time of the blood measurement of dioxin.

<sup>b</sup> Relative risk for a twofold increase in initial dioxin.

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

<b>(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED</b>			
<b>Analysis Results for Log<sub>2</sub> (Initial Dioxin)</b>			
<b>n</b>	<b>Adjusted Relative Risk (95% C.I.)<sup>a</sup></b>		<b>p-Value</b>
482	1.12 (0.94,1.33)		0.213

<sup>a</sup> Relative risk for a twofold increase in initial dioxin.

<b>(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED</b>				
<b>Dioxin Category</b>	<b>n</b>	<b>Number (%) High</b>	<b>Est. Relative Risk (95% C.I.)<sup>ab</sup></b>	<b>p-Value</b>
Comparison	1,213	343 (28.3)		
Background RH	381	102 (26.8)	0.96 (0.74,1.25)	0.774
Low RH	239	59 (24.7)	0.82 (0.60,1.13)	0.234
High RH	243	73 (30.0)	1.05 (0.78,1.43)	0.731
Low plus High RH	482	132 (27.4)	0.93 (0.74,1.18)	0.566

<sup>a</sup> Relative risk and confidence interval relative to Comparisons.

<sup>b</sup> 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 16-29. Analysis of Estradiol (Discrete) (Continued)**

<b>(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED</b>			
<b>Dioxin Category</b>	<b>n</b>	<b>Adjusted Relative Risk (95% C.I.)<sup>a</sup></b>	<b>p-Value</b>
Comparison	1,213		
Background RH	381	0.97 (0.75,1.27)	0.842
Low RH	239	0.79 (0.57,1.09)	0.155
High RH	243	1.05 (0.77,1.44)	0.757
Low plus High RH	482	0.91 (0.72,1.16)	0.460

<sup>a</sup> 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.

<b>(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED</b>				
<b>1987 Dioxin Category Summary Statistics</b>			<b>Analysis Results for Log<sub>2</sub> (1987 Dioxin + 1)</b>	
<b>1987 Dioxin</b>	<b>n</b>	<b>Number (%) High</b>	<b>Estimated Relative Risk (95% C.I.)<sup>a</sup></b>	<b>p-Value</b>
Low	288	79 (27.4)	1.04 (0.94,1.15)	0.430
Medium	287	69 (24.0)		
High	288	86 (29.9)		

<sup>a</sup> Relative risk for a twofold increase in 1987 dioxin.

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

<b>(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED</b>			
<b>Analysis Results for Log<sub>2</sub> (1987 Dioxin + 1)</b>			
<b>n</b>	<b>Adjusted Relative Risk (95% C.I.)<sup>a</sup></b>		<b>p-Value</b>
863	0.99 (0.89,1.12)		0.926

<sup>a</sup> Relative risk for a twofold increase in 1987 dioxin.

A significant relation was seen between estradiol and initial dioxin in the unadjusted Model 2 analysis (Table 16-29(c): Est. RR=1.17, p=0.045). After adjusting for covariates, the results became nonsignificant (Table 16-29(d): p=0.213).

Unadjusted and adjusted analyses for Models 3 and 4 were nonsignificant (Table 13-29(e–h): p>0.15 for each analysis).

#### 16.2.2.3.22 LH (Continuous)

The unadjusted and adjusted analysis of LH did not show a significant relation with dioxin in Models 1 through 3 (Table 16-30(a–f): p>0.13 for each analysis).

**Table 16-30. Analysis of LH (mIU/ml) (Continuous)**

<b>(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED</b>					
Occupational Category	Group	n	Mean <sup>a</sup>	Difference of Means (95% C.I.) <sup>b</sup>	p-Value <sup>c</sup>
<i>All</i>	<i>Ranch Hand</i>	870	3.86	0.00 --	0.979
	<i>Comparison</i>	1,251	3.86		
Officer	Ranch Hand	341	4.09	0.27 --	0.131
	Comparison	494	3.82		
Enlisted Flyer	Ranch Hand	151	3.67	-0.34 --	0.194
	Comparison	187	4.02		
Enlisted Groundcrew	Ranch Hand	378	3.74	-0.11 --	0.491
	Comparison	570	3.85		

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

<sup>c</sup> P-value is based on difference of means on natural logarithm scale.

<b>(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED</b>					
Occupational Category	Group	n	Adjusted Mean <sup>a</sup>	Difference of Adj. Means (95% C.I.) <sup>b</sup>	p-Value <sup>c</sup>
<i>All</i>	<i>Ranch Hand</i>	870	3.84	-0.01 --	0.955
	<i>Comparison</i>	1,251	3.85		
Officer	Ranch Hand	341	3.85	0.22 --	0.185
	Comparison	494	3.63		
Enlisted Flyer	Ranch Hand	151	3.55	-0.37 --	0.147
	Comparison	187	3.92		
Enlisted Groundcrew	Ranch Hand	378	4.03	-0.08 --	0.650
	Comparison	570	4.10		

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

<sup>c</sup> P-value is based on difference of means on natural logarithm scale.

<b>(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED</b>				<b>Analysis Results for Log<sub>2</sub> (Initial Dioxin)<sup>b</sup></b>		
<b>Initial Dioxin Category Summary Statistics</b>				<b>R<sup>2</sup></b>	<b>Slope (Std. Error)<sup>c</sup></b>	<b>p-Value</b>
<b>Initial Dioxin</b>	<b>n</b>	<b>Mean<sup>a</sup></b>	<b>Adj. Mean<sup>ab</sup></b>			
Low	160	3.84	3.84	0.001	-0.016 (0.023)	0.496
Medium	162	3.82	3.82			
High	160	3.66	3.65			

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Adjusted for percent body fat at the time of the blood measurement of dioxin.

<sup>c</sup> Slope and standard error based on natural logarithm of LH versus log<sub>2</sub> (initial dioxin).

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

**Table 16-30. Analysis of LH (mIU/ml) (Continuous) (Continued)**

<b>(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED</b>					
<b>Initial Dioxin Category Summary Statistics</b>			<b>Analysis Results for Log<sub>2</sub> (Initial Dioxin)</b>		
<b>Initial Dioxin</b>	<b>n</b>	<b>Adj. Mean<sup>a</sup></b>	<b>R<sup>2</sup></b>	<b>Adj. Slope (Std. Error)<sup>b</sup></b>	<b>p-Value</b>
Low	160	3.65	0.014	-0.008 (0.027)	0.755
Medium	162	3.67			
High	160	3.56			

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Slope and standard error based on natural logarithm of LH versus log<sub>2</sub> (initial dioxin).

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

<b>(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED</b>					
<b>Dioxin Category</b>	<b>n</b>	<b>Mean<sup>a</sup></b>	<b>Adj. Mean<sup>ab</sup></b>	<b>Difference of Adj. Mean vs. Comparisons (95% C.I.)<sup>c</sup></b>	<b>p-Value<sup>d</sup></b>
Comparison	1,213	3.85	3.85		
Background RH	381	4.04	4.01	0.16 --	0.264
Low RH	239	3.82	3.83	-0.02 --	0.900
High RH	243	3.72	3.74	-0.11 --	0.504
Low plus High RH	482	3.77	3.78	-0.07 --	0.601

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Adjusted for percent body fat at the time of the blood measurement of dioxin.

<sup>c</sup> Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

<sup>d</sup> 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 16-30. Analysis of LH (mIU/ml) (Continuous) (Continued)**

<b>(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED</b>				
Dioxin Category	n	Adj. Mean <sup>a</sup>	Difference of Adj. Mean vs. Comparisons (95% C.I.) <sup>b</sup>	p-Value <sup>c</sup>
Comparison	1,213	3.84		
Background RH	381	4.00	0.16 --	0.281
Low RH	239	3.73	-0.11 --	0.479
High RH	243	3.81	-0.03 --	0.839
Low plus High RH	482	3.77	-0.07 --	0.553

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

<sup>c</sup> 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.

<b>(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED</b>					
1987 Dioxin Category Summary Statistics			Analysis Results for Log <sub>2</sub> (1987 Dioxin + 1)		
1987 Dioxin	n	Mean <sup>a</sup>	R <sup>2</sup>	Adjusted Slope (Std. Error) <sup>b</sup>	p-Value
Low	288	4.15	0.005	-0.030 (0.015)	0.042
Medium	287	3.75			
High	288	3.77			

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Slope and standard error based on natural logarithm of LH versus log<sub>2</sub> (1987 dioxin + 1).

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

<b>(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED</b>					
1987 Dioxin Category Summary Statistics			Analysis Results for Log <sub>2</sub> (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean <sup>a</sup>	R <sup>2</sup>	Adjusted Slope (Std. Error) <sup>b</sup>	p-Value
Low	288	4.13	0.034	-0.024 (0.017)	0.149
Medium	287	3.67			
High	288	3.87			

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Slope and standard error based on natural logarithm of LH versus log<sub>2</sub> (1987 dioxin + 1).

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

The unadjusted Model 4 analysis revealed a significant inverse association between LH in its continuous form and 1987 dioxin (Table 16-30(g): slope=-0.030, p=0.042). After adjusting for covariates, the results became nonsignificant (Table 16-30(h): p=0.149).

#### 16.2.2.3.23 LH (Discrete)

All unadjusted and adjusted analyses in Models 1, 2, and 3 showed no significant relation between group or dioxin and the discrete form of LH (Table 16-31(a-f): p≥0.28 for each analysis). A marginally significant inverse association was seen between 1987 dioxin and LH in the unadjusted Model 4 analysis (Table 16-31(g): Est. RR=0.84, p=0.094). After adjusting for covariates, the results became nonsignificant (Table 16-31(h): p=0.154).

**Table 16-31. Analysis of LH (Discrete)**

<b>(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED</b>					
Occupational Category	Group	n	Number (%) High	Est. Relative Risk (95% C.I.)	p-Value
<i>All</i>	<i>Ranch Hand</i>	870	49 (5.6)	1.01 (0.69,1.47)	0.971
	<i>Comparison</i>	1,251	70 (5.6)		
Officer	Ranch Hand	341	24 (7.0)	1.26 (0.72,2.21)	0.422
	Comparison	494	28 (5.7)		
Enlisted Flyer	Ranch Hand	151	6 (4.0)	0.93 (0.31,2.73)	0.889
	Comparison	187	8 (4.3)		
Enlisted Groundcrew	Ranch Hand	378	19 (5.0)	0.83 (0.47,1.49)	0.538
	Comparison	570	34 (6.0)		

  

<b>(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED</b>		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
<i>All</i>	1.02 (0.70,1.50)	0.907
Officer	1.24 (0.70,2.20)	0.458
Enlisted Flyer	0.86 (0.29,2.55)	0.782
Enlisted Groundcrew	0.88 (0.49,1.59)	0.674

  

<b>(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED</b>				
Initial Dioxin Category Summary Statistics			Analysis Results for Log <sub>2</sub> (Initial Dioxin) <sup>a</sup>	
Initial Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.) <sup>b</sup>	p-Value
Low	160	8 (5.0)	0.93 (0.65,1.32)	0.668
Medium	162	7 (4.3)		
High	160	6 (3.8)		

<sup>a</sup> Adjusted for percent body fat at the time of the blood measurement of dioxin.

<sup>b</sup> Relative risk for a twofold increase in initial dioxin.

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

**Table 16-31. Analysis of LH (Discrete) (Continued)**

<b>(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED</b>		
Analysis Results for Log <sub>2</sub> (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.) <sup>a</sup>	p-Value
482	0.97 (0.65,1.43)	0.873

<sup>a</sup> Relative risk for a twofold increase in initial dioxin.

<b>(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED</b>				
Dioxin Category	n	Number (%) High	Est. Relative Risk (95% C.I.) <sup>ab</sup>	p-Value
Comparison	1,213	67 (5.5)		
Background RH	381	27 (7.1)	1.27 (0.79,2.02)	0.322
Low RH	239	12 (5.0)	0.91 (0.48,1.71)	0.770
High RH	243	9 (3.7)	0.68 (0.33,1.38)	0.280
Low plus High RH	482	21 (4.4)	0.78 (0.47,1.30)	0.345

<sup>a</sup> Relative risk and confidence interval relative to Comparisons.

<sup>b</sup> 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.

<b>(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED</b>			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.) <sup>a</sup>	p-Value
Comparison	1,213		
Background RH	381	1.28 (0.79,2.08)	0.313
Low RH	239	0.83 (0.44,1.58)	0.573
High RH	243	0.76 (0.36,1.60)	0.475
Low plus High RH	482	0.80 (0.47,1.34)	0.392

<sup>a</sup> 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 16-31. Analysis of LH (Discrete) (Continued)**

<b>(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED</b>			
1987 Dioxin Category Summary Statistics			Analysis Results for Log <sub>2</sub> (1987 Dioxin + 1)
1987 Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.) <sup>a</sup>
Low	288	21 (7.3)	0.84 (0.68,1.04)
Medium	287	15 (5.2)	
High	288	12 (4.2)	
			<b>p-Value</b>
			0.094

<sup>a</sup> Relative risk for a twofold increase in 1987 dioxin.

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

<b>(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED</b>		
Analysis Results for Log <sub>2</sub> (1987 Dioxin + 1)		
n	Adjusted Relative Risk (95% C.I.) <sup>a</sup>	p-Value
863	0.84 (0.66,1.07)	0.154

<sup>a</sup> Relative risk for a twofold increase in 1987 dioxin.

**16.2.2.3.24 FSH (Continuous)**

The Model 1 unadjusted analysis of FSH did not show an overall group difference between Ranch Hands and Comparisons (Table 16-32(a): p=0.666). Stratifying by occupation revealed a marginally significant difference between Ranch Hands and Comparisons within the officer stratum (Table 16-32(a): difference of means=0.51 mIU/ml, p=0.071). The mean FSH value for Ranch Hand officers was 6.62 mIU/ml versus 6.11 mIU/ml for Comparison officers. The adjusted analysis of FSH revealed no significant difference between Ranch Hands and Comparisons across all occupations or within each occupational stratum (Table 16-32(b): p>0.11 for each contrast).

**Table 16-32. Analysis of FSH (mIU/ml) (Continuous)**

<b>(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED</b>					
Occupational Category	Group	n	Mean <sup>a</sup>	Difference of Means (95% C.I.) <sup>b</sup>	p-Value <sup>c</sup>
<i>All</i>	<i>Ranch Hand</i>	<i>870</i>	<i>6.05</i>	<i>0.07 --</i>	<i>0.666</i>
	<i>Comparison</i>	<i>1,251</i>	<i>5.98</i>		
Officer	Ranch Hand	341	6.62	0.51 --	0.071
	Comparison	494	6.11		
Enlisted Flyer	Ranch Hand	151	6.02	0.03 --	0.941
	Comparison	187	5.99		
Enlisted Groundcrew	Ranch Hand	378	5.59	-0.27 --	0.257
	Comparison	570	5.86		

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

<sup>c</sup> P-value is based on difference of means on natural logarithm scale.

**Table 16-32. Analysis of FSH (mIU/ml) (Continuous) (Continued)**

<b>(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED</b>					
Occupational Category	Group	n	Adjusted Mean <sup>a</sup>	Difference of Adj. Means (95% C.I.) <sup>b</sup>	p-Value <sup>c</sup>
<i>All</i>	<i>Ranch Hand</i>	870	5.92	0.06 --	0.689
	<i>Comparison</i>	1,251	5.85		
Officer	Ranch Hand	341	6.01	0.40 --	0.112
	Comparison	494	5.62		
Enlisted Flyer	Ranch Hand	151	5.67	-0.03 --	0.928
	Comparison	187	5.70		
Enlisted Groundcrew	Ranch Hand	378	6.06	-0.21 --	0.401
	Comparison	570	6.27		

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

<sup>c</sup> P-value is based on difference of means on natural logarithm scale.

<b>(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED</b>						
Initial Dioxin Category Summary Statistics				Analysis Results for Log <sub>2</sub> (Initial Dioxin) <sup>b</sup>		
Initial Dioxin	n	Mean <sup>a</sup>	Adj. Mean <sup>ab</sup>	R <sup>2</sup>	Slope (Std. Error) <sup>c</sup>	p-Value
Low	160	6.40	6.42	0.008	-0.035 (0.021)	0.099
Medium	162	5.87	5.87			
High	160	5.64	5.62			

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Adjusted for percent body fat at the time of the blood measurement of dioxin.

<sup>c</sup> Slope and standard error based on natural logarithm of FSH versus log<sub>2</sub> (initial dioxin).

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

<b>(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED</b>						
Initial Dioxin Category Summary Statistics				Analysis Results for Log <sub>2</sub> (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean <sup>a</sup>		R <sup>2</sup>	Adj. Slope (Std. Error) <sup>b</sup>	p-Value
Low	160	5.82		0.051	-0.007 (0.024)	0.763
Medium	162	5.50				
High	160	5.53				

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Slope and standard error based on natural logarithm of FSH versus log<sub>2</sub> (initial dioxin).

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

**Table 16-32. Analysis of FSH (mIU/ml) (Continuous) (Continued)**

<b>(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED</b>					
<b>Dioxin Category</b>	<b>n</b>	<b>Mean<sup>a</sup></b>	<b>Adj. Mean<sup>ab</sup></b>	<b>Difference of Adj. Mean vs. Comparisons (95% C.I.)<sup>c</sup></b>	<b>p-Value<sup>d</sup></b>
Comparison	1,213	5.97	5.97		
Background RH	381	6.21	6.21	0.24 --	0.283
Low RH	239	6.28	6.28	0.31 --	0.258
High RH	243	5.66	5.66	-0.31 --	0.229
Low plus High RH	482	5.96	5.96	-0.01 --	0.955

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Adjusted for percent body fat at the time of the blood measurement of dioxin.

<sup>c</sup> Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

<sup>d</sup> 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.

<b>(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED</b>					
<b>Dioxin Category</b>	<b>n</b>	<b>Adj. Mean<sup>a</sup></b>	<b>Difference of Adj. Mean vs. Comparisons (95% C.I.)<sup>b</sup></b>	<b>p-Value<sup>c</sup></b>	
Comparison	1,213	5.87			
Background RH	381	6.02	0.15 --	0.491	
Low RH	239	5.98	0.11 --	0.668	
High RH	243	5.83	-0.04 --	0.855	
Low plus High RH	482	5.90	0.03 --	0.877	

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

<sup>c</sup> 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 16-32. Analysis of FSH (mIU/ml) (Continuous) (Continued)**

<b>(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED</b>					
1987 Dioxin Category Summary Statistics			Analysis Results for Log <sub>2</sub> (1987 Dioxin +1)		
1987 Dioxin	n	Mean <sup>a</sup>	R <sup>2</sup>	Adjusted Slope (Std. Error) <sup>b</sup>	p-Value
Low	288	6.34	0.003	-0.024 (0.015)	0.105
Medium	287	6.19			
High	288	5.70			

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Slope and standard error based on natural logarithm of FSH versus log<sub>2</sub> (1987 dioxin + 1).

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

<b>(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED</b>					
1987 Dioxin Category Summary Statistics			Analysis Results for Log <sub>2</sub> (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean <sup>a</sup>	R <sup>2</sup>	Adjusted Slope (Std. Error) <sup>b</sup>	p-Value
Low	288	6.18	0.066	-0.001 (0.016)	0.958
Medium	287	5.93			
High	288	5.97			

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Slope and standard error based on natural logarithm of FSH versus log<sub>2</sub> (1987 dioxin + 1).

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

A marginally significant inverse association was revealed between initial dioxin and FSH in the unadjusted Model 2 analysis (Table 16-32(c): slope=-0.035, p=0.099). After adjusting for covariates, the results became nonsignificant (Table 16-32(d): p=0.763).

No significant associations were revealed between FSH and dioxin in the unadjusted and adjusted Models 3 and 4 analyses (Table 16-32(e–h): p>0.10 for each analysis).

#### 16.2.2.3.25 FSH (Discrete)

All unadjusted and adjusted analyses in Models 1 through 4 showed no significant relations between dioxin and dichotomized FSH (Table 16-33(a–h): p>0.17 for each analysis).

**Table 16-33. Analysis of FSH (Discrete)**

<b>(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED</b>					
Occupational Category	Group	n	Number (%) High	Est. Relative Risk (95% C.I.)	p-Value
<i>All</i>	<i>Ranch Hand</i>	870	72 (8.3)	<i>1.06 (0.77,1.46)</i>	<i>0.713</i>
	<i>Comparison</i>	1,251	98 (7.8)		
Officer	Ranch Hand	341	39 (11.4)	1.20 (0.77,1.88)	0.424
	Comparison	494	48 (9.7)		
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	16 (4.2)	0.66 (0.36,1.20)	0.171
	Comparison	570	36 (6.3)		

<b>(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED</b>		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
<i>All</i>	<i>1.04 (0.75,1.45)</i>	<i>0.794</i>
Officer	1.18 (0.74,1.85)	0.488
Enlisted Flyer	1.49 (0.70,3.17)	0.297
Enlisted Groundcrew	0.68 (0.37,1.26)	0.221

<b>(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED</b>				
Initial Dioxin Category Summary Statistics			Analysis Results for Log <sub>2</sub> (Initial Dioxin) <sup>a</sup>	
Initial Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.) <sup>b</sup>	p-Value
Low	160	13 (8.1)	0.94 (0.72,1.22)	0.618
Medium	162	14 (8.6)		
High	160	9 (5.6)		

<sup>a</sup> Adjusted for percent body fat at the time of the blood measurement of dioxin.

<sup>b</sup> Relative risk for a twofold increase in initial dioxin.

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

<b>(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED</b>		
Analysis Results for Log <sub>2</sub> (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.) <sup>a</sup>	p-Value
482	1.11 (0.81,1.53)	0.508

<sup>a</sup> Relative risk for a twofold increase in initial dioxin.

**Table 16-33. Analysis of FSH (Discrete) (Continued)**

<b>(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED</b>				
<b>Dioxin Category</b>	<b>n</b>	<b>Number (%) High</b>	<b>Est. Relative Risk (95% C.I.)<sup>ab</sup></b>	<b>p-Value</b>
Comparison	1,213	93 (7.7)		
Background RH	381	35 (9.2)	1.22 (0.81,1.84)	0.341
Low RH	239	20 (8.4)	1.10 (0.66,1.82)	0.713
High RH	243	16 (6.6)	0.85 (0.49,1.47)	0.557
Low plus High RH	482	36 (7.5)	0.96 (0.64,1.44)	0.860

<sup>a</sup> Relative risk and confidence interval relative to Comparisons.

<sup>b</sup> 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.

<b>(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED</b>				
<b>Dioxin Category</b>	<b>n</b>	<b>Adjusted Relative Risk (95% C.I.)<sup>a</sup></b>		<b>p-Value</b>
Comparison	1,213			
Background RH	381	1.10 (0.72,1.69)		0.652
Low RH	239	0.93 (0.55,1.56)		0.781
High RH	243	1.16 (0.64,2.08)		0.621
Low plus High RH	482	1.04 (0.68,1.58)		0.859

<sup>a</sup> 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.

<b>(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED</b>				
<b>1987 Dioxin Category Summary Statistics</b>			<b>Analysis Results for Log<sub>2</sub> (1987 Dioxin + 1)</b>	
<b>1987 Dioxin</b>	<b>n</b>	<b>Number (%) High</b>	<b>Estimated Relative Risk (95% C.I.)<sup>a</sup></b>	<b>p-Value</b>
Low	288	24 (8.3)	0.97 (0.82,1.15)	0.712
Medium	287	28 (9.8)		
High	288	19 (6.6)		

<sup>a</sup> 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 16-33. Analysis of FSH (Discrete) (Continued)**

<b>(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED</b>		
<b>Analysis Results for Log<sub>2</sub> (1987 Dioxin + 1)</b>		
<b>n</b>	<b>Adjusted Relative Risk (95% C.I.)<sup>a</sup></b>	<b>p-Value</b>
863	1.16 (0.93,1.45)	0.188

<sup>a</sup> Relative risk for a twofold increase in 1987 dioxin.

### 16.2.3 Longitudinal Analysis

Longitudinal analyses were conducted on the composite diabetes indicator, TSH, fasting glucose, 2-hour postprandial glucose, and total testosterone 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 the longitudinal analysis 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 and continuous analyses were performed for TSH, fasting glucose, 2-hour postprandial glucose, and total testosterone. The longitudinal analyses for all of these variables investigated the difference between the 1982 and 1997 examinations. These analyses were used to investigate the temporal effects of dioxin during the 15-year period between 1982 and 1997.

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 disease; 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 (50). Summary statistics are provided for reference purposes for the 1985, 1987, and 1992 examinations.

The longitudinal analysis for the discrete form of the dependent 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.

The longitudinal analysis of continuous variables examined the paired difference between the measurements from 1982 and 1997. These paired differences measured the change in the dependent variable 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 cutpoints for TSH, fasting glucose, 2-hour postprandial glucose, and total testosterone differed between examinations. The cutpoints changed between examinations because a different laboratory was used to perform the analysis or because an upgrade in the equipment used caused a change in the reference values. These cutpoints were used for determining abnormal and normal classifications for each of the respective examinations and are shown in Table 16-34.

**Table 16-34. Normal Ranges from Air Force Health Study Examinations for Dependent Variables Used in Endocrine Longitudinal Analysis**

Dependent Variable (Units)	Examination				
	1982	1985	1987	1992	1997
TSH (μIU/ml)	≤10	≤3	≤3	≤5.5	≤5.5
Fasting Glucose (mg/dl)	≤115	≤110	≤110	≤115	≤110
	(Age < 50)				
	≤125				
	(Age ≥ 50)				
2-hour Postprandial Glucose (mg/dl)	≤120	≤140	≤140	≤140	≤140
Total Testosterone (ng/dl)	≥400	≥260	≥260	≥260	≥241
					(Age < 50)
					≥230
					(Age ≥ 50)

16.2.3.1 Medical Records Variables

16.2.3.1.1 Composite Diabetes Indicator

A participant was considered diabetic in the composite diabetes indicator variable if he had a verified history of diabetes or a 2-hour postprandial glucose level of at least 200 mg/dl.

The Model 1 analysis of diabetic participants in 1997 who were nondiabetic in 1982 did not uncover a significant difference between Ranch Hands and Comparisons across all occupations or within each occupational stratum (Table 16-35(a):  $p \geq 0.66$  for each analysis).

**Table 16-35. Longitudinal Analysis of Composite Diabetes Indicator**

(a) MODEL 1: RANCH HANDS VS. COMPARISONS						
Occupational Category	Group	Number (%) Diabetic / (n)				
		Examination				
		1982	1985	1987	1992	1997
<i>All</i>	<i>Ranch Hand</i>	30 (3.7) (808)	52 (6.6) (791)	63 (8.1) (782)	100 (12.8) (779)	143 (17.7) (808)
	<i>Comparison</i>	25 (2.6) (959)	50 (5.3) (940)	64 (6.9) (931)	108 (11.7) (926)	162 (16.9) (959)
Officer	Ranch Hand	13 (4.2) (308)	20 (6.6) (304)	23 (7.7) (300)	38 (12.6) (301)	51 (16.6) (308)
	Comparison	10 (2.6) (378)	20 (5.4) (371)	24 (6.6) (365)	43 (11.5) (373)	60 (15.9) (378)
Enlisted Flyer	Ranch Hand	5 (3.4) (145)	11 (7.7) (143)	12 (8.5) (141)	20 (14.2) (141)	26 (17.9) (145)
	Comparison	5 (3.5) (142)	7 (5.0) (141)	9 (6.4) (140)	18 (13.0) (138)	27 (19.0) (142)
Enlisted Groundcrew	Ranch Hand	12 (3.4) (355)	21 (6.1) (344)	28 (8.2) (341)	42 (12.5) (337)	66 (18.6) (355)
	Comparison	10 (2.3) (439)	23 (5.4) (428)	31 (7.3) (426)	47 (11.3) (415)	75 (17.1) (439)

**Table 16-35. Longitudinal Analysis of Composite Diabetes Indicator (Continued)**

Occupational Category	Group	Normal in 1982		Adj. Relative Risk (95% C.I.) <sup>a</sup>	p-Value <sup>a</sup>
		n in 1997	Number (%) Diabetic in 1997		
<i>All</i>	<i>Ranch Hand Comparison</i>	778 934	113 (14.5) 137 (14.7)	1.00 (0.76,1.31)	0.993
Officer	Ranch Hand	295	38 (12.9)	0.94 (0.60,1.49)	0.801
	Comparison	368	50 (13.6)		
Enlisted Flyer	Ranch Hand	140	21 (15.0)	0.93 (0.48,1.79)	0.821
	Comparison	137	22 (16.1)		
Enlisted Groundcrew	Ranch Hand	343	54 (15.7)	1.09 (0.73,1.63)	0.660
	Comparison	429	65 (15.2)		

<sup>a</sup> 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 were not diabetic in 1982 (see Chapter 7, Statistical Methods).

<b>(b) MODEL 2: RANCH HANDS — INITIAL DIOXIN</b>					
Initial Dioxin	Number (%) Diabetic /(n) Examination				
	1982	1985	1987	1992	1997
Low	6 (4.0) (151)	10 (6.7) (149)	11 (7.3) (151)	23 (16.0) (144)	32 (21.2) (151)
Medium	7 (4.5) (155)	13 (8.6) (152)	12 (7.9) (151)	25 (16.4) (152)	35 (22.6) (155)
High	8 (5.2) (153)	16 (10.7) (150)	21 (14.1) (149)	25 (16.9) (148)	39 (25.5) (153)

Initial Dioxin Category Summary Statistics			Analysis Results for Log <sub>2</sub> (Initial Dioxin) <sup>a</sup>	
Initial Dioxin	Normal in 1982		Adj. Relative Risk (95% C.I.) <sup>b</sup>	p-Value
	n in 1997	Number (%) Diabetic in 1997		
Low	145	26 (17.9)	1.28 (1.04,1.57)	0.019
Medium	148	28 (18.9)		
High	145	31 (21.4)		

<sup>a</sup> Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.

<sup>b</sup> 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 were not diabetic in 1982 (see Chapter 7, Statistical Methods).

**Table 16-35. Longitudinal Analysis of Composite Diabetes Indicator (Continued)**

<b>(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY</b>					
<b>Dioxin Category</b>	<b>Number (%) Diabetic/(n) Examination</b>				
	<b>1982</b>	<b>1985</b>	<b>1987</b>	<b>1992</b>	<b>1997</b>
Comparison	24 (2.6) (932)	47 (5.1) (916)	61 (6.7) (906)	103 (11.4) (900)	154 (16.5) (932)
Background RH	9 (2.6) (345)	13 (13.9) (337)	19 (5.8) (328)	27 (8.1) (332)	35 (10.1) (345)
Low RH	11 (4.9) (226)	18 (8.1) (221)	18 (8.1) (223)	36 (16.6) (217)	49 (21.7) (226)
High RH	10 (4.3) (233)	21 (9.1) (230)	26 (11.4) (228)	37 (16.3) (227)	57 (24.5) (233)
Low plus High RH	21 (4.6) (459)	39 (8.6) (451)	44 (9.8) (451)	73 (16.4) (444)	106 (23.1) (459)
<b>Normal in 1982</b>					
<b>Dioxin Category</b>	<b>n in 1997</b>	<b>Number (%) Diabetic in 1997</b>	<b>Adj. Relative Risk (95% C.I.)<sup>ab</sup></b>	<b>p-Value<sup>b</sup></b>	
Comparison	908	130 (14.3)			
Background RH	336	26 (7.7)	0.55 (0.35,0.88)	0.012	
Low RH	215	38 (17.7)	1.11 (0.72,1.71)	0.634	
High RH	223	47 (21.1)	1.61 (1.07,2.42)	0.023	
Low plus High RH	438	85 (19.4)	1.34 (0.97,1.86)	0.079	

<sup>a</sup> Relative risk and confidence interval relative to Comparisons.

<sup>b</sup> 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  $\leq$  10 ppt.

Background (Ranch Hand): 1987 Dioxin  $\leq$  10 ppt.

Low (Ranch Hand): 1987 Dioxin  $>$ 10 ppt, 10 ppt  $<$  Initial Dioxin  $\leq$  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 were not diabetic in 1982 (see Chapter 7, Statistical Methods).

The Model 2 longitudinal analysis revealed a significant positive association between initial dioxin and the percentage of diabetic participants (Table 16-35(b): Adj. RR=1.28, p=0.019). The percentages of diabetic participants in 1997 who were nondiabetic in 1982 were 17.9, 18.9, and 21.4 in the low, medium, and high initial dioxin categories, respectively.

Three significant contrasts were seen in the Model 3 longitudinal analysis of composite diabetes indicator: Ranch Hands in the background dioxin category versus Comparisons (Table 16-35(c): Adj. RR=0.55, p=0.012), Ranch Hands in the high dioxin category versus Comparisons (Table 16-35(c): Adj. RR=1.61, p=0.023), and Ranch Hands in the low plus high dioxin category versus Comparisons (Table 16-35(c): Adj. RR=1.34, p=0.079). The percentages of participants who were nondiabetic in 1982 and diabetic in 1997 were 7.7, 21.1, 19.4, and 14.3 for Ranch Hands in the background dioxin category, Ranch Hands in

the high dioxin category, Ranch Hands in the low plus high dioxin category, and Comparisons, respectively.

### 16.2.3.2 Laboratory Examination Variables

#### 16.2.3.2.1 TSH (Continuous)

The longitudinal analyses in Models 1 through 3 did not reveal a significant association between dioxin and change in mean TSH level (Table 16-36(a-c):  $p > 0.26$  for each analysis).

**Table 16-36. Longitudinal Analysis of TSH ( $\mu\text{U/ml}$ ) (Continuous)**

<b>(a) MODEL 1: RANCH HANDS VS. COMPARISONS</b>									
Occupational Category	Group	Mean <sup>a</sup> /(n) Examination					Exam. Mean Change <sup>b</sup>	Difference of Exam. Mean Change	p-Value <sup>c</sup>
		1982	1985	1987	1992	1997			
<i>All</i>	<i>Ranch Hand</i>	3.64 (791)	1.21 (773)	0.91 (762)	1.60 (770)	1.87 (791)	-1.76	-0.06	0.525
	<i>Comparison</i>	3.49 (929)	1.16 (911)	0.87 (904)	1.56 (910)	1.79 (929)	-1.70		
Officer	Ranch Hand	3.78 (298)	1.28 (294)	0.99 (289)	1.73 (293)	2.00 (298)	-1.78	-0.15	0.700
	Comparison	3.47 (358)	1.18 (352)	0.89 (347)	1.62 (353)	1.84 (358)	-1.63		
Enlisted Flyer	Ranch Hand	3.46 (141)	1.16 (138)	0.84 (135)	1.43 (139)	1.72 (141)	-1.74	0.03	0.440
	Comparison	3.66 (139)	1.15 (138)	0.87 (137)	1.53 (137)	1.89 (139)	-1.77		
Enlisted Groundcrew	Ranch Hand	3.59 (352)	1.17 (341)	0.89 (338)	1.56 (338)	1.83 (352)	-1.76	-0.02	0.263
	Comparison	3.45 (432)	1.15 (421)	0.84 (420)	1.52 (420)	1.71 (432)	-1.74		

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Difference between 1997 and 1982 examination means after transformation to original scale.

<sup>c</sup> P-value is based on analysis of natural logarithm of TSH; results adjusted for natural logarithm of TSH in 1982 and 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.

**Table 16-36. Longitudinal Analysis of TSH ( $\mu\text{lu/ml}$ ) (Continuous)**

<b>(b) MODEL 2: RANCH HANDS – INITIAL DIOXIN</b>							
Initial Dioxin Category Summary Statistics						Analysis Results for $\text{Log}_2$ (Initial Dioxin) <sup>b</sup>	
Initial Dioxin	Mean <sup>a</sup> /(n) Examination					Adjusted Slope (Std. Error)	p-Value
	1982	1985	1987	1992	1997		
Low	3.62 (151)	1.22 (148)	0.95 (150)	1.60 (146)	1.94 (151)	-0.007 (0.020)	0.717
Medium	3.56 (155)	1.23 (152)	0.91 (151)	1.57 (153)	1.86 (155)		
High	3.59 (145)	1.17 (142)	0.89 (140)	1.55 (142)	1.80 (145)		

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Results based on difference between natural logarithm of 1997 TSH and natural logarithm of 1982 TSH versus  $\text{log}_2$  (initial dioxin); results adjusted for percent body fat at the date of the blood measurement of dioxin, natural logarithm of 1982 TSH, and age in 1997.

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.

<b>(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY</b>								
Dioxin Category	Mean <sup>a</sup> /(n) Examination					Exam. Mean Change <sup>b</sup>	Difference of Exam. Mean Change	p-Value <sup>c</sup>
	1982	1985	1987	1992	1997			
Comparison	3.49 (901)	1.16 (886)	0.86 (878)	1.56 (883)	1.79 (901)	-1.70		
Background RH	3.69 (334)	1.21 (326)	0.91 (316)	1.63 (324)	1.87 (334)	-1.81	-0.11	0.934
Low RH	3.58 (224)	1.23 (218)	0.95 (221)	1.61 (217)	1.90 (224)	-1.67	0.03	0.514
High RH	3.60 (227)	1.18 (224)	0.88 (220)	1.54 (224)	1.83 (227)	-1.77	-0.07	0.681
Low plus High RH	3.59 (451)	1.21 (442)	0.91 (441)	1.57 (441)	1.87 (451)	-1.72	-0.02	0.492

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Difference between 1997 and 1982 examination means after transformation to original scale.

<sup>c</sup> P-value is based on analysis of natural logarithm of 1997 TSH; results adjusted for percent body fat at the date of the blood measurement of dioxin, natural logarithm of 1982 TSH, and age in 1997.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin  $\leq$  10 ppt.

Background (Ranch Hand): 1987 Dioxin  $\leq$  10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin  $\leq$  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.

16.2.3.2.2 TSH (Discrete)

The longitudinal analysis of high 1997 TSH levels for participants who had normal TSH levels in 1982 was not significantly associated with group or dioxin in Models 1 through 3 (Table 16-37(a-c):  $p > 0.23$  for each analysis).

**Table 16-37. Longitudinal Analysis of TSH (Discrete)**

<b>(a) MODEL 1: RANCH HANDS VS. COMPARISONS</b>						
Occupational Category	Group	Number (%) High/(n) Examination				
		1982	1985	1987	1992	1997
<i>All</i>	<i>Ranch Hand</i>	5 (0.6) (791)	9 (1.2) (773)	10 (1.3) (762)	10 (1.3) (770)	32 (4.0) (791)
	<i>Comparison</i>	4 (0.4) (929)	14 (1.5) (911)	11 (1.2) (904)	19 (2.1) (910)	29 (3.1) (929)
Officer	Ranch Hand	2 (0.7) (298)	4 (1.4) (294)	5 (1.7) (289)	4 (1.4) (293)	12 (4.0) (298)
	Comparison	1 (0.3) (359)	6 (1.7) (352)	5 (1.4) (347)	12 (3.4) (353)	11 (3.1) (358)
Enlisted Flyer	Ranch Hand	0 (0.0) (141)	1 (0.7) (138)	1 (0.7) (135)	2 (1.4) (139)	3 (2.1) (141)
	Comparison	1 (0.7) (139)	2 (1.4) (138)	1 (0.7) (137)	1 (0.7) (137)	5 (3.6) (139)
Enlisted Groundcrew	Ranch Hand	3 (0.9) (352)	4 (1.2) (341)	4 (1.2) (338)	4 (1.2) (338)	17 (4.8) (352)
	Comparison	2 (0.5) (432)	6 (1.4) (421)	5 (1.2) (420)	6 (1.4) (420)	13 (3.0) (432)

  

Occupational Category	Group	Normal in 1982		Adj. Relative Risk (95% C.I.) <sup>a</sup>	p-Value <sup>a</sup>
		n in 1997	Number (%) High in 1997		
<i>All</i>	<i>Ranch Hand</i>	786	28 (3.6)	1.23 (0.72,2.10)	0.454
	<i>Comparison</i>	925	27 (2.9)		
Officer	Ranch Hand	296	11 (3.7)	1.20 (0.51,2.81)	0.675
	Comparison	357	11 (3.1)		
Enlisted Flyer	Ranch Hand	141	3 (2.1)	0.57 (0.13,2.45)	0.452
	Comparison	138	5 (3.6)		
Enlisted Groundcrew	Ranch Hand	349	14 (4.0)	1.63 (0.73,3.65)	0.233
	Comparison	430	11 (2.6)		

<sup>a</sup> 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 a normal TSH level in 1982 (see Chapter 7, Statistical Methods).

**Table 16-37. Longitudinal Analysis of TSH (Discrete) (Continued)**

<b>(b) MODEL 2: RANCH HANDS — INITIAL DIOXIN</b>					
<b>Initial Dioxin</b>	<b>Number (%) High/(n) Examination</b>				
	<b>1982</b>	<b>1985</b>	<b>1987</b>	<b>1992</b>	<b>1997</b>
Low	0 (0.0) (151)	1 (0.7) (148)	1 (0.7) (150)	0 (0.0) (146)	6 (4.0) (151)
Medium	1 (0.6) (155)	3 (2.0) (152)	2 (1.3) (151)	1 (0.7) (153)	4 (2.6) (155)
High	1 (0.7) (145)	1 (0.7) (142)	2 (1.4) (140)	5 (3.5) (142)	7 (4.8) (145)

<b>Initial Dioxin Category Summary Statistics</b>			<b>Analysis Results for Log<sub>2</sub> (Initial Dioxin)<sup>a</sup></b>	
<b>Initial Dioxin</b>	<b>Normal in 1982</b>		<b>Adj. Relative Risk (95% C.I.)<sup>b</sup></b>	<b>p-Value</b>
	<b>n in 1997</b>	<b>Number (%) High in 1997</b>		
Low	151	6 (4.0)	1.16 (0.78,1.72)	0.486
Medium	154	3 (1.9)		
High	144	6 (4.2)		

<sup>a</sup> Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.

<sup>b</sup> 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 a normal TSH level in 1982 (see Chapter 7, Statistical Methods).

<b>(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY</b>					
<b>Dioxin Category</b>	<b>Number (%) High/(n) Examination</b>				
	<b>1982</b>	<b>1985</b>	<b>1987</b>	<b>1992</b>	<b>1997</b>
Comparison	4 (0.4) (901)	14 (1.6) (886)	11 (1.3) (878)	19 (2.2) (883)	29 (3.2) (901)
Background RH	3 (0.9) (334)	4 (1.2) (326)	5 (1.6) (316)	4 (1.2) (324)	14 (4.2) (334)
Low RH	0 (0.0) (224)	2 (0.9) (218)	2 (0.9) (221)	1 (0.5) (217)	7 (3.1) (224)
High RH	2 (0.9) (227)	3 (1.3) (224)	3 (1.4) (220)	5 (2.2) (224)	10 (4.4) (227)
Low plus High RH	2 (0.4) (451)	5 (1.1) (442)	5 (1.1) (441)	6 (1.4) (441)	17 (3.8) (451)

**Table 16-37. Longitudinal Analysis of TSH (Discrete) (Continued)**

Dioxin Category	Normal in 1982		Adj. Relative Risk (95% C.I.) <sup>ab</sup>	p-Value <sup>b</sup>
	n in 1997	Number (%) High in 1997		
Comparison	897	27 (3.0)		
Background RH	331	12 (3.6)	1.10 (0.55,2.22)	0.782
Low RH	224	7 (3.1)	1.01 (0.43,2.35)	0.984
High RH	225	8 (3.6)	1.42 (0.63,3.22)	0.399
Low plus High RH	449	15 (3.3)	1.20 (0.63,2.29)	0.585

<sup>a</sup> Relative risk and confidence interval relative to Comparisons.

<sup>b</sup> 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 a normal TSH level in 1982 (see Chapter 7, Statistical Methods).

#### 16.2.3.2.3 Fasting Glucose (Continuous)

Analysis of Models 1 through 3 showed no significant relations between dioxin and the change in mean fasting glucose between 1982 and 1997 (Table 16-38(a-c): p>0.14 for each analysis).

**Table 16-38. Longitudinal Analysis of Fasting Glucose (mg/dl) (Continuous)**

(a) MODEL 1: RANCH HANDS VS. COMPARISONS									
Occupational Category	Group	Mean <sup>a</sup> /(n) Examination					Exam. Mean Change <sup>b</sup>	Difference of Exam. Mean Change	p-Value <sup>c</sup>
		1982	1985	1987	1992	1997			
All	Ranch Hand	97.4 (817)	98.9 (799)	100.2 (790)	104.5 (795)	101.7 (817)	4.3	-0.3	0.817
	Comparison	96.8 (974)	98.0 (956)	99.8 (948)	104.1 (954)	101.5 (974)			
Officer	Ranch Hand	98.1 (310)	100.1 (306)	101.4 (302)	105.1 (305)	101.6 (310)	3.5	-0.1	0.962
	Comparison	96.9 (380)	97.9 (374)	100.3 (368)	104.4 (375)	100.5 (380)			
Enlisted Flyer	Ranch Hand	98.2 (148)	98.4 (145)	100.5 (143)	104.4 (145)	102.8 (148)	4.6	-1.0	0.693
	Comparison	97.9 (145)	99.0 (144)	100.3 (143)	104.7 (143)	103.5 (145)			

**Table 16-38. Longitudinal Analysis of Fasting Glucose (mg/dl) (Continuous) (Continued)**

<b>(a) MODEL 1: RANCH HANDS VS. COMPARISONS</b>									
Occupational Category	Group	Mean <sup>a</sup> /(n) Examination					Exam. Mean Change <sup>b</sup>	Difference of Exam. Mean Change	p-Value <sup>c</sup>
		1982	1985	1987	1992	1997			
Enlisted Groundcrew	Ranch Hand	96.5 (359)	98.0 (348)	99.1 (345)	104.1 (345)	101.4 (359)	4.8	-0.4	0.871
	Comparison	96.4 (449)	97.7 (438)	99.3 (437)	103.6 (436)	101.6 (449)			

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Difference between 1997 and 1982 examination means after transformation to original scale.

<sup>c</sup> P-value is based on analysis of natural logarithm of fasting glucose; results adjusted for natural logarithm of fasting glucose in 1982 and 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.

<b>(b) MODEL 2: RANCH HANDS – INITIAL DIOXIN</b>						Analysis Results for Log <sub>2</sub> (Initial Dioxin) <sup>b</sup>	
Initial Dioxin Category Summary Statistics						Adjusted Slope (Std. Error)	p-Value
Initial Dioxin	Mean <sup>a</sup> /(n) Examination						
	1982	1985	1987	1992	1997		
Low	97.5 (153)	99.7 (150)	101.4 (152)	105.1 (148)	101.5 (153)	0.008 (0.007)	0.261
	Medium	98.3 (158)	99.4 (155)	100.7 (155)	105.0 (155)		
High	99.2 (153)	101.3 (150)	103.4 (148)	109.6 (150)	105.5 (153)		

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Results based on difference between natural logarithm of 1997 fasting glucose and natural logarithm of 1982 fasting glucose versus log<sub>2</sub> (initial dioxin); results adjusted for percent body fat at the date of the blood measurement of dioxin, natural logarithm of 1982 fasting glucose, and age in 1997.

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.

**Table 16-38. Longitudinal Analysis of Fasting Glucose (mg/dl) (Continuous) (Continued)**

<b>(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY</b>								
<b>Dioxin Category</b>	<b>Mean<sup>a</sup>/(n) Examination</b>					<b>Exam. Mean Change<sup>b</sup></b>	<b>Difference of Exam. Mean Change</b>	<b>p-Value<sup>c</sup></b>
	<b>1982</b>	<b>1985</b>	<b>1987</b>	<b>1992</b>	<b>1997</b>			
Comparison	96.8 (946)	97.9 (931)	99.7 (922)	103.9 (927)	101.3 (946)	4.5		
Background RH	96.2 (347)	97.3 (339)	98.1 (330)	101.8 (337)	98.6 (347)	2.4	-2.1	0.484
Low RH	97.9 (229)	100.0 (223)	100.9 (226)	105.3 (222)	101.5 (229)	3.5	-1.0	0.312
High RH	98.7 (235)	100.1 (232)	102.7 (229)	107.7 (231)	106.3 (235)	7.5	3.0	0.146
Low plus High RH	98.3 (464)	100.1 (455)	101.8 (455)	106.5 (453)	103.9 (464)	5.5	1.0	0.755

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Difference between 1997 and 1982 examination means after transformation to original scale.

<sup>c</sup> P-value is based on analysis of natural logarithm of 1997 fasting glucose; results adjusted for percent body fat at the date of the blood measurement of dioxin, natural logarithm of 1982 fasting glucose, 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.

#### 16.2.3.2.4 Fasting Glucose (Discrete)

The Model 1 longitudinal analysis of high fasting glucose levels in 1997 did not reveal a significant difference between Ranch Hands and Comparisons across all occupations or within each occupational stratum (Table 16-39(a):  $p > 0.25$  for each analysis).

**Table 16-39. Longitudinal Analysis of Fasting Glucose (Discrete)**

<b>(a) MODEL 1: RANCH HANDS VS. COMPARISONS</b>						
<b>Occupational Category</b>	<b>Group</b>	<b>Number (%) High /(n) Examination</b>				
		<b>1982</b>	<b>1985</b>	<b>1987</b>	<b>1992</b>	<b>1997</b>
<i>All</i>	<i>Ranch Hand</i>	<i>37 (4.5)</i> <i>(817)</i>	<i>76 (9.5)</i> <i>(799)</i>	<i>94 (11.9)</i> <i>(790)</i>	<i>106 (13.3)</i> <i>(795)</i>	<i>149 (18.2)</i> <i>(817)</i>
	<i>Comparison</i>	<i>34 (3.5)</i> <i>(974)</i>	<i>88 (9.2)</i> <i>(956)</i>	<i>122 (12.9)</i> <i>(948)</i>	<i>125 (13.1)</i> <i>(954)</i>	<i>158 (16.2)</i> <i>(974)</i>
Officer	Ranch Hand	12 (3.9) (310)	27 (8.8) (306)	40 (13.2) (302)	39 (12.8) (305)	54 (17.4) (310)
	Comparison	11 (2.9) (380)	33 (8.8) (374)	48 (13.0) (368)	50 (13.3) (375)	58 (15.3) (380)
Enlisted Flyer	Ranch Hand	11 (7.4) (148)	16 (11.0) (145)	18 (12.6) (143)	20 (13.8) (145)	28 (18.9) (148)
	Comparison	6 (4.1) (145)	14 (9.7) (144)	20 (14.0) (143)	17 (11.9) (143)	25 (17.2) (145)
Enlisted Groundcrew	Ranch Hand	14 (3.9) (359)	33 (9.5) (348)	36 (10.4) (345)	47 (13.6) (345)	67 (18.7) (359)
	Comparison	17 (3.8) (449)	41 (9.4) (438)	54 (12.4) (437)	58 (13.3) (436)	75 (16.7) (449)

<b>Occupational Category</b>	<b>Group</b>	<b>Normal in 1982</b>		<b>Adj. Relative Risk (95% C.I.)<sup>a</sup></b>	<b>p-Value<sup>a</sup></b>
		<b>n in 1997</b>	<b>Number (%) High in 1997</b>		
<i>All</i>	<i>Ranch Hand</i>	<i>780</i>	<i>116 (14.9)</i>	<i>1.16 (0.88,1.52)</i>	<i>0.303</i>
	<i>Comparison</i>	<i>940</i>	<i>124 (13.2)</i>		
Officer	Ranch Hand	298	44 (14.8)	1.18 (0.76,1.85)	0.462
	Comparison	369	47 (12.7)		
Enlisted Flyer	Ranch Hand	137	17 (12.4)	0.89 (0.44,1.81)	0.758
	Comparison	139	19 (13.7)		
Enlisted Groundcrew	Ranch Hand	345	55 (15.9)	1.26 (0.84,1.89)	0.256
	Comparison	432	58 (13.4)		

<sup>a</sup> 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 a normal fasting glucose level in 1982 (see Chapter 7, Statistical Methods).

**Table 16-39. Longitudinal Analysis of Fasting Glucose (Discrete) (Continued)**

<b>(b) MODEL 2: RANCH HANDS — INITIAL DIOXIN</b>					
<b>Initial Dioxin</b>	<b>Number (%) High / (n) Examination</b>				
	<b>1982</b>	<b>1985</b>	<b>1987</b>	<b>1992</b>	<b>1997</b>
Low	10 (6.5) (153)	15 (10.0) (150)	21 (13.8) (152)	25 (16.9) (148)	28 (18.3) (153)
Medium	9 (5.7) (158)	21 (13.5) (155)	20 (12.9) (155)	23 (14.8) (155)	35 (22.2) (158)
High	11 (7.2) (153)	20 (13.3) (150)	25 (16.9) (148)	26 (17.3) (150)	38 (24.8) (153)

<b>Initial Dioxin Category Summary Statistics</b>			<b>Analysis Results for Log<sub>2</sub> (Initial Dioxin)<sup>a</sup></b>	
<b>Initial Dioxin</b>	<b>Normal in 1982</b>		<b>Adj. Relative Risk (95% C.I.)<sup>b</sup></b>	<b>p-Value</b>
	<b>n in 1997</b>	<b>Number (%) High in 1997</b>		
Low	143	19 (13.3)	1.26 (1.02,1.56)	0.029
Medium	149	27 (18.1)		
High	142	28 (19.7)		

<sup>a</sup> Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.

<sup>b</sup> 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 a normal fasting glucose level in 1982 (see Chapter 7, Statistical Methods).

<b>(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY</b>					
<b>Dioxin Category</b>	<b>Number (%) High/(n) Examination</b>				
	<b>1982</b>	<b>1985</b>	<b>1987</b>	<b>1992</b>	<b>1997</b>
Comparison	32 (3.4) (946)	84 (9.0) (931)	117 (12.7) (922)	120 (12.9) (927)	152 (16.1) (946)
Background RH	7 (2.0) (347)	20 (5.9) (339)	27 (8.2) (330)	31 (9.2) (337)	46 (13.3) (347)
Low RH	14 (6.1) (229)	25 (11.2) (223)	31 (13.7) (226)	38 (17.1) (222)	43 (18.8) (229)
High RH	16 (6.8) (235)	31 (13.4) (232)	35 (15.3) (229)	36 (15.6) (231)	58 (24.7) (235)
Low plus High RH	30 (6.5) (464)	56 (12.3) (455)	66 (14.5) (455)	74 (16.3) (453)	101 (21.8) (464)

**Table 16-39. Longitudinal Analysis of Fasting Glucose (Discrete) (Continued)**

Dioxin Category	Normal in 1982		Adj. Relative Risk (95% C.I.) <sup>ab</sup>	p-Value <sup>b</sup>
	n in 1997	Number (%) High in 1997		
Comparison	914	120 (13.1)		
Background RH	340	40 (11.8)	1.04 (0.69,1.55)	0.867
Low RH	215	30 (14.0)	0.89 (0.56,1.42)	0.636
High RH	219	44 (20.1)	1.58 (1.04,2.39)	0.033
Low plus High RH	434	74 (17.1)	1.19 (0.84,1.68)	0.319

<sup>a</sup> Relative risk and confidence interval relative to Comparisons.

<sup>b</sup> 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  $\leq$  10 ppt.

Background (Ranch Hand): 1987 Dioxin  $\leq$  10 ppt.

Low (Ranch Hand): 1987 Dioxin  $>$ 10 ppt, 10 ppt  $<$  Initial Dioxin  $\leq$  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 a normal fasting glucose level in 1982 (see Chapter 7, Statistical Methods).

The Model 2 longitudinal analysis of fasting glucose revealed a significant positive association between initial dioxin and high fasting glucose values (Table 16-39(b): Adj. RR=1.26, p=0.029). In the low, medium, and high initial dioxin categories, 13.3 percent, 18.1 percent, and 19.7 percent of participants, respectively, who had normal fasting glucose levels in 1982 had high fasting glucose levels in 1997.

The Model 3 analysis of the change in percentage of abnormal fasting glucose values revealed a significant difference between Ranch Hands in the high dioxin category and Comparisons (Table 16-39(c): Adj. RR=1.58, p=0.033). For Ranch Hands in the high dioxin category, 20.1 percent had normal fasting glucose levels in 1982 and high fasting glucose levels in 1997. For Comparisons, 13.1 percent had normal fasting glucose levels in 1982 and high fasting glucose levels in 1997.

#### 16.2.3.2.5 2-Hour Postprandial Glucose (Continuous)

The Model 1 analysis of the mean change in 2-hour postprandial glucose did not uncover a significant difference between all Ranch Hands and Comparisons (Table 16-40(a): p=0.982). Stratifying by occupation showed a marginally significant group difference in the officer stratum (Table 16-40(a): difference of means=3.8 mg/dl, p=0.096). The Ranch Hand officers had a mean increase of 17.0 mg/dl between 1982 and 1997 versus 13.2 mg/dl for the Comparison officers.

The mean change in 2-hour postprandial glucose between 1982 and 1997 was not significantly associated with dioxin in Models 2 and 3 (Table 16-40(b,c): p $>$ 0.67 for each analysis).

**Table 16-40. Longitudinal Analysis of 2-Hour Postprandial Glucose (mg/dl) (Continuous)**

<b>(a) MODEL 1: RANCH HANDS VS. COMPARISONS</b>									
<b>Occupational Category</b>	<b>Group</b>	<b>Mean<sup>a</sup>/(n) Examination</b>					<b>Exam. Mean Change<sup>b</sup></b>	<b>Difference of Exam. Mean Change</b>	<b>p-Value<sup>c</sup></b>
		<b>1982</b>	<b>1985</b>	<b>1987</b>	<b>1992</b>	<b>1997</b>			
<i>All</i>	<i>Ranch Hand</i>	<i>89.9</i> <i>(665)</i>	<i>101.8</i> <i>(651)</i>	<i>106.7</i> <i>(641)</i>	<i>102.6</i> <i>(641)</i>	<i>105.5</i> <i>(665)</i>	<i>15.6</i>	<i>0.2</i>	<i>0.982</i>
	<i>Comparison</i>	<i>90.2</i> <i>(797)</i>	<i>104.1</i> <i>(781)</i>	<i>106.4</i> <i>(775)</i>	<i>104.0</i> <i>(773)</i>	<i>105.6</i> <i>(797)</i>	<i>15.4</i>		
Officer	Ranch Hand	89.5 (257)	104.5 (254)	107.0 (250)	103.5 (251)	106.5 (257)	17.0	3.8	0.096
	Comparison	88.8 (318)	102.6 (311)	104.8 (305)	102.1 (315)	102.1 (318)	13.2		
Enlisted Flyer	Ranch Hand	91.7 (119)	100.6 (117)	108.4 (115)	103.8 (116)	107.5 (119)	15.8	-3.2	0.332
	Comparison	92.8 (115)	107.5 (115)	108.6 (114)	108.9 (114)	111.9 (115)	19.0		
Enlisted Groundcrew	Ranch Hand	89.5 (289)	99.8 (280)	105.8 (276)	101.3 (274)	103.8 (289)	14.3	-2.0	0.326
	Comparison	90.6 (364)	104.2 (355)	107.1 (356)	104.1 (344)	106.9 (364)	16.3		

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Difference between 1997 and 1982 examination means after transformation to original scale.

<sup>c</sup> P-value is based on analysis of natural logarithm of 2-hour postprandial glucose; results adjusted for natural logarithm of 2-hour postprandial glucose in 1982 and 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.

**Table 16-40. Longitudinal Analysis of 2-Hour Postprandial Glucose (mg/dl) (Continuous) (Continued)**

<b>(b) MODEL 2: RANCH HANDS – INITIAL DIOXIN</b>							
<b>Initial Dioxin Category Summary Statistics</b>					<b>Analysis Results for Log<sub>2</sub> (Initial Dioxin)<sup>b</sup></b>		
<b>Initial Dioxin</b>	<b>Mean<sup>a</sup>/(n) Examination</b>					<b>Adjusted Slope (Std. Error)</b>	<b>p-Value</b>
	<b>1982</b>	<b>1985</b>	<b>1987</b>	<b>1992</b>	<b>1997</b>		
Low	90.8 (119)	105.4 (117)	112.3 (119)	102.0 (113)	107.8 (119)	-0.005 (0.012)	0.670
Medium	91.1 (120)	102.3 (117)	105.4 (116)	106.6 (117)	105.9 (120)		
High	92.0 (114)	99.6 (112)	106.5 (110)	102.5 (112)	107.3 (114)		

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Results based on difference between natural logarithm of 1997 2-hour postprandial glucose and natural logarithm of 1982 2-hour postprandial glucose versus log<sub>2</sub> (initial dioxin); results adjusted for percent body fat at the date of the blood measurement of dioxin, natural logarithm of 1982 2-hour postprandial glucose, and age in 1997.

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.

**Table 16-40. Longitudinal Analysis of 2-Hour Postprandial Glucose (mg/dl) (Continuous) (Continued)**

<b>(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY</b>								
<b>Dioxin Category</b>	<b>Mean<sup>a</sup>/(n) Examination</b>					<b>Exam. Mean Change<sup>b</sup></b>	<b>Difference of Exam. Mean Change</b>	<b>p-Value<sup>c</sup></b>
	<b>1982</b>	<b>1985</b>	<b>1987</b>	<b>1992</b>	<b>1997</b>			
Comparison	90.1 (778)	103.9 (764)	106.5 (757)	103.7 (755)	105.7 (778)	15.6		
Background RH	88.4 (310)	101.1 (303)	105.4 (294)	101.5 (297)	103.9 (310)	15.5	-0.1	0.991
Low RH	91.3 (177)	103.9 (12)	109.8 (174)	103.1 (169)	107.6 (177)	16.3	0.7	0.689
High RH	91.2 (176)	101.0 (174)	106.4 (171)	104.3 (173)	106.4 (176)	15.1	-0.5	0.999
Low plus High RH	91.3 (353)	102.5 (346)	108.1 (345)	103.7 (342)	107.0 (353)	15.7	0.1	0.795

<sup>a</sup> Transformed from natural logarithm scale.

<sup>b</sup> Difference between 1997 and 1982 examination means after transformation to original scale.

<sup>c</sup> P-value is based on analysis of natural logarithm of 1997 2-hour postprandial glucose; results adjusted for percent body fat at the date of the blood measurement of dioxin, natural logarithm of 1982 2-hour postprandial glucose, 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.

#### 16.2.3.2.6 2-Hour Postprandial Glucose (Discrete)

The Model 1 analysis of the change in percentage of abnormal 2-hour postprandial glucose levels did not reveal a significant difference between Ranch Hands and Comparisons across all occupations (Table 16-41(a): p=0.795). Stratifying by occupation revealed a significant difference between Ranch Hands and Comparison officers (Table 16-41(a): Adj. RR=1.65, p=0.045). For officers with normal 2-hour postprandial glucose levels in 1982, 17.7 percent of the Ranch Hands and 11.4 percent of the Comparisons had impaired 2-hour postprandial glucose levels in 1997.

**Table 16-41. Longitudinal Analysis of 2-Hour Postprandial Glucose (Discrete)**

<b>(a) MODEL 1: RANCH HANDS VS. COMPARISONS</b>						
<b>Occupational Category</b>	<b>Group</b>	<b>Number (%) Impaired/(n) Examination</b>				
		<b>1982</b>	<b>1985</b>	<b>1987</b>	<b>1992</b>	<b>1997</b>
<i>All</i>	<i>Ranch Hand</i>	<i>40 (6.0)</i> <i>(665)</i>	<i>53 (8.1)</i> <i>(651)</i>	<i>88 (13.7)</i> <i>(641)</i>	<i>80 (12.5)</i> <i>(641)</i>	<i>110 (16.5)</i> <i>(665)</i>
	<i>Comparison</i>	<i>57 (7.2)</i> <i>(797)</i>	<i>83 (10.6)</i> <i>(781)</i>	<i>84 (10.8)</i> <i>(775)</i>	<i>91 (11.8)</i> <i>(773)</i>	<i>132 (16.6)</i> <i>(797)</i>
Officer	Ranch Hand	14 (5.4) (257)	23 (9.1) (254)	31 (12.4) (250)	31 (12.4) (251)	50 (19.5) (257)
	Comparison	19 (6.0) (318)	27 (8.7) (311)	23 (7.5) (305)	33 (10.5) (315)	41 (12.9) (318)
Enlisted Flyer	Ranch Hand	9 (7.6) (119)	10 (8.5) (117)	21 (18.3) (115)	12 (10.3) (116)	22 (18.5) (119)
	Comparison	16 (13.9) (115)	17 (14.8) (115)	17 (14.9) (114)	20 (17.5) (114)	25 (21.7) (115)
Enlisted Groundcrew	Ranch Hand	17 (5.9) (289)	20 (7.1) (280)	36 (13.0) (276)	37 (13.5) (274)	38 (13.1) (289)
	Comparison	22 (6.0) (364)	39 (11.0) (355)	44 (12.4) (356)	38 (11.0) (344)	66 (18.1) (364)

<b>Occupational Category</b>	<b>Group</b>	<b>Normal in 1982</b>		<b>Adj. Relative Risk (95% C.I.)<sup>a</sup></b>	<b>p-Value<sup>a</sup></b>
		<b>n in 1997</b>	<b>Number (%) Impaired in 1997</b>		
<i>All</i>	<i>Ranch Hand</i>	<i>625</i>	<i>92 (14.7)</i>	<i>1.04 (0.77,1.41)</i>	<i>0.795</i>
	<i>Comparison</i>	<i>740</i>	<i>106 (14.3)</i>		
Officer	Ranch Hand	243	43 (17.7)	1.65 (1.01,2.71)	0.045
	Comparison	299	34 (11.4)		
Enlisted Flyer	Ranch Hand	110	18 (16.4)	0.90 (0.44,1.87)	0.783
	Comparison	99	18 (18.2)		
Enlisted Groundcrew	Ranch Hand	272	31 (11.4)	0.73 (0.45,1.18)	0.199
	Comparison	342	54 (15.8)		

<sup>a</sup> 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 a normal 2-hour postprandial glucose level in 1982 (see Chapter 7, Statistical Methods).

**Table 16-41. Longitudinal Analysis of 2-Hour Postprandial Glucose (Discrete)  
(Continued)**

<b>(b) MODEL 2: RANCH HANDS — INITIAL DIOXIN</b>					
<b>Initial Dioxin</b>	<b>Number (%) Impaired/(n) Examination</b>				
	<b>1982</b>	<b>1985</b>	<b>1987</b>	<b>1992</b>	<b>1997</b>
Low	6 (5.0) (119)	11 (9.4) (117)	21 (17.6) (119)	15 (13.3) (113)	23 (19.3) (119)
Medium	10 (8.3) (120)	8 (6.8) (117)	14 (12.1) (116)	18 (15.4) (117)	22 (18.3) (120)
High	7 (6.1) (114)	10 (8.9) (112)	16 (14.5) (110)	14 (12.5) (112)	20 (17.5) (114)

<b>Initial Dioxin Category Summary Statistics</b>			<b>Analysis Results for Log<sub>2</sub> (Initial Dioxin)<sup>a</sup></b>	
<b>Initial Dioxin</b>	<b>Normal in 1982</b>		<b>Adj. Relative Risk (95% C.I.)<sup>b</sup></b>	<b>p-Value</b>
	<b>n in 1997</b>	<b>Number (%) Impaired in 1997</b>		
Low	113	20 (17.7)	1.04 (0.81,1.34)	0.765
Medium	110	17 (15.5)		
High	107	18 (16.8)		

<sup>a</sup> Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.

<sup>b</sup> 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 a normal 2-hour postprandial glucose level in 1982 (see Chapter 7, Statistical Methods).

<b>(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY</b>					
<b>Dioxin Category</b>	<b>Number (%) Impaired/(n) Examination</b>				
	<b>1982</b>	<b>1985</b>	<b>1987</b>	<b>1992</b>	<b>1997</b>
Comparison	54 (6.9) (778)	80 (10.5) (764)	82 (10.8) (757)	87 (11.5) (755)	129 (16.6) (778)
Background RH	17 (5.5) (310)	24 (7.9) (303)	37 (12.6) (294)	33 (11.1) (297)	45 (14.5) (310)
Low RH	13 (7.3) (117)	15 (8.7) (172)	26 (14.9) (174)	22 (13.0) (169)	34 (19.2) (177)
High RH	10 (5.7) (176)	14 (8.0) (174)	25 (14.6) (171)	25 (14.5) (173)	31 (17.6) (176)
Low plus High RH	23 (6.5) (353)	29 (8.4) (346)	51 (14.8) (345)	47 (13.7) (342)	65 (18.4) (353)

**Table 16-41. Longitudinal Analysis of 2-Hour Postprandial Glucose (Discrete)  
(Continued)**

Dioxin Category	Normal in 1982		Adj. Relative Risk (95% C.I.) <sup>ab</sup>	p-Value <sup>b</sup>
	n in 1997	Number (%) Impaired in 1997		
Comparison	724	105 (14.5)		
Background RH	293	37 (12.6)	0.87 (0.58,1.32)	0.524
Low RH	164	28 (17.1)	1.14 (0.71,1.83)	0.584
High RH	166	27 (16.3)	1.24 (0.77,2.01)	0.382
Low plus High RH	330	55 (16.7)	1.19 (0.82,1.72)	0.356

<sup>a</sup> Relative risk and confidence interval relative to Comparisons.

<sup>b</sup> 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 a normal 2-hour postprandial glucose level in 1982 (see Chapter 7, Statistical Methods).

The longitudinal analyses in Models 2 and 3 did not reveal a significant association between dioxin and the change in 2-hour postprandial glucose levels between 1982 and 1997 (Table 16-41(b,c):  $p > 0.35$  for each analysis).

#### 16.2.3.2.7 Total Testosterone (Continuous)

The Model 1 analysis of the change in mean total testosterone did not reveal a significant difference between Ranch Hands and Comparisons across all occupations or within each occupational stratum (Table 16-42(a):  $p > 0.35$  for each analysis).

**Table 16-42. Longitudinal Analysis of Total Testosterone (ng/dl) (Continuous)**

<b>(a) MODEL 1: RANCH HANDS VS. COMPARISONS</b>									
Occupational Category	Group	Mean <sup>a</sup> /(n) Examination					Exam. Mean Change <sup>b</sup>	Difference of Exam. Mean Change	p-Value <sup>c</sup>
		1982	1985	1987	1992	1997			
<i>All</i>	<i>Ranch Hand</i>	<i>640.8</i> <i>(800)</i>	<i>600.6</i> <i>(780)</i>	<i>532.1</i> <i>(773)</i>	<i>509.6</i> <i>(775)</i>	<i>424.1</i> <i>(800)</i>	<i>-216.7</i>	<i>-13.1</i>	<i>0.380</i>
	<i>Comparison</i>	<i>626.7</i> <i>(953)</i>	<i>581.6</i> <i>(936)</i>	<i>525.9</i> <i>(929)</i>	<i>498.3</i> <i>(929)</i>	<i>423.1</i> <i>(953)</i>	<i>-203.6</i>		
Officer	Ranch Hand	601.7 (302)	573.8 (295)	502.0 (294)	490.5 (295)	401.9 (302)	-199.8	-11.1	0.353
	Comparison	601.8 (371)	556.0 (367)	499.4 (361)	475.5 (365)	413.1 (371)	-188.7		
Enlisted Flyer	Ranch Hand	651.3 (143)	611.6 (140)	530.9 (138)	518.9 (140)	446.3 (143)	-205.0	-2.8	0.788
	Comparison	634.3 (140)	588.3 (139)	537.0 (138)	508.4 (138)	432.0 (140)	-202.2		
Enlisted Groundcrew	Ranch Hand	670.9 (355)	619.5 (345)	559.4 (341)	522.7 (340)	434.5 (355)	-236.3	-19.5	0.472
	Comparison	645.5 (442)	601.7 (430)	545.2 (430)	515.0 (426)	428.6 (442)	-216.8		

<sup>a</sup> Transformed from the square root of total testosterone.

<sup>b</sup> Difference between 1997 and 1982 examination means after transformation to original scale.

<sup>c</sup> P-value is based on analysis of the square root of total testosterone; results adjusted for the square root of total testosterone in 1982 and 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.

**Table 16-42. Longitudinal Analysis of Total Testosterone (ng/dl) (Continuous) (Continued)**

<b>(b) MODEL 2: RANCH HANDS – INITIAL DIOXIN</b>							
<b>Initial Dioxin Category Summary Statistics</b>						<b>Analysis Results for Log<sub>2</sub> (Initial Dioxin)<sup>b</sup></b>	
<b>Initial Dioxin</b>	<b>Mean<sup>a</sup>/(n) Examination</b>					<b>Adjusted Slope (Std. Error)</b>	<b>p-Value</b>
	<b>1982</b>	<b>1985</b>	<b>1987</b>	<b>1992</b>	<b>1997</b>		
Low	639.7 (150)	573.0 (146)	515.1 (149)	507.1 (145)	404.3 (150)	0.280 (0.143)	0.051
Medium	621.7 (157)	559.1 (154)	518.1 (154)	472.9 (154)	394.7 (157)		
High	616.6 (149)	586.4 (147)	515.2 (144)	486.7 (146)	421.6 (149)		

<sup>a</sup> Transformed from square root of total testosterone.

<sup>b</sup> Results based on difference between the square root of 1997 total testosterone and the square root of 1982 total testosterone versus log<sub>2</sub> (initial dioxin); results adjusted for percent body fat at the date of the blood measurement of dioxin, square root of 1982 total testosterone, and age in 1997.

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.

**Table 16-42. Longitudinal Analysis of Total Testosterone (ng/dl) (Continuous) (Continued)**

<b>(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY</b>								
<b>Dioxin Category</b>	<b>Mean<sup>a</sup>/(n) Examination</b>					<b>Exam. Mean Change<sup>b</sup></b>	<b>Difference of Exam. Mean Change</b>	<b>p-Value<sup>c</sup></b>
	<b>1982</b>	<b>1985</b>	<b>1987</b>	<b>1992</b>	<b>1997</b>			
Comparison	628.1 (925)	581.6 (911)	527.1 (903)	498.4 (902)	423.6 (925)	-204.5		
Background	662.6 (339)	639.4 (329)	554.6 (322)	540.7 (326)	448.7 (339)	-213.9	-9.4	0.789
Low RH	630.9 (225)	564.5 (218)	513.9 (222)	498.8 (218)	400.9 (225)	-230.0	-25.5	0.070
High RH	621.1 (231)	580.3 (229)	518.4 (225)	478.6 (227)	412.1 (231)	-209.0	-4.5	0.885
Low plus High RH	625.9 (456)	572.5 (447)	516.2 (447)	488.4 (445)	406.6 (456)	-219.3	-14.8	0.287

<sup>a</sup> Transformed from the square root of total testosterone.

<sup>b</sup> Difference between 1997 and 1982 examination means after transformation to original scale.

<sup>c</sup> P-value is based on analysis of the square root of 1997 total testosterone; results adjusted for percent body fat at the date of the blood measurement of dioxin, the square root of 1982 total testosterone, and age in 1997.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin  $\leq$  10 ppt.

Background (Ranch Hand): 1987 Dioxin  $\leq$  10 ppt.

Low (Ranch Hand): 1987 Dioxin  $>$  10 ppt, 10 ppt  $<$  Initial Dioxin  $\leq$  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.

The Model 2 longitudinal analysis revealed a marginally significant positive association between initial dioxin and change in mean total testosterone levels (Table 16-42(b): adjusted slope=0.280, p=0.051).

The Model 3 analysis of change in mean total testosterone levels between 1982 and 1997 revealed a marginally significant difference between Ranch Hands in the low dioxin category and Comparisons (Table 16-42(c): difference of means=-25.5 ng/dl, p=0.070). The mean decrease between 1982 and 1997 for Ranch Hands in the low dioxin category was 230.0 ng/dl versus 204.5 ng/dl for Comparisons.

#### 16.2.3.2.8 Total Testosterone (Discrete)

The longitudinal analysis in Models 1 through 3 of low total testosterone levels was not significantly associated with group or dioxin (Table 16-43(a-c): p>0.15 for each analysis).

**Table 16-43. Longitudinal Analysis of Total Testosterone (Discrete)**

<b>(a) MODEL 1: RANCH HANDS VS. COMPARISONS</b>						
Occupational Category	Group	Number (%) Low / (n) Examination				
		1982	1985	1987	1992	1997
<i>All</i>	<i>Ranch Hand</i>	37 (4.6) (800)	21 (2.7) (780)	14 (1.8) (773)	34 (4.4) (775)	67 (8.4) (800)
	<i>Comparison</i>	47 (4.9) (953)	24 (2.6) (936)	13 (1.4) (929)	50 (5.4) (929)	80 (8.4) (953)
Officer	Ranch Hand	15 (5.0) (302)	10 (3.4) (295)	6 (2.0) (294)	14 (4.7) (295)	27 (8.9) (302)
	Comparison	20 (5.4) (371)	14 (3.8) (367)	7 (1.9) (361)	19 (5.2) (365)	30 (8.1) (371)
Enlisted Flyer	Ranch Hand	8 (5.6) (143)	4 (2.9) (140)	5 (3.6) (138)	5 (3.6) (140)	11 (7.7) (143)
	Comparison	8 (5.7) (140)	2 (1.4) (139)	1 (0.7) (138)	7 (5.1) (138)	10 (7.1) (140)
Enlisted Groundcrew	Ranch Hand	14 (3.9) (355)	7 (2.0) (345)	3 (0.9) (341)	15 (4.4) (340)	29 (8.2) (355)
	Comparison	19 (4.3) (442)	8 (1.9) (430)	5 (1.2) (430)	24 (5.6) (426)	40 (9.1) (442)

  

Occupational Category	Group	Normal in 1982		Adj. Relative Risk (95% C.I.) <sup>a</sup>	p-Value <sup>a</sup>
		n in 1997	Number (%) Low in 1997		
<i>All</i>	<i>Ranch Hand</i>	763	54 (7.1)	1.00 (0.69,1.46)	0.984
	<i>Comparison</i>	906	64 (7.1)		
Officer	Ranch Hand	287	21 (7.3)	1.03 (0.56,1.87)	0.935
	Comparison	351	25 (7.1)		
Enlisted Flyer	Ranch Hand	135	9 (6.7)	1.28 (0.46,3.54)	0.637
	Comparison	132	7 (5.3)		
Enlisted Groundcrew	Ranch Hand	341	24 (7.0)	0.94 (0.54,1.62)	0.817
	Comparison	423	32 (7.6)		

<sup>a</sup> 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 a normal total testosterone level in 1982 (see Chapter 7, Statistical Methods).

**Table 16-43. Longitudinal Analysis of Total Testosterone (Discrete) (Continued)**

<b>(b) MODEL 2: RANCH HANDS — INITIAL DIOXIN</b>					
<b>Initial Dioxin</b>	<b>Number (%) Low/(n) Examination</b>				
	<b>1982</b>	<b>1985</b>	<b>1987</b>	<b>1992</b>	<b>1997</b>
Low	6 (4.0) (150)	2 (1.4) (146)	5 (3.4) (149)	5 (3.4) (145)	13 (8.7) (150)
Medium	8 (5.1) (157)	6 (3.9) (154)	2 (1.3) (154)	10 (6.5) (154)	18 (11.5) (157)
High	10 (6.7) (149)	3 (2.0) (147)	3 (2.1) (144)	10 (6.8) (146)	16 (10.7) (149)

<b>Initial Dioxin Category Summary Statistics</b>			<b>Analysis Results for Log<sub>2</sub> (Initial Dioxin)<sup>a</sup></b>	
<b>Initial Dioxin</b>	<b>Normal in 1982</b>		<b>Adj. Relative Risk (95% C.I.)<sup>b</sup></b>	<b>p-Value</b>
	<b>n in 1997</b>	<b>Number (%) Low In 1997</b>		
Low	144	10 (6.9)	1.04 (0.80,1.35)	0.760
Medium	149	16 (10.7)		
High	139	14 (10.1)		

<sup>a</sup> Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.

<sup>b</sup> 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 a normal total testosterone level in 1982 (see Chapter 7, Statistical Methods).

<b>(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY</b>					
<b>Dioxin Category</b>	<b>Number (%) Low/(n) Examination</b>				
	<b>1982</b>	<b>1985</b>	<b>1987</b>	<b>1992</b>	<b>1997</b>
Comparison	45 (4.9) (925)	24 (2.6) (911)	13 (1.4) (903)	49 (5.4) (902)	78 (8.4) (925)
Background RH	13 (3.8) (339)	10 (3.0) (329)	4 (1.2) (322)	9 (2.8) (326)	20 (5.9) (339)
Low RH	11 (4.9) (225)	5 (2.3) (218)	7 (3.2) (222)	7 (3.2) (218)	19 (8.4) (225)
High RH	13 (5.6) (231)	6 (2.6) (229)	3 (1.3) (225)	18 (7.9) (227)	28 (12.1) (231)
Low plus High RH	24 (5.3) (456)	11 (2.5) (447)	10 (2.2) (447)	25 (5.6) (445)	47 (10.3) (456)

**Table 16-43. Longitudinal Analysis of Total Testosterone (Discrete) (Continued)**

Dioxin Category	Normal in 1982		Adj. Relative Risk (95% C.I.) <sup>ab</sup>	p-Value <sup>b</sup>
	n in 1997	Number (%) Low in 1997		
Comparison	880	64 (7.3)		
Background RH	326	14 (4.3)	0.71 (0.39,1.31)	0.278
Low RH	214	16 (7.5)	0.93 (0.52,1.67)	0.812
High RH	218	24 (11.0)	1.46 (0.87,2.44)	0.153
Low plus High RH	432	40 (9.3)	1.17 (0.76,1.79)	0.482

<sup>a</sup> Relative risk and confidence interval relative to Comparisons.

<sup>b</sup> 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 a normal total testosterone level in 1982 (see Chapter 7, Statistical Methods).

### 16.3 DISCUSSION

The historical, physical examination, and laboratory data analyzed in this chapter provide a comprehensive assessment of thyroid, gonadal, and endocrine pancreatic function in the population under study. The current laboratory database includes several indices relevant to the possibility that dioxin may influence glucose metabolism. The  $\alpha$ -1-C hemoglobin measurement reflects the average blood sugar over a 3- to 4-month period and is a more accurate index of diabetic control than random or fasting blood sugar measurements. In general, participants with diabetes were of the adult-onset variety (Type 2), as associated with obesity and characterized by an acquired defect in insulin receptors with elevated serum insulin levels.

Serum levels of TSH, LH, and FSH are indices of pituitary and hypothalamic function, while the T<sub>4</sub> and testosterone levels reflect the integrity of the thyroid gland and testicles, respectively. Additional physical examination variables pertinent to endocrine function—body habitus, ocular signs, and deep tendon reflexes—were included in the general and neurological examinations and are reported in Chapters 9 and 11, respectively.

In the analysis of historical variables verified by a medical records review, the prevalence of thyroid disorders and diabetes was similar in the Ranch Hand and Comparison cohorts (7.5% versus 8.4% and 16.9% versus 17.0%, respectively). For Ranch Hands, in a pattern consistent with a dose-response, a significant positive association was noted between the current body burden of dioxin and the development of diabetes, specifically in the later stages requiring oral hypoglycemic and insulin therapy. Ranch Hands with higher levels of initial and 1987 serum dioxin were significantly more likely to develop diabetes sooner after their exposure than those with lower serum dioxin levels.

After analyzing the physical examination and all laboratory indices of thyroid function ( $T_4$ , TSH, and anti-thyroid antibodies), no significant group differences were defined. Consistent with the 1985, 1987, and 1992 examinations, Ranch Hands continued to have a slightly higher mean serum TSH than Comparisons (1.88  $\mu$ IU/ml versus 1.81  $\mu$ IU/ml), but the difference is not statistically significant. By discrete analysis, the prevalence of abnormal  $T_4$  results was identical in the two cohorts (2.7%). In the assessment of glucose metabolism without regard to dioxin levels, no significant group differences were noted in any of the historical or laboratory variables examined, and the history of diabetes by the composite indicator was similar in the Ranch Hand and Comparison cohorts. With respect to the possibility that dioxin exposure might be a risk factor for the development of diabetes, 1987 serum dioxin levels were strongly associated, in a dose-response pattern, with abnormal elevations in fasting blood sugar in both discrete and continuous forms and with the occurrence of fasting glycosuria. Similar statistical significance ( $p < 0.001$ ) was found, by both continuous and discrete analyses, in the association of both initial and 1987 serum dioxin with elevations in  $\alpha$ -1-C hemoglobin which, as noted above, is a more accurate reflection of blood sugar levels over time.

In the analyses of diabetic severity, Ranch Hands were significantly more likely than Comparisons to require insulin for control (2.8% versus 1.4%), particularly in the officer and enlisted groundcrew occupational groups (3.6% versus 1.4% and 2.4% versus 1.1%, respectively). Further, in a dose-response pattern, requiring insulin to treat diabetes was significantly more common in Ranch Hands with high 1987 levels of serum dioxin than in Comparisons.

In 1992, a significant association was noted between serum insulin and 1987 serum dioxin in nondiabetics. In the 1997 examination, after adjustment for covariates, no significant association was found between serum insulin and 1987 serum dioxin.

In the assessment of gonadal function, no significant group differences were defined on physical examination or with respect to the laboratory indices analyzed. Consistent with all previous examinations, mean serum levels of free and total testosterone were slightly higher in Ranch Hands than in Comparisons but differences were minimal. The unadjusted analysis of total serum testosterone yielded results consistent with a dioxin effect: total testosterone decreased as the 1987 dioxin level increased in Ranch Hands. After adjustment for covariates, the difference was no longer significant. Similar results were noted in the analyses of the biologically active free form of testosterone.

Dependent variable-covariate analyses confirmed associations that are well established in clinical practice. The classic risk factors of age, obesity, and family history of diabetes were strongly and positively associated with all diabetic indices. A significant negative association was noted between age and testicular size and serum testosterone. Blacks were at significantly greater risk for the development of diabetes by the composite indicator and by all laboratory indices of glucose metabolism.

The longitudinal analyses yielded results that would be anticipated in this aging population with no significant group differences defined. The increasing history of diabetes by the composite indicator was similar in Ranch Hands and Comparisons (17.7% versus 16.9%, respectively), as were abnormal elevations in both fasting and two-hour postprandial blood sugar (18.2% versus 16.2% and 16.5% versus 16.6%, respectively). Evidence for a dioxin effect was apparent in several analyses. In a dose-response pattern, an increasing history of diabetes was noted in Ranch Hands in the low, medium, and high initial dioxin categories (17.9%, 18.9%, and 21.4%, respectively;  $p = 0.019$ ), and Ranch Hands in the high serum dioxin category were at significantly greater risk for the development of diabetes relative to Comparisons ( $RR = 1.61$ ,  $p = 0.023$ ). In both cohorts, serum testosterone continues to decrease with advancing years.

In summary, after 15 years of observation, the prevalence of diabetes, thyroid disorders, and gonadal dysfunction remains similar in Ranch Hands and Comparisons, although significant adverse relations exist between glucose intolerance and dioxin among Ranch Hands. Although cause and effect have not

been established, the results cited above provide additional evidence for an association between diabetes and elevated serum dioxin levels.

## 16.4 SUMMARY

Dependent variables to assess thyroid, gonadal, and pancreatic function were examined in the endocrine assessment. Each health endpoint was examined for an association with exposure group (Model 1), initial dioxin (Model 2), categorized dioxin (Model 3), and 1987 dioxin levels (Model 4). Significant results based on adjusted analyses are discussed below.

### 16.4.1 Model 1: Group Analysis

The adjusted group analysis of diabetic severity showed that a greater percentage of Ranch Hands than Comparisons required insulin to treat diabetes when combining all occupations. Stratifying by occupation revealed a marginally significant increase in the need for insulin to treat diabetes for Ranch Hand officers and enlisted groundcrew. A marginally significant increase in the presence of 2-hour postprandial urinary glucose in Ranch Hands was observed when combining all occupations. Stratifying the adjusted analysis by occupation revealed Ranch Hand officers had a significantly higher prevalence of 2-hour postprandial urinary glucose than did Comparison officers.

Significant results for the thyroid function revealed a significantly greater percentage of abnormally high TSH values in Ranch Hand enlisted groundcrew than Comparison enlisted groundcrew. In addition, Comparison officers had a significantly lower mean estradiol level than Ranch Hand officers.

The results of all unadjusted and adjusted Model 1 analyses are summarized in Table 16-44.

**Table 16-44. Summary of Group Analysis (Model 1) for Endocrine Variables (Ranch Hands vs. Comparisons)**

Variable	UNADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
<b>Medical Records</b>				
Past Thyroid Disease (D)	ns	ns	NS	ns
Composite Diabetes Indicator (D)	ns	NS	ns	ns
Diabetic Severity (D):				
No Treatment vs. None	NS	ns	ns	NS
Diet Only vs. None	NS	NS	NS	NS
Oral Hypoglycemics vs. None	ns*	ns	ns	ns
Requiring Insulin vs. None	+0.026	NS*	ns	NS
Time to Diabetes Onset (C) <sup>a</sup>	NS	ns	NS	NS
<b>Physical Examination</b>				
Thyroid Gland (D)	ns	ns	NS	ns
Testicular Exam (D)	NS	ns	NS	NS
<b>Laboratory</b>				
TSH (C)	NS	NS	ns	NS
TSH (D):				
Low vs. Normal	NS	NS	NS	ns
High vs. Normal	NS	NS	ns	+0.044
Thyroxine (C) <sup>a</sup>	NS	ns	NS	NS
Thyroxine (D)	NS	NS	NS	ns

**Table 16-44. Summary of Group Analysis (Model 1) for Endocrine Variables (Ranch Hands vs. Comparisons) (Continued)**

Variable	UNADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Anti-Thyroid Antibodies (D)	NS	ns	NS	ns
Fasting Glucose (C)	ns	NS	ns	ns
Fasting Glucose (D)	NS	NS	NS	NS
2-Hour Postprandial Glucose (C)	NS	NS*	ns	ns
2-Hour Postprandial Glucose (D)	NS	NS*	ns	ns
Fasting Urinary Glucose (D)	ns	NS	NS	ns
2-Hour Postprandial Urinary Glucose (D)	NS	+0.034	ns	NS
Serum Insulin (C)	NS	NS	ns	ns
Serum Insulin (D):				
Low vs. Normal	ns	ns	NS	ns
High vs. Normal	ns	NS	ns	ns
$\alpha$ -1-C Hemoglobin (C)	ns	NS	ns	ns
$\alpha$ -1-C Hemoglobin (D)	NS	NS	ns	NS
Total Testosterone (C) <sup>a</sup>	NS	ns	NS	NS
Total Testosterone (D)	NS	NS	NS	NS
Free Testosterone (C) <sup>a</sup>	NS	ns	NS	NS
Free Testosterone (D)	NS	NS	NS*	ns
Estradiol (C)	ns	-0.003	NS	NS
Estradiol (D)	ns	ns	ns	NS
LH (C)	NS	NS	ns	ns
LH (D)	NS	NS	ns	ns
FSH (C)	NS	NS*	NS	ns
FSH (D)	NS	NS	NS	ns

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

NS\* or ns\*: Marginally significant ( $0.05<p\leq 0.10$ ).

C: Continuous analysis.

D: Discrete analysis.

+: Relative risk  $\geq 1.00$ .

-: Difference of means negative.

<sup>a</sup> Negative difference considered adverse for this variable.

P-value given if  $p\leq 0.05$ .

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or differences of means nonnegative for continuous analysis. A lowercase "ns" denotes a relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

Variable	ADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
<b>Medical Records</b>				
Past Thyroid Disease (D)	ns	ns	NS	ns
Composite Diabetes Indicator (D)	NS	NS	ns	NS
Diabetic Severity (D):				
No Treatment vs. None	NS	ns	ns	NS
Diet Only vs. None	NS	NS	NS	NS
Oral Hypoglycemics vs. None	ns	ns	ns	ns
Requiring Insulin vs. None	+0.017	NS*	NS	NS*
Time to Diabetes Onset (C) <sup>a</sup>	NS	ns	NS	ns

**Table 16-44. Summary of Group Analysis (Model 1) for Endocrine Variables (Ranch Hands vs. Comparisons) (Continued)**

Variable	ADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
<b>Physical Examination</b>				
Thyroid Gland (D)	ns	ns	NS	ns
Testicular Exam (D)	NS	ns	NS	NS
<b>Laboratory</b>				
TSH (C)	NS	NS	ns	NS*
TSH (D):				
Low vs. Normal	NS	NS	NS	ns
High vs. Normal	NS	NS	ns	+0.037
Thyroxine (C) <sup>a</sup>	NS	ns	NS	NS
Thyroxine (D)	NS	NS	NS	ns
Anti-Thyroid Antibodies (D)	NS	ns	NS	ns
Fasting Glucose (C)	NS	NS	ns	ns
Fasting Glucose (D)	NS	NS	ns	NS
2-Hour Postprandial Glucose (C)	NS	NS*	ns	ns
2-Hour Postprandial Glucose (D)	ns	NS	ns	ns
Fasting Urinary Glucose (D)	ns	NS	NS	ns
2-Hour Postprandial Urinary Glucose (D)	NS*	+0.044	ns	NS
Serum Insulin (C)	NS	NS	ns	NS
Serum Insulin (D):				
Low vs. Normal	ns	ns	ns	ns
High vs. Normal	ns	NS	ns	ns
α-1-C Hemoglobin (C)	NS	NS	ns	NS
α-1-C Hemoglobin (D)	NS	NS	ns	NS*
Total Testosterone (C) <sup>a</sup>	ns	ns	NS	ns
Total Testosterone (D)	NS	NS	NS	NS
Free Testosterone (C) <sup>a</sup>	NS	ns	NS	NS
Free Testosterone (D)	NS	NS	NS*	ns
Estradiol (C)	ns	-0.003	NS	NS
Estradiol (D)	ns	ns	ns	NS
LH (C)	ns	NS	ns	ns
LH (D)	NS	NS	ns	ns
FSH (C)	NS	NS	ns	ns
FSH (D)	NS	NS	NS	ns

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

NS\* or ns\*: Marginally significant ( $0.05 < p \leq 0.10$ ).

C: Continuous analysis.

D: Discrete analysis.

+: Relative risk  $\geq 1.00$ .

-: Difference of means negative.

<sup>a</sup> Negative difference considered adverse for this variable.

P-value given if  $p \leq 0.05$ .

A capital “NS” denotes a relative risk of 1.00 or greater for discrete analysis or differences of means nonnegative for continuous analysis. A lowercase “ns” denotes a relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

### 16.4.2 Model 2: Initial Dioxin Analysis

A positive association between initial dioxin and diabetes was observed. The need for insulin to treat diabetes increased as initial dioxin increased. A marginally significant increase in the percentage of Ranch Hands taking oral hypoglycemics also was observed. The time to diabetes onset was significantly shorter for Ranch Hands with higher initial dioxin levels. The adjusted analysis of laboratory measures of diabetes revealed a positive association between initial dioxin and both fasting glucose and  $\alpha$ -1-C hemoglobin, in both continuous and discrete forms.

A marginally significant decrease in low free testosterone levels was observed as initial dioxin increased. The results of all unadjusted and adjusted Model 2 analyses are summarized in Table 16-45.

**Table 16-45. Summary of Initial Dioxin Analysis (Model 2) for Endocrine Variables (Ranch Hands Only)**

Variable	Unadjusted	Adjusted
<b>Medical Records</b>		
Past Thyroid Disease (D)	NS	NS
Composite Diabetes Indicator (D)	NS	+0.005
Diabetic Severity (D):		
No Treatment vs. None	NS	NS
Diet Only vs. None	NS	NS
Oral Hypoglycemics vs. None	NS	NS*
Requiring Insulin vs. None	NS	+0.001
Time to Diabetes Onset (C) <sup>a</sup>	ns	-0.013
<b>Physical Examination</b>		
Thyroid Gland (D)	ns	NS
Testicular Exam (D)	ns	NS
<b>Laboratory</b>		
TSH (C)	ns	ns
TSH (D):		
Low vs. Normal	NS	NS
High vs. Normal	NS	NS
Thyroxine (C) <sup>a</sup>	NS	ns
Thyroxine (D)	NS	NS
Anti-Thyroid Antibodies (D)	ns	NS
Fasting Glucose (C)	NS	+0.014
Fasting Glucose (D)	NS	+0.013
2-Hour Postprandial Glucose (C)	ns	NS
2-Hour Postprandial Glucose (D)	ns	ns
Fasting Urinary Glucose (D)	NS	NS
2-Hour Postprandial Urinary Glucose (D)	ns	ns
Serum Insulin (C)	NS	NS
Serum Insulin (D):		
Low vs. Normal	ns	ns
High vs. Normal	NS	NS
$\alpha$ -1-C Hemoglobin (C)	+0.009	+0.001
$\alpha$ -1-C Hemoglobin (D)	+0.013	+0.001
Total Testosterone (C) <sup>a</sup>	+0.047	ns
Total Testosterone (D)	NS	NS
Free Testosterone (C) <sup>a</sup>	+0.003	ns
Free Testosterone (D)	-0.019	ns*

**Table 16-45. Summary of Initial Dioxin Analysis (Model 2) for Endocrine Variables (Ranch Hands Only) (Continued)**

Variable	Unadjusted	Adjusted
Estradiol (C)	NS*	NS
Estradiol (D)	+0.045	NS
LH (C)	ns	ns
LH (D)	ns	ns
FSH (C)	ns*	ns
FSH (D)	ns	NS

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

NS\* or ns\*: Marginally significant ( $0.05 < p \leq 0.10$ ).

C: Continuous analysis.

D: Discrete analysis.

+: Relative risk  $\geq 1.00$  for discrete analysis; slope nonnegative for continuous analysis.

-: Relative risk  $< 1.00$  for discrete analysis; slope negative for continuous analysis.

<sup>a</sup> Negative slope considered adverse for this variable.

P-value given if  $p \leq 0.05$ .

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or slope nonnegative for continuous analysis. A lowercase "ns" denotes a relative risk less than 1.00 for discrete analysis or slope negative for continuous analysis.

### 16.4.3 Model 3: Categorized Dioxin Analysis

The percentages of diabetes for Ranch Hands in the high dioxin category and in the low plus high dioxin category were significantly greater than for Comparisons. Ranch Hands in the background dioxin category had fewer participants taking oral hypoglycemics than did Comparisons. Ranch Hands in the low dioxin category used insulin for the treatment of diabetes more often than Comparisons. The percentages of Ranch Hands in the high dioxin category and Ranch Hands in the low plus high dioxin category requiring insulin also were significantly greater than Comparisons.

The time to diabetes onset was significantly longer for Ranch Hands in the background dioxin category than for Comparisons. Relative to Comparisons, a marginally significant decrease in the time to diabetes onset was seen for Ranch Hands in the high dioxin category and Ranch Hands in the low plus high dioxin category.

Analysis of laboratory measures of diabetes revealed a significantly higher mean  $\alpha$ -1-C hemoglobin level for Ranch Hands in the high dioxin category than for Comparisons. A greater percentage of high  $\alpha$ -1-C hemoglobin values was seen for Ranch Hands in the high dioxin category than for Comparisons.

The results of all unadjusted and adjusted Model 3 analyses are summarized in Table 16-46.

**Table 16-46. Summary of Categorized Dioxin Analysis (Model 3) for Endocrine Variables (Ranch Hands vs. Comparisons)**

Variable	UNADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
<b>Medical Records</b>				
Past Thyroid Disease (D)	ns	ns	ns	ns
Composite Diabetes Indicator (D)	-0.041	NS	NS	NS*
Diabetic Severity (D):				
No Treatment vs. None	ns	NS	NS	NS
Diet Only vs. None	NS	NS	NS	NS
Oral Hypoglycemics vs. None	-0.006	ns	NS	NS
Requiring Insulin vs. None	NS	+0.042	+0.046	+0.013
Time to Diabetes Onset (C) <sup>a</sup>	+0.013	ns	ns	ns
<b>Physical Examination</b>				
Thyroid Gland (D)	ns	ns	ns	ns
Testicular Exam (D)	ns	NS*	NS	NS
<b>Laboratory</b>				
TSH (C)	NS	NS	NS	NS
TSH (D):				
Low vs. Normal	NS	ns	NS	ns
High vs. Normal	NS	ns	NS	NS
Thyroxine (C) <sup>a</sup>	ns	NS	NS*	NS*
Thyroxine (D)	NS	ns	NS	ns
Anti-Thyroid Antibodies (D)	NS	ns	ns	ns
Fasting Glucose (C)	ns	ns	NS	NS
Fasting Glucose (D)	ns	NS	NS*	NS
2-Hour Postprandial Glucose (C)	NS	NS	ns	NS
2-Hour Postprandial Glucose (D)	ns	NS	NS	NS
Fasting Urinary Glucose (D)	ns	ns	NS	NS
2-Hour Postprandial Urinary Glucose (D)	NS	+0.050	NS	NS
Serum Insulin (C)	ns	NS	NS	+0.046
Serum Insulin (D):				
Low vs. Normal	ns	ns	ns*	ns
High vs. Normal	ns	NS	ns	NS
α-1-C Hemoglobin (C)	ns	ns	+0.005	NS
α-1-C Hemoglobin (D)	ns	ns	+0.006	NS
Total Testosterone (C) <sup>a</sup>	NS	ns	NS	ns
Total Testosterone (D)	NS	NS	NS	NS
Free Testosterone (C) <sup>a</sup>	ns	-0.022	+0.006	NS
Free Testosterone (D)	ns	NS	ns	ns
Estradiol (C)	ns	ns	NS	ns
Estradiol (D)	ns	ns	NS	ns
LH (C)	NS	ns	ns	ns
LH (D)	NS	ns	ns	ns
FSH (C)	NS	NS	ns	ns
FSH (D)	NS	NS	ns	NS

**Table 16-46. Summary of Categorized Dioxin Analysis (Model 3) for Endocrine Variables (Ranch Hands vs. Comparisons) (Continued)**

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

NS\* or ns\*: Marginally significant ( $0.05 < p \leq 0.10$ ).

C: Continuous analysis.

D: Discrete analysis.

+: Relative risk  $\geq 1.00$  for discrete analysis; difference of means nonnegative for continuous analysis.

-: Relative risk  $< 1.00$ .

<sup>a</sup> Negative difference considered adverse for this variable.

P-value given if  $p \leq 0.05$ .

A capital “NS” denotes a relative risk of 1.00 or greater for discrete analysis or differences of means nonnegative for continuous analysis. A lowercase “ns” denotes a relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

Variable	ADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
<b>Medical Records</b>				
Past Thyroid Disease (D)	ns	ns	NS	ns
Composite Diabetes Indicator (D)	ns*	NS	+0.048	+0.049
Diabetic Severity (D):				
No Treatment vs. None	ns	ns	NS	NS
Diet Only vs. None	NS	NS	NS*	NS
Oral Hypoglycemics vs. None	-0.008	ns	NS	NS
Requiring Insulin vs. None	NS	+0.050	+0.009	+0.004
Time to Diabetes Onset (C) <sup>a</sup>	+0.021	ns	ns*	ns*
<b>Physical Examination</b>				
Thyroid Gland (D)	ns	ns	ns	ns
Testicular Exam (D)	ns	NS	NS	NS
<b>Laboratory</b>				
TSH (C)	NS	NS	NS	NS
TSH (D):				
Low vs. Normal	NS	ns	NS	ns
High vs. Normal	NS	ns	NS	NS
Thyroxine (C) <sup>a</sup>	NS	NS	NS	NS
Thyroxine (D)	NS	ns	NS	ns
Anti-Thyroid Antibodies (D)	NS	ns	NS	ns
Fasting Glucose (C)	ns	ns	NS	NS
Fasting Glucose (D)	ns	NS	NS*	NS
2-Hour Postprandial Glucose (C)	NS	NS	ns	NS
2-Hour Postprandial Glucose (D)	ns	NS	NS	NS
Fasting Urinary Glucose (D)	ns	ns	NS	NS
2-Hour Postprandial Urinary Glucose (D)	NS*	NS*	ns	NS
Serum Insulin (C)	ns	NS	NS	NS
Serum Insulin (D):				
Low vs. Normal	ns	ns	ns*	ns*
High vs. Normal	ns	NS	ns	ns
$\alpha$ -1-C Hemoglobin (C)	ns	ns	+0.022	NS
$\alpha$ -1-C Hemoglobin (D)	ns	ns	+0.008	NS
Total Testosterone (C) <sup>a</sup>	NS	ns	ns	ns
Total Testosterone (D)	ns	ns	NS*	NS

**Table 16-46. Summary of Categorized Dioxin Analysis (Model 3) for Endocrine Variables (Ranch Hands vs. Comparisons) (Continued)**

Variable	ADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Free Testosterone (C) <sup>a</sup>	NS	ns	NS	ns
Free Testosterone (D)	ns	NS	ns	ns
Estradiol (C)	ns	ns	NS	ns
Estradiol (D)	ns	ns	NS	ns
LH (C)	NS	ns	ns	ns
LH (D)	NS	ns	ns	ns
FSH (C)	NS	NS	ns	NS
FSH (D)	NS	ns	NS	NS

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

NS\* or ns\*: Marginally significant ( $0.05 < p \leq 0.10$ ).

C: Continuous analysis.

D: Discrete analysis.

+: Relative risk  $\geq 1.00$  for discrete analysis; difference of means nonnegative for continuous analysis.

-: Relative risk  $< 1.00$ .

<sup>a</sup> Negative difference considered adverse for this variable.

P-value given if  $p \leq 0.05$ .

A capital “NS” denotes a relative risk of 1.00 or greater for discrete analysis or differences of means nonnegative for continuous analysis. A lowercase “ns” denotes a relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

#### 16.4.4 Model 4: 1987 Dioxin Level Analysis

As 1987 dioxin levels increased, the prevalence of diabetes increased. In addition, the use of diet and oral hypoglycemics to treat diabetes increased as 1987 dioxin levels increased. Marginally significant increases with 1987 dioxin also were seen for Ranch Hands using no treatment and Ranch Hands who required insulin to treat diabetes. The time to diabetes onset was significantly shorter for Ranch Hands with higher 1987 dioxin levels.

Analyses of laboratory examination variables revealed significant positive associations between 1987 dioxin and both the continuous and discrete forms of fasting glucose and  $\alpha$ -1-C hemoglobin. The presence of fasting urinary glucose also increased with 1987 dioxin. The results of all unadjusted and adjusted Model 4 analyses are summarized in Table 16-47.

**Table 16-47. Summary of 1987 Dioxin Analysis (Model 4) for Endocrine Variables (Ranch Hands Only)**

Variable	Unadjusted	Adjusted
<b>Medical Records</b>		
Past Thyroid Disease (D)	NS	NS
Composite Diabetes Indicator (D)	+<0.001	+<0.001
Diabetic Severity (D):		
No Treatment vs. None	+0.010	NS*
Diet Only vs. None	NS	+0.048

**Table 16-47. Summary of 1987 Dioxin Analysis (Model 4) for Endocrine Variables (Ranch Hands Only) (Continued)**

Variable	Unadjusted	Adjusted
Oral Hypoglycemics vs. None	+<0.001	+<0.001
Requiring Insulin vs. None	NS	NS*
Time to Diabetes Onset (C) <sup>a</sup>	-<0.001	-<0.001
<b>Physical Examination</b>		
Thyroid Gland (D)	ns	NS
Testicular Exam (D)	NS	NS
<b>Laboratory</b>		
TSH (C)	ns	NS
TSH (D):		
Low vs. Normal	ns	NS
High vs. Normal	ns	ns
Thyroxine (C) <sup>a</sup>	+0.009	ns
Thyroxine (D)	ns	NS
Anti-Thyroid Antibodies (D)	ns	ns
Fasting Glucose (C)	+<0.001	+0.002
Fasting Glucose (D)	+<0.001	+0.003
2-Hour Postprandial Glucose (C)	NS	NS
2-Hour Postprandial Glucose (D)	NS	NS
Fasting Urinary Glucose (D)	+0.004	+0.006
2-Hour Postprandial Urinary Glucose (D)	ns	ns
Serum Insulin (C)	+<0.001	NS
Serum Insulin (D):		
Low vs. Normal	-0.050	ns
High vs. Normal	+0.008	NS
α-1-C Hemoglobin (C)	+<0.001	+<0.001
α-1-C Hemoglobin (D)	+<0.001	+<0.001
Total Testosterone (C) <sup>a</sup>	-0.003	ns
Total Testosterone (D)	+0.013	NS
Free Testosterone (C) <sup>a</sup>	ns	ns*
Free Testosterone (D)	ns	ns
Estradiol (C)	NS	NS
Estradiol (D)	NS	ns
LH (C)	-0.042	ns
LH (D)	ns*	ns
FSH (C)	ns	ns
FSH (D)	ns	NS

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

NS\* or ns\*: Marginally significant ( $0.05 < p \leq 0.10$ ).

C: Continuous analysis.

D: Discrete analysis.

+: Relative risk  $\geq 1.00$  for discrete analysis; slope nonnegative for continuous analysis.

-: Relative risk  $< 1.00$  for discrete analysis; slope negative for continuous analysis.

<sup>a</sup> Negative slope considered adverse for this variable.

P-value given if  $p \leq 0.05$ .

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or slope nonnegative for continuous analysis. A lowercase "ns" denotes a relative risk less than 1.00 for discrete analysis or slope negative for continuous analysis.

## 16.5 CONCLUSION

The assessment of the endocrine system included an extensive evaluation of thyroid, pancreatic, and gonadal function and their relation to dioxin exposure. A significantly greater percentage of abnormally high TSH values was found in Ranch Hand enlisted groundcrew.

A positive association between diabetes and initial and 1987 dioxin was observed. Consistent with previous reports, the prevalence of diabetes for Ranch Hands with high dioxin levels was significantly greater than for Comparisons. A greater percentage of Ranch Hands than Comparisons used insulin to control their type 2 diabetes, primarily officers and enlisted groundcrew. The percentage of Ranch Hands requiring insulin to control their type 2 diabetes increased with initial dioxin. A greater percentage of Ranch Hands in the high dioxin category required insulin to control their type 2 diabetes than did Comparisons. The percentage of participants who treated their diabetes through diet only and the percentage of participants who used oral hypoglycemics increased with 1987 dioxin level.

The time to diabetes onset was significantly shorter for Ranch Hands with higher initial and 1987 dioxin levels. Both fasting glucose and  $\alpha$ -1-C hemoglobin increased in Ranch Hands as initial dioxin and 1987 dioxin increased. Increased  $\alpha$ -1-C hemoglobin levels also were observed for Ranch Hands with high dioxin levels. The presence of fasting urinary glucose also increased with 1987 dioxin.

In summary, current data reveal no relation between gonadal disorders and thyroid function and herbicide or dioxin exposure; however, current and past results indicate a consistent and potentially meaningful adverse relation between serum dioxin levels and diabetes. A significant dose-response relation was found, with Ranch Hands in the high dioxin category exhibiting an increase in disease prevalence (relative risk=1.47, 95% confidence interval: [1.00, 2.17]). A dioxin-related increase in disease severity, a decrease in the time from exposure to first diagnosis, and an increase in fasting glucose and  $\alpha$ -1-C hemoglobin support this finding. Similar patterns were observed in 1992 and 1987.

## REFERENCES

---

1. Wilson, J. D., and D. W. Foster, eds. 1992. *Williams Textbook of Endocrinology*. 8th ed. Philadelphia: W. B. Saunders Company.
2. Okey, A. B., D. S. Riddick, and P. A. Harper. 1994. The Ah-receptor: Mediator of toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) and related compounds. *Toxicology Letters* 70(1): 1-22.
3. Lucier, G. W. 1991. Humans are sensitive species to some of the biochemical effects of structural analogs of dioxin. *Environmental Toxicology and Chemistry* 10:727-35.
4. Wang, X., R. Rosengren, V. Morrison, and S. Safe. 1992. Characterization of the human Ah receptor. *Chemosphere* 25(7-10):997-1000.
5. Cuthill, S., A. Wilhelmsson, G. G. Mason, M. Gillner, L. Poelinger, and J. A. Gustafsson. 1988. The dioxin receptor: A comparison with the glucocorticoid receptor. *Journal of Steroid Biochemistry and Molecular Biology* 30:277-80.
6. Potter, C. L., I. G. Sipes, and D. H. Russell. 1983. Hypothyroxinemia and hypothermia in rats in response to 2,3,7,8-tetrachlorodibenzo-p-dioxin administration. *Toxicology and Applied Pharmacology* 69:89-95.
7. Bastomsky, C. H. 1977. Enhanced thyroxine metabolism and high uptake goiters in rats after a single dose of 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Endocrinology* 101:292-6.
8. McKinney, J. D., J. Fawkes, S. Jordan, K. Chae, S. Oatley, R. E. Coleman, and W. Briner. 1985. 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) as a potent and persistent thyroxine agonist: A mechanistic model for toxicity based on molecular reactivity. *Environmental Health Perspectives* 61:41-53.
9. Rozman, K., T. Rozman, E. Scheufler, T. Pazdernik, and H. Greim. 1985. Thyroid hormones modulate the toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). *Journal of Toxicology and Environmental Health* 16:481-91.
10. Roth, W., R. Voorman, and S. D. Aust. 1988. Activity of thyroid hormone-inducible enzymes following treatment with 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Toxicology and Applied Pharmacology* 92(1):65-74.
11. Gorski, J. R., G. Muzi, L. W. D. Weber, D. W. Perera, R. J. Arceo, M. J. Latropoulos, and K. Rozman. 1988. Some endocrine and morphological aspects of the acute toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). *Toxicologic Pathology* 16:313-20.
12. Pohjanvirta, R., T. Kuliu, A. F. W. Morselt, R. Tuominen, R. Juvonen, K. Rozman, P. Mannisto, Y. Collan, E. L. Sainio, and J. Tuomisto. 1989. Target tissue morphology and serum biochemistry following 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) exposure in a TCDD-susceptible and a TCDD-resistant strain. *Fundamental and Applied Toxicology* 12:698-712.
13. Henry, E. C., and T. A. Gasiewicz. 1987. Changes in thyroid hormones and thyroxine glucuronidation in hamsters compared with rats following treatment with 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Toxicology and Applied Pharmacology* 84:439-53.
14. McKinney, J. D., and L. G. Pedersen. 1987. Do residue levels of polychlorinated biphenyls (PCBs) in human blood produce mild hypothyroidism? *Journal of Theoretical Biology* 129:231-41.

15. Capen, C. C. 1992. Pathophysiology of chemical injury of the thyroid gland. *Toxicology Letters* 64-65:381-8.
16. Zober, A., M. G. Ott, and P. Messerer. 1994. Morbidity follow-up study of BASF employees exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) after a 1953 chemical reactor incident. *Occupational and Environmental Medicine* 51:479-86.
17. Ott, M. G., A. Zober, and C. Germann. 1994. Laboratory results for selected target organs in 138 individuals occupationally exposed to TCDD. *Chemosphere* 29:2423-37.
18. Prokipcak, R. D., L. E. Faber, and A. B. Okey. 1989. Characterization of the Ah receptor for 2,3,7,8-tetrachlorodibenzo-p-dioxin: use of chemical crosslinking and a monoclonal antibody directed against a 59kDa protein associated with steroid receptors. *Archives of Biochemistry and Biophysics* 274:648-58.
19. Couture, L. A., B. D. Abbott, and L. S. Birnbaum. 1990. A critical review of the developmental toxicity and teratogenicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin: recent advances toward understanding the mechanism. *Teratology* 42(6):619-27.
20. Mattison, D. R., M. S. Nightingale, and E. K. Silberger. 1984. Reproductive toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin. In Lowrance, W. W., ed. *Public Health Risks of the Dioxins*. Kaufman Inc., Los Altos, California.
21. Dickerson, R., L. Johnson, and S. Safe. 1989. Effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin on androgen function in the male rat. *Toxicologist* 9:32.
22. Johnson, L., R. Dickerson, S. H. Safe, C. L. Nyberg, R. P. Lewis, and T. H. Welsh Jr. 1992. Reduced Leydig cell volume and function in adult rats exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin without a significant effect on spermatogenesis. *Toxicology* 76(2):103-18.
23. Mably, T., R. Moore, and R. Peterson. 1992. In utero and lactational exposure of male rats to 2,3,7,8-tetrachlorodibenzo-para-dioxin: 1. Effects on androgenic status. *Toxicology and Applied Pharmacology* 114(1):97-107.
24. Mably, T. A., D. L. Bjerke, R. W. Moore, A. Gendron-Fitzpatrick, and R. E. Peterson. 1992. In utero and lactational exposure of male rats to 2,3,7,8-tetrachlorodibenzo-p-dioxin: 3. Effects on spermatogenesis and reproductive capability. *Toxicology and Applied Pharmacology* 114:118-26.
25. Moore, R. W., C. L. Potter, H. M. Theobald, J. A. Robinson, and R. E. Peterson. 1985. Androgenic deficiency in male rats treated with 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Toxicology and Applied Pharmacology* 79:99-111.
26. Moore, R. W., and R. E. Peterson. 1988. Androgen catabolism and excretion in 2,3,7,8-tetrachlorodibenzo-p-dioxin-treated rats. *Biochemical Pharmacology* 37:560-2.
27. Moore, R. W., J. A. Parson, R. C. Bookstaff, and R. E. Peterson. 1989. Plasma concentrations of pituitary hormones in 2,3,7,8-tetrachlorodibenzo-p-dioxin-treated male rats. *Journal of Biochemical Toxicology* 4:165-72.
28. Bookstaff, R. C., R. W. Moore, and R. E. Peterson. 1990. 2,3,7,8-tetrachlorodibenzo-p-dioxin increases the potency of androgens and estrogens as feedback inhibitors of luteinizing hormone secretion in male rats. *Toxicology and Applied Pharmacology* 104:212-24.

29. Bookstaff, R. C., F. Kamel, R. W. Moore, D. L. Bjerke, and R. E. Peterson. 1990. Altered regulation of pituitary gonadotropin-releasing hormone (GnRH) receptor number and pituitary responsiveness to GnRH in 2,3,7,8-tetrachlorodibenzo-p-dioxin-treated male rats. *Toxicology and Applied Pharmacology* 105:78-92.
30. Gorski, J. R., M. Lebofsky, and K. Rozman. 1988. Corticosterone decreases toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in hypophysectomized rats. *Journal of Toxicology and Environmental Health* 25:349-60.
31. Bestervelt, L. L., C. J. Nolan, Y. Cai, P. Maimansomsuk, C. A. Mousigian, and W. N. Piper. 1991. Tetrachlorodibenzo-p-dioxin alters rat hypothalamic endorphin and mu-opioid receptors. *Neurotoxicology and Teratology* 13(1-6):495-7.
32. Russell, D. H., A. R. Buckley, G. N. Shah, I. G. Sipes, D. E. Blask, and B. Benson. 1988. Hypothalamic site of action of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). *Toxicology and Applied Pharmacology* 94:496-502.
33. Bestervelt, L. L., Y. Cai, D. W. Piper, C. J. Nolan, J. A. Pitt, and W. N. Piper. 1993. TCDD alters pituitary-adrenal function I: adrenal responsiveness to exogenous ACTH. *Neurotoxicology and Teratology* 15:365-70.
34. Bestervelt, L. L., D. W. Piper, J. A. Pitt, and W. N. Piper. 1994. Lipid peroxidation in the adrenal glands of male rats exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). *Toxicology Letters* 70(32):139-45.
35. Fingerhut, M. A., W. E. Halperin, D. A. Marlow, L. A. Piacitelli, P. A. Honchar, M. H. Sweeney, A. L. Greife, P. A. Dill, K. Steenland, and A. J. Suruda. 1991. Cancer mortality in workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *New England Journal of Medicine* 324(4):212-8.
36. Sweeney, M. H., M. A. Fingerhut, J. C. Arezzo, R. W. Hornung, and L. B. Connally. 1993. Peripheral neuropathy after occupational exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). *American Journal of Industrial Medicine* 23:845-58.
37. Egeland, G. M., M. H. Sweeney, M. A. Fingerhut, K. K. Wille, T. M. Schnorr, and W. E. Halperin. 1994. Total serum testosterone and gonadotropins in workers exposed to dioxin. *American Journal of Epidemiology* 139:272-81.
38. Henriksen, G. L., J. E. Michalek, J. A. Swaby, and A. J. Rahe. 1996. Serum dioxin, testosterone, and gonadotropins in veterans of Operation Ranch Hand. *Epidemiology* 7:352-7.
39. Pazderova-Vejlupkova, J., M. Nemcove, J. Pickova, L. Jirask, and E. Lukas. 1981. The development and prognosis of chronic intoxication by tetrachlorodibenzo-p-dioxin in men. *Archives of Environmental Health* 36:5-11.
40. Henriksen, G. L., N. S. Ketchum, J. E. Michalek, and J. A. Swaby. 1998. Serum dioxin and diabetes mellitus in veterans of Operation Ranch Hand. *Epidemiology* 9:252-8.
41. Roegner, R. H., W. D. Grubbs, M. B. Lustik, A. S. Brockman, S. C. Henderson, D. E. Williams, W. H. Wolfe, J. E. Michalek, and J. C. Miner. 1991. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Serum Dioxin Analysis of 1987 Examination Results. NTIS: AD A 237 516-24. USAF School of Medicine, Brooks Air Force Base, Texas.

42. Grubbs, W. D., W. H. Wolfe, J. E. Michalek, D. E. Williams, M. B. Lustik, A. S. Brockman, S. C. Henderson, F. R. Burnett, R. G. Land, D. J. Osborne, V. K. Rocconi, M. E. Schreiber, J. C. Miner, G. L. Henriksen, and J. A. Swaby. 1995. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Final Report. 1992 Followup Examination Results. NTIS: AD A 304 306, 304 308-316. USAF School of Medicine, Brooks Air Force Base, Texas.
43. Michalek, J. E. 1998. Letter to the editor. *Epidemiology* 9:359-60.
44. Sweeney, M. H., G. M. Calvert, G. A. Egeland, M. A. Fingerhut, W. E. Halperin, L. A. Piacitelli. 1997. Review and update of the results of the NIOSH medical study of workers exposed to chemicals contaminated with 2,3,7,8-tetrachlorodibenzodioxin. *Teratogenesis, Carcinogenesis, and Mutagenesis* 17(4-5):241-7.
45. Von Benner, A., L. Edler, K. Mayer, and A. Zober. 1994. 'Dioxin' investigation program of the chemical industry professional association. *Arbeitsmedizin Sozialmedizin Präventivmedizin* 29:11-6.
46. Institute of Medicine. 1999. *Veterans and Agent Orange: Update 1998*. National Academy Press: Washington, D.C.
47. Jenkins, C. D., R. H. Roseman, and S. J. Zyzanski. 1974. Prediction of clinical coronary heart disease by a test for the coronary-prone behavior pattern. *New England Journal of Medicine* 290(23):1271-5.
48. Knapik, J. J., A. R. L. Burse, and J. A. Vogel. 1983. Height, weight, percent body fat, and indices of adiposity for young men and women entering the Army. *Aviation, Space, and Environmental Medicine* 54:223-31.
49. Michalek, J. E., J. L. Pirkle, S. P. Caudill, R. C. Tripathi, D. G. Patterson Jr., and L. L. Needham. 1996. Pharmacokinetics of TCDD in Veterans of Operation Ranch Hand: 10-year Followup. *Journal of Toxicology and Environmental Health* 47:209-20.
50. Mausner, J. S., and A. K. Bahn. 1974. *Epidemiology – An Introductory Text*. Philadelphia: W. B. Saunders Company.