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)

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

Occupational Category	Group	n	Number (%) High	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***870***	***49 (5.6)***	***1.01 (0.69,1.47)***	***0.971***
	Comparison	***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) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***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

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

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[b]	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)		

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

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

Table 16-31. Analysis of LH (Discrete) (Continued)

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

Analysis Results for Log_2 (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
482	0.97 (0.65,1.43)	0.873

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

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

Dioxin Category	n	Number (%) High	Est. Relative Risk (95% C.I.)[ab]	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

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

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

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

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,213		
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

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

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

Table 16-31. Analysis of LH (Discrete) (Continued)

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

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	288	21 (7.3)	0.84 (0.68,1.04)	0.094
Medium	287	15 (5.2)		
High	288	12 (4.2)		

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

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

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

Analysis Results for Log_2 (1987 Dioxin + 1)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
863	0.84 (0.66,1.07)	0.154

[a] 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)

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

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***870***	***6.05***	***0.07 --***	***0.666***
	Comparison	***1,251***	***5.98***		
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		

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

Table 16-32. Analysis of FSH (mIU/ml) (Continuous) (Continued)

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

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***870***	***5.92***	***0.06 --***	***0.689***
	Comparison	***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		

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

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

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	160	6.40	6.42	0.008	–0.035 (0.021)	0.099
Medium	162	5.87	5.87			
High	160	5.64	5.62			

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

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

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

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	160	5.82	0.051	–0.007 (0.024)	0.763
Medium	162	5.50			
High	160	5.53			

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

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

Table 16-32. Analysis of FSH (mIU/ml) (Continuous) (Continued)

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

Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,213	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

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

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

Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	1,213	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

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

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

Table 16-32. Analysis of FSH (mIU/ml) (Continuous) (Continued)

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

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	n	Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	288	6.34	0.003	–0.024 (0.015)	0.105
Medium	287	6.19			
High	288	5.70			

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

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

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

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	288	6.18	0.066	–0.001 (0.016)	0.958
Medium	287	5.93			
High	288	5.97			

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

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

Occupational Category	Group	n	Number (%) High	Est. Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*870*	*72 (8.3)*	*1.06 (0.77,1.46)*	*0.713*
	Comparison	*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) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1.04 (0.75,1.45)*	*0.794*
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

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

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[b]	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)		

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

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

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

Analysis Results for Log_2 (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
482	1.11 (0.81,1.53)	0.508

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

Table 16-33. Analysis of FSH (Discrete) (Continued)

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

Dioxin Category	n	Number (%) High	Est. Relative Risk (95% C.I.)[ab]	p-Value
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

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

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

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

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,213		
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

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

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

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

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	288	24 (8.3)	0.97 (0.82,1.15)	0.712
Medium	287	28 (9.8)		
High	288	19 (6.6)		

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

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

Table 16-33. Analysis of FSH (Discrete) (Continued)

(b) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
863	1.16 (0.93,1.45)	0.188

[a] 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 (Age < 50) ≤125 (Age ≥ 50)	≤110	≤110	≤115	≤110
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≥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
All	***Ranch Hand***	***30 (3.7) (808)***	***52 (6.6) (791)***	***63 (8.1) (782)***	***100 (12.8) (779)***	***143 (17.7) (808)***
	Comparison	***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 n in 1997	Normal in 1982 Number (%) Diabetic in 1997	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	***Ranch Hand***	***778***	***113 (14.5)***	***1.00 (0.76,1.31)***	***0.993***
	Comparison	***934***	***137 (14.7)***		
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)		

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

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

(b) MODEL 2: RANCH HANDS — INITIAL DIOXIN

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_2 (Initial Dioxin)[a]	
	Normal in 1982			
Initial Dioxin	n in 1997	Number (%) Diabetic in 1997	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	145	26 (17.9)	1.28 (1.04,1.57)	0.019
Medium	148	28 (18.9)		
High	145	31 (21.4)		

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

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

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

Table 16-35. Longitudinal Analysis of Composite Diabetes Indicator (Continued)

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

Dioxin Category	Number (%) Diabetic/(n) Examination				
	1982	1985	1987	1992	1997
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)

Dioxin Category	Normal in 1982			
	n in 1997	Number (%) Diabetic in 1997	Adj. Relative Risk (95% C.I.)[ab]	p-Value[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

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

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

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who 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 (μIU/ml) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Mean[a]/(n) Examination 1982	1985	1987	1992	1997	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
All	***Ranch Hand***	***3.64***	***1.21***	***0.91***	***1.60***	***1.87***	***–1.76***	***–0.06***	***0.525***
		(791)	***(773)***	***(762)***	***(770)***	***(791)***			
	Comparison	***3.49***	***1.16***	***0.87***	***1.56***	***1.79***	***–1.70***		
		(929)	***(911)***	***(904)***	***(910)***	***(929)***			
Officer	Ranch Hand	3.78	1.28	0.99	1.73	2.00	–1.78	–0.15	0.700
		(298)	(294)	(289)	(293)	(298)			
	Comparison	3.47	1.18	0.89	1.62	1.84	–1.63		
		(358)	(352)	(347)	(353)	(358)			
Enlisted Flyer	Ranch Hand	3.46	1.16	0.84	1.43	1.72	–1.74	0.03	0.440
		(141)	(138)	(135)	(139)	(141)			
	Comparison	3.66	1.15	0.87	1.53	1.89	–1.77		
		(139)	(138)	(137)	(137)	(139)			
Enlisted Groundcrew	Ranch Hand	3.59	1.17	0.89	1.56	1.83	–1.76	–0.02	0.263
		(352)	(341)	(338)	(338)	(352)			
	Comparison	3.45	1.15	0.84	1.52	1.71	–1.74		
		(432)	(421)	(420)	(420)	(432)			

[a] Transformed from natural logarithm scale.
[b] Difference between 1997 and 1982 examination means after transformation to original scale.
[c] 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 (μlu/ml) (Continuous)

(b) MODEL 2: RANCH HANDS – INITIAL DIOXIN

Initial Dioxin Category Summary Statistics						Analysis Results for Log_2 (Initial Dioxin)[b]	
	Mean[a]/(n) Examination						
Initial Dioxin	1982	1985	1987	1992	1997	Adjusted Slope (Std. Error)	p-Value
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)		

[a] Transformed from natural logarithm scale.

[b] Results based on difference between natural logarithm of 1997 TSH and natural logarithm of 1982 TSH versus 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.

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

Dioxin Category	Mean[a]/(n) Examination					Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
	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

[a] Transformed from natural logarithm scale.

[b] Difference between 1997 and 1982 examination means after transformation to original scale.

[c] 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 ≤ 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.

16.2.3.2.2 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)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Number (%) High/(n) Examination				
		1982	1985	1987	1992	1997
All	***Ranch Hand***	***5 (0.6) (791)***	***9 (1.2) (773)***	***10 (1.3) (762)***	***10 (1.3) (770)***	***32 (4.0) (791)***
	Comparison	***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.)[a]	p-Value[a]
		n in 1997	Number (%) High in 1997		
All	***Ranch Hand***	***786***	***28 (3.6)***	***1.23 (0.72,2.10)***	***0.454***
	Comparison	***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)		

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

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had a normal TSH level in 1982 (see Chapter 7, Statistical Methods).

Table 16-37. Longitudinal Analysis of TSH (Discrete) (Continued)

(b) MODEL 2: RANCH HANDS — INITIAL DIOXIN

Initial Dioxin	Number (%) High/(n) Examination				
	1982	1985	1987	1992	1997
Low	0 (0.0)	1 (0.7)	1 (0.7)	0 (0.0)	6 (4.0)
	(151)	(148)	(150)	(146)	(151)
Medium	1 (0.6)	3 (2.0)	2 (1.3)	1 (0.7)	4 (2.6)
	(155)	(152)	(151)	(153)	(155)
High	1 (0.7)	1 (0.7)	2 (1.4)	5 (3.5)	7 (4.8)
	(145)	(142)	(140)	(142)	(145)

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
	Normal in 1982			
Initial Dioxin	n in 1997	Number (%) High in 1997	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	151	6 (4.0)	1.16 (0.78,1.72)	0.486
Medium	154	3 (1.9)		
High	144	6 (4.2)		

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

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

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had a normal TSH level in 1982 (see Chapter 7, Statistical Methods).

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

Dioxin Category	Number (%) High/(n) Examination				
	1982	1985	1987	1992	1997
Comparison	4 (0.4)	14 (1.6)	11 (1.3)	19 (2.2)	29 (3.2)
	(901)	(886)	(878)	(883)	(901)
Background RH	3 (0.9)	4 (1.2)	5 (1.6)	4 (1.2)	14 (4.2)
	(334)	(326)	(316)	(324)	(334)
Low RH	0 (0.0)	2 (0.9)	2 (0.9)	1 (0.5)	7 (3.1)
	(224)	(218)	(221)	(217)	(224)
High RH	2 (0.9)	3 (1.3)	3 (1.4)	5 (2.2)	10 (4.4)
	(227)	(224)	(220)	(224)	(227)
Low plus High RH	2 (0.4)	5 (1.1)	5 (1.1)	6 (1.4)	17 (3.8)
	(451)	(442)	(441)	(441)	(451)

Table 16-37. Longitudinal Analysis of TSH (Discrete) (Continued)

Dioxin Category	Normal in 1982: n in 1997	Normal in 1982: Number (%) High in 1997	Adj. Relative Risk (95% C.L)[a,b]	p-Value[b]
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

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

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

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had 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[a]/(n) Examination: 1982	1985	1987	1992	1997	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
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)***	***4.6***		
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)	3.6		
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)	5.6		

Table 16-38. Longitudinal Analysis of Fasting Glucose (mg/dl) (Continuous) (Continued)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Mean[a]/(n) Examination 1982	1985	1987	1992	1997	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
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)	5.2		

[a] Transformed from natural logarithm scale.
[b] Difference between 1997 and 1982 examination means after transformation to original scale.
[c] 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) MODEL 2: RANCH HANDS – INITIAL DIOXIN

Initial Dioxin Category Summary Statistics						Analysis Results for Log_2 (Initial Dioxin)[b]	
	Mean[a]/(n) Examination						
Initial Dioxin	1982	1985	1987	1992	1997	Adjusted Slope (Std. Error)	p-Value
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)	104.6 (158)		
High	99.2 (153)	101.3 (150)	103.4 (148)	109.6 (150)	105.5 (153)		

[a] Transformed from natural logarithm scale.
[b] Results based on difference between natural logarithm of 1997 fasting glucose and natural logarithm of 1982 fasting glucose versus log_2 (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)

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

Dioxin Category	Mean[a]/(n) Examination 1982	1985	1987	1992	1997	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
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

[a] Transformed from natural logarithm scale.
[b] Difference between 1997 and 1982 examination means after transformation to original scale.
[c] 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)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Number (%) High /(n) Examination				
		1982	1985	1987	1992	1997
All	***Ranch Hand***	***37 (4.5) (817)***	***76 (9.5) (799)***	***94 (11.9) (790)***	***106 (13.3) (795)***	***149 (18.2) (817)***
	Comparison	***34 (3.5) (974)***	***88 (9.2) (956)***	***122 (12.9) (948)***	***125 (13.1) (954)***	***158 (16.2) (974)***
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)

Occupational Category	Group	Normal in 1982			
		n in 1997	Number (%) High in 1997	Adj. Relative Risk (95% C.L.)[a]	p-Value[a]
All	***Ranch Hand***	***780***	***116 (14.9)***	***1.16 (0.88,1.52)***	***0.303***
	Comparison	***940***	***124 (13.2)***		
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)		

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

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had a normal fasting glucose level in 1982 (see Chapter 7, Statistical Methods).

Table 16-39. Longitudinal Analysis of Fasting Glucose (Discrete) (Continued)

(b) MODEL 2: RANCH HANDS — INITIAL DIOXIN

Initial Dioxin	Number (%) High /(n) Examination				
	1982	1985	1987	1992	1997
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)

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
	Normal in 1982			
Initial Dioxin	n in 1997	Number (%) High in 1997	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	143	19 (13.3)	1.26 (1.02,1.56)	0.029
Medium	149	27 (18.1)		
High	142	28 (19.7)		

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

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

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had a normal fasting glucose level in 1982 (see Chapter 7, Statistical Methods).

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

Dioxin Category	Number (%) High/(n) Examination				
	1982	1985	1987	1992	1997
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: n in 1997	Normal in 1982: Number (%) High in 1997	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
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

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

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

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had 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)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Mean[a]/(n) Examination 1982	1985	1987	1992	1997	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
All	***Ranch Hand***	***89.9***	***101.8***	***106.7***	***102.6***	***105.5***	***15.6***	***0.2***	***0.982***
		(665)	***(651)***	***(641)***	***(641)***	***(665)***			
	Comparison	***90.2***	***104.1***	***106.4***	***104.0***	***105.6***	***15.4***		
		(797)	***(781)***	***(775)***	***(773)***	***(797)***			
Officer	Ranch Hand	89.5	104.5	107.0	103.5	106.5	17.0	3.8	0.096
		(257)	(254)	(250)	(251)	(257)			
	Comparison	88.8	102.6	104.8	102.1	102.1	13.2		
		(318)	(311)	(305)	(315)	(318)			
Enlisted Flyer	Ranch Hand	91.7	100.6	108.4	103.8	107.5	15.8	−3.2	0.332
		(119)	(117)	(115)	(116)	(119)			
	Comparison	92.8	107.5	108.6	108.9	111.9	19.0		
		(115)	(115)	(114)	(114)	(115)			
Enlisted Groundcrew	Ranch Hand	89.5	99.8	105.8	101.3	103.8	14.3	−2.0	0.326
		(289)	(280)	(276)	(274)	(289)			
	Comparison	90.6	104.2	107.1	104.1	106.9	16.3		
		(364)	(355)	(356)	(344)	(364)			

[a] Transformed from natural logarithm scale.
[b] Difference between 1997 and 1982 examination means after transformation to original scale.
[c] 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) MODEL 2: RANCH HANDS – INITIAL DIOXIN

Initial Dioxin Category Summary Statistics						Analysis Results for Log_2 (Initial Dioxin)[b]	
	Mean[a]/(n) Examination						
Initial Dioxin	1982	1985	1987	1992	1997	Adjusted Slope (Std. Error)	p-Value
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)		

[a] Transformed from natural logarithm scale.
[b] Results based on difference between natural logarithm of 1997 2-hour postprandial glucose and natural logarithm of 1982 2-hour postprandial glucose versus log_2 (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)

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

Dioxin Category	Mean[a]/(n) Examination 1982	1985	1987	1992	1997	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
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

[a] Transformed from natural logarithm scale.
[b] Difference between 1997 and 1982 examination means after transformation to original scale.
[c] 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)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Number (%) Impaired/(n) Examination				
		1982	1985	1987	1992	1997
All	***Ranch Hand***	***40 (6.0)***	***53 (8.1)***	***88 (13.7)***	***80 (12.5)***	***110 (16.5)***
		(665)	***(651)***	***(641)***	***(641)***	***(665)***
	Comparison	***57 (7.2)***	***83 (10.6)***	***84 (10.8)***	***91 (11.8)***	***132 (16.6)***
		(797)	***(781)***	***(775)***	***(773)***	***(797)***
Officer	Ranch Hand	14 (5.4)	23 (9.1)	31 (12.4)	31 (12.4)	50 (19.5)
		(257)	(254)	(250)	(251)	(257)
	Comparison	19 (6.0)	27 (8.7)	23 (7.5)	33 (10.5)	41 (12.9)
		(318)	(311)	(305)	(315)	(318)
Enlisted Flyer	Ranch Hand	9 (7.6)	10 (8.5)	21 (18.3)	12 (10.3)	22 (18.5)
		(119)	(117)	(115)	(116)	(119)
	Comparison	16 (13.9)	17 (14.8)	17 (14.9)	20 (17.5)	25 (21.7)
		(115)	(115)	(114)	(114)	(115)
Enlisted Groundcrew	Ranch Hand	17 (5.9)	20 (7.1)	36 (13.0)	37 (13.5)	38 (13.1)
		(289)	(280)	(276)	(274)	(289)
	Comparison	22 (6.0)	39 (11.0)	44 (12.4)	38 (11.0)	66 (18.1)
		(364)	(355)	(356)	(344)	(364)

Occupational Category	Group	Normal in 1982		Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
		n in 1997	Number (%) Impaired in 1997		
All	***Ranch Hand***	***625***	***92 (14.7)***	***1.04 (0.77,1.41)***	***0.795***
	Comparison	***740***	***106 (14.3)***		
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)		

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

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had 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) MODEL 2: RANCH HANDS — INITIAL DIOXIN

Initial Dioxin	Number (%) Impaired/(n) Examination				
	1982	1985	1987	1992	1997
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)

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
	Normal in 1982			
Initial Dioxin	n in 1997	Number (%) Impaired in 1997	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	113	20 (17.7)	1.04 (0.81,1.34)	0.765
Medium	110	17 (15.5)		
High	107	18 (16.8)		

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

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

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had a normal 2-hour postprandial glucose level in 1982 (see Chapter 7, Statistical Methods).

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

Dioxin Category	Number (%) Impaired/(n) Examination				
	1982	1985	1987	1992	1997
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: n in 1997	Normal in 1982: Number (%) Impaired in 1997	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
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

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

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

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had 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)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Mean[a]/(n) Examination 1982	1985	1987	1992	1997	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
All	***Ranch Hand***	***640.8***	***600.6***	***532.1***	***509.6***	***424.1***	***-216.7***	***-13.1***	***0.380***
		(800)	***(780)***	***(773)***	***(775)***	***(800)***			
	Comparison	***626.7***	***581.6***	***525.9***	***498.3***	***423.1***	***-203.6***		
		(953)	***(936)***	***(929)***	***(929)***	***(953)***			
Officer	Ranch Hand	601.7	573.8	502.0	490.5	401.9	-199.8	-11.1	0.353
		(302)	(295)	(294)	(295)	(302)			
	Comparison	601.8	556.0	499.4	475.5	413.1	-188.7		
		(371)	(367)	(361)	(365)	(371)			
Enlisted Flyer	Ranch Hand	651.3	611.6	530.9	518.9	446.3	-205.0	-2.8	0.788
		(143)	(140)	(138)	(140)	(143)			
	Comparison	634.3	588.3	537.0	508.4	432.0	-202.2		
		(140)	(139)	(138)	(138)	(140)			
Enlisted Groundcrew	Ranch Hand	670.9	619.5	559.4	522.7	434.5	-236.3	-19.5	0.472
		(355)	(345)	(341)	(340)	(355)			
	Comparison	645.5	601.7	545.2	515.0	428.6	-216.8		
		(442)	(430)	(430)	(426)	(442)			

[a] Transformed from the square root of total testosterone.
[b] Difference between 1997 and 1982 examination means after transformation to original scale.
[c] 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) MODEL 2: RANCH HANDS – INITIAL DIOXIN

Initial Dioxin Category Summary Statistics						Analysis Results for Log_2 (Initial Dioxin)[b]	
	Mean[a]/(n) Examination						
Initial Dioxin	1982	1985	1987	1992	1997	Adjusted Slope (Std. Error)	p-Value
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)		

[a] Transformed from square root of total testosterone.
[b] Results based on difference between the square root of 1997 total testosterone and the square root of 1982 total testosterone versus log_2 (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)

(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY								
Dioxin Category	Mean[a]/(n) Examination 1982	1985	1987	1992	1997	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
Comparison	628.1 (925)	581.6 (911)	527.1 (903)	498.4 (902)	423.6 (925)	-204.5		
Background RH	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

[a] Transformed from the square root of total testosterone.
[b] Difference between 1997 and 1982 examination means after transformation to original scale.
[c] 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 ≤ 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.

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)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Number (%) Low /(n) Examination				
		1982	1985	1987	1992	1997
All	***Ranch Hand***	***37 (4.6)***	***21 (2.7)***	***14 (1.8)***	***34 (4.4)***	***67 (8.4)***
		(800)	***(780)***	***(773)***	***(775)***	***(800)***
	Comparison	***47 (4.9)***	***24 (2.6)***	***13 (1.4)***	***50 (5.4)***	***80 (8.4)***
		(953)	***(936)***	***(929)***	***(929)***	***(953)***
Officer	Ranch Hand	15 (5.0)	10 (3.4)	6 (2.0)	14 (4.7)	27 (8.9)
		(302)	(295)	(294)	(295)	(302)
	Comparison	20 (5.4)	14 (3.8)	7 (1.9)	19 (5.2)	30 (8.1)
		(371)	(367)	(361)	(365)	(371)
Enlisted Flyer	Ranch Hand	8 (5.6)	4 (2.9)	5 (3.6)	5 (3.6)	11 (7.7)
		(143)	(140)	(138)	(140)	(143)
	Comparison	8 (5.7)	2 (1.4)	1 (0.7)	7 (5.1)	10 (7.1)
		(140)	(139)	(138)	(138)	(140)
Enlisted Groundcrew	Ranch Hand	14 (3.9)	7 (2.0)	3 (0.9)	15 (4.4)	29 (8.2)
		(355)	(345)	(341)	(340)	(355)
	Comparison	19 (4.3)	8 (1.9)	5 (1.2)	24 (5.6)	40 (9.1)
		(442)	(430)	(430)	(426)	(442)

Occupational Category	Group	Normal in 1982		Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
		n in 1997	Number (%) Low in 1997		
All	***Ranch Hand***	***763***	***54 (7.1)***	***1.00 (0.69,1.46)***	***0.984***
	Comparison	***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)		

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

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had a normal total testosterone level in 1982 (see Chapter 7, Statistical Methods).

Table 16-43. Longitudinal Analysis of Total Testosterone (Discrete) (Continued)

(b) MODEL 2: RANCH HANDS — INITIAL DIOXIN

Initial Dioxin	Number (%) Low /(n) Examination				
	1982	1985	1987	1992	1997
Low	6 (4.0)	2 (1.4)	5 (3.4)	5 (3.4)	13 (8.7)
	(150)	(146)	(149)	(145)	(150)
Medium	8 (5.1)	6 (3.9)	2 (1.3)	10 (6.5)	18 (11.5)
	(157)	(154)	(154)	(154)	(157)
High	10 (6.7)	3 (2.0)	3 (2.1)	10 (6.8)	16 (10.7)
	(149)	(147)	(144)	(146)	(149)

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
	Normal in 1982			
Initial Dioxin	n in 1997	Number (%) Low In 1997	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	144	10 (6.9)	1.04 (0.80,1.35)	0.760
Medium	149	16 (10.7)		
High	139	14 (10.1)		

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

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

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had a normal total testosterone level in 1982 (see Chapter 7, Statistical Methods).

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

Dioxin Category	Number (%) Low/(n) Examination				
	1982	1985	1987	1992	1997
Comparison	45 (4.9)	24 (2.6)	13 (1.4)	49 (5.4)	78 (8.4)
	(925)	(911)	(903)	(902)	(925)
Background RH	13 (3.8)	10 (3.0)	4 (1.2)	9 (2.8)	20 (5.9)
	(339)	(329)	(322)	(326)	(339)
Low RH	11 (4.9)	5 (2.3)	7 (3.2)	7 (3.2)	19 (8.4)
	(225)	(218)	(222)	(218)	(225)
High RH	13 (5.6)	6 (2.6)	3 (1.3)	18 (7.9)	28 (12.1)
	(231)	(229)	(225)	(227)	(231)
Low plus High RH	24 (5.3)	11 (2.5)	10 (2.2)	25 (5.6)	47 (10.3)
	(456)	(447)	(447)	(445)	(456)

Table 16-43. Longitudinal Analysis of Total Testosterone (Discrete) (Continued)

Dioxin Category	Normal in 1982: n in 1997	Normal in 1982: Number (%) Low in 1997	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
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

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

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

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had 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 α-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_4 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 μIU/ml versus 1.81 μIU/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 α-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)

	UNADJUSTED			
Variable	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Medical Records				
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) [a]	NS	ns	NS	NS
Physical Examination				
Thyroid Gland (D)	ns	ns	NS	ns
Testicular Exam (D)	NS	ns	NS	NS
Laboratory				
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) [a]	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
α-1-C Hemoglobin (C)	ns	NS	ns	ns
α-1-C Hemoglobin (D)	NS	NS	ns	NS
Total Testosterone (C) [a]	NS	ns	NS	NS
Total Testosterone (D)	NS	NS	NS	NS
Free Testosterone (C) [a]	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 ($0.05<p\leq0.10$).
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥1.00.
−: Difference of means negative.
[a] Negative difference considered adverse for this variable.

P-value given if $p\leq0.05$.

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
Medical Records				
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) [a]	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
Physical Examination				
Thyroid Gland (D)	ns	ns	NS	ns
Testicular Exam (D)	NS	ns	NS	NS
Laboratory				
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) [a]	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) [a]	ns	ns	NS	ns
Total Testosterone (D)	NS	NS	NS	NS
Free Testosterone (C) [a]	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 ($0.05<p\leq0.10$).
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥1.00.
–: Difference of means negative.
[a] Negative difference considered adverse for this variable.

P-value given if $p\leq0.05$.

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 α-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
Medical Records		
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) [a]	ns	−0.013
Physical Examination		
Thyroid Gland (D)	ns	NS
Testicular Exam (D)	ns	NS
Laboratory		
TSH (C)	ns	ns
TSH (D):		
Low vs. Normal	NS	NS
High vs. Normal	NS	NS
Thyroxine (C) [a]	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
α-1-C Hemoglobin (C)	+0.009	+0.001
α-1-C Hemoglobin (D)	+0.013	+0.001
Total Testosterone (C) [a]	+0.047	ns
Total Testosterone (D)	NS	NS
Free Testosterone (C) [a]	+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 ($0.05<p\leq0.10$).
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥1.00 for discrete analysis; slope nonnegative for continuous analysis.
−: Relative risk <1.00 for discrete analysis; slope negative for continuous analysis.
[a] Negative slope considered adverse for this variable.

P-value given if $p\leq0.05$.

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 α-1-C hemoglobin level for Ranch Hands in the high dioxin category than for Comparisons. A greater percentage of high α-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
Medical Records				
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) [a]	+0.013	ns	ns	ns
Physical Examination				
Thyroid Gland (D)	ns	ns	ns	ns
Testicular Exam (D)	ns	NS*	NS	NS
Laboratory				
TSH (C)	NS	NS	NS	NS
TSH (D):				
Low vs. Normal	NS	ns	NS	ns
High vs. Normal	NS	ns	NS	NS
Thyroxine (C) [a]	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) [a]	NS	ns	NS	ns
Total Testosterone (D)	NS	NS	NS	NS
Free Testosterone (C) [a]	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≤0.10).
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥1.00 for discrete analysis; difference of means nonnegative for continuous analysis.
−: Relative risk <1.00.
[a] Negative difference considered adverse for this variable.

P-value given if p≤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.

		ADJUSTED		
Variable	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Medical Records				
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) [a]	+0.021	ns	ns*	ns*
Physical Examination				
Thyroid Gland (D)	ns	ns	ns	ns
Testicular Exam (D)	ns	NS	NS	NS
Laboratory				
TSH (C)	NS	NS	NS	NS
TSH (D):				
Low vs. Normal	NS	ns	NS	ns
High vs. Normal	NS	ns	NS	NS
Thyroxine (C) [a]	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
α-1-C Hemoglobin (C)	ns	ns	+0.022	NS
α-1-C Hemoglobin (D)	ns	ns	+0.008	NS
Total Testosterone (C) [a]	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) [a]	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 ($0.05<p\leq0.10$).
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥1.00 for discrete analysis; difference of means nonnegative for continuous analysis.
–: Relative risk <1.00.
[a] Negative difference considered adverse for this variable.

P-value given if $p\leq0.05$.

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 α-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
Medical Records		
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) [a]	–<0.001	–<0.001
Physical Examination		
Thyroid Gland (D)	ns	NS
Testicular Exam (D)	NS	NS
Laboratory		
TSH (C)	ns	NS
TSH (D):		
Low vs. Normal	ns	NS
High vs. Normal	ns	ns
Thyroxine (C) [a]	+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) [a]	–0.003	ns
Total Testosterone (D)	+0.013	NS
Free Testosterone (C) [a]	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 ($0.05<p\leq0.10$).
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥1.00 for discrete analysis; slope nonnegative for continuous analysis.
–: Relative risk <1.00 for discrete analysis; slope negative for continuous analysis.
[a] Negative slope considered adverse for this variable.

P-value given if $p\leq0.05$.

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 α-1-C hemoglobin increased in Ranch Hands as initial dioxin and 1987 dioxin increased. Increased α-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 α-1-C hemoglobin support this finding. Similar patterns were observed in 1992 and 1987.

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