

TABLE 12-22.
Analysis of Femoral Pulses

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.) ^a	p-Value
a) Minimal (n=442)	Low	109	0.0	0.90 (0.51,1.59)	0.703
	Medium	223	3.6		
	High	110	1.8		
b) Maximal (n=641)	Low	172	1.2	1.02 (0.68,1.53)	0.922
	Medium	318	2.8		
	High	151	1.3		

Ranch Hands - Log₂ (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.) ^a	p-Value	Covariate Remarks
c) Minimal (n=425)	1.01 (0.55,1.86)**	0.984**	INIT*PERS (p=0.027) AGE (p=0.004) CHOL (p=0.078) DIFCORT (p=0.041) HRTDIS (p=0.078)
d) Maximal (n=615)	1.11 (0.69,1.78)**	0.683**	INIT*PERS (p=0.032) AGE (p=0.003) PACKYR (p=0.024) CHOL (p=0.038) %BFAT (p=0.109) HRTDIS (p=0.113)

^aRelative risk for a twofold increase in dioxin.

**Log₂ (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.

TABLE 12-22. (Continued)

Analysis of Femoral Pulses

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

Assumption	Time (Yrs.)	Percent Abnormal/(n)			Est. Relative Risk (95% C.I.) ^a	p-Value
		Low	Medium	High		
e) Minimal (n=442)	≤18.6	0.0 (58)	2.7 (113)	0.0 (46)	0.96 (0.32,2.93)	0.562 ^b 0.950 ^c
	>18.6	6.1 (49)	2.6 (114)	1.6 (62)	0.64 (0.29,1.42)	0.271 ^c
f) Maximal (n=641)	≤18.6	1.0 (102)	1.2 (166)	1.5 (68)	1.05 (0.48,2.30)	0.656 ^b 0.906 ^c
	>18.6	2.9 (68)	3.3 (152)	2.4 (85)	0.84 (0.50,1.43)	0.527 ^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 (n=425)	≤18.6	1.33 (0.41,4.30)	0.407 ^b	AGE (p=0.020)
	>18.6	0.71 (0.30,1.67)	0.634 ^c 0.429 ^c	CHOL (p=0.092) PERS (p=0.136) DIFCORT (p=0.057) HRTDIS (p=0.082)
h) Maximal (n=613)	≤18.6	****	****	CURR*TIME*%BFAT (p<0.001)
	>18.6	****	****	CURR*TIME*DIFCORT (p=0.005) AGE (p=0.004) PACKYR (p=0.025) CHOL (p=0.012) PERS (p=0.017) HRTDIS (p=0.032)

^aRelative risk for a twofold increase in dioxin.^bTest of significance for homogeneity of relative risks (current dioxin continuous, time categorized).^cTest of significance for relative risk equal to 1 (current dioxin continuous, time categorized).****Log₂ (current dioxin)-by-time-by-covariate interaction (p≤0.01); 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 12-22. (Continued)
Analysis of Femoral Pulses

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	694	0.7	All Categories		0.227
Unknown	317	1.9	Unknown vs. Background	2.66 (0.81,8.78)	0.187
Low	176	2.3	Low vs. Background	3.21 (0.85,12.06)	0.175
High	153	2.0	High vs. Background	2.76 (0.65,11.66)	0.322
Total	1,340				

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	660	All Categories		0.141**	DXCAT*PERS (p=0.030)
Unknown	300	Unknown vs. Background	2.43 (0.69,8.57)**	0.169**	AGE (p=0.001)
Low	172	Low vs. Background	3.48 (0.91,13.38)**	0.070**	
High	148	High vs. Background	4.52 (1.00,20.31)**	0.049**	
Total	1,280				

**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.

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 adjustment for covariate information did not change the lack of significance of the minimal analysis of femoral pulses with current dioxin and time since tour (Table 12-22 [g]: $p>0.40$ for interaction and time-specific analyses). However, under the maximal assumption, the adjusted analysis of femoral pulses detected significant interactions among current dioxin, time, and percent body fat and among current dioxin, time, and differential cortisol response (Table 12-22 [h]: $p<0.001$ and $p=0.005$). Stratified analyses were performed for each percent body fat-by-differential cortisol-response stratum (Appendix Table K-1). The absence of femoral pulses was relatively rare in the 12 time and covariate strata. Only four Ranch Hands (all having normal percent body fat) with later tours had an abnormal femoral pulse; three had a differential cortisol response of $0.6 \mu\text{g}/\text{dl}$ or less (two with medium current dioxin and one with high current dioxin) and the other Ranch Hand had greater than $4.0 \mu\text{g}/\text{dl}$ (low current dioxin). The remaining nine Ranch Hands with earlier tours and abnormal femoral pulses were scattered throughout the six covariate strata (see Appendix Table K-1). These interactions were most likely affected by the sparseness of Ranch Hands who had absent femoral pulses.

Results of Analyses Without Adjustment for Cholesterol and Percent Body Fat. After removing cholesterol and percent body fat from the maximal adjusted analysis of femoral pulses, the current dioxin-by-time-by-differential cortisol interaction was no longer significant. The adjusted analysis after the above exclusions did not detect any significant results (Appendix Table K-2: $p\geq0.60$ for the interaction and time-specific analyses).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The unadjusted analysis did not detect any significant differences among the frequencies of absent femoral pulses of the four current dioxin categories (Table 12-22 [i]: $p>0.15$ for each contrast). Ranch Hands in all three current dioxin categories (unknown, low, and high) had a nonsignificant but higher risk of abnormal femoral pulses than the Comparisons in the background category.

The adjusted analysis of femoral pulses revealed a significant interaction between categorized current dioxin and personality type (Table 12-22 [j]: $p=0.030$). Appendix Table K-1 presents stratified analyses for this interaction. Only two type A participants (both Ranch Hands in the high current dioxin category) had absent femoral pulses; the contrast of the Ranch Hands in the high category versus the Comparisons in the background category was marginally significant ($p=0.066$). For type B participants, the overall contrast of the four current dioxin categories was not significant ($p=0.296$). However, the Ranch Hands in the low category had a marginally higher risk of an absent femoral pulse relative to the Comparisons in the background category (Adj. RR=3.47, 95% C.I.: [0.90,13.39], $p=0.071$). The relative frequencies of participants with absent femoral pulses were 1.3, 3.3, 4.1, and 1.2 percent for the background, unknown, low, and high current dioxin categories.

After deletion of the categorized current dioxin-by-personality type interaction from the model and adjusting only for age and personality type, the simultaneous contrast of the frequencies of abnormal femoral pulses of the four current dioxin categories remained nonsignificant (Table 12-22 [j]: $p=0.141$). However, similar to the analysis of type B participants in the stratified analyses, the contrast of the frequency of Ranch Hands having abnormal femoral pulses in the low category was marginally higher than the corresponding frequency of Comparisons in the background category (Adj. RR=3.48, 95% C.I.: [0.91,13.38],

$p=0.070$). Also, Ranch Hands in the high current dioxin category had a significantly higher risk of an absent femoral pulse than the Comparisons in the background category (Adj. RR=4.52, 95% C.I.: [1.00,20.31], $p=0.049$). The relative frequencies of participants with abnormal femoral pulses were 0.7, 1.9, 2.3, and 2.0 percent for the background, unknown, low, and high current dioxin categories. These results may have been affected by the sparse number of abnormalities.

Popliteal Pulses

Model 1: Ranch Hands - Log₂ (Initial Dioxin)

The unadjusted analysis under the minimal and maximal assumptions displayed a nonsignificant association between initial dioxin and the frequency of Ranch Hands with absent popliteal pulses (Table 12-23 [a] and [b]: $p=0.124$ and $p=0.802$, respectively).

After adjustment for covariate information, the results of the minimal and maximal analyses remained nonsignificant (Table 12-23 [c] and [d]: $p=0.230$ and $p=0.865$, respectively).

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

Under the minimal and the maximal assumptions, the unadjusted analyses of popliteal pulses detected nonsignificant interactions between current dioxin and time since tour (Table 12-23 [e] and [f]: $p=0.762$ and $p=0.881$, respectively). The associations between current dioxin and popliteal pulses were also negative and nonsignificant within all time strata.

The minimal adjusted analysis revealed a significant current dioxin-by-time-by-family history of heart disease interaction (Table 12-23 [g]: $p=0.034$). To examine this interaction, Appendix K-1 presents stratified analyses for Ranch Hands with and without a family history of heart disease. Of the participants with a family history of heart disease, only one Ranch Hand with a later tour (low current dioxin) and one Ranch Hand with an earlier tour (medium current dioxin) had an absent popliteal pulse. In addition, for Ranch Hands without a family history of heart disease, the negative associations between current dioxin and the prevalence of absent popliteal pulse did not differ significantly between time strata and were nonsignificant ($p>0.20$ for the interaction and time-specific analyses). After deletion of this interaction, the minimal adjusted analysis exhibited a nonsignificant current dioxin-by-time since tour interaction (Table 12-23 [g]: $p=0.723$) as well as nonsignificant negative associations between current dioxin and the frequency of Ranch Hands having abnormal popliteal pulses with each time stratum.

Under the maximal assumption, the adjusted analysis revealed a significant interaction among current dioxin, time, and lifetime cigarette smoking history (Table 12-23 [h]: $p=0.035$). To investigate this interaction, stratified analyses were performed for each lifetime cigarette smoking history stratum. In the nonsmoking stratum, only one Ranch Hand (≤ 18.6 years since tour, low current dioxin category) had an absent popliteal pulse. Therefore, relative risks, confidence intervals, and p-values were not presented for this stratum.

TABLE 12-23.
Analysis of Popliteal Pulses

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.) ^a	p-Value
a) Minimal (n=442)	Low	109	2.8	0.67 (0.39,1.16)	0.124
	Medium	223	4.9		
	High	110	0.9		
b) Maximal (n=641)	Low	172	1.2	0.96 (0.67,1.37)	0.802
	Medium	318	4.4		
	High	151	1.3		

Ranch Hands - Log₂ (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.) ^a	p-Value	Covariate Remarks
c) Minimal (n=427)	0.72 (0.40,1.28)	0.230	AGE (p=0.024) PERS (p=0.023) DIFCORT (p=0.010)
d) Maximal (n=620)	1.03 (0.71,1.51)	0.865	AGE (p=0.012) DIFCORT (p=0.059)

^aRelative 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 12-23. (Continued)

Analysis of Popliteal Pulses

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

Assumption	Time (Yrs.)	Percent Abnormal/(n)			Est. Relative Risk (95% C.I.) ^a	p-Value
		Low	Medium	High		
e) Minimal (n=442)	≤18.6	3.5 (58)	3.5 (113)	0.0 (46)	0.50 (0.17,1.49)	0.762 ^b 0.211 ^c
	>18.6	4.1 (49)	6.1 (114)	0.0 (62)	0.61 (0.29,1.25)	0.178 ^c
f) Maximal (n=641)	≤18.6	1.0 (102)	3.0 (166)	1.5 (68)	0.91 (0.48,1.72)	0.881 ^b 0.776 ^c
	>18.6	2.9 (68)	4.6 (152)	2.4 (85)	0.86 (0.53,1.38)	0.525 ^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 (n=427)	≤18.6	0.52 (0.15,1.86)**	0.723** ^b 0.317** ^c	CURR*TIME*HRTDIS (p=0.034) AGE (p=0.038)
	>18.6	0.68 (0.33,1.42)**	0.303** ^c	PERS (p=0.018) DIFCORT (p=0.019)
h) Maximal (n=616)	≤18.6	0.94 (0.46,1.95)**	0.880** ^b 0.874** ^c	CURR*TIME*PACKYR (p=0.035)
	>18.6	0.88 (0.53,1.47)**	0.630*** ^c	AGE (p=0.034) RACE (p=0.148) PERS (p=0.008) DIFCORT (p=0.049)

^aRelative risk for a twofold increase in dioxin.^bTest of significance for homogeneity of relative risks (current dioxin continuous, time categorized).^cTest of significance for relative risk equal to 1 (current dioxin continuous, time categorized).**Log₂ (current dioxin)-by-time-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: >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 12-23. (Continued)

Analysis of Popliteal Pulses

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	694	2.0	All Categories		0.471
Unknown	317	2.2	Unknown vs. Background	1.10 (0.44,2.74)	0.999
Low	176	4.0	Low vs. Background	2.01 (0.80,5.06)	0.222
High	153	2.0	High vs. Background	0.97 (0.28,3.42)	0.999
Total	1,340				

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	660	All Categories		0.490	AGE (p=0.001)
Unknown	300	Unknown vs. Background	0.98 (0.37,2.62)	0.973	PACKYR (p=0.049)
Low	172	Low vs. Background	2.07 (0.80,5.35)	0.133	PERS (p=0.026)
High	148	High vs. Background	1.49 (0.41,5.45)	0.548	
Total	1,280				

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.

The interaction between current dioxin and time since tour was nonsignificant in the analyses of moderate and heavy smokers (Appendix Table K-1: >0-10 pack-years, $p=0.625$; >10 pack-years, $p=0.120$). In the moderate smoking stratum, there was a nonsignificant negative relationship between current dioxin and the frequency of absent popliteal pulses for Ranch Hands with later tours and a nonsignificant positive association for Ranch Hands with early tours. In contrast, for the heavy-smoking stratum, there was a nonsignificant positive association between current dioxin and the prevalence of absent popliteal pulses for Ranch Hands with late tours and a nonsignificant negative association for Ranch Hands with early tours.

After deleting the current dioxin-by-time-by-lifetime cigarette smoking history interaction from the model, the maximal adjusted analysis displayed nonsignificant results consistent with the unadjusted analysis (Table 12-23 [h]: $p>0.60$ for the interaction and time-specific analyses).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In the unadjusted and adjusted analyses of the prevalence of abnormal popliteal pulses, the simultaneous contrast of the four current dioxin categories was not significant (Table 12-23 [i] and [j]: $p=0.471$ and $p=0.490$, respectively). The Ranch Hands versus Comparisons contrasts were also nonsignificant.

Dorsalis Pedis Pulses

Model 1: Ranch Hands - Log₂ (Initial Dioxin)

Based on the minimal assumption, the unadjusted analysis displayed a nonsignificant positive association between initial dioxin and the prevalence of abnormal dorsalis pedis pulses (Table 12-24 [a]: $p=0.322$). However, the maximal unadjusted analysis of dorsalis pedis pulses detected a marginally significant positive association with initial dioxin (Table 12-24 [b]: Est. RR=1.16, $p=0.089$). The relative frequencies of Ranch Hands in the maximal cohort who had absent dorsalis pedis pulses were 9.4, 11.6, and 15.2 percent for the low, medium, and high initial dioxin categories.

The minimal adjusted analysis of dorsalis pedis pulses revealed a significant interaction between initial dioxin and differential cortisol response (Table 12-24 [c]: $p=0.014$). The stratified analyses found a nonsignificant negative association between initial dioxin and the prevalence of abnormal dorsalis pedis pulses for Ranch Hands with a differential cortisol response of 0.6 $\mu\text{g}/\text{dl}$ or less (Appendix Table K-1: Adj. RR=0.90, $p=0.578$). In contrast, for Ranch Hands with a differential cortisol response between 0.6 $\mu\text{g}/\text{dl}$ and 4.0 $\mu\text{g}/\text{dl}$, there was a marginally significant positive association between initial dioxin and dorsalis pedis pulses (Adj. RR=1.42, $p=0.056$) and a nonsignificant positive association for Ranch Hands with over 4.0 $\mu\text{g}/\text{dl}$ (Adj. RR=1.55, $p=0.207$). In the moderate differential cortisol-response stratum, the frequencies of Ranch Hands with absent dorsalis pedis pulses increased steadily with increasing initial dioxin (low, 4.8%; medium, 11.3%; high, 20.0%).

After deletion of the interaction, the adjusted minimal analysis displayed a nonsignificant association between initial dioxin and the prevalence of abnormal dorsalis pedis pulses (Table 12-24 [c]: $p=0.153$). After adjustment for age and differential cortisol,

TABLE 12-24.
Analysis of Dorsalis Pedis Pulses

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.) ^a	p-Value
a) Minimal (n=442)	Low	109	9.2	1.13 (0.89,1.42)	0.322
	Medium	223	13.5		
	High	110	15.5		
b) Maximal (n=640)	Low	171	9.4	1.16 (0.98,1.38)	0.089
	Medium	318	11.6		
	High	151	15.2		

Ranch Hands - Log₂ (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.) ^a	p-Value	Covariate Remarks
c) Minimal (n=430)	1.20 (0.94,1.53)**	0.153**	INITIALDIRCORT (p=0.014) AGE (p=0.071)
d) Maximal (n=619)	1.21 (1.01,1.46)	0.041	AGE (p=0.010) DIRCORT (p=0.007)

^aRelative risk for a twofold increase in dioxin.

**Log₂ (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.

TABLE 12-24. (Continued)
Analysis of Dorsalis Pedis Pulses

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

Assumption	Time (Yrs.)	Percent Abnormal/(n)			Est. Relative Risk (95% C.I.) ^a	p-Value
		Low	Medium	High		
e) Minimal (n=442)	≤18.6	10.3 (58)	10.6 (113)	15.2 (46)	1.27 (0.87,1.85)	0.273 ^b 0.208 ^c
	>18.6	12.2 (49)	15.8 (114)	12.9 (62)	0.97 (0.70,1.33)	0.832 ^c
f) Maximal (n=640)	≤18.6	7.9 (101)	10.8 (166)	14.7 (68)	1.21 (0.93,1.58)	0.497 ^b 0.155 ^c
	>18.6	10.3 (68)	15.1 (152)	11.8 (85)	1.07 (0.85,1.36)	0.569 ^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 (n=430)	≤18.6	1.50 (1.00,2.24)	0.129 ^b 0.051 ^c	AGE (p=0.062) DIFCORT (p=0.002)
	>18.6	1.01 (0.73,1.41)	0.941 ^c	
h) Maximal (n=619)	≤18.6	1.34 (1.00,1.78)	0.355 ^b 0.048 ^c	AGE (p=0.010) DIFCORT (p=0.006)
	>18.6	1.12 (0.88,1.44)	0.355 ^c	

^aRelative risk for a twofold increase in dioxin.

^bTest of significance for homogeneity of relative risks (current dioxin continuous, time categorized).

^cTest 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 12-24. (Continued)
Analysis of Dorsalis Pedis Pulses

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	694	9.4	All Categories		0.295
Unknown	316	11.1	Unknown vs. Background	1.21 (0.78,1.86)	0.399
Low	176	13.6	Low vs. Background	1.53 (0.93,2.52)	0.097
High	153	13.1	High vs. Background	1.46 (0.85,2.48)	0.169
Total	1,339				

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	654	All Categories		0.146	AGE (p=0.003) CHOL (p=0.082)
Unknown	296	Unknown vs. Background	1.17 (0.74,1.86)	0.500	PERS (p=0.147)
Low	171	Low vs. Background	1.62 (0.97,2.70)	0.066	DIFCORT (p=0.138)
High	145	High vs. Background	1.72 (0.98,3.04)	0.061	
Total	1,266				

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.

the maximal analysis revealed a significant positive association between initial dioxin and the frequency of Ranch Hands having abnormal dorsalis pedis pulses (Table 12-24 [d]: Adj. RR=1.21, p=0.041).

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

Under the minimal and the maximal assumptions, the unadjusted analyses of dorsalis pedis pulses displayed nonsignificant interactions between current dioxin and time since tour (Table 12-24 [e] and [f]: p=0.273 and p=0.497, respectively).

After including age and differential cortisol in the models of the minimal and maximal analyses, the interactions between current dioxin and time since tour remained nonsignificant (Table 12-24 [g] and [h]: p=0.129 and p=0.355, respectively). However, for Ranch Hands with later tours, there was a marginally significant positive association between current dioxin and the prevalence of abnormal dorsalis pedis pulses in the minimal cohort (Table 12-24 [g]: Adj. RR=1.50, p=0.051) and a significant positive association for this stratum of Ranch Hands in the maximal cohort (Table 12-24 [h]: Adj. RR=1.34, p=0.048). In the 18.6 years or less time stratum, the relative frequencies of Ranch Hands with absent dorsalis pedis pulses were 10.3, 10.6, and 15.2 percent for low, medium, and high current dioxin under the minimal assumption and 7.9, 10.8, and 14.7 percent for low, medium, and high current dioxin based on the maximal assumption.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In the unadjusted analysis of the prevalence of abnormal dorsalis pedis pulses, the simultaneous contrast of the four current dioxin categories was not significant (Table 12-24 [i]: p=0.295). However, the Ranch Hands in the low current dioxin category had a marginally higher risk of an absent dorsalis pedis pulse than the Comparisons in the background category (Adj. RR=1.53, 95% C.I.: [0.93,2.52], p=0.097). The percentages of participants with an abnormal dorsalis pedis pulse for the background, unknown, low, and high current dioxin categories were 9.4, 11.1, 13.6, and 13.1 percent.

After adjusting for age, cholesterol, personality type, and differential cortisol response in the analysis of dorsalis pedis pulses, the overall contrast of the four current dioxin categories remained nonsignificant (Table 12-24 [j]: p=0.146). The Ranch Hands in the low and high current dioxin categories had marginally higher risks of an absent dorsalis pedis pulse relative to the Comparisons in the background category (low vs. background: Adj. RR=1.62, 95% C.I.: [0.97,2.70], p=0.066; high vs. background: Adj. RR=1.72, 95% C.I.: [0.98,3.04], p=0.061).

Results of Analyses Without Adjustment for Cholesterol. After removing cholesterol from the adjusted analysis of dorsalis pedis pulses, the overall contrast of the four current dioxin categories became marginally significant (Appendix Table K-2: p=0.087). Also, the contrast of the Ranch Hands in the high current dioxin category versus the Comparisons in the background category became significant (Adj. RR=1.86, 95% C.I.: [1.07,3.26], p=0.029).

Posterior Tibial Pulses

Model 1: Ranch Hands - Log₂ (Initial Dioxin)

Under the minimal and the maximal assumptions, the unadjusted analysis of the prevalence of absent posterior tibial pulses did not detect a significant association with initial dioxin (Table 12-25 [a] and [b]: $p=0.333$ and $p=0.346$, respectively).

The adjusted minimal analysis of the frequency of Ranch Hands having abnormal posterior tibial pulses and initial dioxin remained nonsignificant (Table 12-25 [c]: $p=0.921$). However, after adjusting for age, percent body fat, personality type, and differential cortisol response, the maximal analysis detected a marginally significant positive association between initial dioxin and the prevalence of absent posterior tibial pulses in Ranch Hands (Table 12-25 [d]: Adj. RR=1.38, $p=0.086$). Under the maximal assumption, there were no Ranch Hands in the low initial dioxin category who had abnormal posterior tibial pulses, but 4.7 and 2.7 percent of the Ranch Hands in the medium and high initial dioxin categories, respectively, had absent posterior tibial pulses.

Results of Analyses Without Adjustment for Percent Body Fat. After excluding percent body fat from the maximal adjusted model and adjusting only for age, personality type, and differential cortisol response, the positive association between initial dioxin and the prevalence of absent posterior tibial pulses in Ranch Hands became nonsignificant (Appendix Table K-2: Adj. RR=1.34, $p=0.124$).

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

Under the minimal and the maximal assumptions, the unadjusted analysis of the frequency of abnormal posterior tibial pulses in Ranch Hands displayed nonsignificant interactions between current dioxin and time since tour (Table 12-25 [e] and [f]: $p=0.756$ and $p=0.733$, respectively). The associations between current dioxin and the prevalence of abnormal posterior tibial pulses were also nonsignificant within each time stratum of the minimal and maximal cohorts.

The adjusted minimal analysis of posterior tibial pulses with current dioxin and time since tour remained nonsignificant (Table 12-25 [g]: $p>0.60$ for the interaction and time-specific analyses). After adjusting the maximal analysis for age, percent body fat, and differential cortisol response, the interaction between current dioxin and time remained nonsignificant (Table 12-25 [h]: $p=0.297$). However, for Ranch Hands in the maximal cohort with 18.6 years or less since tour, there was a marginally significant positive association between current dioxin and the frequency of Ranch Hands with abnormal posterior tibial pulses (Adj. RR=1.88, $p=0.087$). In the maximal cohort, 4.2 percent of the Ranch Hands with medium current dioxin had an abnormal posterior tibial pulse, while none with low or high current dioxin were classified as abnormal.

Results of Analyses Without Adjustment for Percent Body Fat. After removing percent body fat from the maximal adjusted model, the positive association between current dioxin and abnormal posterior tibial pulses became nonsignificant for Ranch Hands with 18.6 years or less since tour (Appendix Table K-2: Adj. RR=1.65, $p=0.146$).

TABLE 12-25.
Analysis of Posterior Tibial Pulses

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Current Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.) ^a	p-Value
a) Minimal (n=442)	Low	109	1.8	0.81 (0.51,1.27)	0.333
	Medium	223	6.3		
	High	110	1.8		
b) Maximal (n=640)	Low	171	0.0	1.17 (0.85,1.61)	0.346
	Medium	318	4.7		
	High	151	2.7		
Ranch Hands - Log₂ (Initial Dioxin) - Adjusted					
Current Assumption	Dioxin	Adj. Relative Risk (95% C.I.) ^a	p-Value	Covariate Remarks	
c) Minimal (n=430)	Unknown vs Background	1.02 (0.64,1.65)	0.921	AGE (p<0.001) %BFAT (p=0.033) DIFCORT (p<0.001)	
	Low vs Background				
	High vs Background				
d) Maximal (n=603)	Unknown vs Background	1.38 (0.97,1.98)	0.086	AGE (p<0.001) %BFAT (p=0.058) PERS (p=0.136) DIFCORT (p<0.001)	
	Low vs Background				
	High vs Background				

^aRelative 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 12-25. (Continued)
Analysis of Posterior Tibial Pulses

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

Assumption	Time (Yrs.)	Percent Abnormal/(n)			Est. Relative Risk (95% C.I.) ^a	p-Value
		Low	Medium	High		
e) Minimal (n=442)	≤18.6	1.7 (58)	5.3 (113)	0.0 (46)	0.60 (0.24,1.50)	0.756 ^b 0.273 ^c
	>18.6	2.0 (49)	7.9 (114)	1.6 (62)	0.71 (0.39,1.30)	0.263 ^c
f) Maximal (n=640)	≤18.6	0.0 (101)	4.2 (166)	0.0 (68)	1.15 (0.65,2.04)	0.733 ^b 0.636 ^c
	>18.6	1.5 (68)	5.9 (152)	2.4 (85)	1.01 (0.67,1.54)	0.946 ^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 (n=430)	≤18.6	1.05 (0.35,3.15)	0.762 ^b	AGE (p<0.001)
	>18.6	0.86 (0.47,1.59)	0.937 ^c	%BFAT (p=0.033)
h) Maximal (n=619)	≤18.6	1.88 (0.91,3.88)	0.297 ^b	DIFCORT (p<0.001)
	>18.6	1.20 (0.77,1.86)	0.087 ^c	AGE (p<0.001)
			0.413 ^c	%BFAT (p=0.036)

^aRelative risk for a twofold increase in dioxin.

^bTest of significance for homogeneity of relative risks (current dioxin continuous, time categorized).

^cTest 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 12-25. (Continued)**Analysis of Posterior Tibial Pulses****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	694	2.2	All Categories		<0.001
Unknown	316	1.0	Unknown vs. Background	0.43 (0.12,1.51)	0.270
Low	176	7.4	Low vs. Background	3.61 (1.68,7.74)	0.003
High	153	1.3	High vs. Background	0.60 (0.14,2.65)	0.764
Total	1,339				

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	694	All Categories		<0.001	AGE (p<0.001) %BFAT (p=0.055)
Unknown	316	Unknown vs. Background	0.38 (0.11,1.34)	0.131	
Low	176	Low vs. Background	4.46 (2.02,9.82)	<0.001	
High	153	High vs. Background	1.12 (0.25,5.14)	0.880	
Total	1,339				

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.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In both the unadjusted and adjusted analyses of abnormal posterior tibial pulses, the simultaneous contrasts of the four current dioxin categories were significant (Table 12-25 [i] and [j]: $p<0.001$ for each analysis). Also, for both analyses, Ranch Hands in the low current dioxin category had a higher risk of abnormal posterior tibial pulses than the Comparisons in the background category (unadjusted: Est. RR=3.61, 95% C.I.: [1.68, 7.74], $p=0.003$; adjusted: Adj. RR=4.46, 95% C.I.: [2.02, 9.82], $p<0.001$). The relative frequencies of participants with absent posterior tibial pulses were 2.2, 1.0, 7.4, and 1.3 percent for the background, unknown, low, and high current dioxin categories.

Leg Pulses

The primary analyses for leg pulses excluded diabetics. However, additional analyses (unadjusted and adjusted for age) were done based on diabetics only. Appendix Table K-5 details the results of these analyses. There were no significant results found in these analyses. The unadjusted categorized current dioxin analysis showed a marginally significant increased risk of leg pulses for diabetic Ranch Hands in the low current dioxin category relative to diabetic Comparisons in the background category (Est. RR=3.34, 95% C.I.: [0.95, 11.59], $p=0.057$), but this contrast became nonsignificant after adjustment for age (Adj. RR=2.76, 95% C.I.: [0.76, 9.94], $p=0.119$). The prevalences of leg pulse abnormalities based on diabetics only were 18.3, 16.7, 42.9, and 17.9 percent for the background, unknown, low, and high current dioxin categories.

The following discussion of the leg pulse analyses is based on participants who were not classified as diabetic.

Model 1: Ranch Hands - Log₂ (Initial Dioxin)

Under the minimal assumption, the analysis of abnormal leg pulses and initial dioxin was nonsignificant (Table 12-26 [a]: $p=0.636$). Based on the maximal assumption, there was a marginally significant positive association between initial dioxin and the prevalence of abnormal leg pulses in Ranch Hands (Table 12-26 [b]: Est. RR=1.15, $p=0.085$). The relative frequencies of Ranch Hands in the maximal cohort with abnormal leg pulses became larger with increasing levels of initial dioxin (low, 10.5%; medium, 15.1%; high, 17.9%).

The minimal adjusted analysis of leg pulses revealed a significant interaction between initial dioxin and age (Table 12-26 [c]: $p=0.017$). The stratified analyses (Appendix Table K-1) exhibited a nonsignificant negative association between initial dioxin and absent leg pulses for the younger Ranch Hands (Adj. RR=0.86, $p=0.396$) and a significant positive association for the older Ranch Hands (Adj. RR=1.41, $p=0.030$). The relative frequencies of older Ranch Hands with abnormal leg pulses in the low, medium, and high initial dioxin categories were 8.8, 25.0, and 27.8 percent.

After deletion of the initial dioxin-by-age interaction, the minimal analysis of initial dioxin and leg pulses was nonsignificant (Table 12-26 [c]: $p=0.289$). Under the maximal assumption, the adjustment for age and differential cortisol response caused the positive association between initial dioxin and the frequency of absent leg pulses to become significant (Table 12-26 [d]: Adj. RR=1.22, $p=0.021$).

TABLE 12-26.

Analysis of Leg Pulses

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.) ^a	p-Value
a) Minimal (n=442)	Low	109	11.9	1.05 (0.85,1.31)	0.636
	Medium	223	17.9		
	High	110	17.3		
b) Maximal (n=640)	Low	171	10.5	1.15 (0.98,1.35)	0.085
	Medium	318	15.1		
	High	151	17.9		

Ranch Hands - Log₂ (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.) ^a	p-Value	Covariate Remarks
c) Minimal (n=430)	1.13 (0.90,1.42)**	0.289**	INIT*AGE (p=0.017) %BFAT (p=0.086) DIFCORT (p=0.025)
d) Maximal (n=619)	1.22 (1.03,1.45)	0.021	AGE (p<0.001) DIFCORT (p=0.040)

^aRelative risk for a twofold increase in dioxin.

**Log₂ (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.

TABLE 12-26. (Continued)

Analysis of Leg Pulses

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

Assumption	Time (Yrs.)	Percent Abnormal/(n)			Est. Relative Risk (95% C.I.) ^a	p-Value
		Low	Medium	High		
e) Minimal (n=442)	≤18.6	12.1 (58)	14.2 (113)	15.2 (46)	1.13 (0.79,1.61)	0.369 ^b
	>18.6	16.3 (49)	21.1 (114)	16.1 (62)	0.91 (0.68,1.22)	0.533 ^c
f) Maximal (n=640)	≤18.6	8.9 (101)	13.9 (166)	14.7 (68)	1.16 (0.91,1.50)	0.609 ^b
	>18.6	11.8 (68)	19.7 (152)	15.3 (85)	1.07 (0.86,1.32)	0.236 ^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 (n=430)	≤18.6	1.31 (0.89,1.91)**	0.220** ^b	CURR*TIME*PACKYR	
	>18.6	0.97 (0.72,1.32)**	0.167** ^c (p=0.031)	AGE (p=0.005)	
h) Maximal (n=619)	≤18.6	1.30 (0.99,1.71)	0.866** ^c %BFAT (p=0.147)	DIFCORT (p=0.018)	
	>18.6	1.14 (0.91,1.43)	0.460 ^b AGE (p<0.001)	DIFCORT (p=0.035)	

^aRelative risk for a twofold increase in dioxin.^bTest of significance for homogeneity of relative risks (current dioxin continuous, time categorized).^cTest of significance for relative risk equal to 1 (current dioxin continuous, time categorized).**Log₂ (current dioxin)-by-time-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: >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 12-26. (Continued)

Analysis of Leg Pulses

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	694	11.4	All Categories		0.077
Unknown	316	12.7	Unknown vs. Background	1.13 (0.75,1.69)	0.560
Low	176	18.8	Low vs. Background	1.80 (1.15,2.80)	0.010
High	153	15.0	High vs. Background	1.38 (0.83,2.27)	0.211
Total	1,339				

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	656	All Categories		0.020	AGE (p<0.001)
Unknown	298	Unknown vs. Background	1.06 (0.69,1.62)	0.798	CHOL (p=0.122)
Low	171	Low vs. Background	1.92 (1.22,3.03)	0.005	PERS (p=0.119)
High	147	High vs. Background	1.71 (1.01,2.91)	0.047	
Total	1,272				

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.

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

Under the minimal and the maximal assumptions, the associations between current dioxin and absent leg pulses did not differ significantly between time since tour strata in the unadjusted analysis (Table 12-26 [e] and [f]: $p=0.369$ and $p=0.609$, respectively). These associations between current dioxin and leg pulses were also nonsignificant for each time stratum of the unadjusted analysis.

The adjusted minimal analysis of the prevalence of abnormal leg pulses revealed a significant interaction among current dioxin, time since tour, and lifetime cigarette smoking history (Table 12-26 [g]: $p=0.031$). In order to investigate this interaction, stratified analyses are presented in Appendix Table K-1 for each lifetime cigarette smoking history and time stratum. In the nonsmoking stratum, the interaction between current dioxin and time was not significant ($p=0.159$), nor were the associations between current dioxin and absent leg pulses within the time strata (≤ 18.6 years: Adj. RR=0.51, $p=0.175$; > 18.6 years: Adj. RR=1.14, $p=0.733$).

Similarly, for Ranch Hands who were moderate smokers, the nonsignificant positive associations between current dioxin and abnormal leg pulses did not differ significantly between time strata (Appendix Table K-1: $p>0.10$ for the interaction and time-specific analyses). However, for heavy smokers, the interaction between current dioxin and time since tour was significant ($p=0.003$). The positive association between current dioxin and the prevalence of abnormal leg pulses was also significant for Ranch Hands with later tours (Adj. RR=2.73, $p=0.008$). The relative frequencies of Ranch Hands in this stratum with leg pulses classified as abnormal were 18.4 and 14.3 percent for medium and high current dioxin and 0.0 percent for low current dioxin. For Ranch Hands with earlier tours, the analysis detected a nonsignificant negative association between current dioxin and abnormal leg pulses (Adj. RR=0.75, $p=0.231$).

After deletion of the current dioxin-by-time-by-lifetime cigarette smoking history interaction, the minimal adjusted analysis of the prevalence of abnormal leg pulses was nonsignificant (Table 12-26 [g]: $p>0.15$ for the interaction and time-specific analyses).

In the maximal analysis of leg pulses, the adjustment for age and differential cortisol response did not alter the lack of significance of the interaction between current dioxin and time since tour (Table 12-26 [h]: $p=0.460$). However, within the 18.6 years or less time stratum, the positive association between current dioxin and abnormal leg pulses became marginally significant (Adj. RR=1.30, $p=0.057$). In the maximal cohort, the percentages of Ranch Hands with later tours who had abnormal leg pulses were 8.9, 13.9, and 14.7 percent for low, medium, and high current dioxin.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The unadjusted analysis of the prevalence of absent leg pulses detected a marginally significant difference among the four current dioxin categories (Table 12-26 [i]: $p=0.077$). Specifically, the Ranch Hands in the low current dioxin category had a significantly higher risk of abnormal leg pulses than the Comparisons in the background category (Est. RR=1.80, 95% C.I.: [1.15, 2.80], $p=0.010$). Even though the low versus background contrast was the only significant contrast, the Ranch Hands in all three current dioxin categories had higher

percentages of absent leg pulses than the Comparisons in the background category (background, 11.4%; unknown, 12.7%; low, 18.8%; high, 15.0%).

After adjusting for age, cholesterol, and personality type, the overall contrast of the four current dioxin categories became significant in the analysis of leg pulses (Table 12-26 [j]: $p=0.020$). The contrast of the Ranch Hands in the low current dioxin category versus the Comparisons in the background category remained significant (Adj. RR=1.92, 95% C.I.: [1.22,3.03], $p=0.005$). Also, the contrast of the Ranch Hands in the high category versus the Comparisons in the background category became significant with the Ranch Hands having a greater risk of abnormal leg pulses than the Comparisons (Adj. RR=1.71, 95% C.I.: [1.01,2.91], $p=0.047$). The risk of absent leg pulses remained nonsignificantly higher for the Ranch Hands in the low category relative to the Comparisons in the background category ($p=0.798$).

Peripheral and All Pulses

The index of all pulses included the peripheral pulse index and the carotid pulse. These indices differed in the number of abnormalities only in the categorized current dioxin analyses, and, therefore, displayed equivalent results for the initial dioxin and current dioxin with time since tour analyses.

Model 1: Ranch Hands - Log₂ (Initial Dioxin)

The unadjusted analyses of peripheral and all pulses displayed positive associations with initial dioxin that were nonsignificant for the minimal cohort (Table 12-27 [a]: Est. RR=1.04, $p=0.718$) and marginally significant for the maximal cohort (Table 12-27 [b]: Est. RR=1.15, $p=0.092$). The relative frequencies of Ranch Hands with abnormal peripheral and all pulses indices were 10.5, 15.4, and 17.9 percent for the low, medium, and high initial dioxin categories.

The adjusted minimal analysis of peripheral and all pulses revealed a significant interaction between initial dioxin and age (Table 12-27 [c]: $p=0.013$). In order to examine this interaction, stratified analyses were performed for the younger and older Ranch Hands (Appendix Table K-1). For the younger Ranch Hands, the stratified analyses exhibited a nonsignificant negative association between initial dioxin and age (Adj. RR=0.83, $p=0.306$). In contrast, the analysis of the older Ranch Hands found a significant positive association between initial dioxin and the prevalence of abnormal peripheral and all pulse indices (Adj. RR=1.41, $p=0.029$). The relative frequencies of the older Ranch Hands with abnormal peripheral and all pulse indices became larger with increasing levels of initial dioxin (low, 8.8%; medium, 25.0%; high, 27.8%).

After deletion of the initial dioxin-by-age interaction from the model, the minimal analysis of peripheral and all pulses was nonsignificant (Table 12-27 [c]: $p=0.349$). However, the adjustment for age and differential cortisol response caused the positive association between initial dioxin and the peripheral and all pulses indices to become significant under the maximal assumption (Table 12-27 [d]: Adj. RR=1.22, $p=0.025$).

TABLE 12-27.
Analysis of Peripheral and All Pulses

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.) ^a	p-Value
a) Minimal (n=442)	Low	109	12.8	1.04 (0.84,1.29)	0.718
	Medium	223	17.9		
	High	110	17.3		
b) Maximal (n=640)	Low	171	10.5	1.15 (0.98,1.34)	0.092
	Medium	318	15.4		
	High	151	17.9		

Ranch Hands - Log₂ (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.) ^a	p-Value	Covariate Remarks
c) Minimal (n=430)	1.12 (0.89,1.40)**	0.349**	INIT*AGE (p=0.013) %BFAT (p=0.140) DIFCORT (p=0.024)
d) Maximal (n=619)	1.22 (1.03,1.44)	0.025	AGE (p<0.001) DIFCORT (p=0.037)

^aRelative risk for a twofold increase in dioxin.

**Log₂ (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.

TABLE 12-27. (Continued)

Analysis of Peripheral and All Pulses

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

Assumption	Time (Yrs.)	Percent Abnormal/(n)			Est. Relative Risk (95% C.I.) ^a	p-Value
		Low	Medium	High		
e) Minimal (n=442)	≤18.6	12.1 (58)	14.2 (113)	15.2 (46)	1.13 (0.79,1.61)	0.321 ^b 0.513 ^c
	>18.6	18.4 (49)	21.1 (114)	16.1 (62)	0.89 (0.67,1.19)	0.439 ^c
f) Maximal (n=640)	≤18.6	8.9 (101)	13.9 (166)	14.7 (68)	1.16 (0.91,1.50)	0.577 ^b 0.236 ^c
	>18.6	11.8 (68)	20.4 (152)	15.3 (85)	1.06 (0.86,1.31)	0.596 ^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 (n=430)	≤18.6	1.33 (0.91,1.95)**	0.172** ^b	CURR*TIME*PACKYR (p=0.041)
	>18.6	0.96 (0.71,1.29)**	0.136** ^c	AGE (p=0.005)
			0.790** ^c	DIFCORT (p=0.016)
h) Maximal (n=619)	≤18.6	1.30 (0.99,1.70)	0.436 ^b	AGE (p=0.001)
	>18.6	1.13 (0.90,1.42)	0.062 ^c	DIFCORT (p=0.032)
			0.285 ^c	

^aRelative risk for a twofold increase in dioxin.^bTest of significance for homogeneity of relative risks (current dioxin continuous, time categorized).^cTest of significance for relative risk equal to 1 (current dioxin continuous, time categorized).**Log₂ (current dioxin)-by-time-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: >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 12-27. (Continued)

Analysis of Peripheral Pulses

i1) 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	694	11.8	All Categories		0.113
Unknown	316	12.7	Unknown vs. Background	1.08 (0.72,1.62)	0.703
Low	176	18.8	Low vs. Background	1.72 (1.11,2.68)	0.016
High	153	15.0	High vs. Background	1.32 (0.80,2.18)	0.276
Total	1,339				

j1) 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	660	All Categories		0.017	AGE (p<0.001) PERS (p=0.114)
Unknown	299	Unknown vs. Background	1.01 (0.66,1.55)	0.963	
Low	172	Low vs. Background	1.87 (1.18,2.94)	0.007	
High	148	High vs. Background	1.76 (1.05,2.97)	0.033	
Total	1,279				

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.

TABLE 12-27. (Continued)

Analysis of All Pulses

j2) 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	694	12.0	All Categories		0.133
Unknown	316	13.0	Unknown vs. Background	1.10 (0.74,1.64)	0.649
Low	176	18.8	Low vs. Background	1.70 (1.09,2.64)	0.019
High	153	15.0	High vs. Background	1.30 (0.79,2.15)	0.300
Total	1,339				

j2) 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	660	All Categories		0.021	AGE (p<0.001) PERS (p=0.124)
Unknown	299	Unknown vs. Background	1.03 (0.67,1.56)	0.904	
Low	172	Low vs. Background	1.84 (1.17,2.90)	0.008	
High	148	High vs. Background	1.75 (1.04,2.95)	0.035	
Total	1,279				

Note: Background (Comparisons): Current Dioxin \leq 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

Under the minimal and the maximal assumptions, the associations between current dioxin and the prevalence of abnormal peripheral and all pulses indices did not differ significantly between the two time since tour strata (Table 12-27 [e] and [f]: $p=0.321$ and $p=0.577$, respectively).

The minimal adjusted analysis detected a significant interaction among current dioxin, time since tour, and lifetime cigarette smoking history (Table 12-27 [g]: $p=0.041$). Stratified analyses displayed nonsignificant current dioxin-by-time interactions for nonsmokers and moderate smokers (Appendix Table K-1: $p=0.295$ and $p=0.807$, respectively). These analyses also showed nonsignificant negative associations between current dioxin and the peripheral and all pulses indices within both time strata for Ranch Hands who did not smoke and nonsignificant positive associations within both time strata for Ranch Hands who smoked moderately.

In contrast, for Ranch Hands who were heavy smokers (>10 pack-years), the interaction between current dioxin and time was significant (Appendix Table K-1: $p=0.003$). The analysis of Ranch Hands with later tours revealed a significant positive association between current dioxin and the peripheral and all pulses indices (Adj. RR=2.71, $p=0.008$). For Ranch Hands with earlier tours, the stratified analysis exhibited a nonsignificant negative association with current dioxin (Adj. RR=0.75, $p=0.237$). The relative frequencies of abnormal peripheral and all pulses indices for Ranch Hands with later tours were 18.4 and 14.3 percent for medium and high current dioxin. There were no Ranch Hands with abnormal peripheral and all pulses indices and low current dioxin.

After deletion of the current dioxin-by-time-by-lifetime cigarette smoking history interaction, the minimal analysis of peripheral and all pulses was not significant (Table 12-27 [g]: $p>0.10$ for the interaction and time-specific analyses). After adjusting for age and differential cortisol response, the interaction between current dioxin and time since tour remained nonsignificant in the maximal analysis (Table 12-27 [h]: $p=0.436$). However, there was a marginally significant positive association between current dioxin and the peripheral and all pulses indices for Ranch Hands with 18.6 years or less since tour (Adj. RR=1.30, $p=0.062$) and a nonsignificant positive association for Ranch Hands with more than 18.6 years since tour (Adj. RR=1.13, $p=0.285$). The percentages of Ranch Hands in the maximal cohort with later tours who had abnormal peripheral and all pulses indices were 8.9, 13.9, and 14.7 percent for low, medium, and high current dioxin.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

Peripheral Pulses. In the unadjusted analysis of peripheral pulses, the simultaneous contrast of the four current dioxin categories was not significant (Table 12-27 [i1]: $p=0.113$). However, the Ranch Hands in the low current dioxin category had a significantly higher risk of an abnormal peripheral pulses index than the Comparisons in the background category (Est. RR=1.72, 95% C.I.: [1.11, 2.68], $p=0.016$). In fact, the three current dioxin categories consisting of Ranch Hands had higher percentages of abnormal peripheral pulses indices than the background category of Comparisons (background, 11.8%; unknown, 12.7%; low, 18.8%; high, 15.0%).

After adjusting for age and personality type, the analysis of peripheral pulses detected a significant difference among the four current dioxin categories (Table 12-27 [j1]: $p=0.017$). Similar to the unadjusted analysis, the Ranch Hands in the low current dioxin category had a significantly higher risk of abnormal peripheral pulses than the Comparisons in the background category (Adj. RR=1.87, 95% C.I.: [1.18,2.94], $p=0.007$). The Ranch Hands in the high current dioxin category also had a significantly higher risk of an abnormal peripheral pulses index than the Comparisons in the background category (Adj. RR=1.76, 95% C.I.: [1.05,2.97], $p=0.033$).

All Pulses. The unadjusted analysis of the all pulses index did not detect a significant overall difference among the four current dioxin categories (Table 12-27 [i2]: $p=0.133$). Similar to the analysis of the peripheral pulses index, the contrast of the Ranch Hands in the low current dioxin category versus the Comparisons in the background category was significant (Est. RR=1.70, 95% C.I.: [1.09,2.64], $p=0.019$). The relative frequencies of abnormal all pulses indices were 12.0, 13.0, 18.8, and 15.0 percent for the background, unknown, low, and high current dioxin categories.

The adjustment for age and personality type caused the analysis of all pulses to detect a significant simultaneous contrast of the four current dioxin categories (Table 12-27 [j2]: $p=0.021$). Also, similar to the analysis of peripheral pulses, Ranch Hands in both the low category and the high category had a significantly higher risk of an abnormal all pulses index than the Comparisons in the background category (low versus background: Adj. RR=1.84, 95% C.I.: [1.17,2.90], $p=0.008$; high versus background: Adj. RR=1.75, 95% C.I.: [1.04,2.95], $p=0.035$).

Longitudinal Analysis

Physical Examination Variable

Overall ECG

For the cardiovascular examination, longitudinal analyses were conducted to examine the percentage of participants having a normal ECG reading at the 1982 examination and an abnormal reading at the 1987 examination for associations with initial dioxin, current dioxin and time since tour, and categorized current dioxin. Table 12-28 presents the results of these analyses.

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

Model 1: Ranch Hands - Log₂ (Initial Dioxin)

In the longitudinal analyses of the minimal and maximal cohorts, the associations between the percentage of Ranch Hands having an abnormal ECG reading at the 1987 examination and initial dioxin were significant (Table 12-28 [a] and [b]: Est. RR=0.65,

TABLE 12-28.
Longitudinal Analysis of Overall Electrocardiograph (ECG)

Assumption	Initial Dioxin	Percent Abnormal/(n)		
		Examination		
		1982	1985	1987
a) Minimal	Low	23.1 (104)	17.5 (103)	16.4 (104)
	Medium	32.9 (216)	14.8 (210)	18.5 (216)
	High	22.4 (107)	10.4 (106)	13.1 (107)
<u>Normal in 1982</u>				
Initial Dioxin	n in 1987	Percent Abnormal in 1987	Est. Relative Risk (95% C.I.) ^a	p-Value
Low	80	13.8	0.65 (0.44,0.94)	0.014
Medium	145	11.0		
High	83	6.0		

^aRelative 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 12-28. (Continued)

Longitudinal Analysis of Overall Electrocardiograph (ECG)

Ranch Hands - Log₂ (Initial Dioxin)

Assumption	Initial Dioxin	Percent Abnormal/(n) Examination		
		1982	1985	1987
b) Maximal	Low	27.9 (158)	11.7 (154)	16.5 (158)
	Medium	28.1 (306)	14.4 (299)	17.7 (306)
	High	24.5 (147)	11.7 (145)	13.6 (147)
	<u>Normal in 1982</u>			
Initial Dioxin	n in 1987	Percent Abnormal in 1987	Est. Relative Risk (95% C.I.) ^a	p-Value
Low	114	12.3	0.78 (0.61,1.00)	0.041
Medium	220	13.2		
High	111	4.5		

^aRelative 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 12-28. (Continued)
Longitudinal Analysis of Overall Electrocardiograph (ECG)

Ranch Hands - Log₂ (Current Dioxin) and Time

Assumption	Time (Yrs.)	Examination	Percent Abnormal/(n) Current Dioxin			
			Low	Medium	High	
c) Minimal	≤ 18.6	1982	19.6 (56)	33.9 (109)	15.9 (44)	
		1985	14.6 (55)	14.2 (106)	9.3 (43)	
		1987	14.3 (56)	16.5 (109)	11.4 (44)	
	> 18.6	1982	23.9 (46)	32.4 (111)	27.9 (61)	
		1985	20.0 (45)	14.7 (109)	13.1 (61)	
		1987	21.7 (46)	18.0 (111)	16.4 (61)	
Normal in 1982: Percent Abnormal/(n) in 1987						
<u>Current Dioxin</u>						
Time (Yrs.)	Low	Medium	High	Est. Relative Risk (95% C.I.) ^a	p-Value	
≤ 18.6	11.1 (45)	9.7 (72)	5.4 (37)	0.81 (0.47,1.41)	0.189 ^b 0.460 ^c	
> 18.6	22.9 (35)	9.3 (75)	6.8 (44)	0.48 (0.27,0.86)	0.013 ^c	

^aRelative risk for a twofold increase in dioxin.

^bTest of significance for homogeneity of relative risks (current dioxin continuous, time categorized).

^cTest 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 12-28. (Continued)
Longitudinal Analysis of Overall Electrocardiograph (ECG)

Ranch Hands - Log₂ (Current Dioxin) and Time

Assumption	Time (Yrs.)	Examination	Percent Abnormal/(n) Current Dioxin		
			Low	Medium	High
d) Maximal	≤ 18.6	1982	25.3 (91)	28.1 (160)	20.0 (65)
		1985	11.4 (88)	12.8 (156)	10.9 (64)
		1987	15.4 (91)	15.0 (160)	12.3 (65)
	> 18.6	1982	29.2 (65)	30.6 (147)	25.3 (83)
		1985	12.7 (63)	16.0 (144)	12.1 (83)
		1987	20.0 (65)	19.1 (147)	15.7 (83)

Normal in 1982:

**Percent Abnormal/(n) in 1987
Current Dioxin**

Time (Yrs.)	Low	Medium	High	Est. Relative Risk (95% C.I.) ^a	p-Value
≤ 18.6	11.8 (68)	9.6 (115)	5.8 (52)	0.88 (0.61,1.27)	0.281 ^b
> 18.6	15.2 (46)	15.7 (102)	4.8 (62)	0.66 (0.46,0.95)	0.025 ^c

^aRelative risk for a twofold increase in dioxin.

^bTest of significance for homogeneity of relative risks (current dioxin continuous, time categorized).

^cTest 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 12-28. (Continued)
Longitudinal Analysis of Overall Electrocardiograph (ECG)

e) Ranch Hands and Comparisons by Current Dioxin Category

Current Dioxin Category	Percent Abnormal/(n) Examination		
	1982	1985	1987
Background	27.7 (606)	13.0 (598)	19.0 (606)
Unknown	24.5 (290)	9.5 (283)	15.2 (290)
Low	36.3 (171)	15.1 (166)	18.1 (171)
High	23.0 (148)	11.6 (147)	14.2 (148)

Normal in 1982

Current Dioxin Category	n in 1987	Percent Abnormal in 1987	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	438	10.5	All Categories		0.224
Unknown	219	11.9	Unknown vs. Background	1.15 (0.69,1.91)	0.597
Low	109	11.0	Low vs. Background	1.05 (0.54,2.06)	0.878
High	114	5.3	High vs. Background	0.47 (0.20,1.14)	0.094

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.
 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).

$p=0.014$ and Est. RR=0.78, $p=0.041$, respectively). For the minimal cohort, the percentage of participants with an abnormal reading in 1987 (based on those with a normal ECG reading in 1982) decreased steadily with increasing current dioxin (low, 13.8%; medium, 11.0%; high, 6.0%). The corresponding percentages for the maximal cohort were 12.3, 13.2, and 4.5 percent for the low, medium, and high initial dioxin categories.

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

The longitudinal analysis of the 1987 ECG did not detect a significant current dioxin-by-time since tour interaction for the minimal cohort (Table 12-28 [c]: $p=0.189$). Thus, the association with current dioxin did not differ for the two time strata. However, there was a significant negative association between current dioxin and the overall ECG reading for Ranch Hands with more than 18.6 years since tour (Est. RR=0.48, $p=0.013$). The percentages of these Ranch Hands with an abnormal 1987 ECG reading (based on those with a normal ECG reading in 1982) were 22.9, 9.3, and 6.8 percent for low, medium, and high current dioxin.

Similarly, under the maximal assumption, the interaction between current dioxin and time since tour in the longitudinal analysis of the 1987 ECG was nonsignificant (Table 12-28 [d]: $p=0.281$). For Ranch Hands with more than 18.6 years since tour, there was a significant negative association between current dioxin and the percentage of Ranch Hands with an abnormal ECG reading in 1987 (Est. RR=0.66, $p=0.025$). For Ranch Hands with early tours, the percentages of abnormal ECG readings in 1987 were 15.2, 15.7, and 4.8 percent for low, medium, and high current dioxin.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The percentages of participants who had abnormal ECG readings in 1987 did not differ significantly among the four current dioxin categories in the overall longitudinal analysis (Table 12-28 [e]: $p=0.224$). However, the percentage of Ranch Hands in the high current dioxin category who had abnormal ECG readings in 1987 was marginally lower than the corresponding percentage of Comparisons in the background category (Est. RR=0.47, 95% C.I.: [0.20, 1.14], $p=0.094$). In contrast, Ranch Hands in the unknown and low current dioxin categories had nonsignificantly higher percentages of abnormal ECG readings than the Comparisons in the background category ($p=0.597$ and $p=0.878$, respectively). The relative frequencies of participants with abnormal ECG readings in 1987 were 10.5, 11.9, 11.0, and 5.3 percent for the background, unknown, low, and high current dioxin categories.

DISCUSSION

Circulatory disorders are among the most common diseases encountered by primary care physicians. The sources of the noninvasive data analyzed in the current section occupy a time-honored place in cardiovascular practice, specifically the history, physical examination, chest x ray, and resting ECG. These four are highly reliable indices that alert the clinician to the presence of underlying cardiovascular disease and point to the need for additional, more specific, noninvasive or invasive studies. Though arbitrary, dividing data collection into central and peripheral cardiovascular functions is convenient and forms a reasonable basis for contrasting study participants.

The limitations of the history in cardiovascular diagnosis deserve emphasis. In peripheral vascular disease, for example, signs and symptoms vary depending on the degree of development of collateral circulatory channels. While hemodynamically significant arterial disease of the lower extremities usually is associated with claudication, severe carotid occlusive disease can be present in the absence of symptoms of transient cerebral ischemia. Furthermore, conclusive evidence shows that advanced coronary artery disease can occur in the absence of angina and be present as "silent" myocardial ischemia (24). Cardiovascular history, as related by patients, is often subject to error. The generic term *heart attack*, for example, can be used to describe any type of cardiac event from an isolated episode of unstable angina or arrhythmia to an actual myocardial infarction. These imperfections highlight the importance of the type of medical record verification conducted in the current study.

The physical examination can provide valuable clues to the presence of asymptomatic but significant underlying disease, particularly in the cardiovascular assessment. Because the examinations in this study were conducted by internists rather than cardiologists, steps were taken to simplify data collection and to reduce interobserver differences among the examining physicians. All blood pressure readings, for example, were taken by automated sphygmomanometric instruments. Auscultatory endpoints (murmurs and bruits) were recorded as present or absent by anatomic location, thus eliminating speculation as to specific valvular or vessel origin and hemodynamic significance. As markers of occult arterial occlusive disease, vascular bruits, which are relatively easy to detect, were carefully sought over the carotid, abdominal, and femoral vessels.

Pertinent to the longitudinal design of the AFHS, several of the physical findings recorded must be viewed in the context of the aging population under study. A gradual increase in systolic blood pressure occurs with advancing years. Related to the normal progression of arteriosclerosis and, more specifically, to arterial tortuosity, vascular bruits may occur in vessels free of occlusive disease, particularly in the carotid arteries. All bruits were recorded by location without attempting to comment on the hemodynamic significance or specific vessel of origin (i.e., internal versus external carotid). The occurrence of abnormal heart sounds, particularly S₄, also increases with age.

The laboratory data collected in the current section were limited to the resting 12-lead ECG and the standard two-view chest x ray (discussed in Chapter 17, Pulmonary Assessment). In current practice, these techniques are supplemented, but not replaced, by such noninvasive studies as the treadmill exercise test, nuclear isotope studies, and the echocardiogram. These more sophisticated procedures generally serve to confirm diagnoses that can be made based on the more basic techniques. For example, when correlated with the history and physical examination, the chest x ray and ECG enable the clinician to draw highly accurate conclusions regarding the presence and hemodynamic significance of valvular heart disease of any etiology. As defined by the chest x ray, the pulmonary vascularity can provide reliable clues to the presence of global left ventricular dysfunction with pulmonary venous congestion and the presence of pulmonary hypertension.

Analysis of the historical variables examined revealed no evidence for any increased incidence of cardiovascular disease associated with the current or extrapolated initial levels of serum dioxin. In several of the analyses, Ranch Hand participants with higher levels of

serum dioxin appeared to be less at risk than Ranch Hands with lower serum levels and Comparisons. In the maximal cohort, for example, the incidence of reported and verified heart disease in Ranch Hands decreased as the initial serum levels of the Ranch Hands became higher (unadjusted: $p=0.007$ and 0.006, respectively; adjusted: $p=0.052$ and $p=0.044$, respectively). Though not as statistically significant, a similar inverse dose-response relationship was noted in the analysis of current serum dioxin levels. Comparisons appeared to be at greater risk for heart disease than Ranch Hands in the high current dioxin category and the incidence of myocardial infarction was similar in both cohorts.

With rare exception, none of the central cardiac physical examination variables was associated positively with the body burden of dioxin. Ranch Hand participants with the highest levels of extrapolated initial serum dioxin had higher systolic blood pressure by continuous analysis than Ranch Hands with medium and lower levels. Though statistically significant ($p=0.049$), the differences were slight (133.12, 129.73, and 128.31 mm Hg for high, medium, and low levels of TCDD). According to the more clinically relevant discrete analysis, there was no evidence for a dose-response effect. None of the other indices of central cardiac function (including ECG) showed any increase in risk related to the current or extrapolated initial levels of serum dioxin.

In the analysis of peripheral vascular function, several positive associations were noted in relation to the current and extrapolated initial levels of serum dioxin. Unadjusted for such established risk factors as serum cholesterol and percent body fat, Ranch Hand participants with the highest levels of current serum dioxin were found to have higher mean diastolic blood pressure than Comparisons. Although consistent with a dose-response effect, the means were both within normal limits and the difference was slight (76.71 mm Hg and 74.64 mm Hg, respectively). Finally, although a higher incidence of dorsalis pedis pulse deficits was noted in association with the extrapolated initial serum dioxin (low, 9.4%; medium, 11.6%; high, 15.2%), only those participants less removed from service in Vietnam showed evidence for a dose-response effect in relation to the current serum dioxin level. However, these were isolated findings limited to one of the peripheral arterial pulses examined and the three highly correlated composite pulse indices (correlation >0.98).

SUMMARY

Table 12-29 summarizes the results of the initial dioxin analyses for the variables investigated in 1987 for the cardiovascular examination, Table 12-30 presents the results of the current dioxin and time since tour analyses, and Table 12-31 displays the results of the categorized current dioxin analyses. Table 12-32 presents a summary of the interactions found in the course of the three primary analyses.

Questionnaire Variables

Three variables—essential hypertension, heart disease (excluding essential hypertension), and myocardial infarction—concerning cardiovascular disease were constructed from questionnaire information and augmented by physical examination determinations. These conditions were later verified by medical records review. All reported cases of essential hypertension and myocardial infarction were verified; however, there were fewer verified cases of heart disease than reported cases of heart disease.

TABLE 12-29.

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

Variable	Unadjusted		Adjusted	
	Minimal	Maximal	Minimal	Maximal
Questionnaire				
Reported/Verified Essential Hypertension (D)	NS	NS*	NS	** (NS)
Reported Heart Disease (Excluding Essential Hypertension) (D)	ns	-0.007	** (ns)	ns*
Verified Heart Disease (Excluding Essential Hypertension) (D)	ns	-0.006	** (ns)	-0.044
Reported/Verified Myocardial Infarction (D)	ns	NS	NS	NS
Physical Examination: Central Cardiac Function				
Systolic Blood Pressure (C)	NS	NS	*** (NS)	** (NS)
Systolic Blood Pressure ^a (C)	--	--	** (NS)	** (+0.049)
Systolic Blood Pressure (D)	ns	NS	** (ns)	NS
Heart Sounds (D)	ns	ns	NS	NS
Overall Electrocardiograph (D)	ns	ns	NS	NS
ECG: Right Bundle Branch Block (D)	NS	NS	--	--
ECG: Nonspecific ST- and T-Wave Changes (D)	ns	NS	ns	NS
ECG: Bradycardia (D)	ns	ns*	ns	ns*
ECG: Arrhythmia (D)	NS	NS	** (NS*)	NS
ECG: Other Diagnoses (D)	ns	ns	ns	ns

TABLE 12-29. (Continued)

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

Variable	Unadjusted		Adjusted	
	Minimal	Maximal	Minimal	Maximal
Physical Examination:				
Peripheral Vascular Function				
Diastolic Blood Pressure (C)	NS	NS	NS	****
Diastolic Blood Pressure (D)	ns	NS	ns	NS
Funduscopic Examination (D)	NS	ns	--	--
Carotid Bruits (D)	ns	ns	ns	ns
Femoral Pulses (D)	ns	NS	** (NS)	** (NS)
Popliteal Pulses (D)	ns	ns	ns	NS
Dorsalis Pedis Pulses (D)	NS	NS*	** (NS)	+0.041
Posterior Tibial Pulses (D)	ns	NS	NS	NS*
Posterior Tibial Pulses ^a (D)	--	--	NS	NS
Leg Pulses (D)	NS	NS*	** (NS)	+0.021
Leg Pulses ^a (D)	--	--	** (NS)	--
Peripheral and All Pulses (D)	NS	NS*	** (NS)	+0.025

^aAdjusted results from models without cholesterol and/or percent body fat presented for this variable; see Appendix K-2 for a detailed description of these analyses.

C: Continuous analysis.

D: Discrete analysis.

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

-: Relative risk less than 1.00 for discrete analysis.

--: Analyses not applicable, or analyses were not performed due to the sparse number of abnormalities.

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

NS*/ns*: Marginally significant ($0.05 < p \leq 0.10$).

** (NS)/** (ns): Log_2 (initial dioxin)-by-covariate interaction ($0.01 < p \leq 0.05$); not significant when interaction is deleted; refer to Appendix Table K-1 or K-3 for a detailed description of this interaction.

** (NS*): Log_2 (initial dioxin)-by-covariate interaction ($0.01 < p \leq 0.05$), marginally significant when interaction is deleted; refer to Appendix Table K-1 for a detailed description of this interaction.

** (0.049): Log_2 (initial dioxin)-by-covariate interaction ($0.01 < p \leq 0.05$), significant ($p=0.049$) when interaction is deleted; refer to Appendix Table K-3 for a detailed description of this interaction.

TABLE 12-29. (Continued)

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

*** (NS): Log_2 (initial dioxin)-by-covariate interaction ($p \leq 0.01$); not significant when interaction is deleted; refer to Appendix Table K-1 for a detailed description of this interaction.

****: Log_2 (initial dioxin)-by-covariate interaction ($p \leq 0.01$); refer to Appendix Table K-1 for a detailed description of this interaction.

Note: P-value given if $p \leq 0.05$.

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

TABLE 12-30.

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

Variable	C*T	Unadjusted		Maximal			
		Minimal	<18.6	>18.6	C*T	<18.6	
Questionnaire							
Reported/Verified Essential							
Hypertension (D)	ns	NS	NS	ns	NS	NS	
Reported Heart Disease (Excluding Essential Hypertension) (D)	NS	ns	ns	ns	ns*	-0.015	
Verified Heart Disease (Excluding Essential Hypertension) (D)	NS	ns	ns	ns	ns*	-0.013	
Reported/Verified Myocardial Infarction (D)							
	ns	ns	ns	ns	NS	ns	
Physical Examination: Central Cardiac Function							
Systolic Blood Pressure (C)	NS	NS	NS	NS	NS	NS	
Systolic Blood Pressure (D)	ns	NS	ns	ns	NS	NS	
Heart Sounds (D)	NS	ns	ns	NS	ns	NS	
Overall							
Electrocardiograph (D)	ns	NS	ns	ns	NS	ns	
ECG: Right Bundle Branch Block (D)	--	--	NS	--	--	NS	
ECG: Nonspecific ST- and T-Wave Changes (D)	ns	ns	ns	ns	NS	ns	
ECG: Bradycardia (D)	ns	NS	ns	ns*	NS	ns*	
ECG: Arrhythmia (D)	ns	NS	NS	-0.032	NS*	ns	
ECG: Other Diagnoses (D)	ns	NS	-0.048	-0.040	NS	-0.011	
Physical Examination: Peripheral Vascular Function							
Diastolic Blood Pressure (C)	ns	NS	NS	NS	NS	NS	

TABLE 12-30. (Continued)

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

Variable	C*T	Unadjusted		Minimal		Maximal	
		≤ 18.6	> 18.6	C*T	≤ 18.6	> 18.6	
Physical Examination: Peripheral Vascular Function (continued)							
Diastolic Blood Pressure (D)	NS	ns	ns	NS	ns	ns	NS
Funduscopic Examination (D)	--	NS	--	--	NS	--	--
Carotid Bruits (D)	--	--	ns	--	--	--	ns
Femoral Pulses (D)	ns	ns	ns	ns	NS	ns	ns
Popliteal Pulses (D)	NS	ns	ns	ns	ns	ns	ns
Dorsalis Pedis Pulses (D)	ns	NS	ns	ns	NS	ns	NS
Posterior Tibial Pulses (D)	NS	ns	ns	ns	NS	NS	NS
Leg Pulses (D)	ns	NS	ns	ns	NS	NS	NS
Peripheral and All Pulses (D)	ns	NS	ns	ns	NS	NS	NS

C: Continuous analysis.

D: Discrete analysis.

-: C*T: Relative risk for ≤ 18.6 category greater than relative risk for > 18.6 category. ≤ 18.6 and > 18.6 : Relative risk less than 1.00 for discrete analysis.

--: Analyses were not performed due to the sparse number of abnormalities.

NS/ns: Not significant ($p > 0.10$).NS*/ns*: Marginally significant ($0.05 < p \leq 0.10$).Note: 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 18.6 years or less. > 18.6 : Log_2 (current dioxin) hypothesis test for Ranch Hands with time since end of tour more 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 or relative risk less than 1.00 for discrete analysis.

TABLE 12-30. (Continued)

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

Variable	C*T	Adjusted		C*T	Maximal	
		Minimal	>18.6		Minimal	>18.6
Questionnaire						
Reported/Verified Essential Hypertension (D)	ns	NS	ns	ns	NS	NS
Reported/Verified Essential Hypertension ^a (D)	ns	NS	NS	ns	+0.023	NS
Reported Heart Disease (Excluding Essential Hypertension) (D)	ns	ns	ns	ns	ns	ns*
Verified Heart Disease (Excluding Essential Hypertension) (D)	ns	ns	ns	ns	ns	ns*
Reported/Verified Myocardial Infarction (D)	ns	NS	NS	ns	NS*	NS
Physical Examination: Central Cardiac Function						
Systolic Blood Pressure (C)	** (ns)	** (ns)	** (ns)	** (NS)	** (NS)	** (NS)
Systolic Blood Pressure (D)	****	****	****	** (ns)	** (NS)	** (ns)
Heart Sounds (D)	****	****	****	****	****	****
Overall Electrocardiograph (D)	ns	NS*	ns	ns	NS	ns
ECG: Right Bundle Branch Block (D)	--	--	--	--	--	--
ECG: Nonspecific ST- and T-Wave Changes (D)	ns	NS	ns	** (ns)	** (NS)	** (NS)
ECG: Bradycardia (D)	ns	NS	ns	ns*	NS	ns*
ECG: Arrhythmia (D)	ns	+0.017	NS	** (-0.034)	** (+0.018)	** (ns)
ECG: Other Diagnoses (D)	ns	NS	ns	-0.026	NS	-0.046

TABLE 12-30. (Continued)

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

Variable	C*T	Adjusted		C*T	Minimal		Maximal
		≤ 18.6	> 18.6		≤ 18.6	> 18.6	
Physical Examination:							
Peripheral Vascular Function							
Diastolic Blood Pressure (C)	ns	NS	ns	NS	ns	NS	
Diastolic Blood Pressure (D)	NS	ns	ns	NS	ns	NS	
Funduscopic Examination (D)	--	--	--	--	--	--	
Carotid Bruits (D)	--	--	--	--	--	--	
Femoral Pulses (D)	ns	NS	ns	****	****	****	
Popliteal Pulses (D)	** (NS)	** (ns)	** (ns)	** (ns)	** (ns)	** (ns)	
Dorsalis Pedis Pulses (D)	ns	NS*	NS	ns	+0.048	NS	
Posterior Tibial Pulses (D)	ns	NS	ns	ns	NS*	NS	
Posterior Tibial Pulses ^a (D)	ns	ns	ns	ns	NS	NS	
Leg Pulses (D)	** (ns)	** (NS)	** (ns)	ns	NS*	NS	
Peripheral and All Pulses (D)	** (ns)	** (NS)	** (ns)	ns	NS*	NS	

^aAdjusted results from models without cholesterol and/or percent body fat presented for this variable; see Appendix K-2 for a detailed description of these analyses.

C: Continuous analysis.

D: Discrete analysis.

+: ≤ 18.6 and > 18.6 : Relative risk 1.00 or greater for discrete analysis.

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

≤ 18.6 and > 18.6 : Relative risk less than 1.00 for discrete analysis.

--: Analyses were not performed due to the sparse number of abnormalities.

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

NS*/ns*: Marginally significant ($0.05 < p \leq 0.10$).

** (NS)/** (ns): Log_2 (current dioxin)-by-time-by-covariate interaction ($0.01 < p \leq 0.05$); not significant when interaction is deleted; refer to Appendix Table K-1 for a detailed description of this interaction.

** (...): Log_2 (current dioxin)-by-time-by-covariate interaction ($0.01 < p \leq 0.05$); significant when interaction is deleted and p-value is given in parentheses; refer to Appendix Table K-1 for a detailed description of this interaction.

****: Log_2 (current dioxin)-by-time-by-covariate interaction ($p \leq 0.01$); refer to Appendix Table K-1 for a detailed description of this interaction.

TABLE 12-30. (Continued)

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

Note: 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 18.6 years or less.

> 18.6 : Log_2 (current dioxin) hypothesis test for Ranch Hands with time since end of tour more 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 12-31.
Summary of Categorized Current Dioxin Analyses for
Cardiovascular Variables
(Ranch Hands and Comparisons)

Variable	All	Unadjusted		
		Unknown versus Background	Low versus Background	High versus Background
Questionnaire				
Reported/Verified Essential Hypertension (D)	0.043	ns	NS	NS
Reported Heart Disease (Excluding Essential Hypertension) (D)	0.003	+0.047	ns	-0.010
Verified Heart Disease (Excluding Essential Hypertension) (D)	0.002	NS*	ns	-0.007
Reported/Verified Myocardial Infarction (D)	NS*	ns	NS	ns
Physical Examination: Central Cardiac Function				
Systolic Blood Pressure (C)	NS	ns	NS	NS
Systolic Blood Pressure (D)	NS	ns	ns	NS
Heart Sounds (D)	NS	ns	ns	ns
Overall Electrocardiograph (D)	NS	ns	ns	ns
ECG: Right Bundle Branch Block (D)	NS	ns	NS	ns
ECG: Nonspecific ST- and T-Wave Changes (D)	NS	ns	NS	NS
ECG: Bradycardia (D)	NS	NS	ns	ns
ECG: Arrhythmia (D)	NS	NS	ns	NS
ECG: Other Diagnoses (D)	0.024	NS	NS	-0.007

TABLE 12-31. (Continued)

**Summary of Categorized Current Dioxin Analyses for
Cardiovascular Variables
(Ranch Hands and Comparisons)**

Variable	All	Unadjusted		
		Unknown versus Background	Low versus Background	High versus Background
Physical Examination:				
Peripheral Vascular Function				
Diastolic Blood Pressure (C)	0.017	ns	+0.028	NS*
Diastolic Blood Pressure (D)	NS	ns	NS	NS
Funduscopic Examination (D)	NS	NS	ns	NS
Carotid Bruits (D)	NS	NS	NS	ns
Femoral Pulses (D)	NS	NS	NS	NS
Popliteal Pulses (D)	NS	NS	NS	ns
Dorsalis Pedis Pulses (D)	NS	NS	NS*	NS
Posterior Tibial Pulses (D)	<0.001	ns	+0.003	ns
Leg Pulses (D)	NS*	NS	+0.010	NS
Peripheral Pulses (D)	NS	NS	+0.016	NS
All Pulses (D)	NS	NS	+0.019	NS

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.

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

TABLE 12-31. (Continued)

**Summary of Categorized Current Dioxin Analyses for
Cardiovascular Variables
(Ranch Hands and Comparisons)**

Variable	All	Adjusted		
		Unknown versus Background	Low versus Background	High versus Background
Questionnaire				
Reported/Verified Essential Hypertension (D)		** (NS)	** (ns)	** (NS)
Reported/Verified Essential Hypertension ^a (D)		** (0.002)	** (ns*)	** (NS)
Reported Heart Disease (Excluding Essential Hypertension) (D)	0.024	NS*	ns	ns*
Verified Heart Disease (Excluding Essential Hypertension) (D)	0.021	NS*	ns	-0.049
Reported/Verified Myocardial Infarction (D)	****	****	****	****
Physical Examination: Central Cardiac Function				
Systolic Blood Pressure (C)		*** (NS)	*** (ns)	*** (NS)
Systolic Blood Pressure ^a (C)		** (0.012)	** (ns*)	** (NS)
Systolic Blood Pressure (D)	****	****	****	****
Heart Sounds (D)	NS	ns	ns	NS
Overall Electrocardiograph (D)	NS	ns*	NS	NS
ECG: Right Bundle Branch Block (D)	NS	ns	NS	--
ECG: Nonspecific ST- and T-Wave Changes (D)	NS	ns	NS	NS
ECG: Bradycardia (D)	** (NS)	** (NS)	** (ns)	** (ns)
ECG: Bradycardia ^a (D)	** (NS)	** (NS)	** (ns)	** (ns*)
ECG: Arrhythmia (D)	NS	NS	ns	NS*

TABLE 12-31. (Continued)

**Summary of Categorized Current Dioxin Analyses for
Cardiovascular Variables
(Ranch Hands and Comparisons)**

Variable	Assumption				Adjusted
	All	Unknown versus Background	Low versus Background	High versus Background	
Physical Examination:					
Central Cardiac Function (continued)					
ECG: Other Diagnoses (D)	NS	ns	NS		-0.036
Physical Examination:					
Peripheral Vascular Function					
Diastolic Blood Pressure (C)	*** (NS*)	*** (ns)	*** (+0.032)	*** (NS*)	
Diastolic Blood Pressure ^a (C)	** (0.002)	** (ns)	** (+0.020)	** (+0.017)	
Diastolic Blood Pressure (D)	NS	ns	NS	NS	
Funduscopic Examination (D)	** (NS)	** (NS)	** (ns)	** (NS)	
Carotid Bruits (D)	NS	NS	NS	--	
Femoral Pulses (D)	** (NS)	** (NS)	** (NS*)	** (+0.049)	
Popliteal Pulses (D)	NS	ns	NS	NS	
Dorsalis Pedis Pulses (D)	NS	NS	NS*	NS*	
Dorsalis Pedis Pulses ^a (D)	NS*	NS	NS*	+0.029	
Posterior Tibial Pulses (D)	<0.001	ns	+<0.001	NS	
Leg Pulses (D)	0.020	NS	+0.005	+0.047	
Peripheral Pulses (D)	0.017	NS	+0.007	+0.033	
All Pulses (D)	0.021	NS	+0.008	+0.035	

TABLE 12-31. (Continued)

**Summary of Categorized Current Dioxin Analyses for
Cardiovascular Variables
(Ranch Hands and Comparisons)**

^aAdjusted results from models without cholesterol and/or percent body fat presented for this variable; see Appendix K-2 for a detailed description of these analyses.

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.

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

NS*/ns*: Marginally significant ($0.05 < p \leq 0.10$).

** (NS)** (ns): Categorized current dioxin-by-covariate interaction ($0.01 < p \leq 0.05$); not significant when interaction is deleted; refer to Appendix Table K-1 or K-3 for a detailed description of this interaction.

*** (NS)*** (ns): Categorized current dioxin-by-covariate interaction ($p \leq 0.01$); not significant when interaction is deleted; refer to Appendix Table K-1 for a detailed description of this interaction.

** (NS*)** (ns*): Categorized current dioxin-by-covariate interaction ($0.01 < p \leq 0.05$); marginally significant when interaction is deleted; refer to Appendix Table K-1 or K-3 for a detailed description of this interaction.

*** (NS*): Categorized current dioxin-by-covariate interaction ($p \leq 0.01$); marginally significant when interaction is deleted; refer to Appendix Table K-1 for a detailed description of this interaction.

** (...): Categorized current dioxin-by-covariate interaction ($0.01 < p \leq 0.05$); significant when interaction is deleted and p-value is given in parentheses; refer to Appendix Table K-1 or K-3 for a detailed description of this interaction.

*** (...): Categorized current dioxin-by-covariate interaction ($p \leq 0.01$); significant when interaction is deleted and p-value is given in parentheses; refer to Appendix Table K-1 for a detailed description of this interaction.

****: Categorized current dioxin-by-covariate interaction ($p \leq 0.01$); refer to Appendix Table K-1 for a detailed description of this interaction.

Note: P-value given if $p \leq 0.05$.

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