TABLE 10-25. (Continued)

Analysis of Direct Bilirubin (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						0.961[b]
(n=517)	≤18.6	6.9 (72)	4.0 (126)	1.9 (53)	0.67 (0.34,1.33)	0.255[c]
	>18.6	5.2 (58)	4.6 (131)	1.3 (77)	0.69 (0.37,1.27)	0.233[c]
f) Maximal						0.893[b]
(n=737)	≤18.6	1.9 (105)	4.2 (189)	4.9 (82)	0.93 (0.59,1.45)	0.748[c]
	>18.6	2.5 (79)	5.1 (178)	1.0 (104)	0.89 (0.58,1.37)	0.595[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			0.980**[b]	CURR*TIME*DC (p=0.040)
(n=517)	≤18.6	0.74 (0.37,1.47)**	0.388**[c]	
	>18.6	0.75 (0.41,1.38)**	0.351**[c]	
h) Maximal			0.656[b]	RACE (p=0.102)
(n=737)	≤18.6	1.02 (0.64,1.61)	0.936[c]	IC (p=0.052)
	>18.6	0.88 (0.56,1.39)	0.586[c]	DC (p=0.003)

[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 10-25. (Continued)

Analysis of Direct Bilirubin (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	3.9	All Categories		0.500
Unknown	341	2.3	Unknown vs. Background	0.60 (0.27,1.32)	0.205
Low	193	4.1	Low vs. Background	1.08 (0.49,2.39)	0.850
High	186	2.7	High vs. Background	0.69 (0.26,1.80)	0.448
Total	1,499				

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

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	779	All Categories		0.461	AGE*DC (p=0.039)
Unknown	341	Unknown vs. Background	0.61 (0.28,1.35)	0.224	
Low	193	Low vs. Background	1.06 (0.47,2.36)	0.891	
High	186	High vs. Background	0.61 (0.23,1.61)	0.317	
Total	1,499				

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

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

Both the unadjusted and adjusted categorized current dioxin analyses did not find a significant difference in the prevalence of abnormally high direct bilirubin levels among the four current dioxin categories (Table 10-25 [i] and [j]: $p>0.20$ for all contrasts).

LDH (Continuous)

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

For both cohorts, the unadjusted and adjusted analyses did not show a significant association between LDH and initial dioxin (Table 10-26 [a-d]: $p>0.50$ for all analyses).

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 for either the unadjusted or adjusted analyses of LDH (Table 10-26 [e-h]: $p>0.25$ for each analysis).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The mean levels of LDH did not differ significantly among the four current dioxin categories for both the unadjusted (Table 10-26 [i]: $p=0.751$) and adjusted (Table 10-26 [j]: $p=0.725$) analyses.

LDH (Discrete)

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

There were only two abnormally high levels of LDH in the minimal cohort and five for the maximal cohort. The unadjusted initial dioxin analysis was not significant under the minimal assumption (Table 10-27 [a]: $p=0.470$), but the estimated relative risk of an abnormal level of LDH was marginally less than 1 under the maximal assumption (Table 10-27 [b]: Est. RR=0.47, $p=0.083$). No adjusted analyses were done because there were so few abnormalities.

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 evaluated because only one Ranch Hand with an early tour had an abnormal level of LDH. Also, only one Ranch Hand with a later tour had an abnormality under the minimal assumption. The association between current dioxin and discretized LDH was not significant for Ranch Hands with a later tour in the unadjusted maximal analysis (Table 10-27 [d]: $p=0.116$). No adjusted analyses were done because the abnormal data were sparse.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The prevalence of abnormally high levels did not differ significantly among current dioxin categories for the unadjusted analysis (Table 10-27 [e]: 1.5%, 1.5%, 0.0%, and 0.5% for the background, unknown, low, and high current dioxin categories, $p=0.262$). No adjusted analysis was done because there were few abnormalities.

TABLE 10-26.

Analysis of LDH (U/L)
(Continuous)

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Mean[a]	Slope (Std. Error)[b]	p-Value
a) Minimal	Low	130	130.0	-0.0031 (0.0058)	0.599
(n=517)	Medium	257	128.3		
(R^2<0.001)	High	130	128.7		
b) Maximal	Low	184	127.6	0.0003 (0.0042)	0.935
(n=737)	Medium	368	129.1		
(R^2<0.001)	High	185	128.4		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Initial Dioxin	n	Adj. Mean[a]	Adj. Slope (Std. Error)[b]	p-Value	Covariate Remarks
c) Minimal	Low	130	130.0	-0.0024 (0.0059)	0.687	RACE*ALC (p=0.007)
(n=514)	Medium	255	129.0			RACE*IC (p=0.029)
(R^2=0.031)	High	129	129.2			
d) Maximal	Low	184	125.6	0.0008 (0.0044)	0.864	IC (p=0.118)
(n=737)	Medium	368	126.6			AGE*RACE (p=0.016)
(R^2=0.023)	High	185	126.3			RACE*DC (p=0.030)

[a]Transformed from natural logarithm scale.

[b]Slope and standard error based on natural logarithm LDH 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 10-26. (Continued)

Analysis of LDH (U/L)
(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						0.252[c]
(n=517)	≤18.6	130.9	126.2	126.5	-0.0141 (0.0095)	0.139[d]
(R^2=0.008)		(72)	(126)	(53)		
	>18.6	130.7	130.0	129.6	-0.0000 (0.0078)	0.999[d]
		(58)	(131)	(77)		
f) Maximal						0.611[c]
(n=737)	≤18.6	126.2	128.2	126.0	-0.0047 (0.0066)	0.473[d]
(R^2=0.006)		(105)	(189)	(82)		
	>18.6	130.0	129.8	130.6	-0.0003 (0.0058)	0.963[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						0.255[c]	RACE*ALC (p=0.007)
(n=514)	≤18.6	130.6	126.2	126.0	-0.0141 (0.0095)	0.140[d]	RACE*IC (p=0.027)
(R^2=0.040)		(72)	(126)	(52)			
	>18.6	130.7	130.4	129.9	-0.0002 (0.0078)	0.982[d]	
		(58)	(129)	(77)			
h) Maximal						0.677[c]	IC (p=0.094)
(n=737)	≤18.6	124.2	125.6	124.3	-0.0045 (0.0068)	0.510[d]	AGE*RACE (p=0.017)
(R^2=0.028)		(105)	(189)	(82)			RACE*DC (p=0.033)
	>18.6	127.9	127.5	128.0	-0.0008 (0.0060)	0.889[d]	
		(79)	(178)	(104)			

[a]Transformed from natural logarithm scale.

[b]Slope and standard error based on natural logarithm LDH 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).

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 10-26. (Continued)

Analysis of LDH (U/L)
(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	127.9	All Categories		0.751
Unknown	341	126.7	Unknown vs. Background	-1.2 --	0.361
Low	193	127.6	Low vs. Background	-0.3 --	0.821
High	186	128.6	High vs. Background	0.7 --	0.715
Total	1,499		(R^2<0.001)		

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

Current Dioxin Category	n	Adj. Mean[a]	Contrast	Difference of Adj. Means (95% C.I.)[e]	p-Value[f]	Covariate Remarks
Background	779	130.3	All Categories		0.725	AGE (p=0.007)
Unknown	341	129.2	Unknown vs. Background	-1.1 --	0.450	RACE (p=0.019)
Low	193	129.8	Low vs. Background	-0.5 --	0.794	DC (p=0.080)
High	186	131.4	High vs. Background	1.1 --	0.518	
Total	1,499		(R^2=0.010)			

[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.

TABLE 10-27.

Analysis of LDH (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	0.8	0.60 (0.13,2.77)	0.470
	Medium	257	0.4		
	High	130	0.0		
b) Maximal (n=737)	Low	184	1.6	0.47 (0.18,1.28)	0.083
	Medium	368	0.3		
	High	185	0.5		

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

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

TABLE 10-27. (Continued)

Analysis of LDH
(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
c) Minimal						--
(n=517)	≤18.6	1.4 (72)	0.0 (126)	0.0 (53)	--	--
	>18.6	0.0 (58)	0.8 (131)	0.0 (77)	--	--
d) Maximal						--
(n=737)	≤18.6	2.9 (105)	0.5 (189)	0.0 (82)	0.27 (0.05,1.38)	0.116[b]
	>18.6	0.0 (79)	0.0 (178)	1.0 (104)	--	--

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

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

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

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

TABLE 10-27. (Continued)

Analysis of LDH
(Discrete)

e) 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	1.5	All Categories		0.262
Unknown	341	1.5	Unknown vs. Background	0.95 (0.33,2.72)	0.999
Low	193	0.0	Low vs. Background	--	0.138
High	186	0.5	High vs. Background	0.35 (0.05,2.67)	0.504
Total	1,499				

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

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

Cholesterol (Continuous)

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Under both the minimal and maximal assumptions, the unadjusted initial dioxin analyses did not find a significant association with cholesterol in its continuous form (Table 10-28 [a] and [b]: p=0.175 and p=0.179, respectively). However, a significant positive slope was noted under both assumptions after covariate adjustment (Table 10-28 [c] and [d]: p=0.046 and p=0.041 for the minimal and maximal assumptions). The minimal analysis was adjusted for age, current alcohol use, and the degreasing chemical-by-industrial chemical use interaction. Current alcohol use and the age-by-race interaction were used for adjustment in the maximal analysis. Under the minimal assumption, the adjusted mean levels of cholesterol were 213.0, 214.4, and 218.8 mg/dl for the low, medium, and high initial dioxin categories. The corresponding means for the maximal cohort were 210.8, 211.1, and 216.0 mg/dl.

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

Under the minimal assumption, the unadjusted current dioxin and time since tour analysis for cholesterol detected a marginally significant interaction between current dioxin and time (Table 10-28 [e]: p=0.069). The association between current dioxin and cholesterol was significantly positive for Ranch Hands with an early tour in contrast to a nonsignificant negative association for Ranch Hands with a later tour (time>18.6: Adj. slope=0.0195, p=0.024; time≤18.6: Adj. slope=-0.0053, p=0.612). For Ranch Hands with an early tour, the mean levels of cholesterol were 210.3, 216.2, and 221.4 mg/dl for the low, medium, and high current dioxin categories. The unadjusted analysis for the maximal cohort did not find a significant current dioxin-by-time interaction (Table 10-28 [f]: p=0.335).

After covariate adjustment, the current dioxin-by-time interaction became significant for the minimal cohort (Table 10-28 [g]: p=0.049), with the association between current dioxin and cholesterol remaining significant for Ranch Hands with an early tour (time>18.6: Adj. slope=0.0277, p=0.002; Adj. means: 205.6, 213.7, and 221.5 mg/dl for the low, medium, and high current dioxin categories). The association between current dioxin and cholesterol was not significant for Ranch Hands with a later tour (time≤18.6: Adj. slope=0.0011, p=0.921).

The adjusted maximal analysis detected a significant current dioxin-by-time-by-lifetime alcohol history interaction (Table 10-28 [h]: p=0.034). The lifetime alcohol history covariate was trichotomized (0 drink-years, >0-40 drink-years, >40 drink-years) to explore the interaction. Appendix Table I-1 shows that the current dioxin-by-time interaction was not significant for each lifetime alcohol history stratum (0 drink-years: p=0.952; >0-40 drink-years: p=0.916; >40 drink-years: p=0.152). The association between current dioxin and cholesterol was not significant within each time stratum, except for a marginally significant positive finding for heavy lifetime drinkers who had an early tour (>40 drink-years, time>18.6: p=0.059). The current dioxin-by-time interaction was not significant (Table 10-28 [h]: p=0.415) after excluding the current dioxin-by-time-by-lifetime alcohol history interaction. The association between current dioxin and cholesterol was significant for Ranch Hands with an early tour (time>18.6: p=0.030).

TABLE 10-28.

Analysis of Cholesterol (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	215.7	0.0088 (0.0065)	0.175
(n=517)	Medium	257	215.9		
(R^2=0.004)	High	130	218.1		
b) Maximal	Low	184	215.2	0.0066 (0.0049)	0.179
(n=737)	Medium	368	215.5		
(R^2=0.002)	High	185	217.9		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Initial Dioxin	n	Adj. Mean[a]	Adj. Slope (Std. Error)[b]	p-Value	Covariate Remarks
c) Minimal	Low	130	213.0	0.0133 (0.0066)	0.046	AGE (p=0.007)
(n=514)	Medium	255	214.4			ALC (p=0.016)
(R^2=0.041)	High	129	218.8			DC*IC (p=0.049)
d) Maximal	Low	183	210.8	0.0102 (0.0050)	0.041	ALC (p=0.006)
(n=732)	Medium	365	211.1			AGE*RACE (p=0.035)
(R^2=0.030)	High	184	216.0			

[a]Transformed from natural logarithm scale.

[b]Slope and standard error based on natural logarithm cholesterol 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 10-28. (Continued)

Analysis of Cholesterol (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						0.069[c]
(n=517)	≤18.6	216.6	218.4	211.4	-0.0053 (0.0105)	0.612[d]
(R^2=0.010)		(72)	(126)	(53)		
	>18.6	210.3	216.2	221.4	0.0195 (0.0086)	0.024[d]
		(58)	(131)	(77)		
f) Maximal						0.335[c]
(n=737)	≤18.6	213.1	216.7	215.8	0.0007 (0.0076)	0.931[d]
(R^2=0.003)		(105)	(189)	(82)		
	>18.6	217.6	213.5	221.0	0.0104 (0.0067)	0.120[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						0.049[c]	AGE (p=0.004)
(n=514)	≤18.6	214.3	218.4	213.2	0.0011 (0.0108)	0.921[d]	ALC (p=0.013)
(R^2=0.053)		(72)	(126)	(52)			DC*IC (p=0.028)
	>18.6	205.6	213.7	221.5	0.0277 (0.0088)	0.002[d]	
		(58)	(129)	(77)			
h) Maximal						0.415**[c]	CURR*TIME*DRKYR
(n=728)	≤18.6	208.7**	213.2**	215.5**	0.0065 (0.0077)**	0.398**[d]	(p=0.034)
(R^2=0.040)		(104)	(188)	(80)			ALC (p=0.018)
	>18.6	212.5**	208.3**	218.5**	0.0147 (0.0068)**	0.030**[d]	AGE*RACE (p=0.033)
		(78)	(176)	(102)			

[a]Transformed from natural logarithm scale.

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

[c]Test of significance for homogeneity of relative risks (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 10-28. (Continued)

Analysis of Cholesterol (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	213.3	All Categories		0.386
Unknown	341	214.3	Unknown vs. Background	1.0 --	0.669
Low	193	215.0	Low vs. Background	1.7 --	0.570
High	186	218.7	High vs. Background	5.4 --	0.085
Total	1,499		(R^2=0.002)		

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	212.9	All Categories		0.229	ALC (p=0.029)
						IC (p=0.099)
Unknown	338	214.1	Unknown vs. Background	1.2 --	0.612	AGE*DRKYR
Low	191	214.5	Low vs. Background	1.6 --	0.608	(p=0.022)
High	182	219.5	High vs. Background	6.6 --	0.038	
Total	1,488		(R^2=0.020)			

[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.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The unadjusted analysis of categorized current dioxin found that the mean cholesterol for the high current dioxin category was marginally more than the background mean (Table 10-28 [i]: 218.7 mg/dl versus 213.3 mg/dl, p=0.085), although the overall contrast was not significant (p=0.386). After covariate adjustment, the high versus background contrast became significant (Table 10-28 [j]: 219.5 mg/dl versus 212.9 mg/dl, p=0.038), and the overall category contrast remained nonsignificant (p=0.229). The unknown versus background and the low versus background contrasts were not significant for either the unadjusted or adjusted analysis (p>0.50 for each contrast).

Cholesterol (Discrete)

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

For both cohorts, the unadjusted and adjusted initial dioxin analyses did not detect a significant relative risk of abnormally high cholesterol levels (Table 10-29 [a-d]: p>0.35 for all analyses).

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

The unadjusted analyses of discretized cholesterol did not find a significant current dioxin-by-time since tour interaction under either the minimal (Table 10-29 [e]: p=0.388) or maximal (Table 10-29 [f]: p=0.837) assumption.

The current dioxin-by-time interaction remained nonsignificant for the maximal cohort (Table 10-29 [h]: p=0.872) after adjustment for age and industrial chemical exposure. However, the adjusted minimal analysis detected a significant current dioxin-by-time-by-industrial chemical exposure interaction (Table 10-29 [g]: p=0.008). Stratified results showed a marginally significant interaction between current dioxin and time for Ranch Hands who had never been exposed to industrial chemicals (Appendix Table I-1: p=0.060), but the association between current dioxin and cholesterol was not significant within each time stratum (time≤18.6: Adj. RR=1.73, p=0.102; time>18.6: Adj. RR= 0.75, p=0.369). The current dioxin-by-time interaction was significant for Ranch Hands who had been exposed to industrial chemicals (p=0.030). The adjusted relative risk of an abnormally high level of cholesterol was marginally less than 1 for these Ranch Hands with a later tour (time≤18.6: Adj. RR=0.67, p=0.083), and it was greater than 1, but not significant, for those with an early tour (time>18.6: Adj. RR=1.22, p=0.261).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In the unadjusted analysis, the percentages of abnormally high levels of cholesterol did not differ significantly among the four current dioxin categories (Table 10-29 [i]: p=0.164), although the prevalence rate was significantly more in the unknown current dioxin category than in the background category (16.1% versus 11.2%, Est. RR=1.53, 95% C.I.: [1.06,2.20], p=0.022). The prevalence rates in the low (13.0%) and high (12.4%) current dioxin categories were not significantly different from the background rate (p=0.487 and p=0.644, respectively). The adjusted analysis displayed similar results. The overall contrast was not significant (Table 10-29 [j]: p=0.141), but the unknown versus background contrast was significant (Adj. RR=1.56, 95% C.I.: [1.08,2.24], p=0.018).

TABLE 10-29.

Analysis of Cholesterol (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	16.2	0.93 (0.75,1.15)	0.472
	Medium	257	14.0		
	High	130	10.8		
b) Maximal (n=737)	Low	184	15.2	0.94 (0.80,1.09)	0.392
	Medium	368	15.5		
	High	185	11.4		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=517)	0.95 (0.76,1.18)	0.625	AGE (p=0.053) IC (p=0.044)
d) Maximal (n=737)	0.94 (0.80,1.11)	0.482	AGE (p=0.033) IC (P=0.110)

[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 10-29. (Continued)

Analysis of Cholesterol (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						0.388[b]
(n=517)	≤18.6	15.3 (72)	15.9 (126)	9.4 (53)	0.83 (0.58,1.19)	0.309[c]
	>18.6	15.5 (58)	13.0 (131)	11.7 (77)	1.01 (0.77,1.34)	0.924[c]
f) Maximal						0.837[b]
(n=737)	≤18.6	15.2 (105)	14.8 (189)	13.4 (82)	0.91 (0.71,1.15)	0.427[c]
	>18.6	15.2 (79)	15.2 (178)	11.5 (104)	0.94 (0.76,1.16)	0.556[c]

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

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal			****	CURR*TIME*IC (p=0.008)
(n=517)	≤18.6	****	****	AGE (p=0.053)
	>18.6	****	****	
h) Maximal			0.872[b]	AGE (p=0.037)
(n=737)	≤18.6	0.93 (0.72,1.19)	0.560[c]	IC (p=0.114)
	>18.6	0.95 (0.76,1.19)	0.672[c]	

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

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

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

****Log_2 (current dioxin)-by-time-by-covariate interaction ($p \leq 0.01$); adjusted relative risk, confidence interval, and p-value not presented.

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

TABLE 10-29. (Continued)

Analysis of Cholesterol (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	11.2	All Categories		0.164
Unknown	341	16.1	Unknown vs. Background	1.53 (1.06,2.20)	0.022
Low	193	13.0	Low vs. Background	1.18 (0.74,1.90)	0.487
High	186	12.4	High vs. Background	1.12 (0.69,1.83)	0.644
Total	1,499				

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

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	779	All Categories		0.141	ALC (p=0.053)
Unknown	339	Unknown vs. Background	1.56 (1.08,2.24)	0.018	
Low	191	Low vs. Background	1.16 (0.72,1.88)	0.545	
High	185	High vs. Background	1.13 (0.69,1.84)	0.629	
Total	1,494				

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.

HDL (Continuous)

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

The unadjusted initial dioxin analyses did not find a significant association with HDL under the minimal assumption (Table 10-30 [a]: p=0.169), but the association was significantly negative under the maximal assumption (Table 10-30 [b]: p<0.001). For the maximal cohort, the unadjusted mean levels of HDL decreased with initial dioxin (47.56, 44.39, and 43.31 mg/dl for the low, medium, and high initial dioxin categories).

The association between HDL and initial dioxin remained nonsignificant for the adjusted minimal analysis (Table 10-30 [c]: p=0.218). The adjusted analysis for the maximal cohort detected a significant interaction between initial dioxin and degreasing chemical exposure (Table 10-30 [d]: p=0.006). Stratified results showed a highly significant negative association between initial dioxin and HDL for Ranch Hands who had never been exposed to degreasing chemicals (Appendix Table I-1, p<0.001). The adjusted mean levels of HDL for the low, medium, and high initial dioxin categories in this stratum were 51.55, 45.34, and 44.65 mg/dl. The association between initial dioxin and HDL was negative, but not significant, for Ranch Hands who had been exposed to degreasing chemicals (p=0.200, Adj. means: 45.69, 44.80, and 44.12 for the low, medium, and high initial dioxin categories). After deleting the interaction, the adjusted maximal analysis displayed a highly significant negative association between initial dioxin and HDL (Table 10-30 [d]: p<0.001), supporting the unadjusted analysis.

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

Under both the minimal and maximal assumptions, the unadjusted current dioxin and time since tour analyses of HDL in its continuous form did not find a significant current dioxin-by-time interaction (Table 10-30 [e] and [f]: p=0.920 and p=0.727, respectively). However, under the maximal assumption, the association between current dioxin and HDL was significantly negative within each time stratum (time≤18.6: p=0.008; time>18.6: p=0.014). The unadjusted mean levels of HDL decreased with current dioxin in both time strata (time≤18.6: 48.51, 44.60, and 43.65 mg/dl for the low, medium, and high current dioxin categories; time>18.6: 47.58, 43.91, and 42.63 mg/dl for the corresponding categories).

The adjusted minimal analysis detected a significant current dioxin-by-time-by-industrial chemical exposure interaction (Table 10-30 [g]: p=0.026). However, stratified results did not show a significant interaction between current dioxin and time, either for Ranch Hands who had never been exposed to industrial chemicals (Appendix Table I-1: p=0.115) or for Ranch Hands who had been exposed to industrial chemicals (p=0.110). The association between current dioxin and HDL was marginally negative for Ranch Hands with an early tour who had been exposed to industrial chemicals (time>18.6: p=0.065). After excluding the current dioxin-by-time-by-industrial chemical exposure interaction, the adjusted minimal analysis did not find a significant interaction between current dioxin and time (Table 10-30 [g]: p=0.914).

The adjusted maximal analysis supported the unadjusted findings. The current dioxin-by-time interaction was not significant (Table 10-30 [h]: p=0.748), but a significant negative

TABLE 10-30.

Analysis of HDL (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=517) (R^2=0.004)	Low	130	45.42	-0.0126 (0.0091)	0.169
	Medium	257	42.83		
	High	130	44.23		
b) Maximal (n=737) (R^2=0.021)	Low	184	47.56	-0.0266 (0.0067)	<0.001
	Medium	368	44.39		
	High	185	43.31		

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=514) (R^2=0.086)	Low	130	46.16	-0.0115 (0.0093)	0.218	ALC (p<0.001) AGE*RACE (p=0.017) RACE*IC (p=0.044)
	Medium	255	44.04			
	High	129	45.72			
d) Maximal (n=728) (R^2=0.105)	Low	182	48.52***	-0.0231 (0.0069)***	<0.001***	INIT*DC (p=0.006) AGE*RACE (p=0.012) AGE*DC (p=0.010) ALC*DRKYR (p=0.005)
	Medium	365	45.35***			
	High	181	44.86***			

[a]Transformed from natural logarithm scale.

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

***Log_2 (initial dioxin)-by-covariate interaction ($p \leq 0.01$); 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 10-30. (Continued)

Analysis of HDL (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						0.920[c]
(n=517)	≤18.6	45.15	43.63	45.12	-0.0086 (0.0149)	0.566[d]
(R^2=0.004)		(72)	(126)	(53)		
	>18.6	45.24	42.37	43.47	-0.0105 (0.0122)	0.389[d]
		(58)	(131)	(77)		
f) Maximal						0.727[c]
(n=737)	≤18.6	48.51	44.60	43.65	-0.0276 (0.0104)	0.008[d]
(R^2=0.020)		(105)	(189)	(82)		
	>18.6	47.58	43.91	42.63	-0.0227 (0.0092)	0.014[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						0.914**[c]	CURR*TIME*IC
(n=514)	≤18.6	46.13**	45.02**	46.94**	-0.0069 (0.0151)**	0.648**[d]	(p=0.026)
(R^2=0.100)		(72)	(126)	(52)			ALC (p<0.001)
							AGE*RACE (p=0.012)
	>18.6	45.93**	43.66**	45.09**	-0.0090 (0.0123)**	0.466**[d]	RACE*IC (p=0.050)
		(58)	(129)	(77)			
h) Maximal						0.748[c]	DC (p=0.049)
(n=728)	≤18.6	49.29	45.74	45.06	-0.0235 (0.0106)	0.027[d]	AGE*RACE (p=0.021)
(R^2=0.090)		(104)	(188)	(80)			ALC*DRKYR (p=0.012)
	>18.6	48.96	44.73	44.08	-0.0191 (0.0094)	0.042[d]	
		(78)	(176)	(102)			

[a]Transformed from natural logarithm scale.

[b]Slope and standard error based on natural logarithm HDL 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 10-30. (Continued)

Analysis of HDL (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	44.98	All Categories		<0.001
Unknown	341	47.81	Unknown vs. Background	2.83 --	<0.001
Low	193	43.60	Low vs. Background	-1.38 --	0.115
High	186	43.07	High vs. Background	-1.91 --	0.031
Total	1,499		(R^2=0.019)		

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	45.92**	All Categories		<0.001**	DXCAT*DRKYR (p=0.017)
Unknown	338	48.93**	Unknown vs. Background	3.01 -- **	<0.001**	AGE*RACE
Low	191	44.85**	Low vs. Background	-1.07 -- **	0.219**	(p=0.025)
High	182	44.59**	High vs. Background	-1.33 -- **	0.137**	RACE*IC (p=0.023)
Total	1,488		(R^2=0.106)			RACE*DC (p=0.023)
						ALC*DRKYR (p=0.012)

[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 ($0.01<p\leq0.05$); 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.

association between current dioxin and HDL was noted within each time stratum (time≤18.6: p=0.027; time>18.6: p=0.042).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The unadjusted categorized current dioxin analysis found that the mean levels of HDL differed significantly among current dioxin categories (Table 10-30 [i]: 44.98, 47.81, 43.60, and 43.07 mg/dl for the background, unknown, low, and high current dioxin categories, p<0.001). The low current dioxin category mean was significantly more than the background mean (p<0.001), while the high current dioxin category mean was significantly less than the background mean (p=0.031).

The adjusted analysis detected a significant current dioxin-by-lifetime alcohol history interaction (Table 10-30 [j]: p=0.017). To explore the interaction, the lifetime alcohol history covariate was categorized into three levels: never (0 drink-years), moderate (>0-40 drink-years), and heavy (>40 drink-years). The adjusted mean levels of HDL did not differ significantly among current dioxin categories for participants who never had drunk alcohol (Appendix Table I-1: 43.77, 45.01, 46.00, and 46.62 mg/dl for the background, unknown, low, and high current dioxin categories, p=0.657) or for heavy lifetime drinkers (46.77, 46.65, 43.78, and 44.63 for the corresponding categories, p=0.315). Of the four current dioxin categories, the background mean was lowest for participants who never had drunk alcohol, but it was highest for heavy drinkers. The overall difference among adjusted mean levels was significant for moderate drinkers (46.01, 50.16, 45.24, and 44.06 mg/dl for the background, unknown, low, and high current dioxin categories, p<0.001). The mean HDL for the unknown category was significantly more than the background mean (p<0.001), but the mean for the high category was marginally less than the background mean (p=0.083). The low versus background contrast was not significant (p=0.455).

After excluding the interaction, the adjusted analysis found a highly significant overall difference in mean levels of HDL among the current dioxin categories (Table 10-30 [j]: 45.92, 48.93, 44.85, and 44.59 mg/dl for the background, unknown, low, and high current dioxin categories, p<0.001). As in the unadjusted analysis, the unknown versus background contrast was highly significant (p<0.001), but the high versus background contrast became nonsignificant after covariate adjustment (p=0.137).

HDL (Discrete)

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Both the unadjusted and adjusted initial dioxin analyses of discretized HDL did not detect a significant relative risk of an abnormally low level of HDL (Table 10-31 [a-d]: p>0.35 for the minimal and maximal analyses).

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

The current dioxin-by-time since tour interaction was not significant for the discrete analyses of HDL (Table 10-31 [e-h]: p>0.50 for each unadjusted and adjusted analysis).

TABLE 10-31.

Analysis of HDL
(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=517)	Low	130	0.8	1.18 (0.83,1.68)	0.357
	Medium	257	5.1		
	High	130	3.8		
b) Maximal (n=737)	Low	184	2.7	1.11 (0.85,1.46)	0.439
	Medium	368	3.3		
	High	185	4.9		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=514)	1.17 (0.82,1.67)	0.391	ALC (p=0.024)
d) Maximal (n=732)	1.11 (0.84,1.45)	0.476	RACE (p=0.111) ALC (p=0.053)

[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 10-31. (Continued)

Analysis of HDL
(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 (n=517)						0.705[b]
	≤18.6	0.0 (72)	4.8 (126)	1.9 (53)	1.24 (0.64,2.38)	0.519[c]
	>18.6	1.7 (58)	6.1 (131)	3.9 (77)	1.06 (0.68,1.66)	0.787[c]
f) Maximal (n=737)						0.587[b]
	≤18.6	3.8 (105)	2.6 (189)	3.7 (82)	0.99 (0.62,1.59)	0.982[c]
	>18.6	1.3 (79)	3.4 (178)	6.7 (104)	1.17 (0.82,1.65)	0.382[c]

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

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal (n=514)			0.648[b]	RACE (p=0.141)
	≤18.6	1.23 (0.64,2.35)	0.538[c]	ALC (p=0.023)
	>18.6	1.02 (0.65,1.60)	0.936[c]	
h) Maximal (n=732)			0.578[b]	RACE (p=0.106)
	≤18.6	0.98 (0.61,1.57)	0.937[c]	ALC (p=0.052)
	>18.6	1.16 (0.82,1.64)	0.413[c]	

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

TABLE 10-31. (Continued)

Analysis of HDL
(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	779	3.6	All Categories		0.721
Unknown	341	3.5	Unknown vs. Background	0.98 (0.49,1.95)	0.950
Low	193	4.1	Low vs. Background	1.16 (0.52,2.59)	0.717
High	186	5.4	High vs. Background	1.52 (0.73,3.20)	0.265
Total	1,499				

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

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	779	All Categories		0.834**	DXCAT*DC (p=0.025) ALC (p=0.002)
Unknown	339	Unknown vs. Background	1.01 (0.50,2.02)**	0.978**	
Low	191	Low vs. Background	1.12 (0.50,2.51)**	0.778**	
High	185	High vs. Background	1.42 (0.67,3.00)**	0.356**	
Total	1,494				

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

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

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

For the unadjusted analysis, the prevalence of abnormally low levels of HDL did not differ significantly among the four current dioxin categories (Table 10-31 [i]: 3.6%, 3.5%, 4.1%, and 5.4% for the background, unknown, low, and high current dioxin categories, p=0.721).

The adjusted analysis detected a significant categorized current dioxin-by-degreasing chemical exposure interaction (Table 10-31 [j]: p=0.025). Stratified results found a marginally significant overall contrast for participants who had never been exposed to degreasing chemicals (Appendix Table I-1: p=0.058). The percentages of abnormally low levels of HDL in this stratum were 2.0, 4.8, 0.0, and 7.1 percent for the background, unknown, low, and high current dioxin categories. The adjusted relative risk for the high versus background contrast was of borderline significance (Adj. RR=3.43, 95% C.I.: [0.82,14.37], p=0.091). The overall contrast was not significant for participants who had been exposed to degreasing chemicals (p=0.429). After excluding the interaction, the results of the adjusted analysis were not significant (Table 10-31 [j]: p>0.35 for all contrasts).

Cholesterol-HDL Ratio (Continuous)

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Under both the minimal and maximal assumptions, the unadjusted initial dioxin analyses found a significant positive association with the cholesterol-HDL ratio (Table 10-32 [a] and [b]: p=0.031 and p<0.001, respectively). For the low, medium, and high initial dioxin categories, the mean ratios were 4.75, 5.04, and 4.93 in the minimal cohort and 4.52, 4.85, and 5.03 in the maximal cohort.

Adjusting for age, race, current alcohol use, and industrial chemical exposure, the association between initial dioxin and the cholesterol-HDL ratio remained significant under the minimal assumption (Table 10-32 [c]: p=0.009). The adjusted mean ratios for the low, medium, and high initial dioxin categories were 4.42, 4.70, and 4.61. The adjusted analysis under the maximal assumption detected a significant initial dioxin-by-degreasing chemical exposure interaction (Table 10-32 [d]: p=0.010). Appendix Table I-1 presents stratified results that show a highly significant positive association between initial dioxin and the cholesterol-HDL ratio for Ranch Hands who never had been exposed to degreasing chemicals (Adj. slope=0.0633, p<0.001; Adj. means: 3.98, 4.63, and 4.87 for the low, medium, and high initial dioxin categories). The positive association between initial dioxin and the cholesterol-HDL ratio also was significant for Ranch Hands who had been exposed to degreasing chemicals (Adj. slope=0.0221, p=0.015; Adj. means: 4.64, 4.64, and 4.87 for the low, medium, and high initial dioxin categories).

After excluding the interaction, the adjusted analysis under the maximal assumption displayed a highly significant positive association between initial dioxin and the cholesterol-HDL ratio (Table 10-32 [d]: Adj. slope=0.0350, p<0.001). The adjusted mean ratios were 4.30, 4.60, and 4.79 for the low, medium, and high initial dioxin categories.

TABLE 10-32.

Analysis of Cholesterol-HDL Ratio (Continuous)

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Mean[a]	Slope (Std. Error)[b]	p-Value
a) Minimal (n=517) (R^2=0.009)	Low	130	4.75	0.0214 (0.0099)	0.031
	Medium	257	5.04		
	High	130	4.93		
b) Maximal (n=737) (R^2=0.027)	Low	184	4.52	0.0332 (0.0074)	<0.001
	Medium	368	4.85		
	High	185	5.03		

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=514) (R^2=0.066)	Low	130	4.42	0.0263 (0.0101)	0.009	AGE (p=0.001) RACE (p=0.005) ALC (p=0.003) IC (p=0.111)
	Medium	255	4.70			
	High	129	4.61			
d) Maximal (n=732) (R^2=0.063)	Low	183	4.30***	0.0350 (0.0076)***	<0.001***	INIT*DC (p=0.010) AGE (p=0.006) RACE (p=0.065) ALC (p=0.003)
	Medium	365	4.60***			
	High	184	4.79***			

[a]Transformed from natural logarithm scale.

[b]Slope and standard error based on natural logarithm cholesterol-HDL ratio versus log_2 dioxin.

***Log_2 (initial dioxin)-by-covariate interaction ($p \leq 0.01$); 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 10-32. (Continued)

Analysis of Cholesterol-HDL Ratio (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						0.200[c]
(n=517)	≤18.6	4.80	5.01	4.69	0.0032 (0.0162)	0.841[d]
(R^2=0.012)		(72)	(126)	(53)		
	>18.6	4.65	5.10	5.09	0.0300 (0.0132)	0.023[d]
		(58)	(131)	(77)		
f) Maximal						0.749[c]
(n=737)	≤18.6	4.39	4.86	4.94	0.0282 (0.0115)	0.015[d]
(R^2=0.025)		(105)	(189)	(82)		
	>18.6	4.57	4.86	5.18	0.0331 (0.0101)	0.001[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						****	CURR*TIME*IC
(n=514)	≤18.6	****	****	****	****	****	(p=0.010)
(R^2=0.093)		(72)	(126)	(52)			AGE (p=0.002)
	>18.6	****	****	****	****	****	ALC (p=0.002)
		(58)	(129)	(77)			RACE*IC (p=0.019)
h) Maximal						0.711[c]	AGE (p=0.007)
(n=732)	≤18.6	4.22	4.63	4.78	0.0315 (0.0118)	0.008[d]	RACE (p=0.078)
(R^2=0.054)		(105)	(188)	(81)			ALC (p=0.003)
	>18.6	4.32	4.63	4.98	0.0371 (0.0104)	<0.001[d]	IC (p=0.056)
		(78)	(176)	(104)			

[a]Transformed from natural logarithm scale.

[b]Slope and standard error based on natural logarithm cholesterol-HDL ratio 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 ($p \leq 0.01$); adjusted mean, adjusted slope, standard error, and p-value not presented.

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

TABLE 10-32. (Continued)

Analysis of Cholesterol-HDL Ratio (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	4.74	All Categories		<0.001
Unknown	341	4.48	Unknown vs. Background	-0.26 --	0.002
Low	193	4.93	Low vs. Background	0.19 --	0.082
High	186	5.08	High vs. Background	0.34 --	0.003
Total	1,499		(R^2=0.019)		

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	4.63	All Categories		<0.001	AGE (p=0.021) RACE (p=0.134)
Unknown	338	4.36	Unknown vs. Background	-0.27 --	<0.001	IC (p=0.004)
Low	191	4.79	Low vs. Background	0.16 --	0.136	ALC*DRKYR
High	182	4.96	High vs. Background	0.33 --	0.003	(p=0.031)
Total	1,488		(R^2=0.061)			

[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.

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 for the cholesterol-HDL ratio under both the minimal (Table 10-32 [e]: p=0.200) and maximal (Table 10-32 [f]: p=0.749) assumptions. However, under both assumptions, the association between current dioxin and the cholesterol-HDL ratio was significantly positive for Ranch Hands with an early tour (time>18.6: p=0.023 and p=0.001 under the minimal and maximal assumptions). The mean ratios for the low, medium, and high current dioxin categories were 4.65, 5.10, and 5.09 under the minimal assumption. Under the maximal assumption, the corresponding means were 4.57, 4.86, and 5.18. For Ranch Hands with a later tour, the unadjusted association between current dioxin and the cholesterol-HDL ratio was not significant under the minimal assumption (p=0.841), but it was significant under the maximal assumption (p=0.015).

The adjusted minimal analysis detected a significant current dioxin-by-time-by-industrial chemical exposure interaction (Table 10-32 [g]: p=0.010). Stratified results showed that the current dioxin-by-time interaction was not significant for Ranch Hands who never had been exposed to industrial chemicals (Appendix Table I-1: p=0.217), although the association between current dioxin and the cholesterol-HDL ratio was marginally positive for these Ranch Hands with a later tour (time≤18.6: p=0.080, Adj. means: 4.56, 4.64, and 5.25 for the low, medium, and high current dioxin categories). By contrast, the interaction between current dioxin and time was significant for Ranch Hands who had been exposed to industrial chemicals (p=0.008), with a significantly positive association between current dioxin and the cholesterol-HDL ratio for those with an early tour (time>18.6: p<0.001, Adj. means: 3.86, 4.61, and 4.70 for the low, medium, and high current dioxin categories).

Results from the adjusted maximal analysis supported the unadjusted findings. The interaction between current dioxin and time was not significant (Table 10-32 [h]: p=0.711), but the association between current dioxin and the cholesterol-HDL ratio was significantly positive within each time stratum (time≤18.6: p=0.008; time>18.6: p<0.001).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The unadjusted categorized current dioxin analysis found that the mean cholesterol-HDL ratios differed significantly among the categories (Table 10-32 [i]: 4.74, 4.48, 4.93, and 5.08 for the background, unknown, low, and high current dioxin categories, p<0.001). All three Ranch Hand versus background contrasts were significant or marginally significant. The mean cholesterol-HDL ratio for the unknown current dioxin category was significantly less than the background mean (p=0.002), the low current dioxin category mean ratio was marginally more than the background mean (p=0.082), and the high current dioxin category mean was significantly more than the background mean (p=0.003).

The adjusted analysis displayed similar findings except that the low versus background contrast was not significant. The overall contrast remained highly significant (Table 10-32 [j]: p<0.001). The adjusted mean cholesterol-HDL ratios were 4.63, 4.36, 4.79, and 4.96 for the background, unknown, low, and high current dioxin categories. The mean ratio for the unknown category was significantly less than the mean background ratio (p<0.001), and the high current dioxin category mean ratio was significantly more than the mean background ratio (p=0.003).

Cholesterol-HDL Ratio (Discrete)

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

In the unadjusted initial dioxin analyses, the estimated relative risk of an abnormally high cholesterol-HDL ratio was marginally significant under the minimal assumption (Table 10-33 [a]: Est. RR=1.14, p=0.077) and highly significant under the maximal assumption (Table 10-33 [b]: Est. RR=1.22, p<0.001). The percentages of abnormally high ratios for the low, medium, and high initial dioxin categories were 44.6, 50.2, and 48.5 percent in the minimal cohort, and 37.0, 45.9, and 50.3 percent in the maximal cohort.

After adjusting for current alcohol use and the age-by-degreasing chemical exposure interaction, the relative risk became significant for the minimal cohort (Table 10-33 [c]: Adj. RR=1.25, p=0.004). The adjusted maximal analysis detected two significant initial dioxin-by-covariate interactions: initial dioxin-by-age (Table 10-33 [d]: p=0.008) and initial dioxin-by-degreasing chemical exposure (p=0.001). Age was dichotomized to explore the interaction. Appendix Table I-1 presents stratified results for the four combinations of age and degreasing chemical exposure categories. The adjusted relative risk was significantly greater than 1 in three of the four strata (born≥1942, never had been exposed to degreasing chemicals: Adj. RR=1.49, p=0.001; born≥1942, had been exposed to degreasing chemicals: Adj. RR=1.00, p=0.999; born<1942, never had been exposed to degreasing chemicals: Adj. RR=1.89, p<0.001; born<1942, had been exposed to degreasing chemicals: Adj. RR=1.27, p=0.012). After deleting the interactions, the adjusted maximal analysis displayed a highly significant relative risk (Table 10-33 [d]: Adj. RR=1.25, p<0.001), supporting the unadjusted finding.

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

Under both the minimal and maximal assumptions, the interaction between current dioxin and time since tour was not significant for the unadjusted analyses of the discretized cholesterol-HDL ratio (Table 10-33 [e] and [f]: p=0.113 and p=0.399, respectively), although the estimated relative risk of an abnormally high ratio was significant for Ranch Hands with an early tour (time>18.6: Est. RR=1.23, p=0.039 in the minimal analysis; Est. RR=1.24, p=0.005 in the maximal analysis). In this time stratum, the percentages of abnormally high ratios were 39.7, 55.7, and 55.8 percent for the minimal low, medium, and high current dioxin categories and 40.5, 48.9, and 55.8 percent for the corresponding maximal categories.

The adjusted minimal analysis detected a significant current dioxin-by-time-by-industrial chemical exposure interaction (Table 10-33 [g]: p=0.033). Stratified results showed a significant current dioxin-by-time interaction for Ranch Hands who had been exposed to industrial chemicals (Appendix Table I-1: p=0.008). For these Ranch Hands, there was a significant relative risk of an abnormally high cholesterol-HDL ratio for those with an early tour (time>18.6: Adj. RR=1.55, p=0.002; % abnormal: 22.7%, 51.4%, and 57.4% for the low, medium, and high current dioxin categories). The relative risk was less than 1 but not significant for those with a later tour (time≤18.6: Adj. RR=0.90, p=0.532). The current dioxin-by-time interaction was not significant for Ranch Hands who never had been exposed to industrial chemicals (p=0.527), although there was a marginally significant increased risk for those with a later tour (time≤18.6: Adj. RR=1.46, p=0.089; % abnormal: 43.8%, 36.7%, and 69.2% for the low, medium, and high current dioxin categories).

TABLE 10-33.

Analysis of Cholesterol-HDL Ratio (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	44.6	1.14 (0.99,1.31)	0.077
	Medium	257	50.2		
	High	130	48.5		
b) Maximal (n=737)	Low	184	37.0	1.22 (1.09,1.35)	<0.001
	Medium	368	45.9		
	High	185	50.3		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=514)	1.25 (1.07,1.46)	0.004	AGE*DC (p=0.016) ALC (p=0.006)
d) Maximal (n=732)	1.25 (1.12,1.40)***	<0.001***	INIT*AGE (p=0.008) INIT*DC (p=0.001) ALC (p=0.023)

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

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

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

TABLE 10-33. (Continued)

Analysis of Cholesterol-HDL Ratio (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 (n=517)						0.113[b]
	≤18.6	47.2 (72)	45.2 (126)	37.7 (53)	0.96 (0.76,1.22)	0.741[c]
	>18.6	39.7 (58)	55.7 (131)	55.8 (77)	1.23 (1.01,1.50)	0.039[c]
f) Maximal (n=737)						0.399[b]
	≤18.6	32.4 (105)	44.4 (189)	42.7 (82)	1.12 (0.95,1.33)	0.168[c]
	>18.6	40.5 (79)	48.9 (178)	55.8 (104)	1.24 (1.07,1.44)	0.005[c]

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

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal (n=514)			0.119**[b]	CURR*TIME*IC (p=0.033)
	≤18.6	1.07 (0.84,1.37)**	0.582**[c]	ALC (p=0.007)
	>18.6	1.38 (1.11,1.70)**	0.003**[c]	AGE*DC (p=0.015)
h) Maximal (n=732)			0.283[b]	ALC (p=0.026)
	≤18.6	1.14 (0.96,1.36)	0.132[c]	AGE*DC (p=0.038)
	>18.6	1.29 (1.11,1.51)	0.001[c]	

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

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

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

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

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

TABLE 10-33. (Continued)

Analysis of Cholesterol-HDL Ratio (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	43.4	All Categories		0.021
Unknown	341	38.1	Unknown vs. Background	0.80 (0.62,1.04)	0.100
Low	193	49.2	Low vs. Background	1.26 (0.92,1.73)	0.145
High	186	50.0	High vs. Background	1.30 (0.95,1.80)	0.104
Total	1,499				

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

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	779	All Categories		0.023	AGE (p=0.132)
					ALC (p<0.001)
Unknown	339	Unknown vs. Background	0.80 (0.61,1.04)	0.091	DC (p=0.100)
Low	191	Low vs. Background	1.23 (0.89,1.70)	0.202	
High	185	High vs. Background	1.33 (0.96,1.85)	0.087	
Total	1,494				

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

After excluding the interaction, the adjusted minimal results were comparable to the unadjusted findings. The adjusted maximal analysis also displayed similar results. The interaction between current dioxin and time was not significant for either cohort (Table 10-33 [g] and [h]: p=0.119 for the minimal cohort and p=0.283 for the maximal cohort), but the relative risk was significant for Ranch Hands with an early tour (time>18.6: Adj. RR=1.38, p=0.003 for the minimal cohort; Adj. RR=1.29, p=0.001 for the maximal cohort).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The percentage of abnormally high cholesterol-HDL ratios differed significantly among the current dioxin categories in the unadjusted analysis (Table 10-33 [i]: 43.4%, 38.1%, 49.2%, and 50.0% for the background, unknown, low, and high current dioxin categories, p=0.021). The estimated relative risk for the unknown versus background contrast was marginally less than 1 (Adj. RR=0.80, 95% C.I.: [0.62,1.04], p=0.100). The estimated relative risks for the low versus background and the high versus background contrasts were more than 1, but not significant (p=0.145 and p=0.104, respectively). After adjustment for age, current alcohol use, and degreasing chemical exposure, the overall contrast remained significant (Table 10-33 [j]: p=0.023) and the low versus background relative risk remained marginally less than 1 (Adj. RR=0.80, 95% C.I.: [0.61,1.04], p=0.091). The relative risk for the high versus background contrast became marginally more than 1 (Adj. RR=1.33, 95% C.I.: [0.96,1.85], p=0.087).

Triglycerides (Continuous)

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

The unadjusted continuous analyses of triglycerides found a positive association with initial dioxin that was marginally significant for the minimal cohort (Table 10-34 [a]: p=0.068) and highly significant for the maximal cohort (Table 10-34 [b]: p<0.001). The mean levels of triglycerides for the low, medium, and high initial dioxin categories were 115.8, 144.2, and 125.9 mg/dl for the minimal cohort. The corresponding means increased with initial dioxin for the maximal cohort (104.3, 128.9, and 137.5 mg/dl).

The adjusted analyses revealed a significant positive association between initial dioxin and triglycerides for both cohorts (Table 10-34 [c] and [d]: p=0.040 and p<0.001 for the minimal and maximal cohorts). The adjusted mean levels of triglycerides exhibited patterns similar to the unadjusted findings. For the minimal cohort, the adjusted mean level of triglycerides was highest for the medium initial dioxin category (101.3, 126.1, and 111.2 mg/dl for the low, medium, and high initial dioxin categories). The means increased for the maximal categories (90.3, 111.2, 119.8 mg/dl for the low, medium, and high categories).

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

The current dioxin-by-time since tour interaction was not significant for the unadjusted analysis of triglycerides under the minimal assumption (Table 10-34 [e]: p=0.476), but it was of borderline significance for the maximal assumption (Table 10-34 [f]: p=0.086). For the maximal cohort, the positive association between current dioxin and triglycerides was highly significant for Ranch Hands with a later tour (time≤18.6: p<0.001), and marginally significant for Ranch Hands with an early tour (time>18.6: p=0.094). The mean levels of triglycerides for the later time stratum were 98.0, 125.2, and 141.9 mg/dl for the low, medium,

TABLE 10-34.

Analysis of Triglycerides (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	115.8	0.0416 (0.0227)	0.068
(n=517)	Medium	257	144.2		
(R^2=0.006)	High	130	125.9		
b) Maximal	Low	184	104.3	0.0733 (0.0169)	<0.001
(n=737)	Medium	368	128.9		
(R^2=0.025)	High	185	137.5		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Initial Dioxin	n	Adj. Mean[a]	Adj. Slope (Std. Error)[b]	p-Value	Covariate Remarks
c) Minimal	Low	130	101.3	0.0487 (0.0236)	0.040	RACE (p=0.016)
(n=511)	Medium	253	126.1			AGE*DRKYR (p=0.041)
(R^2=0.031)	High	128	111.2			
d) Maximal	Low	182	90.3	0.0762 (0.0176)	<0.001	RACE (p=0.024)
(n=728)	Medium	365	111.2			AGE*DRKYR (p=0.014)
(R^2=0.055)	High	181	119.8			DRKYR*DC (p=0.035)

[a]Transformed from natural logarithm scale.

[b]Slope and standard error based on natural logarithm triglycerides 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 10-34. (Continued)

Analysis of Triglycerides (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						0.476[c]
(n=517)	≤18.6	111.0	143.5	128.7	0.0551 (0.0372)	0.139[d]
(R^2=0.006)		(72)	(126)	(53)		
	>18.6	123.5	142.2	126.8	0.0208 (0.0303)	0.493[d]
		(58)	(131)	(77)		
f) Maximal						0.086[c]
(n=737)	≤18.6	98.0	125.2	141.9	0.0993 (0.0264)	<0.001[d]
(R^2=0.025)		(105)	(189)	(82)		
	>18.6	114.7	133.9	131.2	0.0389 (0.0232)	0.094[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						0.525[c]	RACE (p=0.011)
(n=517)	≤18.6	98.1	124.7	110.5	0.0472 (0.0371)	0.205[d]	
(R^2=0.018)		(72)	(126)	(53)			
	>18.6	108.3	125.2	110.1	0.0168 (0.0302)	0.580[d]	
		(58)	(131)	(77)			
h) Maximal						0.135[c]	RACE (p=0.027)
(n=728)	≤18.6	86.2	109.5	124.9	0.1011 (0.0273)	<0.001[d]	AGE*DRKYR
(R^2=0.054)		(104)	(188)	(80)			(p=0.018)
	>18.6	98.7	114.8	115.1	0.0483 (0.0240)	0.045[d]	DRKYR*DC
		(78)	(176)	(102)			(p=0.049)

[a]Transformed from natural logarithm scale.

[b]Slope and standard error based on natural logarithm triglycerides 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).

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 10-34. (Continued)

Analysis of Triglycerides (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	116.8	All Categories		<0.001
Unknown	341	104.1	Unknown vs. Background	-12.7 --	0.005
Low	193	140.0	Low vs. Background	23.2 --	<0.001
High	186	135.8	High vs. Background	19.0 --	0.004
Total	1,499		(R^2=0.024)		

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	104.8**	All Categories		<0.001**	DXCAT*ALC (p=0.038) RACE (p=0.002)
Unknown	338	93.1**	Unknown vs. Background	-11.7 -- **	0.004**	AGE*DRKYR (p=0.014)
Low	191	124.1**	Low vs. Background	19.3 -- **	<0.001**	DRKYR*DC (p=0.041)
High	182	123.0**	High vs. Background	18.2 -- **	0.002**	
Total	1,488		(R^2=0.051)			

[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 ($0.01<p\leq0.05$); 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.

and high current dioxin categories. The corresponding means for the early time stratum were 114.7, 133.9, and 131.2 mg/dl.

The interaction between current dioxin and time remained nonsignificant for the minimal cohort (Table 10-34 [g]: p=0.525) and became nonsignificant for the maximal cohort (Table 10-34 [h]: p=0.135) after adjustment for race, the age-by-lifetime alcohol history interaction, and the lifetime alcohol history-by-degreasing chemical exposure interaction. However, under the maximal assumption, the positive association between current dioxin and triglycerides was significant for both time strata (time≤18.6: p<0.001; time>18.6: p=0.045).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The unadjusted mean levels of triglycerides differed significantly among the four current dioxin categories (Table 10-34 [i]: 116.8, 104.1, 140.0, and 135.8 mg/dl for the background, unknown, low, and high current dioxin categories, p<0.001). Each contrast relative to the background category also was significant (unknown versus background: p=0.005; low versus background: p<0.001; high versus background: p=0.004).

The adjusted analysis detected a significant interaction between categorized current dioxin and current alcohol use (Table 10-34 [j]: p=0.038). To explore the interaction, the current alcohol use covariate was categorized into three levels: light (≤1 drink/day), moderate (>1-4 drinks/day), and heavy (>4 drinks/day). The adjusted mean levels of triglycerides differed significantly among current dioxin categories for light drinkers (Appendix Table I-1: 106.2, 92.4, 122.2, and 126.7 mg/dl for the background, unknown, low, and high current dioxin categories, p<0.001). In this stratum, the adjusted mean for the unknown current dioxin category was significantly less than the adjusted background mean (p=0.002), but the adjusted means for the low and high categories were significantly more than the adjusted background mean (p=0.014 and p=0.002, respectively).

The overall contrast was marginally significant for moderate drinkers (p=0.076). The low current dioxin category had the largest adjusted mean triglycerides, which was significantly more than the background mean (133.8 mg/dl versus 103.2 mg/dl, p=0.030). The adjusted means for the unknown current dioxin category (95.6 mg/dl) and the high current dioxin category (96.6 mg/dl) were not significantly different from the background mean (p=0.435 and p=0.641, respectively). The overall current dioxin category contrast was not significant for heavy drinkers (p=0.129), but the adjusted means increased by current dioxin category (72.7, 85.3, 103.0, and 134.4 mg/dl for the background, unknown, low, and high current dioxin categories). The high versus background contrast was significant (p=0.021).

Excluding the interaction, the adjusted results paralleled the unadjusted findings. The overall difference in adjusted mean levels of triglycerides among current dioxin categories was highly significant (Table 10-34 [j]: 104.8, 93.1, 124.1, and 123.0 mg/dl for the background, unknown, low, and high current dioxin categories, p<0.001) as were the three Ranch Hand versus background category contrasts (p<0.01 for each contrast).

Triglycerides (Discrete)

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Under both the minimal and maximal assumptions, the unadjusted initial dioxin analyses showed a significant relative risk of abnormally high levels of triglycerides (Table 10-35 [a]: Est. RR=1.32, p=0.021 for the minimal cohort; Table 10-35 [b]: Est. RR=1.31, p=0.004 for the maximal cohort). The percentages of abnormal triglycerides levels were 3.8, 10.1, and 10.8 percent for the low, medium, and high initial dioxin categories of the minimal cohort. The corresponding percentages for the maximal cohort were 4.9, 6.8, and 11.9 percent.

The adjusted analyses results also were significant, with relative risk estimates essentially unchanged from the unadjusted analyses (Table 10-35 [c] and [d]: Adj. RR=1.32, p=0.026 for the minimal cohort; Adj. RR=1.30, p=0.005 for the maximal cohort).

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

The interaction between current dioxin and time since tour was not significant for the unadjusted analyses of discretized triglycerides (Table 10-35 [e] and [f]: p=0.948 and p=0.814, for the minimal and maximal assumptions). However, the relative risk of an abnormally high level of triglycerides was significant in both time strata under the maximal assumption (time≤18.6: Est. RR=1.35, p=0.045; time>18.6: Est. RR=1.29, p=0.044). Under the minimal assumption, the relative risk was marginally significant for Ranch Hands with an early tour (time>18.6: Est. RR=1.30, p=0.094).

The current dioxin-by-time interaction remained nonsignificant in the adjusted analyses (Table 10-35 [g] and [h]: p=0.862 and p=0.812 for the minimal and maximal cohorts). Under the maximal assumption, the adjusted relative risks within each time stratum were essentially unchanged from the unadjusted findings (time≤18.6: Adj. RR=1.34, p=0.050; time>18.6: Adj. RR=1.28, p=0.052). The adjusted relative risk remained marginally significant under the minimal assumption for Ranch Hands with an early tour (time>18.6: Adj. RR=1.32, p=0.078).

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 triglycerides differed significantly among the four current dioxin categories (Table 10-35 [i]: 5.4%, 3.2%, 9.3%, and 11.8% for the background, unknown, low, and high current dioxin categories, p<0.001). There was a significant increased risk relative to the background group for the low (Est. RR=1.80, 95% C.I.: [1.01,3.21], p=0.045) and high (Est. RR=2.35, 95% C.I.: [1.37,4.05], p=0.002) categories.

The adjusted analysis detected a significant interaction between categorized current dioxin and current alcohol use (Table 10-35 [j]: p=0.039). This interaction also was noted in the categorized current dioxin analysis of triglycerides in its continuous form. Stratified results showed that the prevalence of abnormally high levels of triglycerides differed significantly among current dioxin categories for participants who currently consume no more than one drink per day (Appendix Table I-1: 5.2%, 2.2%, 8.4%, and 13.7% for the background, unknown, low, and high current dioxin categories, p<0.001). The prevalence for the unknown category was significantly less than the background prevalence (p=0.035), but the prevalence

TABLE 10-35.

Analysis of Triglycerides (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	3.8	1.32 (1.05,1.67)	0.021
	Medium	257	10.1		
	High	130	10.8		
b) Maximal (n=737)	Low	184	4.9	1.31 (1.10,1.57)	0.004
	Medium	368	6.8		
	High	185	11.9		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=517)	1.32 (1.04,1.67)	0.026	RACE (p=0.031) DC*IC (p=0.025)
d) Maximal (n=732)	1.30 (1.09,1.56)	0.005	RACE (p=0.020) ALC (p=0.060)

[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 10-35. (Continued)

Analysis of Triglycerides (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						0.948[b]
(n=517)	≤18.6	4.2 (72)	9.5 (126)	11.3 (53)	1.32 (0.89,1.95)	0.162[c]
	>18.6	3.4 (58)	9.9 (131)	11.7 (77)	1.30 (0.96,1.76)	0.094[c]
f) Maximal						0.814[b]
(n=737)	≤18.6	3.8 (105)	6.9 (189)	12.2 (82)	1.35 (1.01,1.80)	0.045[c]
	>18.6	5.1 (79)	7.3 (178)	11.5 (104)	1.29 (1.01,1.64)	0.044[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			0.862[b]	RACE (p=0.030)
(n=517)	≤18.6	1.27 (0.86,1.87)	0.238[c]	DC*IC (p=0.024)
	>18.6	1.32 (0.97,1.81)	0.078[c]	
h) Maximal			0.812[b]	RACE (p=0.020)
(n=732)	≤18.6	1.34 (1.00,1.79)	0.050[c]	ALC (p=0.060)
	>18.6	1.28 (1.00,1.63)	0.052[c]	

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

TABLE 10-35. (Continued)

Analysis of Triglycerides (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	5.4	All Categories		<0.001
Unknown	341	3.2	Unknown vs. Background	0.58 (0.30,1.15)	0.120
Low	193	9.3	Low vs. Background	1.80 (1.01,3.21)	0.045
High	186	11.8	High vs. Background	2.35 (1.37,4.05)	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	779	All Categories		<0.001**	DXCAT*ALC (p=0.039)
					AGE (p=0.143)
Unknown	339	Unknown vs. Background	0.56 (0.29,1.11)**	0.097**	RACE (p=0.025)
Low	191	Low vs. Background	1.81 (1.01,3.22)**	0.045**	
High	185	High vs. Background	2.55 (1.46,4.45)**	0.001**	
Total	1,494				

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

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

for the high current dioxin category was significantly more than the background prevalence ($p<0.001$). There was no significant difference among current dioxin categories for moderate current drinkers (>1-4: 7.1%, 6.8%, 11.8%, and 0.0% for the background, unknown, low, and high current dioxin categories, $p=0.225$), but the overall contrast was marginally significant for heavy current heavy drinkers (>4: $p=0.051$). For the heavy current drinkers, the prevalences of abnormal triglycerides levels were 0.0 percent in the background category (n=28), 14.3 percent in the unknown category (n=7), 0.0 percent in the low category (n=3), and 12.5 percent in the high category (n=8).

After excluding the interaction, the adjusted analysis displayed results comparable to the unadjusted findings. The overall contrast was highly significant (Table 10-35 [j]: $p<0.001$) and the relative risk of an abnormal level of triglycerides was significantly more than 1 for the low versus background contrast (Adj. RR=1.81, 95% C.I.: [1.01,3.22], $p=0.045$) and also for the high versus background contrast (Adj. RR=2.55, 95% C.I.: [1.46,4.45], $p=0.001$). The relative risk for the unknown versus background contrast became marginally less than 1 after covariate adjustment (Adj. RR=0.56, 95% C.I.: [0.29,1.11], $p=0.097$).

Creatine Kinase (Continuous)

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

The unadjusted initial dioxin analyses did not detect a significant association with creatine kinase in its continuous form under either the minimal (Table 10-36 [a]: $p=0.830$) or maximal (Table 10-36 [b]: $p=0.955$) assumptions. The adjusted analyses revealed a significant initial dioxin-by-age interaction under both assumptions (Table 10-36 [c] and [d]: $p=0.049$ and $p=0.040$ for the minimal and maximal assumptions). Age was dichotomized to explore the interaction. Under both assumptions, there was a significant negative association between initial dioxin and creatine kinase for Ranch Hands born before 1942 (Appendix Table I-1: $p=0.024$ and $p=0.039$ for the minimal and maximal assumptions). This contrasted with a positive association between initial dioxin and creatine kinase for Ranch Hands born in or after 1942. This association was marginally significant under the minimal assumption ($p=0.051$), but it was not significant under the maximal assumption ($p=0.158$). The adjusted analyses were not significant under both assumptions after excluding the initial dioxin-by-age interaction (Table 10-36 [c] and [d]: $p=0.824$ and $p=0.706$ for the minimal and maximal analyses).

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

Under both the minimal and maximal assumptions, the current dioxin and time since tour analyses for creatine kinase did not detect a significant interaction between current dioxin and time (Table 10-36 [e-h]: $p>0.45$ for the unadjusted and adjusted analyses).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The unadjusted categorized current dioxin analysis of creatine kinase did not find a significant overall difference in the mean levels of creatine kinase (Table 10-36 [i]: $p=0.504$). However, the adjusted analysis detected a significant interaction between categorized current dioxin and race (Table 10-36 [j]: $p=0.027$). Stratified analyses found that the adjusted mean levels of creatine kinase differed significantly among current dioxin categories for Blacks (Appendix Table I-1: 247.4, 173.1, 176.3, and 182.4 mg/dl for the background,

TABLE 10-36.

Analysis of Creatine Kinase (U/L) (Continuous)

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Mean[a]	Slope (Std. Error)[b]	p-Value
a) Minimal (n=517) (R^2<0.001)	Low	130	113.4	-0.0036 (0.0170)	0.830
	Medium	257	109.1		
	High	130	112.8		
b) Maximal (n=737) (R^2<0.001)	Low	184	111.6	-0.0007 (0.0124)	0.955
	Medium	368	109.5		
	High	185	113.1		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Initial Dioxin	n	Adj. Mean[a]	Adj. Slope (Std. Error)[b]	p-Value	Covariate Remarks
c) Minimal (n=514) (R^2=0.111)	Low	130	139.5**	-0.0038 (0.0169)**	0.824**	INIT*AGE (p=0.049) RACE*ALC (p=0.002) ALC*IC (p=0.049)
	Medium	255	135.6**			
	High	129	139.5**			
d) Maximal (n=737) (R^2=0.090)	Low	184	148.8**	-0.0046 (0.0121)**	0.706**	INIT*AGE (p=0.040) RACE (p<0.001)
	Medium	368	142.5**			
	High	185	147.2**			

[a]Transformed from natural logarithm scale.

[b]Slope and standard error based on natural logarithm creatine kinase 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 10-36. (Continued)

Analysis of Creatine Kinase (U/L) (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						0.507[c]
(n=517)	≤18.6	119.9	108.5	116.7	-0.0134 (0.0277)	0.629[d]
(R^2=0.003)		(72)	(126)	(53)		
	>18.6	104.3	109.3	111.7	0.0103 (0.0226)	0.647[d]
		(58)	(131)	(77)		
f) Maximal						0.655[c]
(n=737)	≤18.6	108.5	111.3	115.7	0.0079 (0.0193)	0.682[d]
(R^2<0.001)		(105)	(189)	(82)		
	>18.6	114.1	107.8	111.9	-0.0036 (0.0170)	0.834[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						0.472[c]	AGE (p=0.072)
(n=514)	≤18.6	147.4	136.5	145.5	-0.0115 (0.0275)	0.676[d]	RACE*ALC (p=0.013)
(R^2=0.099)		(72)	(126)	(52)			
	>18.6	130.9	135.2	141.1	0.0131 (0.0223)	0.556[d]	
		(58)	(129)	(77)			
h) Maximal						0.482[c]	AGE (p=0.043)
(n=737)	≤18.6	143.1	145.4	150.8	0.0057 (0.0189)	0.761[d]	RACE (p<0.001)
(R^2=0.085)		(105)	(189)	(82)			
	>18.6	155.0	140.8	144.6	-0.0116 (0.0167)	0.486[d]	
		(79)	(178)	(104)			

[a]Transformed from natural logarithm scale.

[b]Slope and standard error based on natural logarithm creatine kinase 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).

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 10-36. (Continued)

Analysis of Creatine Kinase (U/L) (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	109.4	All Categories		0.504
Unknown	341	106.2	Unknown vs. Background	-3.2 --	0.368
Low	193	107.1	Low vs. Background	-2.3 --	0.604
High	186	113.5	High vs. Background	4.1 --	0.374
Total	1,499		(R^2=0.002)		

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	779	151.6**	All Categories		0.683**	DXCAT*RACE (p=0.027)
Unknown	341	149.5**	Unknown vs. Background	-2.1 -- **	0.659**	AGE*DC (p=0.028)
Low	193	149.2**	Low vs. Background	-2.4 -- **	0.680**	
High	186	157.3**	High vs. Background	5.7 -- **	0.363**	
Total	1,499		(R^2=0.114)			

[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 ($0.01<p\leq0.05$); 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.

unknown, low, and high current dioxin categories, p=0.031). The adjusted means for the unknown and low categories were both significantly less than the background mean (p=0.023 and p=0.045, respectively). The adjusted means did not differ significantly for non-Blacks (105.2, 105.4, 105.4, and 111.0 mg/dl for the background, unknown, low, and high current dioxin categories, p=0.613). No significant findings were noted for the adjusted analysis after excluding the interaction (Table 10-36 [j]: p>0.35 for each contrast).

Creatine Kinase (Discrete)

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

The unadjusted initial dioxin analyses of discretized creatine kinase were not significant (Table 10-37 [a] and [b]: p=0.144 and p=0.228 for the minimal and maximal cohorts).

After adjustment for race and the age-by-degreasing chemical interaction, the adjusted relative risk was not significant for the minimal cohort (Table 10-37 [c]: p=0.123), but was marginally less than 1 for the maximal cohort (Table 10-37 [d]: Adj. RR=0.79, p=0.084). For the maximal cohort, the percentages of Ranch Hands with an abnormal level of creatine kinase were 5.4, 6.5, and 2.7 percent for the low, medium, and high initial dioxin categories.

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

Under the minimal assumption, the interaction between current dioxin and time since tour was marginally significant in the unadjusted analysis of discretized creatine kinase (Table 10-37 [e]: p=0.065). The relative risk was marginally less than 1 for Ranch Hands with a later tour (time≤18.6: Est. RR=0.49, p=0.053). The percentages of abnormally high levels of creatine kinase decreased with current dioxin (9.7%, 5.6%, and 0.0% for the low, medium, and high current dioxin categories) in this time stratum. By contrast, the percentages of abnormal creatine kinase values increased with dioxin for Ranch Hands with an early tour (3.4%, 4.6%, and 5.2% for the low, medium, and high current dioxin categories), although the relative risk was not significant (time>18.6: Est. RR=1.05, p=0.836). The current dioxin-by-time interaction was not significant in the unadjusted maximal analysis (Table 10-37 [f]: p=0.413).

After adjustment for race and the age-by-degreasing chemical exposure interaction, the current dioxin-by-time interaction was not significant under either assumption (Table 10-37 [g] and [h]: p=0.119 and p=0.677 for the minimal and maximal assumptions). For the minimal cohort, the relative risk of an abnormal creatine kinase level remained marginally less than 1 for Ranch Hands with a later tour (Adj. RR=0.48, p=0.070).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The unadjusted categorized current dioxin analysis found a marginally significant difference among the prevalences of abnormally high levels of creatine kinase (Table 10-37 [i]: 7.8%, 5.3%, 5.2%, and 3.8% for the background, unknown, low, and high current dioxin categories, p=0.099). The estimated relative risk was marginally less than 1 for the high versus background contrast (Est. RR=0.46, 95% C.I.: [0.21,1.02], p=0.057).

The adjusted analysis revealed a significant current dioxin-by-race interaction (Table 10-37 [j]: p=0.011). Stratifying by race, a significant difference among prevalence rates was

TABLE 10-37.

Analysis of Creatine Kinase (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	7.7	0.77 (0.53,1.11)	0.144
	Medium	257	4.7		
	High	130	3.1		
b) Maximal (n=737)	Low	184	5.4	0.86 (0.67,1.11)	0.228
	Medium	368	6.5		
	High	185	2.7		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=517)	0.74 (0.49,1.10)	0.123	RACE (p<0.001) AGE*DC (p<0.001)
d) Maximal (n=737)	0.79 (0.60,1.04)	0.084	RACE (p<0.001) AGE*DC (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 10-37. (Continued)

Analysis of Creatine Kinase (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						0.065[b]
(n=517)	≤18.6	9.7 (72)	5.6 (126)	0.0 (53)	0.49 (0.24,1.01)	0.053[c]
	>18.6	3.4 (58)	4.6 (131)	5.2 (77)	1.05 (0.67,1.64)	0.836[c]
f) Maximal						0.413[b]
(n=737)	≤18.6	4.8 (105)	7.4 (189)	2.4 (82)	0.77 (0.51,1.16)	0.210[c]
	>18.6	6.3 (79)	4.5 (178)	4.8 (104)	0.96 (0.68,1.35)	0.813[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			0.119[b]	RACE (p<0.001)
(n=517)	≤18.6	0.48 (0.22,1.06)	0.070[c]	AGE*DC (p<0.001)
	>18.6	0.98 (0.58,1.64)	0.925[c]	
h) Maximal			0.677[b]	RACE (p<0.001)
(n=737)	≤18.6	0.74 (0.47,1.15)	0.182[c]	AGE*DC (p<0.001)
	>18.6	0.84 (0.57,1.23)	0.363[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.