TABLE 15-13. (Continued)

Analysis of Testosterone (ng/dl) (Continuous)

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

Assumption	Time (Yrs.)	Mean[a]/(n) Current Dioxin Low	Medium	High	Slope (Std. Error)[b]	p-Value
e) Minimal						0.669[c]
(n=516)	≤18.6	521.9	545.2	517.8	-0.0063 (0.2062)	0.976[d]
(R^2=0.010)		(71)	(127)	(54)		
	>18.6	496.3	503.8	503.5	0.1077 (0.1687)	0.524[d]
		(57)	(130)	(77)		
f) Maximal						0.509[c]
(n=736)	≤18.6	555.4	532.5	528.7	-0.1240 (0.1453)	0.394[d]
(R^2=0.011)		(105)	(189)	(83)		
	>18.6	509.0	505.6	504.2	0.0042 (0.1282)	0.974[d]
		(79)	(176)	(104)		

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

Assumption	Time (Yrs.)	Adj. Mean[a]/(n) Current Dioxin Low	Medium	High	Adj. Slope (Std. Error)[b]	p-Value	Covariate Remarks
g) Minimal						0.410[c]	AGE (p<0.001)
(n=516)	≤18.6	526.3	531.9	495.1	-0.1935 (0.1869)	0.301[d]	%BFAT (p<0.001)
(R^2=0.243)		(71)	(127)	(54)			
	>18.6	517.3	509.9	511.0	-0.0009 (0.1531)	0.995[d]	
		(57)	(130)	(77)			
h) Maximal						0.690[c]	AGE (p<0.001)
(n=736)	≤18.6	550.5	545.5	527.6	-0.1147 (0.1336)	0.391[d]	RACE (p=0.126)
(R^2=0.224)		(105)	(189)	(83)			%BFAT (p<0.001)
	>18.6	539.8	536.2	526.3	-0.0461 (0.1177)	0.696[d]	
		(79)	(176)	(104)			

[a]Transformed from square root scale.

[b]Slope and standard error based on square root testosterone versus log_2 dioxin.

[c]Test of significance for homogeneity of slopes (current dioxin continuous, time categorized).

[d]Test of significance for slope equal to 0 (current dioxin continuous, time categorized).

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

TABLE 15-13. (Continued)
Analysis of Testosterone (ng/dl)
(Continuous)

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

Current Dioxin Category	n	Mean[a]	Contrast	Difference of Means (95% C.I.)[e]	p-Value[f]
Background	785	525.3	All Categories		0.016
Unknown	343	554.2	Unknown vs. Background	28.9 --	0.005
Low	193	525.6	Low vs. Background	0.3 --	0.977
High	187	515.0	High vs. Background	-10.3 --	0.422
Total	1,508		(R^2=0.007)		

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

Current Dioxin Category	n	Adj. Mean[a]	Contrast	Difference of Adj. Means (95% C.I.)[e]	p-Value[f]	Covariate Remarks
Background	785	519.0	All Categories		0.248	%BFAT (p<0.001)
Unknown	343	531.4	Unknown vs. Background	12.4 --	0.180	AGE*RACE (p=0.041)
Low	193	521.6	Low vs. Background	2.6 --	0.821	
High	187	505.1	High vs. Background	-13.9 --	0.230	
Total	1,508		(R^2=0.203)			

[a]Transformed from square root scale.

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

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

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

and marginally negative for Ranch Hands with an early tour under the maximal assumption (Appendix Table N-2: p=0.012 for time≤18.6 years and p=0.069 and time>18.6 years). This demonstrates the percent body fat-dioxin effect seen in Chapter 6. The current dioxin-by-time interaction remained nonsignificant for both assumptions.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The mean testosterone differed significantly among the four current dioxin categories in the unadjusted analysis (Table 15-13 [i]: p=0.016). Of the three Ranch Hand versus background contrasts, the only significant finding was that the mean for the unknown category was significantly more than the background mean (p=0.005). The mean levels of testosterone were 525.3, 554.2, 525.6, and 515.0 ng/dl for the background, unknown, low, and high current dioxin categories.

After adjustment for percent body fat and the age-by-race interaction, no significant findings were noted (Table 15-13 [j]: p>0.15 for all contrasts). However, the overall contrast became significant when percent body fat was deleted from the model (Appendix Table N-2: p<0.001). For this analysis, the adjusted mean for the unknown current dioxin category was significantly more than the background mean (p=0.001) and the adjusted mean for the high current dioxin category was significantly less than the background mean (p=0.010). The adjusted means were 514.0, 545.9, 513.3, and 482.9 ng/dl for the background, unknown, low, and high current dioxin categories.

Testosterone (Discrete)

Model 1: Ranch Hands – Log_2 (Initial Dioxin)

The prevalence of abnormally low testosterone levels was not significantly associated with initial dioxin in both the unadjusted minimal and maximal analyses (Table 15-14 [a] and [b]: p=0.589 and p=0.581).

These findings did not change after adjusting for age and percent body fat (Table 15-14 [c] and [d]: minimal, p=0.568; maximal, p=0.846).

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

Under both the minimal and maximal assumptions, the current dioxin-by-time since tour interaction was not significant in either the unadjusted or adjusted analyses (Table 15-14 [e-h]: p>0.40 for each analysis).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The prevalence of abnormally low testosterone levels did not differ significantly among current dioxin categories in the unadjusted analysis of categorized current dioxin (Table 15-14 [i]: p=0.649). However, relatively more abnormally low values were found in the high current dioxin category than in the other categories (1.7%, 0.9%, 1.6%, and 2.1% for the background, unknown, low, and high current dioxin categories).

The adjusted analysis found a significant categorized current dioxin-by-personality type interaction (Table 15-14 [j]: p=0.028). For type A participants, the overall current dioxin

TABLE 15-14.

Analysis of Testosterone (Discrete)

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal Low	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=516)	Low	128	3.1	0.88 (0.54,1.43)	0.589
	Medium	257	1.9		
	High	131	3.1		
b) Maximal (n=736)	Low	184	0.0	1.10 (0.78,1.56)	0.581
	Medium	366	3.3		
	High	186	2.2		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=516)	0.87 (0.53,1.43)	0.568	AGE (p=0.044) %BFAT (p<0.001)
d) Maximal (n=736)	1.04 (0.71,1.52)	0.846	AGE (p=0.010) %BFAT (p<0.001)

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

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

TABLE 15-14. (Continued)

Analysis of Testosterone (Discrete)

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

Assumption	Time (Yrs.)	Percent Abnormal Low/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.983[b]
(n=516)	≤18.6	1.4 (71)	1.6 (127)	1.9 (54)	0.75 (0.26,2.18)	0.600[c]
	>18.6	7.0 (57)	1.5 (130)	3.9 (77)	0.74 (0.40,1.38)	0.347[c]
f) Maximal						0.444[b]
(n=736)	≤18.6	0.0 (105)	1.6 (189)	1.2 (83)	1.22 (0.59,2.55)	0.592[c]
	>18.6	2.5 (79)	4.0 (176)	2.9 (104)	0.87 (0.56,1.34)	0.528[c]

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

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal			0.796[b]	%BFAT (p<0.001)
(n=516)	≤18.6	0.53 (0.17,1.69)	0.285[c]	
	>18.6	0.63 (0.33,1.19)	0.154[c]	
h) Maximal			0.762[b]	AGE (p=0.045)
(n=736)	≤18.6	1.00 (0.44,2.25)	0.992[c]	%BFAT (p<0.001)
	>18.6	0.86 (0.54,1.37)	0.536[c]	

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

TABLE 15-14. (Continued)

Analysis of Testosterone (Discrete)

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

Current Dioxin Category	n	Percent Abnormal Low	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	785	1.7	All Categories		0.649
Unknown	343	0.9	Unknown vs. Background	0.52 (0.15,1.85)	0.315
Low	193	1.6	Low vs. Background	0.94 (0.26,3.32)	0.921
High	187	2.1	High vs. Background	1.30 (0.42,4.03)	0.652
Total	1,508				

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

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	750	All Categories		0.899**	DXCAT*PERS (p=0.028)
Unknown	326	Unknown vs. Background	0.72 (0.20,2.58)**	0.610**	AGE (p=0.020)
Low	189	Low vs. Background	0.89 (0.24,3.21)**	0.854**	RACE (p=0.109)
High	181	High vs. Background	1.30 (0.39,4.31)**	0.667**	%BFAT (p<0.001)
Total	1,446				

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

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

effect was marginally significant (Appendix Table N-1: p=0.096) and the relative risk of abnormally low testosterone levels for the high versus background contrast was significant (Adj. RR=6.72, 95% C.I.: [1.06,42.73], p=0.044). The results for type B individuals did not show a significant difference among current dioxin categories (p>0.25 for all contrasts).

The interaction was then excluded from the model. After adjusting for age, race, and percent body fat, no significant difference was found among current dioxin categories (Table 15-14 [j]: p=0.899).

Fasting Glucose (Continuous)

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Under both the minimal and maximal assumptions, the unadjusted initial dioxin analyses found a significant association with fasting glucose in its continuous form (Table 15-15 [a] and [b]: p=0.027 and p<0.001, respectively). The mean levels of fasting glucose were 102.4, 103.1, and 102.2 mg/dl for the low, medium, and high initial dioxin categories under the minimal assumption. The corresponding means under the maximal assumption were 99.4, 101.6, and 104.6 mg/dl.

The adjusted analyses under both assumptions found a highly significant positive association between initial dioxin and fasting glucose (Table 15-15 [c] and [d]: p<0.001 for both the minimal and maximal assumptions). The adjusted means increased with initial dioxin (minimal: 104.1, 105.6, and 106.8 mg/dl; maximal: 103.5, 104.7, and 110.4 mg/dl for the low, medium, and high initial dioxin categories).

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

The unadjusted current dioxin and time since tour analysis for fasting glucose in its continuous form found that the interaction between current dioxin and time was marginally significant under the minimal assumption (Table 15-15 [e]: p=0.096), but it was not significant under the maximal assumption (Table 15-15 [f]: p=0.242). For both cohorts, the association between current dioxin and fasting glucose was significantly positive for Ranch Hands with an early tour (time>18.6: slope=0.0251, p=0.009 for the minimal cohort; slope=0.0205, p=0.002 for the maximal cohort). The mean levels of fasting glucose for the low, medium, and high current dioxin categories in this time stratum were 102.6, 102.9, and 105.7 mg/dl for the minimal cohort, and 99.8, 102.5, and 106.0 mg/dl for the maximal cohort. The association between current dioxin and fasting glucose was not significant for Ranch Hands with an early tour (p=0.993 and p=0.241 for the minimal and maximal cohorts).

The adjusted minimal analysis displayed findings similar to the unadjusted analysis. The current dioxin-by-time interaction was of borderline significance (Table 15-15 [g]: p=0.097). A significant association between current dioxin and fasting glucose was seen for Ranch Hands with an early tour (time>18.6: Adj. slope=0.0393, p<0.001), but the association was not significant for Ranch Hands with a later tour (time≤18.6: Adj. slope=0.0149, p=0.209). The adjusted mean levels of fasting glucose for Ranch Hands with an early tour were 102.4, 104.5, and 109.7 mg/dl for the low, medium, and high current dioxin categories.

TABLE 15-15.

Analysis of Fasting Glucose (mg/dl) (Continuous)

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Mean[a]	Slope (Std. Error)[b]	p-Value
a) Minimal	Low	130	102.4	0.0160 (0.0072)	0.027
(n=517)	Medium	257	103.1		
(R^2=0.010)	High	130	102.2		
b) Maximal	Low	184	99.4	0.0168 (0.0048)	<0.001
(n=737)	Medium	368	101.6		
(R^2=0.016)	High	185	104.6		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Initial Dioxin	n	Adj. Mean[a]	Adj. Slope (Std. Error)[b]	p-Value	Covariate Remarks
c) Minimal	Low	130	104.1	0.0262 (0.0073)	<0.001	AGE (p<0.001)
(n=511)	Medium	253	105.6			RACE*ALC (p=0.021)
(R^2=0.095)	High	128	106.8			RACE*DRKYR (p=0.002)
d) Maximal	Low	182	103.5	0.0216 (0.0048)	<0.001	AGE*RACE (p=0.005)
(n=728)	Medium	365	104.7			AGE*DRKYR (p=0.018)
(R^2=0.106)	High	181	110.4			RACE*DRKYR (p=0.034)

[a]Transformed from natural logarithm scale.

[b]Slope and standard error based on natural logarithm fasting glucose versus log_2 dioxin.

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

TABLE 15-15. (Continued)

Analysis of Fasting Glucose (mg/dl) (Continuous)

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

Assumption	Time (Yrs.)	Mean[a]/(n) Current Dioxin Low	Medium	High	Slope (Std. Error)[b]	p-Value
e) Minimal						0.096[c]
(n=517)	≤18.6	101.3	103.5	98.4	-0.0001 (0.0117)	0.993[d]
(R^2=0.015)		(72)	(126)	(53)		
	>18.6	102.6	102.9	105.7	0.0251 (0.0096)	0.009[d]
		(58)	(131)	(77)		
f) Maximal						0.242[c]
(n=737)	≤18.6	98.2	100.7	104.0	0.0088 (0.0075)	0.241[d]
(R^2=0.018)		(105)	(189)	(82)		
	>18.6	99.8	102.5	106.0	0.0205 (0.0066)	0.002[d]
		(79)	(178)	(104)		

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

Assumption	Time (Yrs.)	Adj. Mean[a]/(n) Current Dioxin Low	Medium	High	Adj. Slope (Std. Error)[b]	p-Value	Covariate Remarks
g) Minimal						0.097[c]	AGE*RACE
(n=511)	≤18.6	103.4	107.4	104.5	0.0149 (0.0118)	0.209[d]	(p=0.019)
(R^2=0.103)		(72)	(125)	(52)			RACE*DRKYR
	>18.6	102.4	104.5	109.7	0.0393 (0.0096)	<0.001[d]	(p=0.043)
		(58)	(128)	(76)			
h) Maximal						0.194**[c]	CURR*TIME*AGE
(n=728)	≤18.6	102.3**	104.9**	110.8**	0.0168 (0.0075)**	0.024**[d]	(p=0.041)
(R^2=0.122)		(104)	(188)	(80)			AGE*RACE
	>18.6	101.7**	104.5**	111.1**	0.0294 (0.0066)**	<0.001**[d]	(p=0.004)
		(78)	(176)	(102)			AGE*DRKYR
							(p=0.015)
							RACE*DRKYR
							(p=0.030)

[a]Transformed from natural logarithm scale.

[b]Slope and standard error based on natural logarithm fasting glucose versus log_2 dioxin.

[c]Test of significance for homogeneity of slopes (current dioxin continuous, time categorized).

[d]Test of significance for slope different from 0 (current dioxin continuous, time categorized).

**Log_2 (current dioxin)-by-time-by-covariate interaction ($0.01<p\leq0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of this interaction.

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

TABLE 15-15. (Continued)

Analysis of Fasting Glucose (mg/dl) (Continuous)

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

Current Dioxin Category	n	Mean[a]	Contrast	Difference of Means (95% C.I.)[e]	p-Value[f]
Background	779	99.5	All Categories		<0.001
Unknown	341	98.3	Unknown vs. Background	-1.2 --	0.206
Low	193	100.7	Low vs. Background	1.2 --	0.331
High	186	105.1	High vs. Background	5.6 --	<0.001
Total	1,499		(R^2=0.017)		

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

Current Dioxin Category	n	Adj. Mean[a]	Contrast	Difference of Adj. Means (95% C.I.)[e]	p-Value[f]	Covariate Remarks
Background	777	101.3***	All Categories		<0.001***	DXCAT*AGE (p<0.001)
Unknown	338	99.9***	Unknown vs. Background	-1.4 -- ***	0.151***	DXCAT*DRKYR
Low	191	102.7***	Low vs. Background	1.4 -- ***	0.250***	(p=0.044)
High	182	108.9***	High vs. Background	7.6 -- ***	<0.001***	AGE*RACE (p=0.018)
Total	1,488		(R^2=0.101)			AGE*DRKYR (p=0.046)

[a]Transformed from natural logarithm scale.

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

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

***Categorized current dioxin-by-covariate interaction ($p \leq 0.01$); adjusted mean and p-value derived from a model fitted after deletion of this interaction.

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

The adjusted maximal analysis detected a significant current dioxin-by-time-by-age interaction (Table 15-15 [h]: p=0.041). Stratified analyses found a significant interaction between current dioxin and time for younger Ranch Hands, those born in or after 1942 (Appendix Table N-1: p=0.031). The association between current dioxin and fasting glucose was significant for younger Ranch Hands with an early tour (time>18.6: Adj. slope=0.0319, p=0.002), but it was not significant for those with a later tour (time ≤18.6: Adj. slope=0.0017, p=0.854). The adjusted mean levels of fasting glucose for the early time stratum were 94.3, 95.3, and 100.1 mg/dl for the low, medium, and high current dioxin categories.

The interaction between current dioxin and time was not significant for older Ranch Hands (born<1942: p=0.451), but the association between current dioxin and fasting glucose was significant within each time stratum (time≤18.6: Adj. slope=0.0370, p=0.003; time>18.6: Adj. slope=0.0254, p=0.006). The adjusted mean levels of fasting glucose increased for the low, medium, and high current dioxin categories for both time strata (time≤18.6: 103.4, 109.1, and 122.8 mg/dl; time>18.6: 105.1, 109.0, and 114.8 mg/dl).

Ignoring the current dioxin-by-time-by-age interaction, the adjusted maximal analysis did not find a significant interaction between current dioxin and time (Table 15-15 [h]: p=0.194). However, the association between current dioxin and fasting glucose was significant within each time stratum (time≤18.6: Adj. slope=0.0168, p=0.024; time>18.6: Adj. slope=0.0294, p<0.001). The adjusted mean levels of fasting glucose increased with current dioxin for both time strata (time≤18.6: 102.3, 104.9, and 110.8 mg/dl; time>18.6: 101.7, 104.5, and 111.1 mg/dl for the low, medium, and high current dioxin categories).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The unadjusted analysis of categorized current dioxin found that the mean levels of fasting glucose differed significantly among current dioxin categories (Table 15-15 [i]: 99.5, 98.3, 100.7, and 105.1 mg/dl for the background, unknown, low, and high current dioxin categories, p<0.001). The mean for the high current dioxin category was significantly more than the background mean (p<0.001). The means for the unknown and low categories did not differ significantly from the background mean (p=0.206 and p=0.331, respectively).

The adjusted analysis detected two significant categorized current dioxin-by-covariate interactions—categorized current dioxin-by-age (Table 15-15 [j]: p<0.001) and categorized current dioxin-by-lifetime alcohol history (p=0.044). Age and lifetime alcohol history were categorized to explore these interactions. Separate analyses were done for younger Ranch Hands (born≥1942) and older Ranch Hands (born<1942). The categorized current dioxin-by-lifetime alcohol history interaction was not significant for younger Ranch Hands (p=0.807), but it was significant for older Ranch Hands (p=0.050). The mean level of fasting glucose differed significantly among current dioxin categories for younger Ranch Hands (Appendix Table N-1: 96.1, 95.5, 96.5, and 100.0 mg/dl for the background, unknown, low, and high current dioxin categories, p=0.017), with the mean for the high current dioxin category being significantly more than the background mean (p=0.004).

Appendix Table N-1 presents results stratified by lifetime alcohol history for older Ranch Hands because of the significant interaction. They show that the overall contrast was

not significant for older Ranch Hands who never had drunk (p=0.567), but that the overall difference among adjusted mean levels of fasting glucose was significant for older Ranch Hands who were moderate lifetime drinkers (>0-40: 102.5, 100.7, 106.1, and 112.2 mg/dl for the background, unknown, low, and high current dioxin categories, p=0.003) and for those who were heavy lifetime drinkers (>40: 107.2, 105.4, 105.8, and 127.4 mg/dl for the background, unknown, low, and high current dioxin categories, p<0.001). The low versus background contrast was marginally significant for older Ranch Hands who were moderate drinkers (p=0.091). The high versus background contrast was significant for older Ranch Hands who were moderate drinkers (p=0.004) and for those who were heavy drinkers (p<0.001). For older Ranch Hands, the difference in adjusted means for the high versus background contrast increased with lifetime alcohol consumption (0: 7.1 mg/dl; >0-40: 9.7 mg/dl; >40: 20.2 mg/dl).

The adjusted results paralleled the unadjusted findings after deleting the interactions. The overall contrast was highly significant (Table 15-15 [j]: p<0.001), as was the high versus background contrast (p<0.001). The adjusted means for the background, unknown, low, and high current dioxin categories were 101.3, 99.9, 102.7, and 108.9 mg/dl.

Fasting Glucose (Discrete)

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

The unadjusted initial dioxin analyses of discretized fasting glucose detected a significant relative risk of an abnormally high level of fasting glucose for each cohort (Table 15-16 [a]: Est. RR=1.25, p=0.022 for the minimal cohort; Table 15-16 [b]: Est. RR=1.29, p<0.001 for the maximal cohort). For the minimal cohort, the percentages of abnormal fasting glucose levels were 15.4, 14.8, and 17.7 percent for the low, medium, and high initial dioxin categories. The corresponding percentages for the maximal cohort were 8.2, 13.9, and 19.5 percent.

The adjusted analyses displayed a highly significant increased risk of an abnormally high level of fasting glucose for both cohorts (Table 15-16 [c] and [d]: p<0.001 for both analyses). Adjusting for age, the relative risk of an abnormally high level of fasting glucose was 1.45 for the minimal cohort. The relative risk was 1.48 for the maximal cohort, adjusting for age and race.

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

The interaction between current dioxin and time since tour was not significant in either the unadjusted minimal (Table 15-16 [e]: p=0.256) or maximal (Table 15-16 [f]: p=0.531) analysis of discretized fasting glucose. Under both assumptions, the estimated relative risk was significantly greater than 1 for Ranch Hands with an early tour (Est. RR=1.32, p=0.023 for the minimal cohort; Est. RR=1.30, p=0.006 for the maximal cohort).

In the adjusted minimal analysis, the current dioxin-by-time interaction remained nonsignificant (Table 15-16 [g]: p=0.396) and the relative risk of an abnormally high level of fasting glucose remained significant for Ranch Hands with an early tour (Adj. RR=1.59, p<0.001). However, the adjusted maximal analysis detected a significant current dioxin-by-time-by-race interaction (Table 15-16 [h]: p=0.038). Appendix Table N-1 presents

TABLE 15-16.

Analysis of Fasting Glucose (Discrete)

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal High	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=517)	Low	130	15.4	1.25 (1.03,1.50)	0.022
	Medium	257	14.8		
	High	130	17.7		
b) Maximal (n=737)	Low	184	8.2	1.29 (1.12,1.49)	<0.001
	Medium	368	13.9		
	High	185	19.5		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=517)	1.45 (1.18,1.77)	<0.001	AGE (p<0.001)
d) Maximal (n=737)	1.48 (1.26,1.74)	<0.001	AGE (p<0.001) RACE (p=0.100)

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

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

TABLE 15-16. (Continued)

Analysis of Fasting Glucose (Discrete)

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

Assumption	Time (Yrs.)	Percent Abnormal High/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.256[b]
(n=517)	≤18.6	13.9 (72)	14.3 (126)	11.3 (53)	1.04 (0.74,1.45)	0.821[c]
	>18.6	13.8 (58)	16.0 (131)	23.4 (77)	1.32 (1.04,1.67)	0.023[c]
f) Maximal						0.531[b]
(n=737)	≤18.6	5.7 (105)	12.7 (189)	17.1 (82)	1.18 (0.93,1.50)	0.183[c]
	>18.6	11.4 (79)	14.6 (178)	22.1 (104)	1.30 (1.08,1.56)	0.006[c]

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

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal			0.396[b]	AGE (p<0.001)
(n=517)	≤18.6	1.33 (0.93,1.89)	0.118[c]	
	>18.6	1.59 (1.23,2.05)	<0.001[c]	
h) Maximal			0.666**[b]	CURR*TIME*RACE
(n=728)	≤18.6	1.44 (1.10,1.88)**	0.007**[c]	(p=0.038)
	>18.6	1.55 (1.26,1.91)**	<0.001**[c]	DRKYR (p=0.122)
				AGE*RACE (p=0.040)

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

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

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

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

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

TABLE 15-16. (Continued)

Analysis of Fasting Glucose (Discrete)

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

Current Dioxin Category	n	Percent Abnormal High	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	779	11.4	All Categories		0.001
Unknown	341	7.9	Unknown vs. Background	0.67 (0.42,1.05)	0.078
Low	193	12.4	Low vs. Background	1.10 (0.68,1.78)	0.695
High	186	19.9	High vs. Background	1.93 (1.26,2.94)	0.002
Total	1,499				

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

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	777	All Categories		<0.001	AGE (p<0.001) RACE (p=0.042)
Unknown	338	Unknown vs. Background	0.66 (0.42,1.05)	0.081	DRKYR (p=0.033)
Low	191	Low vs. Background	1.18 (0.72,1.94)	0.510	
High	182	High vs. Background	2.95 (1.87,4.66)	<0.001	
Total	1,488				

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

stratified results that show sparse data for Blacks. The current dioxin-by-time interaction was not significant for non-Blacks (p=0.477), but the relative risk of an abnormally high level of fasting glucose was significantly more than 1 in each time stratum (time≤18.6: Adj. RR=1.39, p=0.015; time>18.6: Adj. RR=1.57, p<0.001). After excluding the current dioxin-by-time-by-race interaction, the adjusted maximal results were comparable to the stratified findings for non-Blacks. The current dioxin-by-time interaction was not significant (Table 15-16 [h]: p=0.666), but the association between current dioxin and fasting glucose was significant within both time strata (time≤18.6: Adj. RR=1.44, p=0.007; time>18.6: Adj. RR=1.55, p<0.001).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The unadjusted categorized current dioxin analysis found that the prevalence of abnormally high levels of fasting glucose differed significantly among the current dioxin categories (Table 15-16 [i]: 11.4%, 7.9%, 12.4%, and 19.9% for the background, unknown, low, and high current dioxin categories, p=0.001). The estimated relative risk for the unknown versus background contrast was marginally less than 1 (Est. RR=0.67, 95% C.I.: [0.42,1.05], p=0.078), and it was significantly more than 1 for the high versus background contrast (Est. RR=1.93, 95% C.I.: [1.26,2.94], p=0.002).

Adjusting for age, race, and lifetime alcohol history, the overall contrast remained highly significant (Table 15-16 [j]: p<0.001), with the unknown versus background contrast essentially unchanged (Adj. RR=0.66, 95% C.I.: [0.42,1.05], p=0.081). However, the adjusted relative risk for the high versus background contrast increased more than 50 percent to 2.95 (95% C.I.: [1.87,4.66], p<0.001).

2-Hour Postprandial Glucose (Continuous)

Model 1: Ranch Hands – Log_2 (Initial Dioxin)

Under the minimal assumption, the association between initial dioxin and 2-hour postprandial glucose was not significant in the unadjusted analysis (Table 15-17 [a]: p=0.177). However, the unadjusted maximal analysis detected a significant positive association (Table 15-17 [b]: p=0.021). The unadjusted mean postprandial glucose levels for the maximal cohort were 108.0, 112.1, and 114.0 mg/dl for the low, medium, and high initial dioxin categories.

The adjusted minimal analysis revealed a significant initial dioxin-by-percent body fat interaction (Table 15-17 [c]: p=0.045). Percent body fat was categorized to explore the interaction. Stratified analyses showed that a positive association between initial dioxin and 2-hour postprandial glucose was stronger for obese Ranch Hands than for normal/lean Ranch Hands, but neither finding was significant (Appendix Table N-1).

The interaction between initial dioxin and percent body fat was then removed from the model. Adjusting for age and percent body fat, the relationship between initial dioxin and 2-hour postprandial glucose was not significant (Table 15-17 [c]: p=0.114). However, similar to the testosterone findings, the association became significant when percent body fat was excluded from the model (Appendix Table N-2: p=0.020).

TABLE 15-17.

Analysis of 2-Hour Postprandial Glucose (mg/dl) (Continuous)

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Mean[a]	Slope (Std. Error)[b]	p-Value
a) Minimal (n=467) (R^2=0.004)	Low	117	112.3	0.0146 (0.0108)	0.177
	Medium	231	112.9		
	High	119	113.8		
b) Maximal (n=678) (R^2=0.008)	Low	177	108.0	0.0178 (0.0077)	0.021
	Medium	337	112.1		
	High	164	114.0		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Initial Dioxin	n	Adj. Mean[a]	Adj. Slope (Std. Error)[b]	p-Value	Covariate Remarks
c) Minimal (n=467) (R^2=0.111)	Low	117	111.9**	0.0169 (0.0107)**	0.114**	INIT*%BFAT (p=0.045) AGE (p<0.001)
	Medium	231	113.6**			
	High	119	113.6**			
d) Maximal (n=654) (R^2=0.105)	Low	168	110.2	0.0118 (0.0079)	0.135	AGE (p<0.001) PERS (p=0.127) %BFAT (p<0.001)
	Medium	328	111.6			
	High	158	113.4			

[a]Transformed from natural logarithm scale.

[b]Slope and standard error based on natural logarithm 2-hour postprandial glucose versus log_2 dioxin.

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

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

TABLE 15-17. (Continued)

Analysis of 2-Hour Postprandial Glucose (mg/dl) (Continued)

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

Assumption	Time (Yrs.)	Mean[a]/(n) Current Dioxin Low	Medium	High	Slope (Std. Error)[b]	p-Value
e) Minimal						0.555[c]
(n=467)	≤18.6	107.3	110.2	110.5	0.0137 (0.0170)	0.421[d]
(R^2=0.014)		(63)	(117)	(51)		
	>18.6	126.7	110.5	119.3	0.0005 (0.0145)	0.975[d]
		(52)	(116)	(68)		
f) Maximal						0.406[c]
(n=678)	≤18.6	109.3	109.0	111.3	0.0073 (0.0116)	0.530[d]
(R^2=0.010)		(105)	(174)	(74)		
	>18.6	104.0	116.7	116.6	0.0204 (0.0107)	0.057[d]
		(74)	(159)	(92)		

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

Assumption	Time (Yrs.)	Adj. Mean[a]/(n) Current Dioxin Low	Medium	High	Adj. Slope (Std. Error)[b]	p-Value	Covariate Remarks
g) Minimal						0.486**[c]	CURR*TIME*PERS
(n=453)	≤18.6	106.9**	111.6**	111.6**	0.0188 (0.0168)**	0.264**[d]	(p=0.038)
(R^2=0.112)		(60)	(114)	(48)			AGE (p=0.001)
	>18.6	124.6**	110.5**	117.9**	0.0039 (0.0143)**	0.785**[d]	%BFAT (p<0.001)
		(51)	(113)	(67)			
h) Maximal						0.252[c]	AGE (p<0.001)
(n=654)	≤18.6	112.3	109.9	112.4	0.0012 (0.0120)	0.921[d]	PERS (p=0.110)
(R^2=0.107)		(98)	(168)	(70)			%BFAT (p<0.001)
	>18.6	103.1	115.5	114.3	0.0190 (0.0107)	0.077[d]	
		(72)	(156)	(90)			

[a]Transformed from natural logarithm scale.

[b]Slope and standard error based on natural logarithm 2-hour postprandial glucose versus log_2 dioxin.

[c]Test of significance for homogeneity of slopes (current dioxin continuous, time categorized).

[d]Test of significance for slope equal to 0 (current dioxin continuous, time categorized).

**Log_2 (current dioxin)-by-time-by-covariate interaction ($0.01<p\leq0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of this interaction.

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

TABLE 15-17. (Continued)

Analysis of 2-Hour Postprandial Glucose (mg/dl) (Continuous)

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

Current Dioxin Category	n	Mean[a]	Contrast	Difference of Means (95% C.I.)[e]	p-Value[f]
Background	740	111.3	All Categories		0.082
Unknown	331	107.5	Unknown vs. Background	-3.8 --	0.049
Low	179	109.8	Low vs. Background	-1.5 --	0.527
High	166	114.2	High vs. Background	2.9 --	0.263
Total	1,416		(R^2=0.005)		

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

Current Dioxin Category	n	Adj. Mean[a]	Contrast	Difference of Adj. Means (95% C.I.)[e]	p-Value[f]	Covariate Remarks
Background	705	110.9	All Categories		0.557	AGE (p<0.001) %BFAT (p<0.001)
Unknown	314	109.5	Unknown vs. Background	-1.4 --	0.471	PERS (p=0.076)
Low	175	109.3	Low vs. Background	-1.6 --	0.507	
High	160	113.1	High vs. Background	2.2 --	0.380	
Total	1,354		(R^2=0.107)			

[a]Transformed from natural logarithm scale.

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

[f]p-value is based on difference of means on natural logarithm scale.

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

The maximal analyses were comparable. Adjusting for age, percent body fat, and personality type, the association between initial dioxin and 2-hour postprandial glucose was not significant (Table 15-17 [d]: p=0.135). But when percent body fat was removed from the model, the association was highly significant (Appendix Table N-2: p=0.003). The adjusted mean postprandial glucose levels for the low, medium, and high initial dioxin categories were 108.0, 111.6, and 115.8 mg/dl.

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

In the unadjusted analyses, the current dioxin-by-time since tour interaction was not significant under either the minimal (Table 15-17 [e]: p=0.555) or maximal (Table 15-17 [f]: p=0.406) assumption. Under the maximal assumption, the association between current dioxin and 2-hour postprandial glucose was marginally positive for Ranch Hands with more than 18.6 years since exposure (p=0.057). For these participants, the mean postprandial glucose levels were 104.0, 116.7, and 116.6 mg/dl for low, medium, and high current dioxin.

The current dioxin-by-time-by-personality type interaction was significant for the adjusted minimal analysis (Table 15-17 [g]: p=0.038). Stratified results showed that the current dioxin-by-time interaction was marginally significant for type B participants (Appendix Table N-1: p=0.074), but not significant for type A participants (p=0.221). The association between current dioxin and 2-hour postprandial glucose was not significant for each time stratum. The three-way interaction can be partly explained by noting that the adjusted slopes for the corresponding time strata were in the opposite direction for type A participants versus type B participants.

Excluding the interaction and adjusting for age and percent body fat, the current dioxin-by-time interaction was not significant for the minimal cohort (Table 15-17 [g]: p=0.486).

The results for the adjusted maximal analysis were consistent with the unadjusted findings. After adjusting for age, percent body fat, and personality type, the test of homogeneity of slopes was not significant (Table 15-17 [h]: p=0.252). However, a marginally significant association between current dioxin and 2-hour postprandial glucose (p=0.077) was found for Ranch Hands with an early tour of duty. This finding was significant when percent body fat was removed from the model (Appendix Table N-2: p=0.009).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The mean 2-hour postprandial glucose differed marginally among the four current dioxin categories in the unadjusted analysis (Table 15-17 [i]: p=0.082). The mean for the unknown category was significantly less than the background mean (107.5 mg/dl versus 111.3 mg/dl, p=0.049).

No significant results were found after adjusting for age, percent body fat, and personality type (Table 15-17 [j]: p>0.35 for all contrasts). However, the overall contrast became significant (Appendix Table N-2: p=0.010) when percent body fat was excluded from the model. The adjusted means were 111.1, 107.0, 110.1, and 116.5 mg/dl for the background, unknown, low, and high current dioxin categories. The adjusted mean for the high category was significantly more than the background mean (p=0.041), and the adjusted mean for the unknown category was significantly less than the background mean (p=0.035).

2-Hour Postprandial Glucose (Discrete)

Model 1: Ranch Hands – Initial Dioxin (Categorized)

The unadjusted analyses of discretized 2-hour postprandial glucose did not detect an overall association with initial dioxin for either the minimal (p=0.174) or maximal (p=0.243) cohorts (Table 15-18 [a] and [b]). However, the high versus low initial dioxin category contrast showed a marginally significant risk of diabetic glucose levels for both cohorts (minimal: Est. RR=7.00, 95% C.I.: [0.85,58.00], p=0.071; maximal: Est. RR=2.85, 95% C.I.: [0.97,8.33], p=0.056). The percentage of Ranch Hands with diabetic glucose levels increased for the low, medium, and high initial dioxin categories (0.9%, 2.6%, and 5.9% for the minimal cohort; 2.1%, 2.6%, and 5.9% for the maximal cohort).

Adjusting for age and percent body fat, similar findings were noted. The overall association with initial dioxin was not significant (Table 15-18 [c] and [d]: p=0.229 and p=0.237 for the minimal and maximal assumptions), but the high versus low initial dioxin category contrast of diabetic glucose levels was marginally significant under each assumption (minimal: Adj. RR=5.95, 95% C.I.: [0.91,38.81], p=0.062; maximal: Adj. RR=2.98, 95% C.I.: [0.97,9.14], p=0.057).

Further adjusted analyses were done excluding percent body fat from the model. They found a marginally significant overall association with initial dioxin for the maximal cohort (Appendix Table N-2: p=0.091). The high versus low initial dioxin category contrast of diabetic glucose levels was significant for both cohorts (Adj. RR=7.99, 95% C.I.: [1.10,57.96], p=0.040 for the minimal cohort; Adj. RR=3.85, 95% C.I.: [1.28,11.57], p=0.016 for the maximal cohort).

Model 2: Ranch Hands – Current Dioxin (Categorized) and Time

The current dioxin-by-time since tour interaction was not significant for either the unadjusted minimal (p=0.444) or maximal (p=0.781) analysis of discretized 2-hour postprandial glucose (Table 15-18 [e] and [f]). However, for the minimal cohort, the medium versus low current dioxin category contrast for the risk of impaired glucose levels was significantly less than 1 for Ranch Hands with more than 18.6 years since exposure (Est. RR=0.44, 95% C.I.: [0.21,0.92], p=0.029) and the high versus low contrast was marginally less than 1 for this time stratum (Est. RR=0.47, 95% C.I.: [0.20,1.08], p=0.074). For Ranch Hands with time 18.6 years or less, the relative risk of diabetic glucose levels for the high versus low contrast was significant under the maximal assumption (Est. RR=5.02, 95% C.I.: [1.08,23.32], p=0.039). The percentages of diabetic glucose levels for this time stratum were 1.6, 1.7, and 7.8 percent for the low, medium, and high current dioxin categories.

Adjusting for age, race, and percent body fat, the current dioxin-by-time interaction remained nonsignificant for both assumptions (Table 15-18 [g] and [h]: p=0.358 and p=0.813 for the minimal and maximal assumptions). However, within each time stratum, particular category contrasts were significant or marginally significant. For Ranch Hands with a later tour, the risk of diabetic glucose levels was greater for the high current dioxin category relative to the low current dioxin category (Adj. RR=5.20, 95% C.I.: [0.82,32.91], p=0.080 for the minimal cohort; Adj. RR=5.33, 95% C.I.: [1.22,23.28], p=0.026 for the maximal cohort). Also, similar to the unadjusted results for Ranch Hands with an early tour, the risk of impaired glucose levels was significantly less for the medium current dioxin category relative

TABLE 15-18.

Analysis of 2-Hour Postprandial Glucose (Discrete)

Ranch Hands - Initial Dioxin (Categorized) - Unadjusted

Assumption	Initial Dioxin	n	Percent Normal	Percent Impaired	Percent Diabetic	Initial Dioxin Contrast	Est. Relative Risk (95% C.I.)	p-Value
a) Minimal (n=467)	Low	117	81.2	17.9	0.9	Overall†		0.174
	Medium	231	78.4	19.0	2.6	M vs. L[a]	1.10 (0.62,1.96)	0.749
	High	119	79.8	14.3	5.9	H vs. L[a]	0.81 (0.40,1.63)	0.554
						M vs. L[b]	3.15 (0.37,26.54)	0.291
						H vs. L[b]	7.00 (0.85,58.00)	0.071
b) Maximal (n=678)	Low	326	82.8	15.0	2.1	Overall†		0.243
	Medium	233	78.5	18.9	2.6	M vs. L[a]	1.32 (0.85,2.07)	0.219
	High	119	79.8	14.3	5.9	H vs. L[a]	0.99 (0.54,1.80)	0.963
						M vs. L[b]	1.26 (0.42,3.82)	0.677
						H vs. L[b]	2.85 (0.97,8.33)	0.056

Ranch Hands - Initial Dioxin (Categorized) - Adjusted

Assumption	Initial Dioxin Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
c) Minimal (n=467)	Overall†		0.229	AGE (p=0.002)
	M vs. L[a]	1.17 (0.65,2.10)	0.609	%BFAT (p<0.001)
	H vs. L[a]	0.93 (0.45,1.93)	0.319	
	M vs. L[b]	2.57 (0.40,16.44)	0.845	
	H vs. L[b]	5.95 (0.91,38.81)	0.062	
d) Maximal (n=678)	Overall†		0.237	AGE (p<0.001)
	M vs. L[a]	1.39 (0.87,2.19)	0.164	%BFAT (p<0.001)
	H vs. L[a]	1.15 (0.61,2.15)	0.671	
	M vs. L[b]	1.28 (0.43,3.81)	0.657	
	H vs. L[b]	2.98 (0.97,9.14)	0.057	

[a]Impaired contrasted with normal.
[b]Diabetic contrasted with normal.
†Overall test of independence of initial dioxin and 2-hour postprandial glucose.
Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
M vs. L: Medium initial dioxin category versus low initial dioxin category.
H vs. L: High initial dioxin category versus low initial dioxin category.

TABLE 15-18. (Continued)

Analysis of 2-Hour Postprandial Glucose (Discrete)

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

Assumption	Time (Yrs.)	Glucose Category	Percent/(n) Current Dioxin Low	Medium	High	Current Dioxin Contrast	Est. Relative Risk (95% C.I.)	p-Value
e) Minimal						C-by-T[a]		0.444
(n=467)	≤18.6	Normal	87.3	83.8	82.4	Overall[†]		0.297
		Impaired	11.1	14.5	9.8	M vs. L[b]	1.36 (0.53,3.49)	0.519[d]
		Diabetic	1.6	1.7	7.8	H vs. L[b]	0.94 (0.28,3.16)	0.915[d]
			(63)	(117)	(51)	M vs. L[c]	1.12 (0.10,12.66)	0.925[d]
						H vs. L[c]	5.24 (0.56,48.61)	0.145[d]
	>18.6	Normal	63.5	79.3	75.0	Overall[†]		0.105
		Impaired	34.6	19.0	19.1	M vs. L[b]	0.44 (0.21,0.92)	0.029[d]
		Diabetic	1.9	1.7	5.9	H vs. L[b]	0.47 (0.20,1.08)	0.074[d]
			(52)	(116)	(68)	M vs. L[c]	0.72 (0.06,8.18)	0.789[d]
						H vs. L[c]	2.59 (0.28,24.18)	0.406[d]
f) Maximal						C-by-T[a]		0.781
(n=678)	≤18.6	Normal	85.4	83.8	82.4	Overall[†]		0.251
		Impaired	13.0	14.5	9.8	M vs. L[b]	1.14 (0.58,2.23)	0.700[d]
		Diabetic	1.6	1.7	7.8	H vs. L[b]	0.78 (0.28,2.18)	0.641[d]
			(185)	(117)	(51)	M vs. L[c]	1.07 (0.18,6.55)	0.938[d]
						H vs. L[c]	5.02 (1.08,23.32)	0.039[d]
	>18.6	Normal	75.9	79.3	75.0	Overall[†]		0.658
		Impaired	20.6	19.0	19.1	M vs. L[b]	0.88 (0.47,1.64)	0.690[d]
		Diabetic	3.5	1.7	5.9	H vs. L[b]	0.94 (0.45,1.96)	0.866[d]
			(141)	(116)	(68)	M vs. L[c]	0.46 (0.09,2.45)	0.365[d]
						H vs. L[c]	1.68 (0.43,6.51)	0.456[d]

[a]Test of significance of current dioxin-by-time interaction.
[b]Impaired contrasted with normal.
[c]Diabetic contrasted with normal.
[d]Test of significance for relative risk equal to 1 (current dioxin and time categorized).
[†]Overall test of independence of current dioxin and 2-hour postprandial glucose within time stratum.
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
M vs. L: Medium current dioxin category versus low current dioxin category.
H vs. L: High current dioxin category versus low current dioxin category.

TABLE 15-18. (Continued)

Analysis of 2-Hour Postprandial Glucose (Discrete)

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

Assumption	Time (Yrs.)	Current Dioxin Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
g) Minimal (n=467)	≤18.6	C-by-T[a]		0.358	AGE (p=0.007)
		Overall[†]		0.177	RACE (p=0.138)
		M vs. L[b]	1.51 (0.60,3.82)	0.387[d]	%BFAT (p<0.001)
		H vs. L[b]	1.22 (0.37,4.02)	0.748[d]	
		M vs. L[c]	1.14 (0.16,7.88)	0.895[d]	
		H vs. L[c]	5.20 (0.82,32.91)	0.080[d]	
	>18.6	Overall[†]		0.140	
		M vs. L[b]	0.46 (0.21,0.97)	0.040[d]	
		H vs. L[b]	0.53 (0.22,1.27)	0.154[d]	
		M vs. L[c]	0.53 (0.08,3.71)	0.525[d]	
		H vs. L[c]	1.95 (0.32,12.02)	0.471[d]	
h) Maximal (n=678)	≤18.6	C-by-T[a]		0.813	AGE (p<0.001)
		Overall[†]		0.102	RACE (p=0.054)
		M vs. L[b]	1.19 (0.61,2.34)	0.616[d]	%BFAT (p<0.001)
		H vs. L[b]	0.99 (0.36,2.70)	0.988[d]	
		M vs. L[c]	1.14 (0.23,5.62)	0.870[d]	
		H vs. L[c]	5.33 (1.22,23.28)	0.026[d]	
	>18.6	Overall[†]		0.518	
		M vs. L[b]	0.97 (0.52,1.83)	0.933[d]	
		H vs. L[b]	1.17 (0.55,2.49)	0.686[d]	
		M vs. L[c]	0.51 (0.11,2.29)	0.381[d]	
		H vs. L[c]	1.93 (0.52,7.22)	0.329[d]	

[a]Overall test of significance of current dioxin-by-time interaction.
[b]Impaired contrasted with normal.
[c]Diabetic contrasted with normal.
[d]Test of significance for relative risk equal to 1 (current dioxin and time categorized).
[†]Overall test of independence of current dioxin and 2-hour postprandial glucose within time stratum.
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
M vs. L: Medium current dioxin category versus low current dioxin category.
H vs. L: High current dioxin category versus low current dioxin category.

TABLE 15-18. (Continued)

Analysis of 2-Hour Postprandial Glucose (Discrete)

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

Current Dioxin Category	n	Percent Normal	Percent Impaired	Percent Diabetic	Contrast	Impaired versus Normal: Est. Relative Risk (95% C.I.)	Impaired versus Normal: p-Value	Diabetic versus Normal: Est. Relative Risk (95% C.I.)	Diabetic versus Normal: p-Value
Background	740	82.4	14.6	3.0					
Unknown	331	83.7	14.5	1.8	Unknown vs. Background	0.98 (0.68,1.41)	0.907	0.60 (0.24,1.50)	0.275
Low	179	83.2	15.6	1.1	Low vs. Background	1.06 (0.37,1.67)	0.795	0.37 (0.09,1.60)	0.185
High	166	78.3	15.7	6.0	High vs. Background	1.13 (0.71,1.80)	0.610	2.14 (0.99,4.62)	0.053
Total	1,416						All categories: p=0.174		

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

Current Dioxin Category	n	Contrast	Impaired versus Normal: Adj. Relative Risk (95% C.I.)	Impaired versus Normal: p-Value	Diabetic versus Normal: Adj. Relative Risk (95% C.I.)	Diabetic versus Normal: p-Value	Covariate Remarks
Background	705						AGE (p<0.001) RACE (p=0.142)
Unknown	314	Unknown vs. Background	1.03 (0.71,1.51)	0.872	0.88 (0.37,2.06)	0.760	%BFAT (p<0.001)
Low	175	Low vs. Background	1.10 (0.70,1.73)	0.685	0.60 (0.19,1.89)	0.386	PERS (p=0.092)
High	160	High vs. Background	1.41 (0.87,2.27)	0.160	2.35 (1.06,5.19)	0.035	
Total	1,354			All categories: p=0.267			

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

to the low current dioxin category under the minimal assumption (Adj. RR=0.46, 95% C.I.: [0.21,0.97], p=0.040).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The unadjusted analysis of categorized current dioxin was not significant for discretized 2-hour postprandial glucose (Table 15-18 [i]: p=0.174), although the high versus background contrast indicated a marginal risk of diabetic glucose levels (Est. RR=2.14, 95% C.I.: [0.99,4.62], p=0.053).

Adjusting for age, race, percent body fat, and personality type, the overall current dioxin effect remained nonsignificant (Table 15-18 [j]: p=0.267), and the risk of a diabetic glucose level became significant for the high versus background contrast (Adj. RR=2.35, 95% C.I.: [1.06,5.19], p=0.035). The overall current dioxin effect became marginally significant with percent body fat excluded from the model (Appendix Table N-2: p=0.092).

Composite Diabetes Indicator

Model 1: Ranch Hands – Log_2 (Initial Dioxin)

Under both the minimal and maximal assumptions, the unadjusted analysis of the composite diabetes indicator revealed a significant positive association with initial dioxin (Table 15-19 [a] and [b]: p=0.023 and p<0.001, respectively). The estimated relative risk of diabetes for a twofold increase in initial dioxin was 1.27 for the minimal cohort and 1.33 for the maximal cohort. The percentage of Ranch Hands with a verified history of diabetes or a 2-hour postprandial glucose level above 200 mg/dl increased with initial dioxin under both assumptions (minimal: 10.1%, 12.5%, and 14.5% for the low, medium, and high initial dioxin categories; maximal: 5.4%, 10.6%, and 16.7% for the low, medium, and high initial dioxin categories).

Under both assumptions, the association became stronger after covariate adjustment. The relative risk was 1.46 (p=0.001) for the minimal analysis, adjusting for age and percent body fat. For the maximal analysis, the relative risk was 1.48 (p<0.001) after adjusting for age, race, and percent body fat.

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

The current dioxin and time since tour analyses of the composite diabetes indicator failed to detect a significant current dioxin-by-time interaction for both the minimal and maximal assumptions (Table 15-19 [e-h]: p>0.50 for all analyses). However, in most time strata, current dioxin was significantly associated with an increased risk of diabetes. This finding is consistent with the results for model 1, which found a significant association between initial dioxin and the composite diabetes indicator, because initial dioxin and current dioxin are highly correlated.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The unadjusted analysis of categorized current dioxin was highly significant for the composite diabetes indicator (Table 15-19 [i]: p<0.001). The high current dioxin category had more than twice as many diabetics as the background category (16.6% versus 8.2%,

TABLE 15-19.

Analysis of Composite Diabetes Indicator

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Diabetic	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=517)	Low	129	10.1	1.27 (1.04,1.56)	0.023
	Medium	257	12.5		
	High	131	14.5		
b) Maximal (n=738)	Low	185	5.4	1.33 (1.13,1.55)	<0.001
	Medium	367	10.6		
	High	186	16.7		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=517)	1.46 (1.17,1.82)	0.001	AGE (p<0.001) %BFAT (p=0.003)
d) Maximal (n=738)	1.48 (1.23,1.77)	<0.001	AGE (p<0.001) RACE (p=0.099) %BFAT (p<0.001)

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

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

TABLE 15-19. (Continued)

Analysis of Composite Diabetes Indicator

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

Assumption	Time (Yrs.)	Percent Diabetic/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.527[b]
(n=517)	≤18.6	13.9 (72)	9.4 (127)	13.0 (54)	1.13 (0.80,1.61)	0.488[c]
	>18.6	10.5 (57)	12.3 (130)	16.9 (77)	1.30 (1.00,1.69)	0.047[c]
f) Maximal						0.638[b]
(n=738)	≤18.6	2.8 (106)	9.5 (190)	16.9 (83)	1.34 (1.03,1.74)	0.027[c]
	>18.6	8.9 (79)	11.9 (176)	16.3 (104)	1.24 (1.01,1.52)	0.040[c]

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

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal			0.723[b]	AGE (p<0.001)
(n=517)	≤18.6	1.46 (0.99,2.13)	0.054[c]	%BFAT (p=0.003)
	>18.6	1.58 (1.18,2.11)	0.002[c]	
h) Maximal			0.512[b]	AGE (p<0.001)
(n=738)	≤18.6	1.62 (1.20,2.19)	0.002[c]	RACE (p=0.089)
	>18.6	1.43 (1.14,1.81)	0.002[c]	%BFAT (p<0.001)

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

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

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

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

TABLE 15-19. (Continued)

Analysis of Composite Diabetes Indicator

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

Current Dioxin Category	n	Percent Diabetic	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	782	8.2	All Categories		<0.001
Unknown	344	5.5	Unknown vs. Background	0.66 (0.39,1.11)	0.118
Low	193	8.3	Low vs. Background	1.01 (0.57,1.80)	0.962
High	187	16.6	High vs. Background	2.23 (1.40,3.54)	0.001
Total	1,506				

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

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	782	All Categories		0.003**	DXCAT*AGE (p=0.012) %BFAT (p<0.001)
Unknown	344	Unknown vs. Background	0.82 (0.48,1.43)**	0.491**	
Low	193	Low vs. Background	1.01 (0.56,1.82)**	0.986**	
High	187	High vs. Background	2.51 (1.51,4.16)**	<0.001**	
Total	1,506				

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

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

p=0.001). The incidence of diabetes in both the unknown (5.5%) and low (8.3%) categories was not significantly different from the background incidence.

The adjusted analysis detected a significant categorized current dioxin-by-age interaction (Table 15-19 [j]: p=0.012) for the composite diabetes indicator. Stratified analyses were done to explore the interaction. They showed that the incidence of diabetes differed significantly among the four current dioxin categories for older participants (Appendix Table N-1: born before 1942: p=0.002), but the overall current dioxin effect was not significant for younger participants (born in or after 1942: p=0.595). For older participants, the percentages of diabetics were 10.2, 6.6, 12.4, and 28.6 percent for the background, unknown, low, and high current dioxin categories. Adjusting for percent body fat, older Ranch Hands in the high current dioxin category were more than three times as likely to be positive for diabetes than similar-aged Comparisons in the background category (Adj. RR=3.09, 95% C.I.: [1.64,5.82], p<0.001). The high versus background relative risk was greater than 1, but not significant, for younger individuals (Adj. RR=1.49, 95% C.I.: [0.65,3.41], p=0.341). The percentages of younger participants with diabetes were 5.3, 3.4, 2.5, and 9.4 percent for the background, unknown, low, and high current dioxin categories.

Excluding percent body fat from the model, the high versus background relative risk of diabetes increased to 3.52 for the older age stratum (Appendix Table N-3: 95% C.I.: [1.93,6.42], p<0.001) and became 1.86 for the younger age stratum (95% C.I.: [0.84,4.09], p=0.125). The incidences of diabetes in the unknown and low categories were not significantly different from the background incidence in either age stratum.

The adjusted results were comparable to the unadjusted findings after excluding the interaction. Adjusting for age and percent body fat, the overall current dioxin effect was significant (Table 15-19 [j]: p=0.003) and the high versus background contrast was highly significant (Adj. RR=2.51, 95% C.I.: [1.51,4.16], p<0.001). The association became even stronger when percent body fat was dropped from the model. For this analysis, the overall current dioxin effect was highly significant (Appendix Table N-2: p<0.001), the unknown versus background contrast became marginally less than 1 (Adj. RR=0.63, 95% C.I.: [0.37,1.08], p=0.095), and the adjusted relative risk for the high versus background contrast was 2.95 (95% C.I.: [1.82,4.79], p<0.001).

Longitudinal Analysis

Laboratory Examination Variables

Longitudinal analyses were conducted to evaluate the association between various measures of dioxin (initial dioxin, current dioxin and time since tour, and categorized current dioxin) and the change between the 1982 Baseline examination and the 1987 examination in T_3 % uptake, TSH, and testosterone. T_3 % uptake and testosterone were treated as continuous variables. TSH was analyzed in its discrete form because laboratory techniques to measure TSH differed between examinations.

For a specific longitudinal analysis of T_3 % uptake or testosterone (e.g., minimal assumption, initial dioxin analysis), the left side of each subpanel of a table provides the means and sample sizes at each examination for participants who were compliant at both the 1982 and 1987 examinations. Based on the difference between 1987 and 1982 laboratory

values, the right side of each subpanel presents slopes, standard errors, and associated p-values (for models using initial dioxin or models using current dioxin and time), or differences of examination mean changes, 95 percent confidence intervals, and associated p-values (for models using categorized current dioxin).

For a specific longitudinal analysis of TSH, the upper part of each subpanel of a table provides the percents of participants with abnormally high levels of TSH at each examination. The lower part of each subpanel presents sample sizes, percents, relative risks, and associated 95 percent confidence intervals for all participants who had normal TSH levels at the 1982 examination and who were compliant at the 1987 examination.

T_3 % Uptake (Continuous)

Table 15-20 presents the results of the longitudinal analyses for T_3 % uptake (unadjusted for covariate information).

Model 1: Ranch Hands – Log_2 (Initial Dioxin)

Under both the minimal and the maximal assumptions, the longitudinal analysis displayed a nonsignificant negative association between initial dioxin and the change (as measured by the difference from the 1987 examination value relative to the 1982 examination value) in T_3 % uptake (Table 15-20 [a] and [b]; p=0.113 and p=0.699, respectively).

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

For the longitudinal analysis of the change in T_3 % uptake between 1982 and 1987, the interaction between current dioxin and time since tour was not significant under both the minimal and the maximal assumptions (Table 15-20 [c] and [d]: p=0.300 and p=0.167). For the minimal cohort, there was a marginally significant decreasing association between current dioxin and the change in T_3 % uptake for Ranch Hands with more than 18.6 years since the end of their tour (Table 15-20 [d]: p=0.073).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The analysis of categorized current dioxin found a significant overall difference in the mean change in T_3 % uptake (between 1982 and 1987) among the four current dioxin categories (Table 15-20 [e]: p=0.018). The differences between the mean change in T_3 % uptake of the unknown, low, and high categories versus the mean change for those in the background category were -0.3, 0.2, and -0.4 percent, respectively. The mean change in T_3 % uptake for the Comparisons in the background group was significantly greater than the mean change for the Ranch Hands in the low current dioxin category (p=0.036). Also, the difference in the mean change in T_3 % uptake for the background and high current dioxin categories was marginally significant (p=0.055).

TSH (Discrete)

The longitudinal analyses of TSH were based on participants who had a normal level of TSH in 1982 (see Chapter 4). Table 15-21 presents the results of the longitudinal analyses for TSH (unadjusted for covariate information). Due to an inconsistency in the laboratory technique, the normal/abnormal cutpoint for TSH differed at each examination. The cutpoints

TABLE 15-20.

Longitudinal Analysis of T_3 % Uptake (Continuous)

Ranch Hands - Log_2 (Initial Dioxin)

Assumption	Initial Dioxin	Mean[a]/(n) Examination 1982	1985	1987	Slope (Std. Error)[b]	p-Value
a) Minimal (R^2=0.005)	Low	30.1 (122)	27.8 (120)	30.5 (122)	-0.0044 (0.0028)	0.113
	Medium	29.9 (251)	27.6 (246)	30.3 (251)		
	High	29.9 (121)	27.5 (120)	30.1 (121)		
b) Maximal (R^2<0.001)	Low	30.5 (169)	27.8 (166)	30.6 (169)	-0.0008 (0.0021)	0.699
	Medium	30.0 (352)	27.8 (345)	30.5 (352)		
	High	29.9 (173)	27.5 (171)	30.0 (173)		

[a]Transformed from natural logarithm scale.

[b]Slope and standard error based on difference between natural logarithm of 1987 T_3 % uptake and natural logarithm of 1982 T_3 % uptake versus log_2 dioxin.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1987 examinations. P-values given are in reference to a contrast of 1982 and 1987 results.

TABLE 15-20. (Continued)
Longitudinal Analysis of T_3 % Uptake
(Continuous)

Ranch Hands - Log_2 (Current Dioxin) and Time

Assumption	Time (Yrs.)	Examination	Mean[a]/(n) Current Dioxin Low	Medium	High	Slope (Std. Error)[b]	p-Value
c) Minimal							0.300[c]
(R^2=0.010)	≤18.6	1982	29.9	29.9	30.1	-0.0006 (0.0045)	0.896[d]
			(67)	(123)	(51)		
		1985	27.5	27.8	27.8		
			(66)	(120)	(50)		
		1987	30.2	30.6	30.5		
			(67)	(123)	(51)		
	>18.6	1982	30.1	29.9	29.8	-0.0067 (0.0037)	0.073[d]
			(55)	(128)	(70)		
		1985	28.2	27.4	27.3		
			(54)	(126)	(70)		
		1987	31.0	30.0	29.9		
			(55)	(128)	(70)		
d) Maximal							0.167[c]
(R^2=0.004)	≤18.6	1982	30.6	29.9	30.1	0.0029 (0.0032)	0.372[d]
			(95)	(182)	(78)		
		1985	27.8	27.8	27.7		
			(92)	(178)	(77)		
		1987	30.7	30.5	30.5		
			(95)	(182)	(78)		
	>18.6	1982	30.4	30.0	30.0	-0.0031 (0.0029)	0.280[d]
			(74)	(169)	(96)		
		1985	27.8	27.8	27.3		
			(73)	(167)	(95)		
		1987	30.6	30.5	29.7		
			(74)	(169)	(96)		

[a]Transformed from natural logarithm scale.

[b]Slope and standard error based on difference between natural logarithm of 1987 T_3 % uptake and natural logarithm of 1982 T_3 % uptake versus log_2 dioxin.

[c]Test of significance for homogeneity of slopes (current dioxin continuous, time categorized).

[d]Test of significance for slope equal to 0 (current dioxin continuous, time categorized).

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1987 examinations. P-values given are in reference to a contrast of 1982 and 1987 results.

TABLE 15-20. (Continued)

Longitudinal Analysis of T_3 % Uptake (Continuous)

e) Ranch Hands and Comparisons by Current Dioxin Category

Current Dioxin Category	Mean[a]/(n) Examination 1982	1985	1987	Contrast	Difference of Examination Mean Change (95% C.I.)[e]	p-Value[f]
Background	30.2 (674)	27.7 (670)	30.6 (674)	All Categories		0.018
Unknown	30.6 (310)	27.9 (304)	30.6 (310)	Unknown vs. Background	-0.3 --	0.036
Low	29.8 (190)	27.6 (187)	30.4 (190)	Low vs. Background	0.2 --	0.291
High	30.0 (174)	27.5 (172)	30.1 (174)	High vs. Background	-0.4 --	0.055
	(R^2=0.007)					

[a]Transformed from natural logarithm scale.

[e]Difference of 1987 and 1982 examination mean changes after transformation to original scale; confidence interval on difference of 1987 and 1982 examination mean changes not given because analysis was performed on natural logarithm scale.

[f]P-value is based on difference of 1987 and 1982 examination mean changes on natural logarithm scale.

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

TABLE 15-21.

Longitudinal Analysis of TSH (Discrete)

Ranch Hands - Log_2 (Initial Dioxin)

Assumption	Initial Dioxin	Percent Abnormal/(n) Examination 1982	1985	1987
a) Minimal	Low	0.0 (122)	0.0 (120)	0.0 (122)
	Medium	1.2 (251)	1.2 (246)	2.4 (251)
	High	0.8 (121)	0.8 (120)	3.3 (121)

Normal in 1982

Initial Dioxin	n in 1987	Percent Abnormal in 1987	Est. Relative Risk (95% C.I.)[a]	p-Value
Low	122	0.0	1.18 (0.63,2.20)	0.613
Medium	248	1.2		
High	120	2.5		

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

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1987 examinations. P-values given are in reference to a contrast of 1982 and 1987 results. Statistical analyses are based only on participants who were normal in 1982 (see Chapter 4, Statistical Methods).

TABLE 15-21. (Continued)

Longitudinal Analysis of TSH (Discrete)

Ranch Hands - Log_2 (Initial Dioxin)

Assumption	Initial Dioxin	Percent Abnormal/(n) Examination 1982	1985	1987
b) Maximal	Low	0.6 (169)	0.0 (166)	3.6 (169)
	Medium	0.9 (352)	0.6 (345)	1.4 (352)
	High	1.2 (173)	1.2 (171)	2.9 (173)

Initial Dioxin	Normal in 1982: n in 1987	Percent Abnormal in 1987	Est. Relative Risk (95% C.I.)[a]	p-Value
Low	168	3.0	0.87 (0.55,1.40)	0.567
Medium	349	0.9		
High	171	1.8		

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

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1987 examinations. P-values given are in reference to a contrast of 1982 and 1987 results. Statistical analyses are based only on participants who were normal in 1982 (see Chapter 4, Statistical Methods).

TABLE 15-21. (Continued)

Longitudinal Analysis of TSH (Discrete)

Ranch Hands - Log_2 (Current Dioxin) and Time

Assumption	Time (Yrs.)	Examination	Percent Abnormal/(n) Current Dioxin Low	Medium	High
c) Minimal	≤18.6	1982	0.0 (68)	1.6 (123)	0.0 (51)
		1985	0.0 (67)	1.7 (120)	0.0 (50)
		1987	0.0 (68)	2.4 (123)	2.0 (51)
	>18.6	1982	0.0 (54)	0.8 (128)	1.4 (70)
		1985	0.0 (53)	0.8 (126)	1.4 (70)
		1987	1.9 (54)	1.6 (128)	4.3 (70)

Time (Yrs.)	Normal in 1982: Percent Abnormal/(n) in 1987 Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
≤18.6	0.0 (68)	0.8 (121)	2.0 (51)	1.31 (0.40,4.30)	0.691[b] 0.652[c]
>18.6	1.9 (54)	0.8 (127)	2.9 (69)	0.98 (0.44,2.18)	0.961[c]

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

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

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

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1987 examinations. P-values given are in reference to a contrast of 1982 and 1987 results. Statistical analyses are based only on participants who were normal in 1982 (see Chapter 4, Statistical Methods).

TABLE 15-21. (Continued)

Longitudinal Analysis of TSH (Discrete)

Ranch Hands - Log_2 (Current Dioxin) and Time

Assumption	Time (Yrs.)	Examination	Percent Abnormal/(n) Current Dioxin Low	Medium	High
d) Maximal	≤18.6	1982	0.0 (95)	0.0 (183)	2.6 (78)
		1985	0.0 (92)	0.0 (179)	2.6 (77)
		1987	2.1 (95)	0.6 (183)	3.9 (78)
	>18.6	1982	2.7 (74)	0.6 (168)	1.0 (96)
		1985	0.0 (73)	0.6 (166)	1.1 (95)
		1987	5.4 (74)	1.8 (168)	3.1 (96)

Time (Yrs.)	Normal in 1982: Percent Abnormal/(n) in 1987 Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
					0.769[b]
≤18.6	2.1 (95)	0.6 (183)	1.3 (76)	0.89 (0.38,2.09)	0.792[c]
>18.6	4.2 (72)	1.2 (167)	2.1 (95)	0.76 (0.41,1.42)	0.387[c]

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

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

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

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1987 examinations. P-values given are in reference to a contrast of 1982 and 1987 results. Statistical analyses are based only on participants who changed status between 1982 and 1987 (see Chapter 4, Statistical Methods).

TABLE 15-21. (Continued)

Longitudinal Analysis of TSH (Discrete)

e) Ranch Hands and Comparisons by Current Dioxin Category

Current Dioxin Category	Percent Abnormal/(n) Examination		
	1982	1985	1987
Background	1.0 (674)	0.6 (670)	2.1 (674)
Unknown	1.0 (310)	0.3 (304)	2.9 (310)
Low	0.5 (190)	0.5 (187)	1.6 (190)
High	1.7 (174)	1.7 (172)	3.5 (174)

Normal in 1982

Current Dioxin Category	n in 1987	Percent Abnormal in 1987	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	667	1.2	All Categories		0.598
Unknown	307	2.3	Unknown vs. Background	1.92 (0.69,5.35)	0.211
Low	189	1.1	Low vs. Background	0.88 (0.19,4.18)	0.873
High	171	1.8	High vs. Background	1.47 (0.39,5.60)	0.572

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

were 10.0 μIU/ml at the 1982 Baseline examination, 7.5 μIU/ml for the 1985 examination, and 3.0 μIU/ml for the 1987 examination.

Model 1: Ranch Hands – Log_2 (Initial Dioxin)

Under the minimal and the maximal assumptions, the longitudinal analysis exhibited a nonsignificant association between initial dioxin and the percentage of Ranch Hands with abnormal TSH levels at the 1987 examination (Table 15-21 [a] and [b]: p=0.613 and p=0.567, respectively).

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

The longitudinal analysis of current dioxin and time since tour and the proportion of Ranch Hands with abnormal TSH levels at the 1987 examination found no significant current dioxin-by-time interaction under either the minimal or the maximal assumption (Table 15-21 [c] and [d]: p=0.691 and p=0.769).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The percentages of participants with abnormal TSH levels at the 1987 followup examination did not differ significantly among the four current dioxin categories (Table 15-21 [e]: p=0.598).

Testosterone (Continuous)

Table 15-22 presents the results of the longitudinal analyses of testosterone (unadjusted for covariate information).

Model 1: Ranch Hands – Log_2 (Initial Dioxin)

The analysis of the change in the testosterone levels of Ranch Hands between the 1982 and 1987 examinations displayed a marginally significant positive association with initial dioxin under both the minimal and the maximal assumptions (Table 15-22 [a] and [b]: p=0.076 and p=0.072, respectively). Thus, the difference in the 1987 examination testosterone level of Ranch Hands relative to the 1982 examination level increased for increasing levels of initial dioxin.

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

Based on the minimal assumption, the longitudinal analysis of the change in testosterone did not find a significant interaction between current dioxin and time since tour (Table 15-22 [c]: p=0.899). However, for Ranch Hands with more than 18.6 years since the end of their tour, there was a significant positive association between their current dioxin levels and the change in their testosterone levels between the 1982 and 1987 examinations (p=0.048).

For the maximal cohort, the interaction between current dioxin and time since tour was not significant (Table 15-22 [d]: p=0.851). The positive association between the change in testosterone levels and current dioxin exposure was marginally significant for Ranch Hands in both time strata (≤18.6 years: p=0.079; >18.6 years: p=0.084).

TABLE 15-22.

Longitudinal Analysis of Testosterone (ng/dl) (Continuous)

Ranch Hands - Log_2 (Initial Dioxin)

Assumption	Initial Dioxin	Mean[a]/(n) Examination 1982	1985	1987	Slope (Std. Error)[b]	p-Value
a) Minimal (R^2=0.006)	Low	645.3 (122)	570.1 (119)	514.3 (122)	0.2211 (0.1241)	0.076
	Medium	624.5 (252)	565.9 (247)	522.5 (252)		
	High	603.6 (125)	598.5 (124)	508.8 (125)		
b) Maximal (R^2=0.005)	Low	647.1 (170)	619.1 (167)	531.9 (170)	0.1618 (0.0898)	0.072
	Medium	631.8 (354)	573.3 (345)	519.1 (354)		
	High	613.2 (179)	585.2 (177)	511.5 (179)		

[a]Transformed from square root scale.

[b]Slope and standard error based on difference between square root of 1987 testosterone and square root of 1982 testosterone versus log_2 dioxin.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1987 examinations. P-values given are in reference to a contrast of 1982 and 1987 results.

TABLE 15-22. (Continued)

Longitudinal Analysis of Testosterone (ng/dl)
(Continuous)

Ranch Hands - Log_2 (Current Dioxin) and Time

Assumption	Time (Yrs.)	Examination	Mean[a]/(n) Current Dioxin Low	Medium	High	Slope (Std. Error)[b]	p-Value
c) Minimal							0.899[c]
(R^2=0.017)	≤18.6	1982	657.7 (68)	616.8 (124)	616.4 (52)	0.2947 (0.2007)	0.143[d]
		1985	559.9 (67)	570.5 (121)	624.9 (51)		
		1987	521.8 (68)	542.1 (124)	516.2 (52)		
	>18.6	1982	620.8 (54)	638.9 (128)	589.4 (73)	0.3277 (0.1650)	0.048[d]
		1985	551.1 (52)	573.5 (126)	582.5 (73)		
		1987	497.0 (54)	505.3 (128)	506.9 (73)		
d) Maximal							0.851[c]
(R^2=0.012)	≤18.6	1982	662.7 (94)	635.1 (183)	608.4 (80)	0.2460 (0.1400)	0.079[d]
		1985	635.2 (91)	576.1 (179)	592.1 (79)		
		1987	544.4 (94)	531.2 (183)	525.0 (80)		
	>18.6	1982	627.0 (76)	636.7 (170)	603.7 (100)	0.2111 (0.1220)	0.084[d]
		1985	593.5 (74)	576.1 (167)	575.1 (99)		
		1987	506.9 (76)	507.1 (170)	506.7 (100)		

[a]Transformed from square root scale.

[b]Slope and standard error based on difference between square root of 1987 testosterone and square root of 1982 testosterone versus log_2 dioxin.

[c]Test of significance for homogeneity of slopes (current dioxin continuous, time categorized).

[d]Test of significance for slope equal to 0 (current dioxin continuous, time categorized).

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1987 examinations. P-values given are in reference to a contrast of 1982 and 1987 results.

TABLE 15-22. (Continued)

Longitudinal Analysis of Testosterone (ng/dl) (Continuous)

e) Ranch Hands and Comparisons by Current Dioxin Category

Current Dioxin Category	Mean[a]/(n) Examination 1982	1985	1987	Contrast	Difference of Examination Mean Change (95% C.I.)[e]	p-Value[f]
Background	619.0 (685)	574.0 (679)	520.2 (685)	All Categories		0.641
Unknown	663.3 (315)	632.6 (308)	551.5 (315)	Unknown vs. Background	-13.0 --	0.335
Low	628.1 (189)	582.9 (186)	525.8 (189)	Low vs. Background	-3.5 --	0.811
High	605.8 (180)	582.6 (178)	514.8 (180)	High vs. Background	7.8 --	0.560
	(R^2=0.001)					

[a]Transformed from square root scale.

[e]Difference of 1987 and 1982 examination mean changes after transformation to original scale; confidence interval on difference of 1987 and 1982 examination mean changes not given because analysis was performed on square root scale.

[f]P-value is based on difference of 1987 and 1982 examination mean changes on square root scale.

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

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The change in testosterone levels between the 1982 and 1987 examinations did not differ significantly among participants in the four current dioxin categories (Table 15-22 [e]: p=0.641).

DISCUSSION

The historical, physical examination, and laboratory data analyzed in the current assessment provide a valid reflection of thyroid, gonadal, and glucoregulatory pancreatic functions by simple indices that are well established in clinical practice. Additional physical findings—percent body fat, ocular/funduscopic, integumentary, and deep tendon reflexes—were relevant to the clinical evaluation of endocrine function (4). These variables are discussed in other chapters of the current report.

Of the two thyroid laboratory variables examined, the T_3 % uptake, though less sensitive than the serum TSH, assumes importance as the only index common to all three physical examination cycles of the Air Force Health Study. In lacking a lower limit of normal, the radioimmunoassay technique of serum TSH determination employed in the current study may not be sensitive to hyperthyroid states. As a test used in the last two examination cycles, however, it serves as a valid index for contrasting the Ranch Hand and Comparison cohorts over time.

Several of the variables analyzed revealed statistically significant effects related to the body burden of dioxin, though in most instances the clinical significance is limited or uncertain. Dimensional criteria are available to assess testicular size, but rarely are used in practice. At the 1987 physical examination, the determination of testicular abnormality involved subjective judgement on the part of each examiner in distinguishing between normal/small and abnormal/atrophic; there was no attempt to account for prior testicular trauma or infection (e.g., mumps). Analyses were done that showed no statistical difference among examiners in their testicular evaluations (the percentages of abnormalities indicated by the five examiners were 1.8 percent [7/395], 3.9 percent [17/439], 2.9 percent [12/412], 0 percent [0/3], and 3.6 percent [15/421]). On the physical examination, unilateral atrophy of a testicle was noted as a relatively common finding. There were 9 assayed participants with a bilateral testicular abnormality, 16 with a left testicular abnormality, and 26 with a right testicular abnormality.

Because of the wide variation in testicular size in the normal population, the determination of serum testosterone must be considered a more reliable index than palpation of the testes. Although the prevalence of testes abnormalities was associated significantly with both initial and current dioxin, the discrete analyses of testosterone did not find a significant association between dioxin and abnormally low levels of serum testosterone. However, for the continuous analyses of testosterone, a significant decrease was noted in association with increasing initial serum dioxin levels when percent body fat was excluded from the model. Categorizing initial dioxin, the differences between the mean serum testosterone for the low, medium, and high categories (559.9, 544.3, and 508.5 ng/dl) are not considered clinically relevant.

In the analysis of thyroid function, slight differences were found in the serum TSH and T_3 % uptake indices consistent with a dose response effect for initial or categorized current

dioxin. A slightly higher mean serum TSH was noted in the high versus background current dioxin categories (1.026 μIU/ml versus 0.920 μIU/ml) and a slightly lower mean T_3 % uptake in the high versus background groups (29.99 percent versus 30.65 percent). Though these results are internally consistent with subtle decreases in thyroid function related to dioxin exposure, they cannot be considered physiologically significant. Further, by discrete analysis of the thyroid indices, there were no detectable differences in thyroid function related to dioxin.

Analysis of the indices of glucose metabolism revealed a statistically significant association between 2-hour postprandial glucose and initial dioxin. The mean levels for the low, medium, and high initial dioxin categories (108.0, 111.6, and 115.8 mg/dl) were well within normal limits. Though a difference of 7.8 mg/dl between the high and low categories is not considered clinically significant, the data are consistent with a dose-response effect. Further, because the differences were more pronounced in those participants further removed from service in Southeast Asia (>18.6 years), the possibility of a temporal effect is raised. The analyses of fasting glucose were also significant. Ranch Hand participants with the highest levels of serum dioxin were nearly three times as likely to have elevated fasting blood sugars as Comparisons. More important, perhaps, is the significant association between dioxin and the incidence of overt diabetes by verified history or by a 2-hour postprandial blood sugar of more than 200 mg/dl. The apparent association of glucose intolerance with the body burden of dioxin has been noted in a previous study, although the mechanism has not been defined (21). Under the maximal assumption, more than a threefold increase in the incidence of diabetes was found in the high versus the low initial dioxin categories (16.7% versus 5.4%).

SUMMARY

Table 15-23 summarizes the results of the initial dioxin analyses for the 10 variables examined in 1987 to assess the endocrine system. Table 15-24 presents the results for the current dioxin and time since tour analyses, and Table 15-25 displays the results of the categorized current dioxin analyses.

Questionnaire Variables

Two variables were constructed from the review of systems and the health interval questionnaire to determine the status of each participant's thyroid. For all three sets of analyses, there was no evidence of a dioxin association with either the response to current thyroid function or with the verified response to a history of thyroid disease.

Physical Examination Variables

The thyroid gland and the testes were evaluated at the physical examination. None of the results for the thyroid gland analyses was significant. Several of the testes analyses displayed significant associations between dioxin and unilateral atrophy of a testicle, although the number of study participants with bilateral atrophy or absence was equivalent between the total Ranch Hand and Comparison groups (nine in each group).

The adjusted initial dioxin analyses found a significant increased risk of testes abnormalities under both the minimal and maximal assumptions. The association between current dioxin and abnormal testes did not significantly differ between time since tour strata, but the adjusted relative risk was significant for Ranch Hands with a later tour under both

TABLE 15-23.

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

	Unadjusted		Adjusted	
Variable	Minimal	Maximal	Minimal	Maximal
Questionnaire				
Current Thyroid Function (Self-Administered) (D)	ns	ns	ns	ns
History of Thyroid Disease (Interviewer-Administered) (D)	NS	NS	NS	NS
Physical Examination				
Thyroid Gland (D)	ns	NS	ns	NS
Testes (D)	NS	NS*	+0.017	+0.003
Laboratory				
T_3 % Uptake (C)	-0.042	-0.002	-0.034	-0.003
T_3 % Uptake (D)	ns	ns	ns	ns
TSH (C)	ns	ns	ns	NS
TSH (D)	NS	NS	NS	NS
FSH (C)	ns	ns	NS	NS
FSH (D)	NS	NS	NS	NS
Testosterone[a] (C)	ns	ns	** (ns)	** (ns)
Testosterone[a,b] (C)	--	--	** (-0.023)	** (-<0.001)
Testosterone (D)	ns	NS	ns	NS
Fasting Glucose (C)	+0.027	+<0.001	+<0.001	+<0.001
Fasting Glucose (D)	+0.022	+<0.001	+<0.001	+<0.001
2-Hour Postprandial Glucose (C)	NS	+0.021	** (NS)	NS
2-Hour Postprandial Glucose[b] (C)	--	--	+0.020	+0.003
2-Hour Postprandial Glucose (D)	NS	NS	NS	NS
Composite Diabetes Indicator (C)	+0.023	+<0.001	+0.001	+<0.001

[a]Negative slope considered adverse for this variable.

[b]Adjusted results from models without percent body fat presented for this variable; see Appendix Table N-2 for a detailed description of these analyses.

C: Continuous analysis.

D: Discrete analysis.

+: Relative risk 1.00 or greater for discrete analysis; slope nonnegative for continuous analysis.

-: Slope negative.

--: Not applicable.

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

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

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

** (...): Log_2 (initial dioxin)-by-covariate interaction ($p\leq0.05$); significant when interaction is deleted and p-value is given in parentheses; refer to Appendix Table N-1 for a detailed description of this interaction.

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

Table N-2 contains detailed analyses for models without percent body fat.

A capital "NS" denotes relative risk 1.00 or greater for discrete analysis or slope nonnegative for continuous analysis; a lowercase "ns" denotes relative risk less than 1.00 for discrete analysis or slope negative for continuous analysis; a capital "NS" for FSH and 2-hour postprandial glucose does not imply directionality due to log-linear analysis.

TABLE 15-24.

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

	Unadjusted					
	Minimal			Maximal		
Variable	C*T	≤18.6	>18.6	C*T	≤18.6	>18.6
Questionnaire						
Current Thyroid Function (Self-Administered) (D)	NS	ns	NS	ns	ns	ns
History of Thyroid Disease (Interviewer-Administered) (D)	NS	ns	NS	ns	ns	ns
Physical Examination						
Thyroid Gland (D)	NS	ns	ns	NS	NS	NS
Testes (D)	ns	NS	NS	ns	NS	NS
Laboratory						
T_3 % Uptake (C)	ns*	NS	-0.016	ns	ns	-0.003
T_3 % Uptake (D)	ns	ns	ns	ns	ns	ns
TSH (C)	ns	NS	ns	ns	ns	ns
TSH (D)	ns	NS	NS	ns	NS	ns
FSH (C)	NS*	-0.014	ns	+0.014	-0.007	NS
FSH (D)	NS	NS	NS	NS*	NS	NS
Testosterone[a] (C)	NS	ns	NS	NS	ns	NS
Testosterone (D)	ns	ns	ns	ns	NS	ns
Fasting Glucose (C)	NS*	ns	+0.009	NS	NS	+0.002
Fasting Glucose (D)	NS	NS	+0.023	NS	NS	+0.006
2-Hour Postprandial Glucose (C)	ns	NS	NS	NS	NS	NS*
2-Hour Postprandial Glucose (D)	NS	NS	NS	NS	NS	NS
Composite Diabetes Indicator (D)	NS	NS	+0.047	ns	+0.027	+0.040

[a]Negative slope considered adverse for this variable.
C: Continuous analysis.
D: Discrete analysis.
+: C*T: Relative risk/slope for ≤18.6 category less than relative risk/slope for >18.6 category.
≤18.6 and >18.6: Relative risk 1.00 or greater for discrete analysis; slope nonnegative for continuous analysis.
-: ≤18.6 and >18.6: Slope negative.
NS/ns: Not significant ($p>0.10$).
NS*/ns*: Marginally significant ($0.05<p\leq0.10$).
Note: P-value given if $p\leq0.05$.
C*T: Log_2 (current dioxin)-by-time interaction hypothesis test.
≤18.6: Log_2 (current dioxin) hypothesis test for Ranch Hands with time since end of tour of 18.6 years or less.
>18.6: Log_2 (current dioxin) hypothesis test for Ranch Hands with time since end of tour greater than 18.6 years.
A capital "NS" denotes relative risk/slope for ≤18.6 category less than relative risk/slope for >18.6 category, relative risk 1.00 or greater for discrete analysis, or slope nonnegative for continuous analysis; a lowercase "ns" denotes relative risk/slope for ≤18.6 category greater than relative risk/slope for >18.6 category, relative risk less than 1.00 for discrete analysis, or slope negative for continuous analysis; a capital "NS" for FSH and 2-hour postprandial glucose does not imply directionality due to log-linear analysis.

TABLE 15-24. (Continued)

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

	Adjusted					
	Minimal			Maximal		
Variable	C*T	≤18.6	>18.6	C*T	≤18.6	>18.6
Questionnaire						
Current Thyroid Function (Self-Administered) (D)	NS	ns	NS	ns	ns	ns
History of Thyroid Disease (Interviewer-Administered) (D)	NS	ns	NS	ns	ns	ns
Physical Examination						
Thyroid Gland (D)	NS	ns	ns	NS	NS	NS
Testes (D)	ns	+0.006	NS	ns	+0.007	NS*
Laboratory						
T_3 % Uptake (C)	-0.015	NS	-0.004	ns*	ns	-0.002
T_3 % Uptake (D)	ns	ns	ns	ns	ns	ns
TSH (C)	ns	NS	ns	ns	NS	ns
TSH (D)	ns	NS	NS	** (ns)	** (NS)	** (ns)
FSH (C)	NS*	ns	NS	+0.011	ns	+0.015
FSH (D)	NS	NS	NS	0.047	NS	NS
Testosterone[a] (C)	NS	ns	ns	NS	ns	ns
Testosterone[a,b] (C)	NS	ns*	ns	NS	-0.012	ns*
Testosterone (D)	NS	ns	ns	ns	NS	ns
Fasting Glucose (C)	NS*	NS	+<0.001	**(NS)	**(+0.024)	**(+<0.001)
Fasting Glucose (D)	NS	NS	+<0.001	**(NS)	**(+0.007)	**(+<0.001)
2-Hour Postprandial Glucose (C)	** (ns)	** (NS)	** (NS)	NS	NS	NS*
2-Hour Postprandial Glucose[b] (C)	**(ns)	**(NS*)	**(NS)	NS	NS	+0.009
2-Hour Postprandial Glucose (D)	NS	NS	NS	NS	NS	NS
Composite Diabetes Indicator (D)	NS	NS*	+0.002	ns	+0.002	+0.002

[a]Negative slope considered adverse for this variable.

[b]Adjusted results from models without percent body fat presented for this variable; see Appendix Table N-2 for a detailed description of these analyses.

C: Continuous analysis.

D: Discrete analysis.

+: C*T: Slope for ≤18.6 category less than slope for >18.6 category.

≤18.6 and >18.6: Relative risk 1.00 or greater for discrete analysis; slope nonnegative for continuous analysis.

-: C*T: Slope for ≤18.6 category greater than slope for >18.6 category.

≤18.6 and >18.6: Relative risk less than 1.00 for discrete analysis; slope negative for continuous analysis.

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

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

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

**(NS*): Log_2 (current dioxin)-by-time-by-covariate interaction ($p\leq0.05$); marginally significant when interaction is deleted; refer to Appendix Table N-1 for a detailed description of this interaction.

**(...): Log_2 (current dioxin)-by-time-by-covariate interaction ($0.05<p\leq0.10$); significant when interaction is deleted and p-value is given in parentheses; refer to Appendix Table N-1 for a detailed description of this interaction.

TABLE 15-24. (Continued)

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

Note: P-value given if $p \leq 0.05$.
Appendix Table N-2 contains detailed analyses for models without percent body fat.
C*T: Log_2 (current dioxin)-by-time interaction hypothesis test.
≤18.6: Log_2 (current dioxin) hypothesis test for Ranch Hands with time since end of tour of 18.6 years or less.
>18.6: Log_2 (current dioxin) hypothesis test for Ranch Hands with time since end of tour greater than 18.6 years.
A capital "NS" denotes relative risk/slope for ≤18.6 category less than relative risk/slope for >18.6 category, relative risk 1.00 or greater for discrete analysis, or slope nonnegative for continuous analysis; a lowercase "ns" denotes relative risk/slope for ≤18.6 category greater than relative risk/slope for >18.6 category, relative risk less than 1.00 for discrete analysis, or slope negative for continuous analysis; a capital "NS" for FSH and 2-hour postprandial glucose does not imply directionality due to log-linear analysis.

TABLE 15-25.

Summary of Catgeorized Current Dioxin Analyses for Endocrine Variables (Ranch Hands and Comparisons)

		Unadjusted		
Variable	All	Unknown versus Background	Low versus Background	High versus Background
Questionnaire				
Current Thyroid Function (Self-Administered) (D)	NS	NS	ns	ns
History of Thyroid Disease (Interviewer-Administered) (D)	NS	NS	ns	ns
Physical Examination				
Thyroid Gland (D)	NS	ns	NS	ns
Testes (D)	NS	ns	ns	NS
Laboratory				
T_3 % Uptake (C)	0.010	NS	ns	-0.002
T_3 % Uptake (D)	NS	NS	ns	ns
TSH (C)	NS	NS	NS	NS
TSH (D)	NS	NS	ns	NS
FSH (C)	NS	NS	NS	ns
FSH[a] (D)	NS	NS	NS	NS
FSH[b] (D)		NS	NS	NS
Testosterone[c] (C)	0.016	+0.005	NS	ns
Testosterone (D)	NS	ns	ns	NS
Fasting Glucose (C)	<0.001	ns	NS	+<0.001
Fasting Glucose (D)	0.001	ns*	NS	+0.002
2-Hour Postprandial Glucose (C)	NS*	-0.049	ns	NS
2-Hour Postprandial Glucose[d] (D)	NS	ns	NS	NS
2-Hour Postprandial Glucose[e] (D)		ns	ns	NS*
Composite Diabetes Indicator (D)	<0.001	ns	NS	+0.001

[a]Low FSH contrasted with normal FSH for last three columns.

[b]High FSH contrasted with normal FSH for last three columns.

[c]Negative difference considered adverse for this variable.

[d]Impaired contrasted with normal for last three columns.

[e]Diabetic contrasted with normal for last three columns.

C: Continuous analysis.

D: Discrete analysis.

+: Relative risk 1.00 or greater for discrete analysis; difference in means nonnegative for continuous analysis.

-: Difference in means negative.

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

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

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

A capital "NS" denotes relative risk 1.00 or greater for discrete analysis or difference of means nonnegative for continuous analysis; a lowercase "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis; a capital "NS" in the first column does not imply directionality.