TABLE 6-2.

Number of Participants With Missing Data for the General Health Assessment

Variable	Variable Use	Assumption (Ranch Hands Only)		Categorized Current Dioxin	
		Minimal	Maximal	Ranch Hand	Comparison
Self-Perception of Health	DEP	0	0	0	1
Appearance of Illness or Distress by Physician	DEP	0	0	0	1
Personality Type (1985)	COV	15	25	27	35

DEP--Dependent variable (missing data).
COV--Covariate (missing data).

TABLE 6-3.

Analysis of Self-Perception of Health

Ranch Hands - Log$_2$ (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Fair/Poor	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=521)	Low	130	5.4	1.10 (0.85,1.44)	0.471
	Medium	260	7.7		
	High	131	7.6		
b) Maximal (n=742)	Low	185	4.9	1.23 (1.00,1.50)	0.058
	Medium	371	5.9		
	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)	1.14 (0.87,1.49)**	0.360**	INIT*AGE (p=0.045)
d) Maximal (n=717)	1.23 (1.00,1.52)**	0.056**	INIT*PERS (p=0.046)

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

**Log$_2$ (initial dioxin)-by-covariate interaction (0.01<p≤0.05); 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.
   INIT: Log$_2$ (initial dioxin).

TABLE 6-3. (Continued)

Analysis of Self-Perception of Health

Ranch Hands - Log$_2$ (Current Dioxin) and Time - Unadjusted

| Assumption | Time (Yrs.) | Percent Fair or Poor/(n) Current Dioxin | | | Est. Relative Risk (95% C.I.)[a] | p-Value |
		Low	Medium	High		
e) Minimal						0.056[b]
(n=521)	≤18.6	6.9 (72)	5.5 (128)	3.7 (54)	0.64 (0.34,1.20)	0.166[c]
	>18.6	5.2 (58)	8.3 (132)	11.7 (77)	1.22 (0.89,1.67)	0.213[c]
f) Maximal						0.314[b]
(n=742)	≤18.6	1.9 (106)	6.3 (191)	3.6 (83)	1.00 (0.68,1.48)	0.996[c]
	>18.6	3.8 (79)	7.8 (179)	9.6 (104)	1.27 (0.99,1.63)	0.065[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*PERS (p=0.007)
(n=506)	≤18.6	****	****	
	>18.6	****	****	
h) Maximal			****	CURR*TIME*PERS (p=0.005)
(n=717)	≤18.6	****	****	
	>18.6	****	****	

[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≤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.
CURR: Log$_2$ (current dioxin).
TIME: Time since tour.

TABLE 6-3. (Continued)

Analysis of Self-Perception of Health

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

Current Dioxin Category	n	Percent Fair/Poor	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	785	5.0	All Categories		0.253
Unknown	345	3.8	Unknown vs. Background	0.75 (0.39,1.42)	0.377
Low	196	7.1	Low vs. Background	1.47 (0.78,2.77)	0.231
High	187	7.0	High vs. Background	1.43 (0.75,2.73)	0.281
Total	1,513				

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

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	750	All Categories		0.270	AGE*PERS (p=0.041)
Unknown	328	Unknown vs. Background	0.73 (0.37,1.42)	0.350	
Low	192	Low vs. Background	1.46 (0.77,2.75)	0.244	
High	181	High vs. Background	1.40 (0.72,2.71)	0.323	
Total	1,451				

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.

Based on the minimal assumption, there was a significant interaction between initial dioxin and age (Table 6-3 [c]: p=0.045) for the adjusted analysis. To investigate this interaction, the association between self-perception of health and initial dioxin was examined separately for Ranch Hands born in or after 1942, and for Ranch Hands born before 1942. For the younger Ranch Hands, there was a significant positive association between self-perception of health and initial dioxin (Table E-1: p=0.049, Adj. RR=1.49). For the older Ranch Hands, a nonsignificant negative association was found between self-perception of health and initial dioxin (p=0.522). Without the interaction of initial dioxin and age in the model, the association was nonsignificant (p=0.360).

Under the maximal assumption, there was a significant interaction between initial dioxin and personality type (Table 6-3 [d]: p=0.046) for the adjusted analysis. To examine this interaction, the association was investigated for each personality type. For Ranch Hands classified as type A, there was a significant positive association between self-perception of health and initial dioxin (Table E-1: p=0.005, Adj. RR=1.57). For the type B Ranch Hands, a nonsignificant positive association was found (p=0.912). Without the interaction of initial dioxin and personality type in the model, the adjusted relative risk was of borderline significance (Table 6-3 [d]: p=0.056, Est. RR=1.23).

Model 2: Ranch Hands - Log₂ (Current Dioxin) and Time

In the unadjusted analysis of the association between self-perception of health with current dioxin and time since tour, based on the minimal assumption, there was a marginally significant current dioxin-by-time interaction (Table 6-3 [e]: p=0.056); thus, the relationships between self-perception of health and current dioxin differed marginally between time strata (i.e., the estimated relative risks between strata were marginally different). Neither of the associations was significant within time strata ($\leq$18.6 years, p=0.166; >18.6 years, p=0.213).

Under the maximal assumption, the current dioxin-by-time interaction was not significant for the unadjusted analysis (Table 6-3 [f]: p=0.314). However, for Ranch Hands whose time exceeded 18.6 years, the relative frequencies of Ranch Hands with a fair or poor self-perception of health increased marginally with current dioxin (p=0.065, Est. RR=1.27). For the low, medium, and high current dioxin categories, the relative frequencies were 3.8, 7.8, and 9.6 percent.

In the adjusted analysis, there was a significant interaction among current dioxin, time, and personality type under both the minimal and the maximal assumptions (Table 6-3 [g] and [h]: p=0.007 and p=0.005). To investigate these interactions, associations between self-perception and current dioxin are presented separately for each time and personality-type stratum. Under the minimal assumption, Ranch Hands with personality type A had a significant current dioxin-by-time interaction (Appendix Table E-1: p=0.036). There was a significant positive association between self-perception of health and current dioxin for Ranch Hands with personality type A and time greater than 18.6 years (Appendix Table E-1: p=0.014, Adj. RR=1.83). For Ranch Hands with personality type A and time of 18.6 years or less, there was a nonsignificant negative association (p=0.106). The interaction of current dioxin and time was not significant (p=0.747) for Ranch Hands classified as type B. Under the maximal assumption, Ranch Hands with personality type A also exhibited a significant interaction for current dioxin and time (Appendix Table E-1: p=0.014). There also was a

significant positive association with current dioxin for Ranch Hands with personality type A and time greater than 18.6 years (Appendix Table E-1: p=0.001, Adj. RR=2.11). For Ranch Hands with personality type A and time of 18.6 years or less, there was a nonsignificant negative association (p=0.360). The interaction with current dioxin and time was not significant (p=0.270) for type B Ranch Hands.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In both the unadjusted and the adjusted analyses of the frequencies of Ranch Hands with unknown, low, and high current dioxin and Comparisons with background current dioxin reporting a fair or poor self-perception of health, the contrasts of the four current dioxin categories were not significant (Table 6-3 [i] and [j]: p=0.253 and p=0.270, respectively).

Physical Examination Variables

Appearance of Illness or Distress by Physician

Model 1: Ranch Hands - Log$_2$ (Initial Dioxin)

In the unadjusted analysis of the physician's assessment as to whether the study participant displayed illness or distress at the physical examination, there were nonsignificant associations with initial dioxin for both the minimal and the maximal assumptions (Table 6-4 [a] and [b]: p=0.478 and p=0.195). Because none of the candidate covariates was retained in the adjusted models under either the minimal or the maximal assumptions, adjusted relative risks and associated p-values were identical to those presented for the unadjusted analysis.

Model 2: Ranch Hands - Log$_2$ (Current Dioxin) and Time

Under both the minimal and maximal assumptions, the unadjusted analysis of the association between appearance of illness or distress with current dioxin and time since tour contained no significant current dioxin-by-time interaction (Table 6-4 [e] and [f]: p=0.203 and p=0.396, respectively). Similar to the adjusted analyses for initial dioxin, none of the candidate covariates was retained in the adjusted models under either the minimal or the maximal assumption; thus, the adjusted results (Table 6-4 [g] and [h]) were identical to the unadjusted results.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In the unadjusted analysis of the frequencies of Ranch Hands with unknown, low, and high current dioxin and Comparisons with background current dioxin displaying the appearance of illness or distress at the physical examination, the contrast of the four current dioxin categories was not significant (Table 6-4 [i]: p=0.407).

The adjusted analysis of appearance of illness or distress, based on the four dioxin categories, contained a significant interaction between categorized current dioxin and age (Table 6-4 [j]: p=0.034). To investigate the interaction, separate adjusted analyses were performed for Ranch Hands and Comparisons born in or after 1942 and those born prior to 1942 (Appendix Table E-1). For younger participants, no Ranch Hands and only one Comparison were judged to have had an appearance of illness or distress. For older participants, the overall contrast was not significant (p=0.236). An adjusted model without

TABLE 6-4.

Analysis of Appearance of Illness or Distress by Physician

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=521)	Low	130	0.8	1.36 (0.60,3.09)	0.478
	Medium	260	0.0		
	High	131	1.5		
b) Maximal (n=742)	Low	185	0.0	1.61 (0.81,3.21)	0.195
	Medium	371	0.3		
	High	186	1.1		

Ranch Hands - Log₂ (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=521)	1.36 (0.60,3.09)	0.478	--
d) Maximal (n=742)	1.61 (0.81,3.21)	0.195	--

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

Note: <u>Minimal</u>--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.

      <u>Maximal</u>--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 6-4. (Continued)

Analysis of Appearance of Illness or Distress by Physician

Ranch Hands - Log$_2$ (Current Dioxin) and Time - Unadjusted

| | | Percent Yes/(n) Current Dioxin | | | | |
Assumption	Time (Yrs.)	Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.203[b]
(n=521)	≤18.6	0.0 (72)	0.8 (128)	0.0 (54)	0.28 (0.01,10.02)	0.488[c]
	>18.6	0.0 (58)	0.0 (132)	2.6 (77)	1.71 (0.68,4.30)	0.253[c]
f) Maximal						0.396[b]
(n=742)	≤18.6	0.0 (106)	0.5 (191)	0.0 (83)	0.88 (0.16,4.80)	0.880[c]
	>18.6	0.0 (79)	0.0 (179)	1.9 (104)	1.88 (0.82,4.30)	0.138[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=521)	≤18.6	0.28 (0.01,10.02)	0.488[c]	
	>18.6	1.71 (0.68,4.30)	0.253[c]	
h) Maximal				--
(n=742)	≤18.6	0.88 (0.16,4.80)	0.880[c]	
	>18.6	1.88 (0.82,4.30)	0.138[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 6-4. (Continued)

Analysis of Appearance of Illness or Distress by Physician

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

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	785	0.5	All Categories		0.407
Unknown	345	0.6	Unknown vs. Background	1.14 (0.21,6.25)	0.881
Low	196	0.0	Low vs. Background	--	--
High	187	1.1	High vs. Background	2.11 (0.38,11.61)	0.390
Total	1,513				

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	785	All Categories		0.300**	DXCAT*AGE (p=0.034)
Unknown	345	Unknown vs. Background	1.12 (0.20,6.18)**	0.894**	
Low	196	Low vs. Background	--	--	
High	187	High vs. Background	3.12 (0.54,18.12)**	0.204**	
Total	1,513				

**Categorized current dioxin-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction.

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

Notes: 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.
      DXCAT: Categorized current dioxin.

the interaction of categorized current dioxin and age also exhibited a nonsignificant overall contrast (Table 6-4 [j]: p=0.300).

Relative Age

Model 1: Ranch Hands - Log₂ (Initial Dioxin)

In the unadjusted analysis of the physician's assessment of whether the study participant appeared older versus younger or the same than his stated age, there was no significant association with initial dioxin under either the minimal or maximal assumption (Table 6-5 [a] and [b]: p=0.517 and p=0.512).

Under both the minimal and maximal assumptions, the association between relative age and initial dioxin also was not significant when adjusted for covariate information (Table 6-5 [c] and [d]: p=0.660 and p=0.697, respectively).

Model 2: Ranch Hands - Log₂ (Current Dioxin) and Time

In the unadjusted analysis of relative age with current dioxin and time since tour under the minimal assumption, the interaction between current dioxin and time was significant (Table 6-5 [e]: p=0.039); thus, the relationships between relative age and current dioxin differed between time strata (i.e., the estimated relative risks between time strata differed significantly). A significant positive association was found for those Ranch Hands with time of 18.6 years or less (p=0.027, Est. RR=1.73). The relative frequency of individuals that appeared older than their stated age increased as current dioxin increased (low, 2.8%; medium, 4.7%; high, 7.4%). For Ranch Hands with time greater than 18.6 years, there was a negative association between relative age and current dioxin that was not significant (p=0.526).

Under the maximal assumption, the unadjusted analysis also exhibited a significant interaction between current dioxin and time (Table 6-5 [f]: p=0.024). For Ranch Hands with time of 18.6 years or less, a significant positive association was displayed between relative age and current dioxin (p=0.028, Est. RR=1.50). For those individuals having times at or below 18.6 years, the relative frequency of Ranch Hands that appeared older to the physician was about the same for the low and medium current dioxin levels (2.8% and 2.6%). However, the frequency for those Ranch Hands at the high current dioxin level was considerably greater (9.6%). For Ranch Hands with times greater than 18.6 years, there was a nonsignificant negative association (p=0.349).

In the adjusted analysis performed under the minimal assumption, none of the candidate covariates was retained in the model; thus, the relative risks and associated p-values for the adjusted analysis (Table 6-5 [g]) were identical to the unadjusted results (Table 6-5 [e]).

Under the maximal assumption, the interaction between current dioxin and time was significant (Table 6-5 [h]: p=0.026); thus, the adjusted relative risks differed significantly between time strata. For Ranch Hands with time of 18.6 years or less, there was a marginally significant positive association between relative age and current dioxin (p=0.066, Adj. RR=1.42). For the other time stratum, the negative association was not significant (p=0.238).

TABLE 6-5.

Analysis of Relative Age

Ranch Hands - Log$_2$ (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Older	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=521)	Low	130	3.1	1.11 (0.81,1.53)	0.517
	Medium	260	5.4		
	High	131	5.3		
b) Maximal (n=742)	Low	185	3.8	1.08 (0.86,1.37)	0.512
	Medium	371	5.4		
	High	186	4.8		

Ranch Hands - Log$_2$ (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=521)	1.08 (0.77,1.51)	0.660	AGE*RACE (p=0.048)
d) Maximal (n=742)	1.05 (0.82,1.34)	0.697	AGE*RACE (p=0.036)

[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 6-5. (Continued)
Analysis of Relative Age

Ranch Hands - Log$_2$ (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Older/(n) Current Dioxin			Est. Relative Risk (95% C.I.)[a]	p-Value
		Low	Medium	High		
e) Minimal						0.039[b]
(n=521)	≤18.6	2.8	4.7	7.4	1.73 (1.06,2.81)	0.027[c]
		(72)	(128)	(54)		
	>18.6	5.2	5.3	3.9	0.86 (0.53,1.38)	0.526[c]
		(58)	(132)	(77)		
f) Maximal						0.024[b]
(n=742)	≤18.6	2.8	2.6	9.6	1.50 (1.04,2.15)	0.028[c]
		(106)	(191)	(83)		
	>18.6	5.1	6.7	3.8	0.85 (0.60,1.20)	0.349[c]
		(79)	(179)	(104)		

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			0.039[b]	- -
(n=521)	≤18.6	1.73 (1.06,2.81)	0.027[c]	
	>18.6	0.86 (0.53,1.38)	0.526[c]	
h) Maximal			0.026[b]	AGE*RACE (p=0.035)
(n=742)	≤18.6	1.42 (0.98,2.05)	0.066[c]	
	>18.6	0.81 (0.56,1.15)	0.238[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 6-5. (Continued)

Analysis of Relative Age

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

Current Dioxin Category	n	Percent Older	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	786	5.0	All Categories		0.638
Unknown	345	5.2	Unknown vs. Background	1.05 (0.59,1.87)	0.856
Low	196	3.6	Low vs. Background	0.71 (0.31,1.61)	0.412
High	187	6.4	High vs. Background	1.31 (0.67,2.56)	0.424
Total	1,514				

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	786	All Categories		0.638	--
Unknown	345	Unknown vs. Background	1.05 (0.59,1.07)	0.856	
Low	196	Low vs. Background	0.71 (0.31,1.61)	0.412	
High	187	High vs. Background	1.31 (0.67,2.56)	0.424	
Total	1,514				

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

In the unadjusted analysis of the frequencies of Ranch Hands in the unknown, low, and high current dioxin categories and Comparisons in the background current dioxin category appearing older than their stated age, the contrast of the four current dioxin categories was nonsignificant (Table 6-5 [i]: p=0.638). For the adjusted analysis, none of the covariates was retained in the model; therefore, the adjusted and unadjusted analysis results were the same.

Percent Body Fat (Continuous)

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Percent body fat displayed a significant positive association with initial dioxin under both the unadjusted minimal and the unadjusted maximal assumptions (Table 6-6 [a] and [b]: p=0.001 and p<0.001). The unadjusted means for the minimal analysis within the defined low, medium, and high initial dioxin levels were 22.34, 22.15, and 24.01 percent. Under the maximal assumption, the corresponding means were 20.72, 22.13, and 23.40 percent.

The adjusted analysis also displayed a significant association between percent body fat and initial dioxin (Table 6-6 [c] and [d]: p=0.001 and p<0.001). The adjusted means for the low, medium, and high initial dioxin levels were 22.38, 22.07, and 24.05 percent under the minimal assumption, and 20.70, 22.07, and 23.55 percent under the maximal assumption.

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

In the unadjusted analysis based on current dioxin and time since tour, neither the minimal nor the maximal analysis had a significant current dioxin-by-time interaction (Table 6-6 [e] and [f]: p=0.817 and p=0.438, respectively); thus, the positive relationships between percent body fat and current dioxin between the time strata were not statistically different (i.e., the estimated slopes of the two time strata did not differ significantly).

Under the minimal assumption, a marginally significant positive association between percent body fat and current dioxin was found for time of 18.6 years or less (p=0.086) and a significant positive association (Table 6-6 [e]: p=0.014) was found between percent body fat and current dioxin for time greater than 18.6 years. However, the interaction of current dioxin and time was not significant (p=0.817). Within the time of 18.6 years or less stratum, the percent body fat means for low, medium, and high current dioxin were 22.21, 22.12, and 23.64 percent. For the time greater than 18.6 years stratum, the means also increased with current dioxin (low, 22.11 percent; medium, 22.43 percent; and high, 24.12 percent).

Under the maximal assumption, each time stratum displayed a significant positive association between percent body fat and current dioxin (Table 6-6 [f]: ≤18.6 years: p<0.001; >18.6 years: p<0.001). For time of 18.6 years or less, the percent body fat means increased with current dioxin (low, 20.19 percent; medium, 22.03 percent; and high, 23.11 percent). For time greater than 18.6 years, the percent body fat means also increased with current dioxin (low, 21.39 percent; medium, 22.09 percent; and high, 23.90 percent). Similar to the minimal analysis, the interaction of current dioxin and time was not significant (p=0.438).

TABLE 6-6.

Analysis of Percent Body Fat
(Continuous)

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Mean	Slope (Std. Error)	p-Value
a) Minimal	Low	130	22.34	0.627 (0.195)	0.001
(n=521)	Medium	260	22.15		
(R^2=0.019)	High	131	24.01		
b) Maximal	Low	185	20.72	0.792 (0.136)	<0.001
(n=742)	Medium	371	22.13		
(R^2=0.044)	High	186	23.40		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Initial Dioxin	n	Adj. Mean	Adj. Slope (Std. Error)	p-Value	Covariate Remarks
c) Minimal	Low	130	22.38	0.648 (0.202)	0.001	AGE*RACE
(n=521)	Medium	260	22.07			(p=0.024)
(R^2=0.037)	High	131	24.05			
d) Maximal	Low	185	20.70	0.859 (0.138)	<0.001	AGE (p=0.016)
(n=742)	Medium	371	22.07			
(R^2=0.051)	High	186	23.55			

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 6-6. (Continued)

Analysis of Percent Body Fat
(Continuous)

Ranch Hands - Log$_2$ (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Mean/(n) Current Dioxin			Slope (Std. Error)	p-Value
		Low	Medium	High		
e) Minimal						0.817[a]
(n=521)	≤18.6	22.21	22.12	23.64	0.549 (0.319)	0.086[b]
(R^2=0.018)		(72)	(128)	(54)		
	>18.6	22.11	22.43	24.12	0.644 (0.261)	0.014[b]
		(58)	(132)	(77)		
f) Maximal						0.438[a]
(n=742)	≤18.6	20.19	22.03	23.11	0.893 (0.211)	<0.001[b]
(R^2=0.045)		(106)	(191)	(83)		
	>18.6	21.39	22.09	23.90	0.674 (0.187)	<0.001[b]
		(79)	(179)	(104)		

Ranch Hands - Log$_2$ (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Mean/(n) Current Dioxin			Adj. Slope (Std. Error)	p-Value	Covariate Remarks
		Low	Medium	High			
g) Minimal						0.775[a]	AGE*RACE (p=0.024)
(n=521)	≤18.6	22.19	22.17	23.73	0.596 (0.330)	0.071[b]	
(R^2=0.037)		(72)	(128)	(54)			
	>18.6	22.03	22.25	24.11	0.713 (0.268)	0.008[b]	
		(58)	(132)	(77)			
h) Maximal						0.431[a]	AGE (p=0.011)
(n=742)	≤18.6	20.19	22.05	23.39	0.999 (0.214)	<0.001[b]	
(R^2=0.053)		(106)	(191)	(83)			
	>18.6	21.20	21.95	24.02	0.777 (0.190)	<0.001[b]	
		(79)	(179)	(104)			

[a]Test of significance for homogeneity of slopes (current dioxin continuous, time categorized).
[b]Test of significance for slope equal to 0 (current dioxin continuous, time categorized).
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 6-6. (Continued)

Analysis of Percent Body Fat
(Continuous)

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

Current Dioxin Category	n	Mean	Contrast	Difference of Means (95% C.I.)	p-Value
Background	786	21.91	All Categories		<0.001
Unknown	345	20.03	Unknown vs. Background	-1.88 (-2.51,-1.24)	<0.001
Low	196	22.15	Low vs. Background	0.24 (-0.54,1.02)	0.549
High	187	23.55	High vs. Background	1.64 (0.84,2.44)	<0.001
Total	1,514		$(R^2=0.042)$		

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

Current Dioxin Category	n	Adj. Mean	Contrast	Difference of Adj. Means (95% C.I.)	p-Value	Covariate Remarks
Background	786	21.90	All Categories		<0.001	AGE (p=0.145)
Unknown	345	20.01	Unknown vs. Background	-1.89 (-2.53,-1.26)	<0.001	
Low	196	22.15	Low vs. Background	0.24 (-0.54,1.03)	0.541	
High	187	23.63	High vs. Background	1.73 (0.92,2.54)	<0.001	
Total	1,514		$(R^2=0.044)$			

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.

In the adjusted analysis of percent body fat using current dioxin and time, neither the minimal nor maximal cohort exhibited a significant current dioxin-by-time interaction (Table 6-6 [g] and [h]: p=0.775 and p=0.431, respectively); therefore, the positive associations between percent body fat and current dioxin of each time stratum were not significantly different from one another. Under the minimal assumption, percent body fat for Ranch Hands with 18.6 years or less since tour exhibited a marginally significant positive association (p=0.071). For those Ranch Hands with time greater than 18.6 years, percent body fat displayed a significant positive association (p=0.008). Under the maximal assumption of the adjusted analysis, each time stratum displayed a significant positive association (p<0.001 for both time strata).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In the unadjusted analysis of percent body fat, the contrast of the four current dioxin categories was significant (Table 6-6 [i]: p<0.001). The unadjusted percent body fat means for the background, unknown, low, and high current dioxin categories were 21.91, 20.03, 22.15, and 23.55 percent. The contrasts of unknown versus background current dioxin category and high versus background current dioxin category were also significant (for both contrasts, p<0.001). Relative to the background mean for Comparisons, Ranch Hands in the unknown current dioxin category had a lower mean percent body fat and Ranch Hands in the high current dioxin category had a higher mean percent body fat. An adjusted model containing the covariate age produced similar results.

Percent Body Fat (Discrete)

A small number of participants, two Ranch Hands and three Comparisons, were classified as lean (<10 percent body fat). The current serum dioxin levels for the Ranch Hands were 1.33 ppt and 18.10 ppt, and the current dioxin levels for the Comparisons ranged from 0.00 ppt to 2.45 ppt. Due to the sparse number of lean participants, statistical analyses were performed with the lean and normal participants combined.

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Unadjusted and adjusted analyses of percent body fat as a discrete variable (obese versus lean/normal) indicated that there was a significant positive association with initial dioxin.

Under the minimal assumption, the estimated relative risk in the unadjusted analysis was 1.23 (Table 6-7 [a]: p=0.012) and the corresponding relative frequencies of obese Ranch Hands within the low, medium, and high initial dioxin categories were 20.8, 23.8, and 32.8 percent. Under the maximal assumption, the estimated relative risk was 1.32 (Table 6-7 [b]: p<0.001) with increasing percentages of obese Ranch Hands for the low, medium, and high initial dioxin categories (12.4%, 23.2%, and 29.0%).

Incorporating covariate information into the models, the adjusted relative risk was 1.25 (Table 6-7 [c]: p=0.010) and 1.37 (Table 6-7 [d]: p<0.001) under the minimal and maximal assumptions.

TABLE 6-7.

Analysis of Percent Body Fat
(Discrete)

Ranch Hands - Log$_2$ (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Obese	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal	Low	130	20.8	1.23 (1.05,1.44)	0.012
(n=521)	Medium	260	23.8		
	High	131	32.8		
b) Maximal	Low	185	12.4	1.32 (1.17,1.49)	<0.001
(n=742)	Medium	371	23.2		
	High	186	29.0		

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 (1.05,1.47)	0.010	AGE*RACE (p=0.022)
d) Maximal (n=742)	1.37 (1.20,1.55)	<0.001	AGE (p=0.026)

[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 6-7. (Continued)

Analysis of Percent Body Fat
(Discrete)

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Obese/(n) Current Dioxin			Est. Relative Risk (95% C.I.)[a]	p-Value
		Low	Medium	High		
e) Minimal						0.776[b]
(n=521)	≤18.6	23.6 (72)	22.7 (128)	29.6 (54)	1.18 (0.91,1.54)	0.217[c]
	>18.6	17.2 (58)	25.8 (132)	33.8 (77)	1.24 (1.01,1.53)	0.045[c]
f) Maximal						0.320[b]
(n=742)	≤18.6	8.5 (106)	23.0 (191)	26.5 (83)	1.40 (1.15,1.70)	0.001[c]
	>18.6	19.0 (79)	21.8 (179)	32.7 (104)	1.23 (1.04,1.45)	0.013[c]

Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal			0.755[b]	AGE*RACE (p=0.022)
(n=521)	≤18.6	1.21 (0.92,1.59)	0.176[c]	
	>18.6	1.28 (1.02,1.59)	0.029[c]	
h) Maximal			0.299[b]	AGE (p=0.022)
(n=742)	≤18.6	1.48 (1.20,1.81)	<0.001[c]	
	>18.6	1.29 (1.09,1.52)	0.003[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 6-7. (Continued)

Analysis of Percent Body Fat
(Discrete)

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

Current Dioxin Category	n	Percent Obese	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	786	23.7	All Categories		<0.001
Unknown	345	11.9	Unknown vs. Background	0.44 (0.30,0.63)	<0.001
Low	196	23.5	Low vs. Background	0.99 (0.68,1.43)	0.954
High	187	30.0	High vs. Background	1.38 (0.97,1.96)	0.075
Total	1,514				

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	786	All Categories		<0.001	--
Unknown	345	Unknown vs. Background	0.44 (0.30,0.63)	<0.001	
Low	196	Low vs. Background	0.99 (0.68,1.43)	0.954	
High	187	High vs. Background	1.38 (0.97,1.96)	0.075	
Total	1,514				

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 - Log₂ (Current Dioxin) and Time

In the unadjusted analysis of percent body fat, under both the minimal and maximal assumptions, the interactions between current dioxin and time since tour were not significant (Table 6-7 [e] and [f]: p=0.776 and p=0.320, respectively); thus, the estimated relative risks of the two time strata did not differ significantly. Under the minimal assumption, a significant association between obesity and current dioxin was found for Ranch Hands with more than 18.6 years since tour (p=0.045, Est. RR=1.24). For these Ranch Hands, the relative frequencies of obese participants for low, medium, and high current dioxin were 17.2, 25.8, and 33.8 percent.

Under the maximal assumption, an unadjusted analysis revealed significant positive associations between obesity and current dioxin for both time strata (Table 6-7 [f]: p=0.001, Est. RR=1.40 for time≤18.6 years and p=0.013, Est. RR=1.23 for time>18.6 years). For Ranch Hands with 18.6 years or less since tour, the relative frequencies of obese participants increased with current dioxin (low, 8.5%; medium, 23.0%; and high, 26.5%). For the other time stratum, the corresponding relative frequencies were 19.0, 21.8, and 32.7 percent.

In the adjusted analysis based on the minimal assumption, the interaction of current dioxin and time was not significant (Table 6-7 [g]: p=0.755); therefore, the adjusted relative risks of the two time strata did not differ significantly. For time greater than 18.6 years since tour, the adjusted relative risk of 1.28 was significant (p=0.029).

In the adjusted analysis under the maximal assumption, the interaction between current dioxin and time was not significant (Table 6-7 [h]: p=0.299); thus, the adjusted relative risks of the two time strata were not significantly different. Within each time strata, there was a significant association between percent body fat and current dioxin (p<0.001, Adj. RR=1.48 for time≤18.6 years and p=0.003, Adj. RR=1.29 for time>18.6 years).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In the unadjusted analysis of percent body fat, the contrast of the four current dioxin categories was significant (Table 6-7 [i]: p<0.001). The relative frequencies of obese participants for the background, unknown, low, and high current dioxin categories were 23.7, 11.9, 23.5, and 30.0 percent. The unknown versus background current dioxin category contrast produced a significant relative risk less than 1 (p<0.001, Est. RR=0.44, 95% C.I.: [0.30,0.63]) and the high versus background category contrast resulted in an estimated relative risk greater than one that was marginally significant (p=0.075, Est. RR=1.38, 95% C.I.: [0.97,1.96]). For the adjusted model, no covariates were retained in the model from the stepping procedure; therefore, the adjusted and unadjusted results were the same.

Laboratory Examination Variable

Sedimentation Rate (Continuous)

Model 1: Ranch Hands - Log₂ (Initial Dioxin)

In the unadjusted analysis of sedimentation rate in its continuous form, there was a positive association with initial dioxin that was marginally significant under the minimal assumption and significant under the maximal assumption (Table 6-8 [a] and [b]: p=0.092

TABLE 6-8.

Analysis of Sedimentation Rate (mm/hr)
(Continuous)

Ranch Hands - Log$_2$ (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Mean[a]	Slope (Std. Error)[b]	p-Value
a) Minimal	Low	130	4.98	0.053 (0.031)	0.092
(n=521)	Medium	260	5.94		
(R^2=0.006)	High	131	6.01		
b) Maximal	Low	185	4.50	0.078 (0.023)	<0.001
(n=742)	Medium	371	5.64		
(R^2=0.016)	High	186	5.78		

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	4.68	0.099 (0.031)	0.002	AGE (p<0.001)
(n=521)	Medium	260	5.89			
(R^2=0.074)	High	131	6.50			
d) Maximal	Low	185	4.45	0.108 (0.022)	<0.001	AGE (p<0.001)
(n=742)	Medium	371	5.46			
(R^2=0.072)	High	186	6.24			

[a]Transformed from natural logarithm scale.

[b]Slope and standard error based on natural logarithm sedimentation rate versus log$_2$ dioxin.

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

TABLE 6-8. (Continued)

Analysis of Sedimentation Rate (mm/hr)
(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						0.500[c]
(n=521)	≤18.6	5.63 (72)	4.96 (128)	5.05 (54)	-0.007(0.051)	0.892[d]
(R^2=0.014)	>18.6	5.86 (58)	6.36 (132)	6.43 (77)	0.037(0.042)	0.368[d]
f) Maximal						0.311[c]
(n=742)	≤18.6	4.51 (106)	5.21 (191)	5.05 (83)	0.032(0.035)	0.367[d]
(R^2=0.018)	>18.6	4.46 (79)	6.27 (179)	6.24 (104)	0.079(0.031)	0.011[d]

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						0.634[c]	AGE (p<0.001)
(n=521)	≤18.6	5.39 (72)	5.13 (128)	5.83 (54)	0.062 (0.051)	0.221[d]	
(R^2=0.110)	>18.6	5.20 (58)	6.14 (132)	6.66 (77)	0.093 (0.042)	0.026[d]	
h) Maximal						0.309[c]	AGE (p<0.001)
(n=742)	≤18.6	4.52 (106)	5.27 (191)	5.70 (83)	0.075 (0.035)	0.031[d]	
(R^2=0.083)	>18.6	4.10 (79)	5.90 (179)	6.58 (104)	0.122 (0.031)	<0.001[d]	

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm sedimentation rate versus log$_2$ dioxin.
[c]Test of significance for homogeneity of slopes (current dioxin continuous, time categorized).
[d]Test of significance for slope equal to 0 (current dioxin continuous, time categorized).
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
    Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 6-8. (Continued)

Analysis of Sedimentation Rate (mm/hr)
(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	786	5.09	All Categories		0.002
Unknown	345	4.52	Unknown vs. Background	-0.57 --	0.025
Low	196	5.77	Low vs. Background	0.68 --	0.053
High	187	5.68	High vs. Background	0.59 --	0.099
Total	1,514		(R^2=0.010)		

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	751	5.19**	All Categories		<0.001**	DXCAT*AGE (p=0.035)
Unknown	328	4.50**	Unknown vs. Background	-0.69 --**	0.007**	AGE*PERS
Low	192	5.88**	Low vs. Background	0.69 --**	0.054**	(p<0.001)
High	181	6.31**	High vs. Background	1.12 --**	0.004**	
Total	1,452		(R^2=0.074)			

[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 ($0.01 < p \leq 0.05$); adjusted mean and p-value derived from a model fitted after deletion of this interaction.

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

and p<0.001, respectively). Under the minimal assumption, the average sedimentation rates for the low, medium, and high initial dioxin levels were 4.98, 5.94, and 6.01 mm/hr. Similarly, the average sedimentation rates for the low, medium, and high levels under the maximal assumption were 4.50, 5.64, and 5.78 mm/hr.

Under both the minimal and the maximal assumptions, the adjusted analyses exhibited significant positive associations between sedimentation rate and initial dioxin (Table 6-8 [c] and [d]: p=0.002 and p<0.001, respectively). Under the minimal assumption, the adjusted mean sedimentation rates for low, medium, and high initial dioxin were 4.68, 5.89, and 6.50 mm/hr. Under the maximal assumption, the corresponding adjusted means were 4.45, 5.46, and 6.24 mm/hr.

Model 2: Ranch Hands - Log₂ (Current Dioxin) and Time

Under the minimal assumption, the unadjusted analysis of sedimentation rate contained a nonsignificant interaction between current dioxin and time since tour (Table 6-8 [e]: p=0.500); thus, the relationships of the two time strata were not significantly different. Under the maximal assumption, the unadjusted analysis also contained a nonsignificant interaction between current dioxin and time (Table 6-8 [f]: p=0.311). However, Ranch Hands whose time since tour exceeded 18.6 years exhibited a significant positive association with current dioxin (p=0.011). For this time stratum, the sedimentation rate means for low, medium, and high current dioxin were 4.46, 6.27, and 6.24 mm/hr.

In the adjusted analysis under the minimal assumption, which adjusted for age, the current dioxin-by-time interaction was not significant (Table 6-8 [g]: p=0.634); thus, the adjusted slopes did not differ significantly between time strata. However, for time greater than 18.6 years, a positive association between sedimentation rate and current dioxin was significant (p=0.026) with adjusted means of 5.20, 6.14, and 6.66 mm/hr for low, medium, and high current dioxin.

Under the maximal assumption, the adjusted analysis which adjusted for age contained a nonsignificant current dioxin-by-time interaction (Table 6-8 [h]: p=0.309); thus, the estimated slopes were not significantly different between the two time strata. Within each time stratum, the association between sedimentation rate and current dioxin was significant (≤18.6 years, p=0.031, >18.6 years, p<0.001). For the 18.6 years or less time stratum, the adjusted sedimentation rate means were 4.52, 5.27, and 5.70 mm/hr for low, medium, and high current dioxin. For the more than 18.6 years time stratum, the adjusted sedimentation rate means were 4.10, 5.90, and 6.58 mm/hr.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The unadjusted analysis of sedimentation rate for the four current dioxin categories was significant (Table 6-8 [i]: p=0.002). The unadjusted sedimentation rate means for the background, unknown, low, and high current dioxin categories were 5.09, 4.52, 5.77, and 5.68 mm/hr. The contrast for Ranch Hands in the unknown category versus Comparisons in the background category was significant (p=0.025) with the mean sedimentation rate for the Comparisons being higher. The low and high category contrasts versus background category were both marginally significant (p=0.053 and p=0.099, respectively) with the Ranch Hands having the higher sedimentation rate means.

The adjusted analysis of sedimentation rate contained a significant interaction between categorized current dioxin and age (Table 6-8 [j]: p=0.035). To explore the interaction, adjusted analyses were performed for Ranch Hands and Comparisons born in or after 1942 and those born prior to 1942. For the younger participants, the simultaneous contrast of the four current dioxin categories was significant (Appendix Table E-1: p=0.009). The adjusted means for the background, unknown, low, and high categories were 4.36, 3.72, 5.52, and 4.72 mm/hr. The unknown versus background category contrast was marginally significant (p=0.080) with the mean rate for the Comparisons being higher. The contrast for low versus background category was significant (p=0.021) with the Ranch Hands having the higher mean sedimentation rate. The contrast for the high category was not significant (p=0.368). For the older study participants, the overall contrast for the four current dioxin categories was also significant (p<0.001). The adjusted means for background, unknown, low, and high categories were 5.77, 5.01, 6.05, and 7.94 mm/hr. The unknown versus background category contrast was significant (p=0.037) with the mean sedimentation rate for Comparisons being higher. For the older participants, the contrast of high versus background was significant (p=0.003) with the adjusted mean sedimentation rate being higher for Ranch Hands than Comparisons. The contrast for the low category was not significant (p=0.576).

An adjusted analysis without the interaction of categorized current dioxin and age was also performed. For this secondary model, the overall contrast of the four current dioxin categories was significant (Table 6-8 [j]: p<0.001). The adjusted mean sedimentation rates were 5.19, 4.50, 5.88, and 6.31 mm/hr. The contrast of unknown versus background category was significant (p=0.007) with the background category (Comparisons) having the higher adjusted mean. The contrast for low versus background category was marginally significant (p=0.054) and the contrast for high versus background category was significant (p=0.004). For both of these contrasts, the adjusted mean sedimentation rate was higher for Ranch Hands than Comparisons.

Sedimentation Rate (Discrete)

Model 1: Ranch Hands - Log₂ (Initial Dioxin)

Model 1: Ranch Hands - Log$_2$ (Initial Dioxin)

The unadjusted analysis of sedimentation rate in discrete form (abnormal versus normal) exhibited a nonsignificant association with initial dioxin under the minimal assumption (Table 6-9 [a]: p=0.509). Under the maximal assumption, the unadjusted analysis displayed a marginally significant positive association between sedimentation rate and initial dioxin (Table 6-9 [b]: p=0.064, Est. RR=1.20). The relative frequency of Ranch Hands with abnormal sedimentation rates had a positive association with initial dioxin (low, 4.9%; medium, 7.3%; high, 8.1%).

In the adjusted analysis, the association between sedimentation rate and initial dioxin was not significant under the minimal assumption (Table 6-9 [c]: p=0.134), but significant under the maximal assumption (Table 6-9 [d]: p=0.008; Est. RR=1.33). Age was the only covariate retained in these analyses.

Model 2: Ranch Hands - Log$_2$ (Current Dioxin) and Time

For the unadjusted analysis of percent abnormal sedimentation rate, the interaction of current dioxin and time since tour was not significant for the minimal assumption (Table 6-9

TABLE 6-9.

Analysis of Sedimentation Rate
(Discrete)

Ranch Hands - Log$_2$ (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal	Low	130	6.2	1.09 (0.85,1.40)	0.509
(n=521)	Medium	260	9.2		
	High	131	8.4		
b) Maximal	Low	185	4.9	1.20 (0.99,1.46)	0.064
(n=742)	Medium	371	7.3		
	High	186	8.1		

Ranch Hands - Log$_2$ (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal	1.22 (0.95,1.58)	0.134	AGE (p<0.001)
(n=521)			
d) Maximal	1.33 (1.08,1.63)	0.008	AGE (p<0.001)
(n=742)			

[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 6-9. (Continued)

Analysis of Sedimentation Rate
(Discrete)

Ranch Hands - Log$_2$ (Current Dioxin) and Time - Unadjusted

| Assumption | Time (Yrs.) | Percent Abnormal/(n) Current Dioxin | | | Est. Relative Risk (95% C.I.)[a] | p-Value |
		Low	Medium	High		
e) Minimal						0.262[b]
(n=521)	≤18.6	9.7 (72)	6.3 (128)	1.9 (54)	0.78 (0.46,1.33)	0.360[c]
	>18.6	8.6 (58)	10.6 (132)	10.4 (77)	1.10 (0.81,1.49)	0.548[c]
f) Maximal						0.228[b]
(n=742)	≤18.6	3.8 (106)	6.3 (191)	6.0 (83)	0.96 (0.67,1.39)	0.845[c]
	>18.6	3.8 (79)	8.4 (179)	11.5 (104)	1.26 (0.99,1.60)	0.065[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			0.337[b]	AGE (p=0.001)
(n=521)	≤18.6	0.93 (0.54,1.61)	0.808[c]	
	>18.6	1.25 (0.92,1.71)	0.154[c]	
h) Maximal			0.263[b]	AGE (p<0.001)
(n=742)	≤18.6	1.10 (0.75,1.62)	0.619[c]	
	>18.6	1.42 (1.10,1.83)	0.007[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 6-9. (Continued)

Analysis of Sedimentation Rate
(Discrete)

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	786	3.3	All Categories		0.003
Unknown	345	3.5	Unknown vs. Background	1.05 (0.53,2.11)	0.884
Low	196	7.1	Low vs. Background	2.25 (1.15,4.39)	0.018
High	187	9.1	High vs. Background	2.92 (1.55,5.51)	0.001
Total	1,514				

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	786	All Categories		<0.001	AGE (p<0.001)
Unknown	345	Unknown vs. Background	1.03 (0.51,2.07)	0.937	
Low	196	Low vs. Background	2.32 (1.18,4.56)	0.015	
High	187	High vs. Background	3.86 (2.00,7.45)	<0.001	
Total	1,514				

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.

[e]: p=0.262) as well as the maximal assumption (Table 6-9 [f]: p=0.228). Therefore, for each assumption, the estimated relative risks of the two time strata were not significantly different from one another. Under the maximal assumption, the association between percent abnormal sedimentation rate and current dioxin was marginally significant (p=0.065, Est. RR=1.26) within the time greater than 18.6 years stratum. The relative frequencies for abnormal sedimentation rate within that time stratum were 3.8, 8.4, and 11.5 percent for low, medium, and high current dioxin. The other results were not statistically significant.

After adjusting for age in the analysis of percent abnormal sedimentation rate, the interaction of current dioxin and time was not significant under the minimal assumption (Table 6-9 [g]: p=0.337) or the maximal assumption (Table 6-9 [h]: p=0.263). Therefore, the adjusted relative risks of the two time strata were not significantly different from one another. Under the maximal assumption, the adjusted relative risk for time greater than 18.6 years since tour was significant (p=0.007, Adj. RR=1.42). The other adjusted analyses were not significant.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In the unadjusted analysis of the relative frequencies of participants with abnormal sedimentation rates, the simultaneous contrast of the four current dioxin categories was significant (Table 6-9 [i]: p=0.003). The relative frequencies of participants with abnormal sedimentation rates for the background, unknown, low, and high current dioxin categories were 3.3, 3.5, 7.1, and 9.1 percent. The estimated relative risks for low versus background (Est. RR=2.25, 95% C.I.: [1.15,4.39]) and high versus background (Est. RR=2.92, 95% C.I.: [1.55,5.51]) were significant (p=0.018 and p<0.001, respectively).

In the adjusted analysis of sedimentation rate as a discrete variable, the overall contrast of the four current dioxin categories was significant (Table 6-9 [j]: p<0.001). The adjusted relative risks for low versus background (Adj. RR=2.32, 95% C.I.: [1.18,4.56]) and high versus background (Adj. RR=3.86, 95% C.I.: [2.00,7.45]) were significant (p=0.015 and p<0.001, respectively).

Longitudinal Analysis

Questionnaire Variable

Self-Perception of Health

Longitudinal analyses of the percentage of participants who perceived their health as poor/fair at the 1987 examination were conducted to detect associations with initial dioxin in Ranch Hands, current dioxin and time since tour in Ranch Hands, and categorized current dioxin in Ranch Hands and Comparisons. Only participants who reported their health as good or excellent at the 1982 Baseline examination were included in these analyses. Table 6-10 presents the results of the longitudinal analyses. For a specific longitudinal analysis (e.g., minimal assumption, initial dioxin analysis), the upper part of each subpanel of a table provides the percents of participants with fair or poor self-perception of health at each examination. The lower part of each subpanel presents sample sizes, percents, relative risks, and associated 95 percent confidence intervals subject to the requirement that

TABLE 6-10.

Longitudinal Analysis of Self-Perception of Health

Ranch Hands - Log_2 (Initial Dioxin)

Assumption	Initial Dioxin	Percent Fair or Poor/(n) Examination		
		1982	1985	1987
a) Minimal	Low	15.5 (123)	7.4 (121)	5.7 (123)
	Medium	23.2 (254)	12.5 (249)	7.9 (254)
	High	18.4 (125)	12.9 (124)	8.0 (125)

Excellent or Good in 1982

Initial Dioxin	n in 1987	Percent Fair or Poor in 1987	Est. Relative Risk (95% C.I.)[a]	p-Value
Low	104	1.0	1.53 (1.02,2.30)	0.047
Medium	195	3.1		
High	102	5.9		

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

TABLE 6-10. (Continued)

Longitudinal Analysis of Self-Perception of Health

Ranch Hands - Log$_2$ (Initial Dioxin)

Assumption	Initial Dioxin	Percent Fair or Poor/(n) Examination		
		1982	1985	1987
b) Maximal	Low	18.2 (170)	4.2 (167)	4.7 (170)
	Medium	20.7 (357)	10.0 (350)	6.2 (357)
	High	17.9 (179)	12.4 (177)	7.3 (179)

Excellent or Good in 1982

Initial Dioxin	n in 1987	Percent Fair or Poor in 1987	Est. Relative Risk (95% C.I.)[a]	p-Value
Low	139	0.7	1.78 (1.25,2.54)	0.002
Medium	283	2.1		
High	147	4.1		

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

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.

Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1987 examinations. P-values given are in reference to a contrast of 1982 and 1987 results.

Statistical analyses are based only on participants who were classified as excellent or good in 1982 (see Chapter 4, Statistical Methods).

Ranch Hands - Log$_2$ (Current Dioxin) and Time

Assumption	Time (Yrs.)	Examination	Percent Fair or Poor/(n) Current Dioxin		
			Low	Medium	High
c) Minimal	$\leq$18.6	1982	15.9 (69)	25.0 (124)	15.4 (52)
		1985	7.4 (68)	9.1 (121)	5.9 (51)
		1987	7.3 (69)	5.7 (124)	3.9 (52)
	>18.6	1982	14.8 (54)	20.8 (130)	21.9 (73)
		1985	9.4 (53)	14.1 (128)	19.2 (73)
		1987	5.6 (54)	8.5 (130)	12.3 (73)

Excellent or Good in 1982:

Time (Yrs.)	Percent Fair or Poor/(n) in 1987 Current Dioxin			Est. Relative Risk (95% C.I.)[a]	p-Value
	Low	Medium	High		
					0.189[b]
$\leq$18.6	1.7 (58)	2.2 (93)	0.0 (44)	0.76 (0.23,2.48)	0.648[c]
>18.6	2.2 (46)	2.9 (103)	10.5 (57)	1.65 (1.03,2.62)	0.036[c]

[a]Relative risk for a twofold increase in dioxin.
[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).
[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
     Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.
     Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1987 examinations. P-values given are in reference to a contrast of 1982 and 1987 results.
     Statistical analyses are based only on participants who were classified as excellent or good in 1982 (see Chapter 4, Statistical Methods).

TABLE 6-10. (Continued)

Longitudinal Analysis of Self-Perception of Health

Ranch Hands - Log_2 (Current Dioxin) and Time

Assumption	Time (Yrs.)	Examination	Percent Fair or Poor/(n) Current Dioxin		
			Low	Medium	High
d) Maximal	≤18.6	1982	18.1 (94)	21.7 (184)	17.5 (80)
		1985	0.0 (91)	8.3 (180)	6.3 (79)
		1987	1.1 (94)	6.5 (184)	3.8 (80)
	>18.6	1982	13.2 (76)	21.5 (172)	19.0 (100)
		1985	9.3 (75)	11.8 (170)	17.2 (99)
		1987	4.0 (76)	8.1 (172)	10.0 (100)

Excellent or Good in 1982:
Percent Fair or Poor/(n) in 1987

Time (Yrs.)	Current Dioxin			Est. Relative Risk (95% C.I.)[a]	p-Value
	Low	Medium	High		
					0.324[b]
≤18.6	0.0 (77)	1.4 (144)	1.5 (66)	1.18 (0.51,2.73)	0.692[c]
>18.6	0.0 (66)	3.0 (135)	7.4 (81)	1.87 (1.23,2.83)	0.003[c]

[a]Relative risk for a twofold increase in dioxin.
[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).
[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1987 examinations. P-values given are in reference to a contrast of 1982 and 1987 results. Statistical analyses are based only on participants who were classified as excellent or good in 1982 (see Chapter 4, Statistical Methods).

TABLE 6-10. (Continued)
Longitudinal Analysis of Self-Perception of Health

e) Ranch Hands and Comparisons by Current Dioxin Category

Current Dioxin Category	Percent Fair or Poor/(n) Examination		
	1982	1985	1987
Background	14.5 (685)	5.1 (681)	5.0 (685)
Unknown	16.8 (316)	4.8 (310)	3.8 (316)
Low	24.1 (191)	12.2 (188)	7.3 (191)
High	18.3 (180)	12.4 (178)	7.2 (180)

Excellent or Good in 1982

Current Dioxin Category	n in 1987	Percent Fair or Poor in 1987	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	586	2.1	All Categories		0.022
Unknown	263	0.4	Unknown vs. Background	0.19 (0.02,1.44)	0.108
Low	145	2.8	Low vs. Background	1.38 (0.44,4.36)	0.579
High	147	4.8	High vs. Background	2.40 (0.93,6.22)	0.070

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

participants were compliant at both the 1982 and 1987 examinations and the participants had a good or excellent self-perception of health at the 1982 examination.

Model 1: Ranch Hands - Log₂ (Initial Dioxin)

Under both the minimal and the maximal assumptions, there was a significant positive association between initial dioxin and the percentage of Ranch Hands who reported fair or poor health at the 1987 examination (Table 6-10 [a] and [b]: p=0.047, Est. RR=1.53 and p=0.002, Est. RR=1.78, respectively). Under the minimal assumption, of the Ranch Hands with a good or excellent self-perception of health at the 1982 examination, the percentages with a poor or fair opinion of their health at the 1987 examination were 1.0, 3.1, and 5.9 percent for the low, medium, and high initial dioxin categories. The corresponding percentages under the maximal assumption were 0.7, 2.1, and 4.1 percent.

Model 2: Ranch Hands - Log₂ (Current Dioxin) and Time

Under the minimal assumption, the longitudinal analysis of the self-perception of health of Ranch Hands did not detect a significant interaction between current dioxin and time since tour (Table 6-10 [c]: p=0.189). However, for Ranch Hands with more than 18.6 years since their tour, there was a significant positive association between current dioxin and the percentage who reported fair or poor health at the 1987 examination (p=0.036, Est. RR=1.65). Of the Ranch Hands who reported good or excellent health in 1982, the percentages reporting fair or poor health in 1987 were 2.2, 2.9, and 10.5 percent for low, medium, and high current dioxin.

Under the maximal assumption, the longitudinal analysis did not detect a significant interaction between current dioxin and time since tour (Table 6-10 [d]: p=0.324). Similar to the minimal analysis, there was a significant positive association between current dioxin and the percentage of Ranch Hands who reported fair or poor health in 1987 within the greater than 18.6 years time stratum (p=0.003, Est. RR=1.87). Of those Ranch Hands who reported excellent or good health at the 1982 Baseline examination, the percentage who reported fair or poor health at the 1987 examination increased with increasing current dioxin for this time stratum (low, 0.0%; medium, 3.0%; high, 7.4%).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

For the longitudinal analysis, there was a significant difference among the percentage of participants who reported fair or poor health at the 1987 examination for the four current dioxin categories (Table 6-10 [e]: p=0.022). Of the participants who reported excellent or good health in 1982, the percentages who reported fair or poor health in 1987 for the background, unknown, low, and high current dioxin categories were 2.1, 0.4, 2.8, and 4.8 percent. Specifically, the contrast of the percentage of Ranch Hands in the high current dioxin category who reported fair or poor health in 1987 versus the percentage of Comparisons in the background category was of borderline significance (p=0.070, Est. RR=2.40, 95% C.I.: [0.93,6.22]).

Laboratory Examination Variable

Sedimentation Rate (Discrete)

For the longitudinal analyses, the percentages of participants with abnormal sedimentation rates at the 1987 examination were examined for associations with initial dioxin for Ranch Hands, current dioxin and time since tour for Ranch Hands, and categorized current dioxin for Ranch Hands and Comparisons. Only those participants with normal sedimentation rates at the 1982 Baseline examination were included in these analyses. Table 6-11 presents the results of the longitudinal analyses.

For a specific longitudinal analysis (e.g., minimal assumption, initial dioxin analysis), the upper part of each subpanel of a table provides the percents of participants with an abnormal sedimentation rate at each examination. The lower part of each subpanel presents sample sizes, percents, relative risks, and associated 95 percent confidence intervals subject to the requirement that participants were compliant at both the 1982 and 1987 examinations and the participants had a normal sedimentation rate at the 1982 examination.

Due to laboratory differences, the cutpoint for sedimentation rate for the 1982 Baseline examination differed from the cutpoint for the 1985 and 1987 examinations. The normal range for sedimentation rate for the 1982 Baseline examination was less than or equal to 12 mm/hr, and the normal range for the 1985 and 1987 examinations was less than or equal to 20 mm/hr.

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Under both the minimal and the maximal assumptions, the longitudinal analysis of the sedimentation rate detected a nonsignificant positive association between initial dioxin and the percentage of Ranch Hands with an abnormal sedimentation rate at the 1987 examination (Table 6-11 [a] and [b]: p=0.361 and p=0.102, respectively).

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

The longitudinal analysis of sedimentation rate did not detect a significant interaction between current dioxin and time since tour under either the minimal or the maximal assumption (Table 6-11 [c] and [d]: p=0.823 and p=0.922, respectively). The association between current dioxin and the percentage of Ranch Hands with an abnormal sedimentation rate in 1987 was also nonsignificant in the time strata under both assumptions (p>0.30 for all analyses).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

For the longitudinal analysis there was a significant difference among the percentage of participants with abnormal sedimentation rates for the four current dioxin categories (Table 6-11 [e]: p=0.010). Of the participants with normal sedimentation rates at the 1982 Baseline examination, the proportions with abnormal sedimentation rates at the 1987 followup examination for the background, unknown, low, and high current dioxin categories were 2.3, 2.9, 5.4, and 7.4 percent. The percentage of Comparisons in the background category with abnormal sedimentation rates in 1987 was significantly lower than the percentage of Ranch Hands with abnormal sedimentation rates in 1987 in both the low (p=0.033, Est. RR=2.43, 95% C.I.: [1.07,5.51]) and high (p=0.002, Est. RR=3.42, 95% C.I.: [1.59,7.33]) categories.

TABLE 6-11.

Longitudinal Analysis of Sedimentation Rate
(Discrete)

Ranch Hands - Log₂ (Initial Dioxin)

Assumption	Initial Dioxin	Percent Abnormal/(n) Examination		
		1982	1985	1987
a) Minimal	Low	4.0	8.2	6.5
		(124)	(122)	(124)
	Medium	3.1	7.2	9.0
		(255)	(250)	(255)
	High	2.4	4.0	8.0
		(125)	(124)	(125)

Normal in 1982

Initial Dioxin	n in 1987	Percent Abnormal in 1987	Est. Relative Risk (95% C.I.)[a]	p-Value
Low	119	2.5	1.15 (0.85,1.56)	0.361
Medium	247	6.9		
High	122	6.6		

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

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.

Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1987 examinations. P-values given are in reference to a contrast of 1982 and 1987 results. Statistical analyses are based only on participants who were normal in 1982 (see Chapter 4, Statistical Methods).

TABLE 6-11. (Continued)

Longitudinal Analysis of Sedimentation Rate
(Discrete)

Ranch Hands - Log$_2$ (Initial Dioxin)

		Percent Abnormal/(n) Examination		
Assumption	Initial Dioxin	1982	1985	1987
b) Maximal	Low	2.9 (171)	4.8 (168)	4.7 (171)
	Medium	2.8 (359)	7.1 (352)	7.2 (359)
	High	2.8 (179)	4.0 (177)	7.8 (179)

Normal in 1982

Initial Dioxin	n in 1987	Percent Abnormal in 1987	Est. Relative Risk (95% C.I.)[a]	p-Value
Low	166	3.6	1.22 (0.97,1.55)	0.102
Medium	349	5.2		
High	174	5.8		

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

Note: <u>Minimal</u>--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.

      <u>Maximal</u>--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

      Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1987 examinations. P-values given are in reference to a contrast of 1982 and 1987 results. Statistical analyses are based only on participants who were normal in 1982 (see Chapter 4, Statistical Methods).

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	7.3 (69)	1.6 (125)	0.0 (52)
		1985	11.8 (68)	4.9 (122)	2.0 (51)
		1987	10.1 (69)	6.4 (125)	1.9 (52)
	>18.6	1982	3.6 (55)	3.1 (130)	4.1 (73)
		1985	9.3 (54)	7.8 (128)	4.1 (73)
		1987	9.1 (55)	10.0 (130)	9.6 (73)

Normal in 1982:
Percent Abnormal/(n) in 1987
Current Dioxin

Time (Yrs.)	Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
					0.823[b]
≤18.6	3.1 (64)	6.5 (123)	1.9 (52)	1.14 (0.66,1.97)	0.649[c]
>18.6	5.7 (53)	7.1 (126)	7.1 (70)	1.05 (0.71,1.55)	0.798[c]

[a]Relative risk for a twofold increase in dioxin.
[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).
[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
  Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.
  Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1987 examinations. P-values given are in reference to a contrast of 1982 and 1987 results. Statistical analyses are based only on participants who were normal in 1982 (see Chapter 4, Statistical Methods).

TABLE 6-11. (Continued)

Longitudinal Analysis of Sedimentation Rate
(Discrete)

Ranch Hands - Log$_2$ (Current Dioxin) and Time

Assumption	Time (Yrs.)	Examination	Percent Abnormal/(n) Current Dioxin Low	Medium	High
d) Maximal	≤18.6	1982	4.2 (95)	3.8 (185)	0.0 (80)
		1985	3.3 (92)	6.1 (181)	6.3 (79)
		1987	3.2 (95)	6.5 (185)	6.3 (80)
	>18.6	1982	0.0 (76)	2.9 (173)	4.0 (100)
		1985	4.0 (75)	7.6 (171)	5.1 (99)
		1987	4.0 (76)	8.1 (173)	11.0 (100)

Normal in 1982:
Percent Abnormal/(n) in 1987

Time (Yrs.)	Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
					0.922[b]
≤18.6	2.2 (91)	3.9 (178)	6.3 (80)	1.20 (0.80,1.80)	0.390[c]
>18.6	4.0 (76)	5.4 (168)	8.3 (96)	1.17 (0.86,1.57)	0.314[c]

[a]Relative risk for a twofold increase in dioxin.
[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).
[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1987 examinations. P-values given are in reference to a contrast of 1982 and 1987 results. Statistical analyses are based only on participants who were normal in 1982 (see Chapter 4, Statistical Methods).

TABLE 6-11. (Continued)

Longitudinal Analysis of Sedimentation Rate
(Discrete)

e) Ranch Hands and Comparisons by Current Dioxin Category

Current Dioxin Category	Percent Abnormal/(n) Examination		
	1982	1985	1987
Background	4.7 (686)	3.1 (682)	3.5 (686)
Unknown	2.2 (317)	3.5 (311)	3.5 (317)
Low	2.6 (192)	4.8 (189)	6.8 (192)
High	2.2 (180)	5.6 (178)	8.9 (180)

Normal in 1982

Current Dioxin Category	n in 1987	Percent Abnormal in 1987	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	654	2.3	All Categories		0.010
Unknown	310	2.9	Unknown vs. Background	1.29 (0.56,2.99)	0.550
Low	187	5.4	Low vs. Background	2.43 (1.07,5.51)	0.033
High	176	7.4	High vs. Background	3.42 (1.59,7.33)	0.002

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

DISCUSSION

In clinical medicine, the assessment of an individual's general state of health is based on subjective and objective indices derived from the history, physical examination, and laboratory testing. The variables analyzed in the current assessment were selected to be sensitive to the overall state of health rather than specific to any organ system. Of the five clinical variables analyzed in the current assessment, only the percent body fat and sedimentation rate consistently showed strongly positive associations with the current and extrapolated initial serum levels of dioxin.

The percent body fat easily is derived as an objective parameter related to good health. Whereas obesity is a risk factor for cardiovascular disease and can contribute to hypertension and diabetes mellitus, it is often the patient with unexplained weight loss who is clinically of concern. Among the disorders considered in the current study that can induce unintentional weight loss are metabolic diseases, such as diabetes mellitus and hyperthyroidism; occult malignancy, most often lung or colon; drug abuse, for example alcoholism or cocaine addiction; and emotional illness, such as anxiety or depression. To the extent that it can reflect significant weight gain or loss, the percent body fat can serve as a valuable clinical clue to the presence of occult disease.

A significant association between percent body fat and initial dioxin was evident in this study. The relationship between dioxin and body fat was consistent whether dioxin was measured on a lipid-adjusted basis or on a whole-weight basis. In the maximal cohort, 29.0 percent of those participants with high initial levels of dioxin met criteria for obesity by discrete analysis in contrast to a 12.4 percent incidence of obesity in those with low initial levels. Clinically, it would be difficult to explain the finding of higher levels of dioxin in relatively obese participants on the basis of any health detriment. While several studies have documented that a mobile equilibrium exists between serum and adipose tissue levels (11, 37), the pharmacokinetics of dioxin in obese versus lean individuals have not been studied prospectively over time.

The sedimentation rate can be a sensitive, if nonspecific, index of general health. Pertinent to the longitudinal design of the current study is the effect of age: A rate as high as 40 millimeters per hour is considered within the range of normal at age 65. Extreme elevations in the sedimentation rate consistently are associated with serious underlying disease, usually malignancy.

In groups of close to identical size, 4.9 percent of participants with low serum dioxin levels (25 ppt to 56.9 ppt) were found to have elevated sedimentation rates while those with the highest levels (more than 218 ppt) had an 8.1 percent incidence of abnormal elevations. Furthermore, consistent with results described in the 1985 and 1987 reports, a significantly higher incidence of abnormally elevated sedimentation rates was noted in the Ranch Hand versus the Comparison cohort in a pattern strongly suggestive of a dose-response effect. Finally, the possibility of a temporal effect is raised by the significantly higher incidence of sedimentation rate elevations in Ranch Hands who are now more removed from service in SEA (>18.6 years). Though of uncertain cause, these results raise the possibility that some clinically occult disease process may be present in the Ranch Hand cohort and highlight the need for continued evaluation of ESR in subsequent examination cycles.

The longitudinal analyses of sedimentation rate reveal positive but nonsignificant associations for Ranch Hand-only analyses using initial dioxin, as well as current dioxin and time since tour. The longitudinal analysis of categorized current dioxin did reveal a dose-response pattern when considering Ranch Hands and Comparisons.

SUMMARY

For the general health assessment, the following five variables were evaluated for an association with serum dioxin levels: self-perception of health, appearance of illness or distress at physical examination, relative age, percent body fat, and sedimentation rate. All five variables were analyzed in discrete form. Percent body fat and sedimentation rate were also analyzed as continuous variables. Tables 6-12, 6-13, and 6-14 provide the results of analyses based on initial dioxin, current dioxin and time since tour, and categorized current dioxin.

Model 1: Ranch Hands - Log$_2$ (Initial Dioxin)

For the unadjusted analysis of self-perception of health, there was a marginally significant positive association with initial dioxin under the maximal assumption. For the unadjusted analysis of percent body fat expressed in the continuous form, significant positive associations with initial dioxin were found under both the minimal and maximal assumptions (Table 6-12: p=0.001 and p<0.001). Significant positive associations were also found for percent body fat expressed as a discrete variable (p=0.012 and p<0.001). In the unadjusted analyses of sedimentation rate in continuous form, a marginally significant positive association with initial dioxin was found under the minimal assumption and a significant positive association (p<0.001) was found under the maximal assumption. For the discrete form of sedimentation rate, there was a positive association with initial dioxin that was of borderline significance under the maximal assumption. The other two dependent variables displayed nonsignificant, albeit positive associations with initial dioxin for the unadjusted analyses.

Regardless of its form, percent body fat again displayed significant positive associations with initial dioxin under both the minimal and maximal assumptions for the adjusted analyses. For sedimentation rate evaluated in continuous form, the adjusted analyses displayed positive significant associations with initial dioxin (p=0.002 and p<0.001) for the minimal and maximal assumptions. For sedimentation rate expressed in discrete form, there was a significant positive association for the maximal assumption (p=0.008).

For the adjusted analysis of self-perception of health, there was a significant interaction between initial dioxin and age for the minimal analysis, and an interaction of initial dioxin and personality type for the maximal analysis. For the interaction of initial dioxin with age, Ranch Hands born in or after 1942 had a significant positive association with initial dioxin, and those born prior to 1942 had a nonsignificant negative association. For the interaction of initial dioxin with personality type, Ranch Hands classified as type A had a significant positive association with initial dioxin and those classified as type B had a nonsignificant positive association. After excluding these interactions, there was a nonsignificant positive association with initial dioxin for the minimal analysis, and a marginally significant positive association with initial dioxin for the maximal analysis. The adjusted analyses of appearance of illness or distress and relative age were nonsignificant under both assumptions.

TABLE 6-12.

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

Variable	Unadjusted		Adjusted	
	Minimal	Maximal	Minimal	Maximal
Questionnaire				
Self-Perception of Health (D)	NS	NS*	** (NS)	** (NS*)
Physical Examination				
Appearance of Illness or Distress by Physician (D)	NS	NS	NS	NS
Relative Age (D)	NS	NS	NS	NS
Percent Body Fat[a] (C)	+0.001	+<0.001	+0.001	+<0.001
Percent Body Fat (D)	+0.012	+<0.001	+0.010	+<0.001
Laboratory				
Sedimentation Rate (C)	NS*	+<0.001	+0.002	+<0.001
Sedimentation Rate (D)	NS	NS*	NS	+0.008

[a]Negative slope considered adverse for this variable.
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk 1.00 or greater for discrete analysis; slope nonnegative for continuous analysis.
NS: Not significant (p>0.10).
NS*: Marginally significant (0.05<p≤0.10).
** (NS): Log_2 (initial dioxin)-by-covariate interaction (0.01<p≤0.05); not significant when interaction is deleted; refer to Appendix Table E-1 for a detailed description of this interaction.
** (NS*): Log_2 (initial dioxin)-by-covariate interaction (0.01<p≤0.05); marginally significant when interaction is deleted; refer to Appendix Table E-1 for a detailed description of this interaction.
Note: P-value given if p≤0.05.
    A capital "NS" denotes relative risk 1.00 or greater for discrete analysis or nonnegative for continuous analysis.

TABLE 6-13.

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

Variable	Unadjusted					
	Minimal			Maximal		
	C*T	≤18.6	>18.6	C*T	≤18.6	>18.6
Questionnaire						
Self-Perception of Health (D)	NS*	ns	NS	NS	NS	NS*
Physical Examination						
Appearance of Illness or Distress by Physician (D)	NS	ns	NS	NS	ns	NS
Relative Age (D)	-0.039	+0.027	ns	-0.024	+0.028	ns
Percent Body Fat[a] (C)	NS	NS*	+0.014	ns	+<0.001	+<0.001
Percent Body Fat (D)	NS	NS	+0.045	ns	+0.001	+0.013
Laboratory						
Sedimentation Rate (C)	NS	ns	NS	NS	NS	+0.011
Sedimentation Rate (D)	NS	ns	NS	NS	ns	NS*

[a]Negative slope considered adverse for this variable.
C: Continuous analysis.
D: Discrete analysis.
+: ≤18.6 and >18.6: Relative risk 1.00 or greater for discrete analysis; slope nonnegative for continuous analysis.
-: C*T: Relative risk/slope for ≤18.6 category greater than relative risk/slope for >18.6 category.
NS/ns: Not significant ($p > 0.10$).
NS*: Marginally significant ($0.05 < p \leq 0.10$).
Notes: P-value given if $p \leq 0.05$.

C*T: Log_2 (current dioxin)-by-time interaction hypothesis test.

≤18.6: Log_2 (current dioxin) hypothesis test for Ranch Hands with time since end of tour of 18.6 years or less.

>18.6: Log_2 (current dioxin) hypothesis test for Ranch Hands with time since end of tour greater than 18.6 years.

A capital "NS" denotes relative risk/slope for ≤18.6 category less than relative risk/slope for >18.6 category, relative risk 1.00 or greater for discrete analysis, or slope nonnegative for continuous analysis; a lowercase "ns" denotes relative risk/slope for ≤18.6 category greater than relative risk/slope for >18.6 category, relative risk less than 1.00 for the discrete analysis, or slope negative for continuous analysis.

TABLE 6-13. (Continued)

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

| | Adjusted | | | | | |
| | Minimal | | | Maximal | | |
Variable	C*T	≤18.6	>18.6	C*T	≤18.6	>18.6
Questionnaire						
Self-Perception of Health (D)	****	****	****	****	****	****
Physical Examination						
Appearance of Illness or Distress by Physician (D)	NS	ns	NS	NS	ns	NS
Relative Age (D)	-0.039	+0.027	ns	-0.026	NS*	ns
Percent Body Fat[a] (C)	NS	NS*	+0.008	ns	+<0.001	+<0.001
Percent Body Fat (D)	NS	NS	+0.029	ns	+<0.001	+0.003
Laboratory						
Sedimentation Rate (C)	NS	NS	+0.026	NS	+0.031	+<0.001
Sedimentation Rate (D)	NS	.ns	NS	NS	NS	+0.007

[a]Negative slope considered adverse for this variable.

C: Continuous analysis.

D: Discrete analysis.

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

-: C*T: Relative risk/slope for ≤18.6 category greater than relative risk/slope for >18.6 category.

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

NS*: Marginally significant (0.05<p≤0.10).

****: $\log_2$ (current dioxin)-by-time-by-covariate interaction (p≤0.01); refer to Appendix Table E-1 for a detailed description of this interaction.

Notes: P-value given if p≤0.05.

C*T: $\log_2$ (current dioxin)-by-time interaction hypothesis test.

≤18.6: $\log_2$ (current dioxin) hypothesis test for Ranch Hands with time since end of tour of 18.6 years or less.

>18.6: $\log_2$ (current dioxin) hypothesis test for Ranch Hands with time since end of tour greater than 18.6 years.

A capital "NS" denotes relative risk/slope for ≤18.6 category less than relative risk/slope for >18.6 category, relative risk 1.00 or greater for discrete analysis, or slope nonnegative for continuous analysis; a lowercase "ns" denotes relative risk/slope for ≤18.6 category greater than relative risk/slope for >18.6 category, relative risk less than 1.00 for discrete analysis, or slope negative for continuous analysis.

TABLE 6-14.

Summary of Categorized Current Dioxin Analyses for
General Health Variables
(Ranch Hands and Comparisons)

		Unadjusted		
Variable	All	Unknown versus Background	Low versus Background	High versus Background
Questionnaire				
Self-Perception of Health (D)	NS	ns	NS	NS
Physical Examination				
Appearance of Illness or Distress by Physician (D)	NS	NS	--	NS
Relative Age (D)	NS	NS	ns	NS
Percent Body Fat[a] (C)	<0.001	-<0.001	NS	+<0.001
Percent Body Fat (D)	<0.001	-<0.001	ns	NS*
Laboratory				
Sedimentation Rate (C)	0.002	-0.025	NS*	NS*
Sedimentation Rate (D)	0.003	NS	+0.018	+0.001

[a]Negative difference considered adverse for this variable.
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk 1.00 or greater for discrete analysis; difference in means nonnegative for continuous analysis.
-: Relative risk less than 1.00 for discrete analysis; difference in means negative for continuous analysis.
--: Analysis not performed due to category with no abnormalities.
NS/ns: Not significant (p>0.10).
NS*: Marginally significant ($0.05 < p \leq 0.10$).
Note: P-value given if $p \leq 0.05$.
A capital "NS" denotes relative risk 1.00 or greater for discrete analysis or difference in means nonnegative for continuous analysis; a lowercase "ns" denotes relative risk less than 1.00 for discrete analysis; a capital "NS" in the first column does not imply directionality.

TABLE 6-14. (Continued)

Summary of Categorized Current Dioxin Analyses for
General Health Variables
(Ranch Hands and Comparisons)

Variable	Adjusted			
	All	Unknown versus Background	Low versus Background	High versus Background
Questionnaire				
Self-Perception of Health (D)	NS	ns	NS	NS
Physical Examination				
Appearance of Illness or Distress by Physician (D)	** (NS)	** (NS)	--	**(NS)
Relative Age (D)	NS	NS	ns	NS
Percent Body Fat[a] (C)	<0.001	-<0.001	NS	+<0.001
Percent Body Fat (D)	<0.001	-<0.001	ns	NS*
Laboratory				
Sedimentation Rate (C)	** (<0.001)	** (-0.007)	** (NS*)	** (+0.004)
Sedimentation Rate (D)	<0.001	NS	+0.015	+<0.001

[a]Negative difference considered adverse for this variable.
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk 1.00 or greater for discrete analysis; difference in means nonnegative for continuous analysis.
-: Relative risk less than 1.00 for discrete analysis; difference in means negative for continuous analysis.
--: Analysis not performed due to category with no abnormalities.
NS/ns: Not significant ($p>0.10$).
NS*: Marginally significant ($0.05<p\leq0.10$).
** (NS): Categorized current dioxin-by-covariate interaction ($0.01<p\leq0.05$); not significant when interaction is deleted; refer to Appendix Table E-1 for a detailed description of this interaction.
** (NS*): Categorized current dioxin-by-covariate interaction ($0.01<p\leq0.05$); marginally significant when interaction is deleted; refer to Appendix Table E-1 for a detailed description of this interaction.
** (...): Categorized current dioxin-by-covariate interaction ($0.01<p\leq0.05$); significant when interaction is deleted, and p-value is given in parentheses; refer to Appendix Table E-1 for a detailed description of this interaction.
Note: P-value given if $p\leq0.05$.
A capital "NS" denotes relative risk 1.00 or greater for discrete analysis or difference in means nonnegative for continuous analysis; a lowercase "ns" denotes relative risk less than 1.00 for discrete analysis; a capital "NS" in the first column does not imply directionality.