class interaction (Table 8-25 [j]: p=0.019). Stratified results did not reveal a significant contrast for either diabetic (Appendix Table G-1: p>0.30 for all contrasts) or normal participants (p>0.20 for all contrasts). The percentages of muscle status abnormalities differed significantly among categories for diabetically impaired participants (0.0%, 6.4%, 0.0%, and 0.0% for the background, unknown, low, and high current dioxin categories, p=0.022), but this finding was affected by the sparse number of abnormalities (three in the unknown category and none in the other categories). The interaction occurred partly because the high and background categories contained the highest percentage of abnormalities in the normal strata, the unknown category had the most abnormalities in the impaired strata, and the low current dioxin category had the highest percentage of abnormalities in the diabetic stratum.

After excluding the interaction, the adjusted analysis was not significant (Table 8-25 [j]: p>0.55 for all contrasts).

Vibration

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Under both the minimal and maximal assumptions the initial dioxin analyses did not find a significant association with vibration (Table 8-26 [a-d]: p>0.60 for all unadjusted and adjusted analyses).

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

The current dioxin-by-time since tour interaction was not significant in the analyses of vibration under both the minimal and maximal assumptions (Table 8-26 [e-h]: p>0.80 in each unadjusted and adjusted analysis).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The prevalence of vibration abnormalities did not differ significantly among the current dioxin categories in the unadjusted analysis (Table 8-26 [i]: 1.4%, 0.9%, 1.6%, and 1.6% for the background, unknown, low, and high current dioxin categories, p=0.844). The overall contrast remained nonsignificant after covariate adjustment (Table 8-26 [j]: p=0.584).

Patellar Reflex

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

The unadjusted initial dioxin analyses of the patellar reflex were not significant under both the minimal (Table 8-27 [a]: p=0.661) and maximal (Table 8-27 [b]: p=0.304) assumptions. The adjusted analyses were also not significant (Table 8-27 [c] and [d]: p=0.686 for the minimal analysis and p=0.182 for the maximal analysis).

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

Under both the minimal and maximal assumptions, the association between current dioxin and patellar reflex did not differ significantly between time since tour strata (Table 8-27 [e-h]: p>0.50 in each analysis).

TABLE 8-26.

Analysis of Vibration

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=512)	Low	128	2.3	0.87 (0.50,1.52)	0.620
	Medium	255	2.4		
	High	129	0.8		
b) Maximal (n=729)	Low	183	1.1	1.07 (0.72,1.60)	0.737
	Medium	363	1.9		
	High	183	1.6		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=512)	0.87 (0.48,1.59)	0.644	AGE*INS (p=0.005)
d) Maximal (n=729)	1.11 (0.73,1.70)	0.619	AGE*INS (p=0.005)

[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 8-26. (Continued)

Analysis of Vibration

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

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.847[b]
(n=512)	≤18.6	1.4 (71)	1.6 (125)	0.0 (54)	0.87 (0.28,2.72)	0.806[c]
	>18.6	5.3 (57)	2.3 (130)	1.3 (75)	0.76 (0.38,1.53)	0.438[c]
f) Maximal						0.885[b]
(n=729)	≤18.6	1.0 (105)	1.1 (189)	1.2 (81)	1.06 (0.49,2.30)	0.879[c]
	>18.6	1.3 (78)	2.9 (174)	2.0 (102)	0.99 (0.61,1.63)	0.974[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			0.897[b]	AGE*INS (p=0.004)
(n=512)	≤18.6	0.82 (0.25,2.71)	0.751[c]	
	>18.6	0.75 (0.36,1.59)	0.457[c]	
h) Maximal			0.900[b]	AGE*INS (p=0.006)
(n=727)	≤18.6	1.11 (0.50,2.48)	0.794[c]	DIAB (p=0.131)
	>18.6	1.05 (0.62,1.77)	0.862[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 8-26. (Continued)

Analysis of Vibration

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

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	771	1.4	All Categories		0.844
Unknown	339	0.9	Unknown vs. Background	0.62 (0.17,2.22)	0.460
Low	194	1.6	Low vs. Background	1.09 (0.30,3.93)	0.901
High	183	1.6	High vs. Background	1.15 (0.32,4.17)	0.830
Total	1,487				

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	771	All Categories		0.584	AGE*RACE (p=0.017)
Unknown	339	Unknown vs. Background	0.63 (0.17,2.29)	0.478	
Low	194	Low vs. Background	1.21 (0.33,4.46)	0.774	
High	183	High vs. Background	1.99 (0.52,7.57)	0.312	
Total	1,487				

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 8-27.

Analysis of Patellar Reflex

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=521)	Low	130	0.0	1.12 (0.68,1.83)	0.661
	Medium	260	3.1		
	High	131	1.5		
b) Maximal (n=741)	Low	184	1.1	1.23 (0.84,1.79)	0.304
	Medium	371	1.6		
	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=519)	1.11 (0.67,1.85)	0.686	AGE (p=0.641) DIAB (p=0.107)
d) Maximal (n=739)	1.33 (0.89,2.00)	0.182	AGE*DIAB (p=0.021)

[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 8-27. (Continued)

Analysis of Patellar Reflex

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

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.820[b]
(n=521)	≤18.6	0.0 (72)	3.1 (128)	0.0 (54)	1.16 (0.48,2.80)	0.740[c]
	>18.6	1.7 (58)	2.3 (132)	2.6 (77)	1.02 (0.54,1.93)	0.945[c]
f) Maximal						0.786[b]
(n=741)	≤18.6	0.9 (106)	1.1 (191)	2.4 (83)	1.27 (0.66,2.44)	0.470[c]
	>18.6	1.3 (78)	1.7 (179)	2.9 (104)	1.13 (0.69,1.86)	0.615[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			0.738[b]	AGE (p=0.718)
(n=519)	≤18.6	1.19 (0.49,2.93)	0.700[c]	DIAB (p=0.099)
	>18.6	0.99 (0.52,1.91)	0.983[c]	
h) Maximal			0.535[b]	AGE*DIAB (p=0.014)
(n=739)	≤18.6	1.52 (0.75,3.11)	0.248[c]	
	>18.6	1.18 (0.72,1.96)	0.510[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 8-27. (Continued)

Analysis of Patellar Reflex

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

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	783	1.2	All Categories		0.434
Unknown	343	1.2	Unknown vs. Background	1.01 (0.31,3.32)	0.981
Low	196	2.0	Low vs. Background	1.79 (0.55,5.88)	0.336
High	187	2.7	High vs. Background	2.36 (0.78,7.13)	0.127
Total	1,509				

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	783	All Categories		0.343	AGE (p=0.241) RACE (p=0.112)
Unknown	343	Unknown vs. Background	1.05 (0.32,3.45)	0.935	
Low	196	Low vs. Background	1.80 (0.55,5.94)	0.332	
High	187	High vs. Background	2.75 (0.89,8.50)	0.078	
Total	1,509				

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 prevalence of patellar reflex abnormalities did not differ significantly among current dioxin categories in the unadjusted analysis, although the high current dioxin category had relatively more abnormalities than the other categories (Table 8-27 [i]: 1.2%, 1.2%, 2.0%, and 2.7% for the background, unknown, low, and high current dioxin categories, p=0.434). The overall contrast remained nonsignificant after adjustment for age and race (Table 8-27 [j]: p=0.343), but the high versus background contrast became marginally significant (Adj. RR=2.75, 95% C.I.: [0.89,8.50], p=0.078).

Achilles Reflex

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

In the unadjusted analyses, initial dioxin was not significantly associated with the Achilles reflex under either the minimal (Table 8-28 [a]: p=0.718) or maximal (Table 8-28 [b]: p=0.273) assumption. Adjusting for age, race, and the diabetic class-by-lifetime alcohol history interaction, the association remained nonsignificant under both assumptions (Table 8-28 [c] and [d]: p=0.698 for the minimal analysis and p=0.224 for the maximal analysis). However, because of the association between dioxin and diabetes (see Chapter 15 for a discussion of diabetes), an additional model was examined that did not adjust for diabetic class. Adjusting for age and race only (lifetime alcohol history stepped out of the model), the relative risk was marginally more than 1 under the maximal assumption (Appendix Table G-2: Adj. RR=1.26, p=0.063). The percentages of Ranch Hands in the maximal cohort with an abnormal Achilles reflex were 2.7, 6.2, and 5.4 percent for the low, medium, and high initial dioxin categories. The results under the minimal assumption remained nonsignificant after excluding diabetic class (p=0.771).

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

Under the minimal assumption, the association between current dioxin and the Achilles reflex differed significantly between time since tour strata in the unadjusted analysis (Table 8-28 [e]: p=0.049). The relative risk was marginally less than 1 for Ranch Hands in the minimal cohort with a later tour (time$\leq$18.6: Est. RR=0.59, p=0.098) in contrast to a nonsignificant relative risk that was more than 1 for Ranch Hands in the minimal cohort with an early tour (time>18.6: Est. RR=1.17, p=0.387). The current dioxin-by-time interaction was not significant in the unadjusted maximal analysis, nor was there a significant relative risk within either time stratum.

After adjustment for age, race, and the diabetic class-by-lifetime alcohol history interaction, the interaction between current dioxin and time became marginally significant under the minimal assumption (Table 8-28 [g]: p=0.064), with neither of the within time stratum results significant. Adjusting for the same covariates, the current dioxin-by-time interaction was not significant under the maximal assumption, although the relative risk became marginally more than 1 for Ranch Hands with an early tour (time>18.6: Adj. RR=1.33, p=0.073). Adjusting for age and race only, the relative risk was significantly more than 1 in this stratum (Appendix Table G-2: Adj. RR=1.42, p=0.022).

TABLE 8-28.

Analysis of Achilles Reflex

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=520)	Low	130	6.2	0.95 (0.70,1.28)	0.718
	Medium	259	7.3		
	High	131	3.8		
b) Maximal (n=739)	Low	183	2.7	1.14 (0.91,1.42)	0.273
	Medium	370	6.2		
	High	186	5.4		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=512)	0.94 (0.68,1.29)	0.698	AGE (p=0.033) RACE (p=0.040) DIAB*DRKYR (p=0.002)
d) Maximal (n=728)	1.17 (0.91,1.49)	0.224	AGE (p=0.002) RACE (p=0.052) DIAB*DRKYR (p=0.020)

[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 8-28. (Continued)

Analysis of Achilles Reflex

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

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.049[b]
(n=520)	≤18.6	5.6 (72)	8.7 (127)	0.0 (54)	0.59 (0.31,1.10)	0.098[c]
	>18.6	1.7 (58)	8.3 (132)	6.5 (77)	1.17 (0.82,1.69)	0.387[c]
f) Maximal						0.305[b]
(n=739)	≤18.6	2.9 (105)	6.8 (190)	2.4 (83)	0.97 (0.65,1.43)	0.861[c]
	>18.6	3.9 (78)	5.0 (179)	7.7 (104)	1.24 (0.93,1.66)	0.143[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			0.064[b]	AGE (p=0.039)
(n=512)	≤18.6	0.61 (0.33,1.15)	0.126[c]	RACE (p=0.034)
	>18.6	1.17 (0.79,1.74)	0.425[c]	DIAB*DRKYR (p=0.002)
h) Maximal			0.243[b]	AGE (p=0.001)
(n=728)	≤18.6	0.99 (0.65,1.50)	0.950[c]	RACE (p=0.052)
	>18.6	1.33 (0.97,1.81)	0.073[c]	DIAB*DRKYR (p=0.020)

[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 8-28. (Continued)

Analysis of Achilles Reflex

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

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	784	5.6	All Categories		0.290
Unknown	342	3.8	Unknown vs. Background	0.66 (0.35,1.25)	0.205
Low	195	7.7	Low vs. Background	1.40 (0.76,2.57)	0.277
High	187	5.4	High vs. Background	0.95 (0.47,1.92)	0.887
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	782	All Categories		0.313**	DXCAT*RACE (p=0.045)
					AGE (p<0.001)
Unknown	341	Unknown vs. Background	0.66 (0.35,1.26)**	0.211**	DIAB (p=0.002)
Low	193	Low vs. Background	1.39 (0.74,2.60)**	0.303**	
High	187	High vs. Background	1.06 (0.51,2.23)**	0.871**	
Total	1,503				

**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

The unadjusted categorized current dioxin analysis of the Achilles reflex did not find a significant difference in the prevalences among the four categories (Table 8-28 [i]: 5.6%, 3.8%, 7.7%, and 5.4% for the background, unknown, low, and high current dioxin categories, p=0.290). The adjusted analysis detected a significant interaction between categorized current dioxin and race (Table 8-28 [j]: p=0.045). Stratified results show a marginally significant overall contrast for Blacks (Appendix Table G-1: p=0.078), but this finding may be affected by sparse data. Only two Black Ranch Hands (unknown current dioxin category) and three Black Comparisons in the background category had an abnormal Achilles reflex. None of the contrasts was significant for non-Blacks (p>0.10 for each contrast). After excluding the interaction, the overall contrast was not significant in the adjusted analysis (Table 8-28 [j]: p=0.313).

Biceps Reflex

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Under the minimal assumption, no Ranch Hands had an abnormal biceps reflex. One Ranch Hand had an abnormal biceps reflex under the maximal assumption. Table 8-29 [b] shows that he was in the low initial dioxin category. No analyses were done due to sparse data.

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

No current dioxin and time since tour analyses were done for the biceps reflex because there was only one Ranch Hand abnormality. Table 8-29 [d] shows that he was in the low current dioxin category with a time since tour 18.6 years or less.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The unadjusted categorized current dioxin analysis found that 10 Comparisons in the background current dioxin category had an abnormal biceps reflex (1.3%) versus 1 Ranch Hand in the unknown category (0.6%). Neither the overall contrast (Table 8-29 [e]: p=0.135) nor the unknown versus background contrast (p=0.482) was significant.

Babinski Reflex

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Under both the minimal and maximal assumptions there were only two Ranch Hands with an abnormal Babinski reflex. For each cohort, one was in the medium initial dioxin category and the other was in the high initial dioxin category. In the unadjusted analyses, initial dioxin was not associated with the Babinski reflex under both assumptions (Table 8-30 [a] and [b]: p=0.552 under the minimal assumption and p=0.285 under the maximal assumption). No adjusted analyses were done because of the sparse number of abnormalities.

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

The current dioxin-by-time interaction could not be investigated because no Ranch Hands with a time since tour 18.6 years or less had an abnormal Babinski reflex. The

TABLE 8-29.

Analysis of Biceps Reflex

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.)	p-Value
a) Minimal (n=521)	Low	130	0.0	--	--
	Medium	260	0.0		
	High	131	0.0		
b) Maximal (n=741)	Low	184	0.5	--	--
	Medium	371	0.0		
	High	186	0.0		

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

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 8-29. (Continued)

Analysis of Biceps Reflex

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

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)	p-Value
c) Minimal						--
(n=521)	≤18.6	0.0 (72)	0.0 (128)	0.0 (54)	--	--
	>18.6	0.0 (58)	0.0 (132)	0.0 (77)	--	--
d) Maximal						--
(n=741)	≤18.6	0.9 (106)	0.0 (191)	0.0 (83)	--	--
	>18.6	0.0 (78)	0.0 (179)	0.0 (104)	--	--

--: Relative risk, confidence interval, and 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 8-29. (Continued)

Analysis of Biceps Reflex

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

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	784	1.3	All Categories		0.135
Unknown	343	0.6	Unknown vs. Background	0.45 (0.10,2.08)	0.482
Low	196	0.0	Low vs. Background	--	0.212
High	187	0.0	High vs. Background	--	0.232
Total	1,510				

--: 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.

TABLE 8-30.

Analysis of Babinski Reflex

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=521)	Low	130	0.0	1.37 (0.51,3.73)	0.552
	Medium	260	0.4		
	High	131	0.8		
b) Maximal (n=741)	Low	184	0.0	1.62 (0.70,3.75)	0.285
	Medium	371	0.3		
	High	186	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 8-30. (Continued)

Analysis of Babinski Reflex

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

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
c) Minimal						--
(n=521)	≤18.6	0.0 (72)	0.0 (128)	0.0 (54)	--	--
	>18.6	1.7 (58)	0.0 (132)	1.3 (77)	0.96 (0.20,4.72)	0.964[b]
d) Maximal						--
(n=741)	≤18.6	0.0 (106)	0.0 (191)	0.0 (83)	--	--
	>18.6	0.0 (78)	0.6 (179)	1.0 (104)	1.24 (0.36,4.30)	0.734[b]

[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, and 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 8-30. (Continued)

Analysis of Babinski Reflex

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

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	784	0.3	All Categories		0.641
Unknown	343	0.6	Unknown vs. Background	2.29 (0.32,16.35)	0.712
Low	196	0.0	Low vs. Background	--	0.999
High	187	0.5	High vs. Background	2.10 (0.19,23.31)	0.948
Total	1,510				

--: 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.

association between current dioxin and the Babinski reflex was not significant for Ranch Hands with a time since tour more than 18.6 years under both the minimal (Table 8-30 [c]: p=0.964) and maximal (Table 8-30 [d]: p=0.734) assumptions. No adjusted analyses were done due to sparse data.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The overall contrast was not significant in the unadjusted categorized current dioxin analysis of the Babinski reflex (Table 8-30 [e]: p=0.641). No adjusted analysis was done because there were only five participants with an abnormal Babinski reflex (two in the background category, two in the unknown current dioxin category, and one in the high current dioxin category).

Tremor

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Under both the minimal and maximal assumptions, initial dioxin was not associated significantly with tremor (Table 8-31 [a-d]: p>0.60 for all unadjusted and adjusted analyses).

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

The unadjusted current dioxin and time since tour analyses of tremor did not find a significant interaction between current dioxin and time under either the minimal (Table 8-31 [e]: p=0.402) or maximal (Table 8-31 [f]: p=0.101) assumption.

The current dioxin-by-time interaction remained nonsignificant in the adjusted minimal analysis (Table 8-31 [g]: p=0.409), but the adjusted maximal analysis detected a significant interaction among current dioxin, time, and age (Table 8-31 [h]: p=0.044). Age was categorized to explore the interaction. Stratified results revealed a significant current dioxin-by-time interaction for older Ranch Hands, those born before 1942 (Appendix Table G-1: p=0.008). The within time stratum findings showed that there was a significant increased risk of tremor associated with initial dioxin for older Ranch Hands with a later tour (time≤18.6: Adj. RR=2.96, p=0.005; % abnormal: 0.0%, 0.9%, and 11.5% for the low, medium, and high initial dioxin categories). The relative risk was less than 1, but not significant for older Ranch Hands with an early tour (time>18.6: Adj. RR=0.70, p=0.432). For younger Ranch Hands, those born in or after 1942, the current dioxin-by-time interaction was not significant (p=0.954), nor were either of the within time stratum results significant (p=0.670 for time≤18.6 and p=0.440 for time>18.6).

After excluding the interaction, the current dioxin-by-time interaction was not significant for the adjusted maximal analysis (Table 8-31 [h]: p=0.102).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The prevalence of tremor abnormalities did not differ significantly among current dioxin categories in the unadjusted analysis, although the high category had the highest percentage of abnormalities (Table 8-31 [i]: 2.7%, 2.6%, 2.0%, and 3.7% for the background, unknown,

TABLE 8-31.

Analysis of Tremor

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=521)	Low	130	2.3	1.08 (0.69,1.67)	0.744
	Medium	260	2.3		
	High	131	3.1		
b) Maximal (n=741)	Low	184	2.7	1.08 (0.78,1.50)	0.643
	Medium	371	1.9		
	High	186	3.2		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=521)	1.05 (0.66,1.66)	0.850	AGE (p=0.598)
d) Maximal (n=741)	1.08 (0.77,1.51)	0.675	AGE (p=0.861)

[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 8-31. (Continued)

Analysis of Tremor

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

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.402[b]
(n=521)	≤18.6	1.4 (72)	2.3 (128)	3.7 (54)	1.41 (0.71,2.79)	0.326[c]
	>18.6	1.7 (58)	2.3 (132)	3.9 (77)	0.95 (0.52,1.75)	0.877[c]
f) Maximal						0.101[b]
(n=741)	≤18.6	0.0 (106)	2.1 (191)	3.6 (83)	1.56 (0.92,2.65)	0.102[c]
	>18.6	5.1 (78)	1.7 (179)	3.9 (104)	0.87 (0.55,1.37)	0.548[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			0.409[b]	AGE (p=0.631)
(n=521)	≤18.6	1.35 (0.67,2.75)	0.404[c]	
	>18.6	0.92 (0.49,1.73)	0.789[c]	
h) Maximal			0.102**[b]	CURR*TIME*AGE (p=0.044)
(n=741)	≤18.6	1.53 (0.89,2.63)**	0.126**[c]	
	>18.6	0.85 (0.54,1.37)**	0.512**[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 8-31. (Continued)

Analysis of Tremor

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

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	784	2.7	All Categories		0.788
Unknown	343	2.6	Unknown vs. Background	0.98 (0.44,2.16)	0.958
Low	196	2.0	Low vs. Background	0.76 (0.26,2.23)	0.614
High	187	3.7	High vs. Background	1.41 (0.59,3.37)	0.436
Total	1,510				

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	784	All Categories		0.657	AGE (p=0.089) INS (p=0.126)
Unknown	343	Unknown vs. Background	0.90 (0.40,1.99)	0.789	
Low	196	Low vs. Background	0.71 (0.24,2.10)	0.532	
High	187	High vs. Background	1.51 (0.62,3.70)	0.364	
Total	1,510				

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.

low, and high current dioxin categories, p>0.40 for each contrast). All contrasts remained nonsignificant after covariate adjustment (Table 8-31 [j]: p>0.35 for each contrast).

Coordination

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

The unadjusted initial dioxin analyses of coordination did not detect a significant association (Table 8-32 [a] and [b]: p=0.414 under the minimal assumption and p=0.178 under the maximal assumption), although the percentages of abnormalities increased with initial dioxin (0.0%, 1.9%, and 2.3% for the low, medium, and high initial dioxin categories of the minimal cohort; 0.5%, 1.1%, and 2.2% for the corresponding categories of the maximal cohort).

The relative risk remained nonsignificant after adjustment for age and the diabetic class-by-lifetime alcohol history interaction (Table 8-32 [c] and [d]: p=0.296 under the minimal assumption and p=0.101 under the maximal assumption). However, because of the association between dioxin and diabetes, an additional model was examined that excluded the diabetic class-by-lifetime alcohol history interaction under both assumptions. Adjusting for age only, initial dioxin was marginally associated with coordination under the maximal assumption (Table G-2: Adj. RR=1.49, p=0.085), but the association remained nonsignificant under the minimal assumption (Adj. RR=1.41, p=0.220).

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

The interaction between current dioxin and time since tour was not significant in the unadjusted analyses of coordination (Table 8-32 [e] and [f]: p=0.312 under the minimal assumption and p=0.128 under the maximal assumption). The relative risk was marginally more than 1 for Ranch Hands in the maximal cohort with a later tour (time≤18.6: Est. RR=2.00, p=0.051; % abnormal: 0.0%, 0.5%, and 3.6% for the low, medium, and high current dioxin categories).

Adjusting for age, the minimal analysis did not find a significant current dioxin-by-time interaction (Table 8-32 [g]: p=0.257), although the relative risk was marginally more than 1 for Ranch Hands with a later tour (time>18.6: Adj. RR=2.14, p=0.071). Under the maximal assumption, adjusting for age and the diabetic class-by-lifetime alcohol history interaction, the current dioxin-by-time interaction was marginally significant (Table 8-32 [h]: p=0.086) and the relative risk was significantly more than 1 for Ranch Hands with a later tour (time≤18.6: Adj. RR=2.53, p=0.019). The adjusted relative risk was more than 1, but not significant for Ranch Hands in the maximal cohort with an early tour (time>18.6: Adj. RR=1.11, p=0.758).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The prevalence of coordination abnormalities differed marginally among current dioxin categories in the unadjusted analysis (Table 8-32 [i]: 0.4%, 1.2%, 1.0%, and 2.7% for the background, unknown, low, and high current dioxin categories, p=0.056). There was a significant increased risk for the high category relative to the background category (Est. RR=7.14, 95% C.I.: [1.69,30.16], p=0.007).

TABLE 8-32.

Analysis of Coordination

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=521)	Low	130	0.0	1.25 (0.74,2.11)	0.414
	Medium	260	1.9		
	High	131	2.3		
b) Maximal (n=740)	Low	183	0.5	1.35 (0.89,2.06)	0.178
	Medium	371	1.1		
	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=513)	1.35 (0.78,2.36)	0.296	AGE (p=0.050) DIAB*DRKYR (p=0.046)
d) Maximal (n=729)	1.48 (0.94,2.32)	0.101	AGE (p=0.041) DIAB*DRKYR (p=0.047)

[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 8-32. (Continued)

Analysis of Coordination

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

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.312[b]
(n=521)	≤18.6	0.0 (72)	1.6 (128)	3.7 (54)	1.69 (0.75,3.79)	0.206[c]
	>18.6	1.7 (58)	0.8 (132)	2.6 (77)	0.94 (0.42,2.11)	0.885[c]
f) Maximal						0.128[b]
(n=740)	≤18.6	0.0 (105)	0.5 (191)	3.6 (83)	2.00 (1.00,4.03)	0.051[c]
	>18.6	1.3 (78)	1.1 (179)	1.9 (104)	0.99 (0.53,1.84)	0.962[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			0.257[b]	AGE (p=0.032)
(n=521)	≤18.6	2.14 (0.94,4.91)	0.071[c]	
	>18.6	1.14 (0.52,2.51)	0.748[c]	
h) Maximal			0.086[b]	AGE (p=0.025)
(n=729)	≤18.6	2.53 (1.16,5.48)	0.019[c]	DIAB*DRKYR (p=0.049)
	>18.6	1.11 (0.58,2.11)	0.758[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 8-32. (Continued)

Analysis of Coordination

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

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	783	0.4	All Categories		0.056
Unknown	342	1.2	Unknown vs. Background	3.08 (0.68,13.82)	0.143
Low	196	1.0	Low vs. Background	2.68 (0.44,16.15)	0.282
High	187	2.7	High vs. Background	7.14 (1.69,30.16)	0.007
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	781	All Categories		0.006**	DXCAT*AGE (p=0.049) RACE (p=0.093)
Unknown	341	Unknown vs. Background	4.68 (0.84,25.97)**	0.077**	DIAB*INS (p=0.038)
Low	194	Low vs. Background	3.89 (0.53,28.40)**	0.180**	
High	187	High vs. Background	18.30 (3.26,102.7)**	0.001**	
Total	1,503				

**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.

The adjusted analysis detected a significant categorized current dioxin-by-age interaction (Table 8-32 [j]: p=0.049). Age was dichotomized to explore the interaction. There was a significant overall difference in the prevalences of coordination abnormalities among categories for older Ranch Hands, those born before 1942 (Appendix Table G-1: 0.2%, 1.3%, 0.0%, and 5.7% for the background, unknown, low, and high current dioxin categories, p=0.003). The relative risk was significantly more than 1 for the high versus background contrast (Adj. RR=32.71, 95% C.I.: [3.50,306.0], p=0.002). No contrasts were significant in the younger Ranch Hand stratum, but the background category had the fewest percentage of abnormalities (0.3%, 0.9%, 2.5%, and 0.9% for the background, unknown, low, and high current dioxin categories, p>0.10 for each contrast).

After excluding the interaction, the adjusted analysis displayed a significant overall contrast (Table 8-32 [j]: p=0.006). The high versus background contrast was significant (Adj. RR=18.30, 95% C.I.: [3.26,102.7], p=0.001) and the unknown versus background contrast was marginally significant (Adj. RR=4.68, 95% C.I.: [0.84,25.97], p=0.077).

Romberg Sign

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Under both the minimal and maximal assumptions, there were only two assayed Ranch Hands with an abnormal Romberg sign. The association with initial dioxin was not significant (Table 8-33 [a] and [b]: p=0.871 in the unadjusted minimal analysis and p=0.479 in the unadjusted maximal analysis). No adjusted analyses were done because of the sparse number of abnormalities.

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

The current dioxin and time since tour analyses of Romberg sign could not investigate the interaction between current dioxin and time because no Ranch Hands with a later tour had an abnormal Romberg sign. For Ranch Hands with an early tour, the association between current dioxin and Romberg sign was not significant (Table 8-33 [c] and [d]: p=0.921 for the unadjusted minimal analysis and p=0.770 for the unadjusted maximal analysis). No adjusted analyses were done due to sparse data.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The overall contrast among current dioxin categories was not significant in the unadjusted analysis of Romberg sign (Table 8-33 [e]: p=0.117). The low and high current dioxin categories each had one abnormality; there were no abnormalities in the background and unknown categories. No adjusted analysis was done because of the sparse number of abnormalities.

Gait

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Although the percentages of gait abnormalities increased with initial dioxin, the relative risk was not significant in the unadjusted analyses under both the minimal (Table 8-34 [a]: Est. RR=1.27, p=0.236; % abnormal: 0.8%, 3.5%, and 3.8% for the low, medium, and high initial dioxin categories) and maximal (Table 8-34 [b]: Est. RR=1.25, p=0.154; % abnormal:

TABLE 8-33.
Analysis of Romberg Sign

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=521)	Low	130	0.0	1.10 (0.36,3.30)	0.871
	Medium	260	0.4		
	High	131	0.8		
b) Maximal (n=741)	Low	184	0.0	1.39 (0.58,3.34)	0.479
	Medium	371	0.3		
	High	186	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 8-33. (Continued)

Analysis of Romberg Sign

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

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
c) Minimal (n=521)	≤18.6	0.0 (72)	0.0 (128)	0.0 (54)	--	--
	>18.6	0.0 (58)	0.8 (132)	1.3 (77)	0.92 (0.18,4.70)	0.921[b]
d) Maximal (n=741)	≤18.6	0.0 (106)	0.0 (191)	0.0 (83)	--	--
	>18.6	0.0 (78)	0.6 (179)	1.0 (104)	1.21 (0.34,4.24)	0.770[b]

[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, and 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 8-33. (Continued)

Analysis of Romberg Sign

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

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	783	0.0	All Categories		0.117
Unknown	343	0.0	Unknown vs. Background	--	--
Low	196	0.5	Low vs. Background	--	0.400
High	187	0.5	High vs. Background	--	0.386
Total	1,509				

--: Relative risk/confidence interval/p-value 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.

TABLE 8-34.

Analysis of Gait

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=521)	Low	130	0.8	1.27 (0.87,1.87)	0.236
	Medium	260	3.5		
	High	131	3.8		
b) Maximal (n=740)	Low	183	1.6	1.25 (0.93,1.69)	0.154
	Medium	371	2.7		
	High	186	3.2		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=513)	1.24 (0.82,1.87)	0.323	AGE (p=0.514) DIAB (p=0.051) DRKYR (p=0.132) INS (p=0.062)
d) Maximal (n=729)	1.30 (0.94,1.80)	0.123	AGE (p=0.696) DIAB (p=0.042) DRKYR (p=0.034)

[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 8-34. (Continued)

Analysis of Gait

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

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.880[b]
(n=521)	≤18.6	1.4 (72)	1.6 (128)	1.9 (54)	1.18 (0.49,2.84)	0.705[c]
	>18.6	1.7 (58)	4.6 (132)	5.2 (77)	1.10 (0.69,1.73)	0.692[c]
f) Maximal						0.824[b]
(n=740)	≤18.6	1.0 (105)	1.6 (191)	2.4 (83)	1.08 (0.58,2.04)	0.806[c]
	>18.6	1.3 (78)	3.9 (179)	4.8 (104)	1.17 (0.82,1.68)	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			0.901[b]	AGE (p=0.720)
(n=513)	≤18.6	1.14 (0.47,2.75)	0.768[c]	DIAB (p=0.036)
	>18.6	1.07 (0.67,1.73)	0.771[c]	DRKYR (p=0.137)
				INS (p=0.053)
h) Maximal			0.949[b]	AGE (p=0.917)
(n=729)	≤18.6	1.21 (0.61,2.40)	0.577[c]	DIAB (p=0.032)
	>18.6	1.18 (0.81,1.73)	0.379[c]	DRKYR (p=0.037)

[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 8-34. (Continued)

Analysis of Gait

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

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	783	2.2	All Categories		0.657
Unknown	342	2.6	Unknown vs. Background	1.22 (0.54,2.76)	0.637
Low	196	3.1	Low vs. Background	1.42 (0.55,3.66)	0.464
High	187	3.7	High vs. Background	1.75 (0.72,4.29)	0.219
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	779	All Categories		0.482**	DXCAT*DIAB (p=0.047) AGE (p=0.135)
Unknown	338	Unknown vs. Background	1.06 (0.45,2.50)**	0.889**	DRKYR (p=0.044)
Low	192	Low vs. Background	1.50 (0.58,3.88)**	0.399**	
High	183	High vs. Background	2.03 (0.81,5.08)**	0.131**	
Total	1,492				

**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.

1.6%, 2.7%, and 3.2% for the low, medium, and high initial dioxin categories) assumptions. The adjusted analyses displayed essentially the same findings as the unadjusted analyses (Table 8-34 [c] and [d]: Adj. RR=1.24, p=0.323 for the minimal analysis and Adj. RR=1.30, p=0.123 for the maximal analysis).

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 in the analyses of gait (Table 8-34 [e-h]: p>0.80 in each analysis).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The unadjusted categorized current dioxin analysis of gait did not find a significant overall contrast (Table 8-34 [i]: p=0.657), but the high current dioxin category had the highest percentage of abnormalities (2.2%, 2.6%, 3.1%, and 3.7% for the background, unknown, low, and high current dioxin categories). Each Ranch Hand versus background contrast was also not significant (p>0.20 for each contrast).

The adjusted analysis detected a significant categorized current dioxin-by-diabetic class interaction (Table 8-34 [j]: p=0.047). Stratified results showed a marginally significant overall contrast among categories for normal participants (Appendix Table G-1: p=0.095; 2.3%, 0.7%, 2.7%, and 4.0% for the background, unknown, low, and high current dioxin categories), although none of the Ranch Hand versus background contrasts was significant (p>0.10 for each contrast). There was also a marginally significant overall contrast for diabetically impaired individuals (p=0.052), but the only abnormalities were in the unknown (8.5%, n=47) and background (1.9%, n=107) categories; the unknown versus background contrast was marginally significant (Adj. RR=5.27, 95% C.I.: [0.92,30.11], p=0.062). The overall contrast was not significant for diabetic individuals (p=0.630), but the percentages of gait abnormalities increased with current dioxin (1.5%, 5.3%, 5.9%, and 6.5% for the background, unknown, low, and high current dioxin categories). None of the Ranch Hand versus background contrasts was significant in this stratum (p>0.25 for each contrast).

After excluding the interaction, the adjusted analysis did not reveal any significant findings (Table 8-34 [j]: p>0.10 for each contrast).

CNS Index

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

In the unadjusted analyses, initial dioxin was not significantly associated with the CNS index under the minimal assumption (Table 8-35 [a]: p=0.171), but the estimated relative risk was marginally more than 1 under the maximal assumption (Table 8-35 [b]: Est. RR=1.24, p=0.064). In the maximal cohort, the percentages of CNS abnormalities were 3.8, 4.6, and 7.0 percent for the low, medium, and high initial dioxin categories.

Under both assumptions, the adjusted analyses detected a significant initial dioxin-by-age interaction (Table 8-35 [c] and [d]: p=0.019 in the adjusted minimal analysis and p=0.044 in the adjusted maximal analysis). Age was categorized to explore the interactions. Both analyses found a significant increased risk of CNS abnormalities for older Ranch Hands,

TABLE 8-35.

Analysis of CNS Index

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=521)	Low	130	3.1	1.23 (0.92,1.64)	0.171
	Medium	260	5.8		
	High	131	7.6		
b) Maximal (n=740)	Low	183	3.8	1.24 (0.99,1.55)	0.064
	Medium	371	4.6		
	High	186	7.0		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=521)	1.25 (0.93,1.68)**	0.145**	INIT*AGE (p=0.019)
d) Maximal (n=731)	1.26 (1.00,1.59)**	0.050**	INIT*AGE (p=0.044) DRKYR (p=0.077)

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

**Log_2 (initial 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: 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 8-35. (Continued)

Analysis of CNS Index

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

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.383[b]
(n=521)	≤18.6	2.8 (72)	4.7 (128)	7.4 (54)	1.43 (0.87,2.34)	0.159[c]
	>18.6	3.5 (58)	6.1 (132)	9.1 (77)	1.08 (0.74,1.57)	0.686[c]
f) Maximal						0.256[b]
(n=740)	≤18.6	1.0 (105)	3.7 (191)	8.4 (83)	1.44 (0.99,2.10)	0.056[c]
	>18.6	5.1 (78)	5.0 (179)	8.7 (104)	1.09 (0.82,1.46)	0.541[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			0.372[b]	AGE (p=0.628)
(n=521)	≤18.6	1.47 (0.88,2.43)	0.137[c]	
	>18.6	1.11 (0.75,1.63)	0.607[c]	
h) Maximal			0.165[b]	AGE (p=0.768)
(n=731)	≤18.6	1.55 (1.05,2.31)	0.029[c]	DRKYR (p=0.074)
	>18.6	1.10 (0.82,1.48)	0.511[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 8-35. (Continued)

Analysis of CNS Index

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

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	783	4.9	All Categories		0.276
Unknown	342	5.3	Unknown vs. Background	1.09 (0.61,1.94)	0.771
Low	196	4.6	Low vs. Background	0.94 (0.45,1.99)	0.878
High	187	8.6	High vs. Background	1.83 (1.00,3.37)	0.050
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	783	All Categories		0.137**	DXCAT*AGE (p=0.018) RACE*INS (p=0.023)
Unknown	342	Unknown vs. Background	1.01 (0.56,1.81)**	0.973**	
Low	196	Low vs. Background	0.91 (0.43,1.92)**	0.798**	
High	187	High vs. Background	2.08 (1.11,3.89)**	0.023**	
Total	1,508				

**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.

those born before 1942 (Appendix Table G-2: Adj. RR=1.66, p=0.010 in the minimal analysis and Adj. RR=1.53, p=0.009 in the maximal analysis). In both cohorts, the prevalence of abnormalities increased with initial dioxin for older Ranch Hands (2.3%, 4.0%, and 12.5% for the low, medium, and high initial dioxin categories in the minimal cohort; 2.7%, 3.3%, and 10.3% for the corresponding categories in the maximal cohort). For younger Ranch Hands, the relative risk was not significant (Adj. RR=0.87, p=0.523 in the minimal cohort; Adj. RR=1.00, p=0.976 in the maximal cohort).

After excluding the interaction, the adjusted minimal analysis was not significant (Table 8-35 [c]: p=0.145), but the adjusted maximal analysis displayed a significant increased risk (Table 8-35 [d]: Adj. RR=1.26, p=0.050).

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

The unadjusted current dioxin and time since tour analyses of the CNS index did not find a significant interaction between current dioxin and time (Table 8-35 [e] and [f]: p=0.383 under the minimal assumption and p=0.256 under the maximal assumption). There was a marginally significant association between current dioxin and the CNS index for Ranch Hands with a later tour under the maximal assumption (time≤18.6: Est. RR=1.44, p=0.056; % abnormal: 1.0%, 3.7%, and 8.4% for the low, medium, and high current dioxin categories). None of the other within time stratum results was significant in the unadjusted analyses.

The adjusted analyses displayed similar findings. The current dioxin-by-time interaction was not significant under either assumption (Table 8-35 [g] and [h]: p=0.372 under the minimal assumption and p=0.165 under the maximal assumption). Under the maximal assumption, the relative risk of an abnormal CNS index was significant for Ranch Hands with a later tour (Adj. RR=1.55, p=0.029).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The overall contrast was not significant in the unadjusted categorized current dioxin analysis of the CNS index (Table 8-35 [i]: p=0.276), although there were relatively more abnormalities in the high current dioxin category than in the background category (8.6% versus 4.9%; Est. RR=1.83, 95% C.I.: [1.00,3.37], p=0.050). The percentages of abnormalities in the low (4.6%) and unknown (5.3%) current dioxin categories were not significantly different from the background percentage (p>0.75 for both contrasts).

The adjusted analysis detected a significant categorized current dioxin-by-age interaction (Table 8-35 [j]: p=0.018). Stratified results showed that the prevalence of CNS abnormalities differed significantly among current dioxin categories for older participants (Appendix Table G-1: 5.9%, 5.3%, 1.7%, and 12.9% for the background, unknown, low, and high current dioxin categories, p=0.017). For older individuals, the relative risk was significantly more than 1 for the high versus background contrast (Adj. RR=2.39, 95% C.I.: [1.07,5.34], p=0.034) and it was marginally less than 1 for the low versus background contrast (Adj. RR=0.27, 95% C.I.: [0.06,1.16], p=0.079). The overall contrast was not significant for younger men (p=0.401) although the low versus background relative risk was marginally more than 1 (Adj. RR=2.50, 95% C.I.: [0.93,6.72], p=0.069). In this stratum, the prevalences for the background, unknown, low, and high current dioxin categories were 3.4, 5.1, 8.6, and 6.0 percent. The interaction occurred partly because the low category had the

fewest percentage of abnormalities in the older age stratum, but it had the highest percentage of abnormalities in the younger age stratum.

After deleting the interaction, the adjusted analysis supported the unadjusted findings. The overall contrast was not significant (Table 8-35 [j]: p=0.137), but the high current dioxin category had a significant increased risk of CNS abnormalities (Adj. RR=2.08, 95% C.I.: [1.11,3.89], p=0.023).

Longitudinal Analysis

Physical Examination Variables

The neurological assessment conducted longitudinal analyses for the cranial nerve index and the CNS index. These analyses only included participants who were normal at the 1985 examination to determine whether the incidence between 1985 and 1987 for these two variables was associated with dioxin. The longitudinal analyses investigated the change between 1985 and 1987 because SCRF conducted both of these neurological examinations.

Cranial Nerve Index

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Under the minimal assumption, the longitudinal analysis found that initial dioxin was not significantly associated with the percentage of Ranch Hands who developed a cranial nerve index abnormality between the 1985 and 1987 examinations (Table 8-36 [a]: p=0.288). However, under the maximal assumption, there was a marginally significant decreased risk (Table 8-36 [b]: Est. RR= 0.83, p=0.055). The percentages of Ranch Hands in the maximal cohort with an abnormal index in 1987 (based on those who were normal in 1985) were 15.3, 12.7, and 7.3 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 longitudinal analysis of the cranial nerve index did not detect a significant current dioxin-by-time since tour interaction (Table 8-36 [c]: p=0.756). Thus, the association with current dioxin did not differ between time strata.

However, under the maximal assumption, there was a marginally significant interaction between current dioxin and time (Table 8-36 [d]: p=0.086). For Ranch Hands in the maximal cohort with a later tour, the relative risk of developing a cranial nerve index abnormality between 1985 and 1987 was significantly less than 1 (time$\leq$18.6: Est. RR=0.68, p=0.017; % abnormal: 19.8%, 11.7%, and 6.6% for the low, medium, and high current dioxin categories).

The relative risk was less than 1, but not significant for Ranch Hands in the maximal cohort with an early tour (time>18.6: Est. RR=0.97, p=0.816).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The percentage of participants who developed a cranial nerve index abnormality between the 1985 and 1987 examinations did not differ significantly among the four current

TABLE 8-36.

Longitudinal Analysis of Cranial Nerve Index

Ranch Hands - Log_2 (Initial Dioxin)

Assumption	Initial Dioxin	Percent Abnormal/(n) Examination 1982	1985	1987
a) Minimal	Low	51.8 (114)	6.6 (121)	12.4 (121)
	Medium	52.8 (231)	7.2 (251)	15.5 (251)
	High	58.3 (115)	8.0 (125)	12.8 (125)

Initial Dioxin	Normal in 1985: n in 1987	Percent Abnormal in 1987	Est. Relative Risk (95% C.I.)[a]	p-Value
Low	113	10.6	0.87 (0.67,1.13)	0.288
Medium	233	12.5		
High	115	7.8		

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

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Summary statistics for 1982 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 1985 and 1987 results. Statistical analyses are based only on participants who were normal in 1985 (see Chapter 4, Statistical Methods).

TABLE 8-36. (Continued)

Longitudinal Analysis of Cranial Nerve Index

Ranch Hands - Log_2 (Initial Dioxin)

Assumption	Initial Dioxin	Percent Abnormal/(n) Examination 1982	1985	1987
b) Maximal	Low	52.3 (155)	12.8 (172)	18.6 (172)
	Medium	52.5 (326)	6.8 (355)	15.2 (355)
	High	56.4 (163)	7.3 (177)	11.9 (177)

Initial Dioxin	Normal in 1985: n in 1987	Normal in 1985: Percent Abnormal in 1987	Est. Relative Risk (95% C.I.)[a]	p-Value
Low	150	15.3	0.83 (0.69,1.01)	0.055
Medium	331	12.7		
High	164	7.3		

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

Note: Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.
Summary statistics for 1982 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 1985 and 1987 results. Statistical analyses are based only on participants who were normal in 1985 (see Chapter 4, Statistical Methods).

TABLE 8-36. (Continued)

Longitudinal Analysis of Cranial Nerve Index

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	54.7 (64)	52.2 (113)	52.2 (46)
		1985	7.6 (66)	8.3 (121)	0.0 (50)
		1987	10.6 (66)	16.5 (121)	4.0 (50)
	>18.6	1982	49.0 (49)	55.5 (119)	58.0 (69)
		1985	5.4 (56)	6.2 (129)	13.3 (75)
		1987	12.5 (56)	16.3 (129)	17.3 (75)

Time (Yrs.)	Normal in 1985: Percent Abnormal/(n) in 1987 Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
					0.756[b]
≤18.6	9.8 (61)	11.7 (111)	4.0 (50)	0.77 (0.48,1.23)	0.278[c]
>18.6	11.3 (53)	14.1 (121)	9.2 (65)	0.84 (0.60,1.19)	0.338[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.
Summary statistics for 1982 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 1985 and 1987 results. Statistical analyses are based only on participants who were normal in 1985 (see Chapter 4, Statistical Methods).

TABLE 8-36. (Continued)

Longitudinal Analysis of Cranial Nerve Index

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	46.0 (87)	54.4 (169)	51.4 (72)
		1985	11.3 (97)	7.9 (177)	2.6 (78)
		1987	21.7 (97)	14.7 (177)	7.7 (78)
	>18.6	1982	56.1 (66)	52.5 (158)	59.8 (92)
		1985	14.5 (76)	5.7 (176)	11.0 (100)
		1987	14.5 (76)	15.9 (176)	15.0 (100)

Time (Yrs.)	Normal in 1985: Percent Abnormal/(n) in 1987 Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
					0.086[b]
≤18.6	19.8 (86)	11.7 (163)	6.6 (76)	0.68 (0.50,0.93)	0.017[c]
>18.6	7.7 (65)	14.5 (166)	7.9 (89)	0.97 (0.75,1.25)	0.816[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: Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.
Summary statistics for 1982 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 1985 and 1987 results. Statistical analyses are based only on participants who were normal in 1985 (see Chapter 4, Statistical Methods).

TABLE 8-36. (Continued)

Longitudinal Analysis of Cranial Nerve Index

e) Ranch Hands and Comparisons by Current Dioxin Category

Current Dioxin Category	Percent Abnormal/(n) Examination 1982	1985	1987
Background	52.0 (641)	9.0 (733)	16.1 (733)
Unknown	50.0 (286)	10.6 (320)	15.6 (320)
Low	52.8 (176)	7.4 (190)	17.9 (190)
High	56.1 (164)	7.3 (178)	11.8 (178)

Current Dioxin Category	Normal in 1985: n in 1987	Percent Abnormal in 1987	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	667	12.7	All Categories		0.125
Unknown	286	13.3	Unknown vs. Background	1.05 (0.70,1.58)	0.818
Low	176	14.8	Low vs. Background	1.19 (0.74,1.91)	0.479
High	165	7.3	High vs. Background	0.54 (0.29,1.01)	0.053

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 1982 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 1985 and 1987 results. Statistical analyses are based only on participants who were normal in 1985 (see Chapter 4, Statistical Methods).

dioxin categories in the longitudinal analysis (Table 8-36 [e]: 12.7%, 13.3%, 14.8%, and 7.3% for the background, unknown, low, and high current dioxin categories, p=0.125). However, the relative risk of developing an abnormal cranial nerve index for the high versus background contrast was marginally less than 1 (Est. RR=0.54; 95% C.I.: [0.29,1.01], p=0.053).

CNS Index

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Under the minimal assumption, the longitudinal analysis of the CNS index did not find a significant risk associated with initial dioxin (Table 8-37 [a]: Est. RR=1.25, p=0.207), but the relative risk was marginally significant under the maximal assumption (Table 8-37 [b]: Est. RR=1.27, p=0.087). The percentages of Ranch Hands in the maximal cohort with an abnormal CNS index at the 1987 examination (based on those who were normal at the 1985 examination) were 2.4, 3.5, and 5.2 percent for the low, medium, and high initial dioxin categories.

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

The current dioxin-by-time since tour interaction was not significant for the longitudinal analysis of the CNS index under either the minimal or the maximal assumption (Table 8-37 [c] and [d]: p=0.654 and p=0.409, respectively). However, under the maximal assumption, the relative risk was marginally more than 1 for Ranch Hands with a later tour (time$\leq$18.6: Est. RR=1.45, p=0.080). For these Ranch Hands, the percentages with an abnormal CNS index (based on those who were normal in 1985) were 1.0, 2.9, and 7.8 percent for the low, medium, and high current dioxin categories.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The longitudinal analysis did not find a significant difference in the percentages of participants with an abnormal CNS index at the 1987 examination (based on those who were normal in 1985) among the current dioxin categories (Table 8-37 [e]: 4.4%, 3.8%, 3.2%, and 6.8% for the background, unknown, low, and high current dioxin categories, p=0.382). The three Ranch Hand versus background contrasts were also not significant (p>0.15 for each contrast).

DISCUSSION

Although definitive diagnosis usually requires laboratory testing beyond the scope of the current study, the data analyzed in this chapter can be relied upon to detect the presence, if not the cause, of neurologic disease, including disorders of the peripheral nervous system. In clinical practice, the neurological assessment can be divided into examinations of the peripheral and the cranial nerves. The central, cranial, and peripheral nerve variables examined can provide specific clues in the anatomic site of neurological lesions and clarify the need for additional diagnostic studies.

As indices of CNS function, tremor and coordination are less specific and more subject to individual variation in the absence of underlying neurological disease. Tremor, for example, may occur as a benign familial trait, may be reflective of alcohol withdrawal, or may be a marker of extrapyramidal motor system disease as in Parkinson's syndrome. The Romberg sign may signal a lesion in the cerebellum but is more often indicative of impaired position

TABLE 8-37.

Longitudinal Analysis of CNS Index

Ranch Hands - Log_2 (Initial Dioxin)

Assumption	Initial Dioxin	Percent Abnormal/(n) Examination 1982	1985	1987
a) Minimal	Low	30.6 (121)	5.6 (125)	3.2 (125)
	Medium	27.8 (245)	3.5 (255)	5.9 (255)
	High	24.0 (121)	3.9 (128)	7.8 (128)

Initial Dioxin	Normal in 1985: n in 1987	Percent Abnormal in 1987	Est. Relative Risk (95% C.I.)[a]	p-Value
Low	118	2.5	1.25 (0.89,1.75)	0.207
Medium	246	4.1		
High	123	5.7		

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

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Summary statistics for 1982 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 1985 and 1987 results. Statistical analyses are based only on participants who were normal in 1985 (see Chapter 4, Statistical Methods).

TABLE 8-37. (Continued)

Longitudinal Analysis of CNS Index

Ranch Hands - Log_2 (Initial Dioxin)

Assumption	Initial Dioxin	Percent Abnormal/(n) Examination 1982	1985	1987
b) Maximal	Low	22.3 (166)	2.9 (175)	4.0 (175)
	Medium	28.1 (349)	3.6 (361)	4.7 (361)
	High	25.7 (171)	4.4 (182)	7.1 (182)

Initial Dioxin	Normal in 1985: n in 1987	Normal in 1985: Percent Abnormal in 1987	Est. Relative Risk (95% C.I.)[a]	p-Value
Low	170	2.4	1.27 (0.97,1.65)	0.087
Medium	348	3.5		
High	174	5.2		

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

Note: Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.
Summary statistics for 1982 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 1985 and 1987 results. Statistical analyses are based only on participants who were normal in 1985 (see Chapter 4, Statistical Methods).

TABLE 8-37. (Continued)

Longitudinal Analysis of CNS Index

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	23.9 (67)	27.7 (119)	20.4 (49)
		1985	5.9 (68)	3.2 (125)	3.9 (51)
		1987	2.9 (68)	4.8 (125)	7.8 (51)
	>18.6	1982	37.0 (54)	27.6 (127)	28.2 (71)
		1985	5.3 (57)	3.1 (130)	5.2 (77)
		1987	3.5 (57)	6.2 (130)	9.1 (77)

Time (Yrs.)	Normal in 1985: Percent Abnormal/(n) in 1987 Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
≤18.6	3.1 (64)	4.1 (121)	6.1 (49)	1.39 (0.81,2.39)	0.654[b] 0.230[c]
>18.6	0.0 (54)	4.8 (126)	5.5 (73)	1.18 (0.75,1.87)	0.473[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.
Summary statistics for 1982 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 1985 and 1987 results. Statistical analyses are based only on participants who were normal in 1985 (see Chapter 4, Statistical Methods).

TABLE 8-37. (Continued)

Longitudinal Analysis of CNS Index

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	18.7 (91)	25.7 (179)	24.0 (75)
		1985	2.0 (99)	4.4 (183)	3.8 (80)
		1987	1.0 (99)	3.8 (183)	8.8 (80)
	>18.6	1982	25.7 (74)	30.4 (171)	28.1 (96)
		1985	2.6 (76)	4.0 (177)	3.9 (103)
		1987	5.3 (76)	5.1 (177)	8.7 (103)

Time (Yrs.)	Normal in 1985: Percent Abnormal/(n) in 1987 Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
					0.409[b]
≤18.6	1.0 (97)	2.9 (175)	7.8 (77)	1.45 (0.96,2.21)	0.080[c]
>18.6	2.7 (74)	2.9 (170)	6.1 (99)	1.15 (0.80,1.66)	0.448[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: Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.
Summary statistics for 1982 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 1985 and 1987 results. Statistical analyses are based only on participants who were normal in 1985 (see Chapter 4, Statistical Methods).

TABLE 8-37. (Continued)

Longitudinal Analysis of CNS Index

e) Ranch Hands and Comparisons by Current Dioxin Category

Current Dioxin Category	Percent Abnormal/(n) Examination 1982	1985	1987
Background	26.4 (666)	3.1 (748)	5.0 (748)
Unknown	23.7 (304)	3.4 (327)	5.5 (327)
Low	27.1 (188)	3.6 (193)	4.7 (193)
High	26.3 (171)	3.8 (183)	8.7 (183)

Current Dioxin Category	Normal in 1985: n in 1987	Percent Abnormal in 1987	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	725	4.4	All Categories		0.382
Unknown	316	3.8	Unknown vs. Background	0.85 (0.43,1.68)	0.649
Low	186	3.2	Low vs. Background	0.72 (0.30,1.75)	0.472
High	176	6.8	High vs. Background	1.58 (0.80,3.14)	0.187

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 1982 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 1985 and 1987 results. Statistical analyses are based only on participants who were normal in 1985 (see Chapter 4, Statistical Methods).