CHAPTER 8

COVARIATE ASSOCIATIONS WITH ESTIMATES OF DIOXIN EXPOSURE

INTRODUCTION

The associations between the covariates used throughout this report and five estimates of dioxin exposure are evaluated in this chapter. The purpose of studying these associations is to determine if these covariates, which have been determined to be risk factors for one or more particular clinical areas, are associated with an estimate of dioxin exposure, and, therefore, could potentially be confounding variables in subsequent statistical analyses in this report. These covariates and estimates of dioxin exposure are used extensively in the statistical analyses in Chapters 9 through 20, which comprise the clinical portions of the report. The results in this chapter, however, should not be interpreted as indicating causal relationships between dioxin exposure and covariate levels (e.g., diabetes) because these analyses are not adjusted for known and suspected confounders.

Model 1 refers to the relationship of an individual covariate with group (Ranch Hand or Comparison). Model 2 refers to the relationship between an individual covariate and an extrapolated initial dioxin measure for Ranch Hands. The estimate of dioxin exposure in Model 3 dichotomizes the Ranch Hands in Model 2 based on their initial dioxin measures; these two categories of Ranch Hands are referred to as the "low Ranch Hand" category and the "high Ranch Hand" category. Ranch Hands and Comparisons with current lipid-adjusted serum dioxin levels at or below 10 ppt also are used to create a total of four categories. Ranch Hands with current lipid-adjusted serum dioxin levels at or below 10 ppt are referred to as the "background Ranch Hand" category. The relationship between a covariate and the four categories of Ranch Hands and Comparisons is examined.

Models 4, 5, and 6 refer to the relationship between a covariate and 1987 (current) dioxin levels in all Ranch Hands with a dioxin measurement. If a participant did not have a measured 1987 dioxin level, a 1992 measurement was used when available. The 1992 level was extrapolated to the 1987 level using a first-order pharmacokinetics model (additional details are given in Chapter 2, Dioxin Assay and Chapter 7, Statistical Methods). The measure of dioxin in Model 4 is lipid-adjusted, whereas the measure of dioxin (the same for both) in Models 5 and 6 is whole-weight adjusted. Model 6 differs from Model 5 in that a statistical adjustment for total lipids is included in the Model 6 analysis in subsequent chapters. Details on dioxin and the models are found in Chapters 2 and 7 respectively.

The summary statistics listed in the tables in this chapter are either percentages, correlations (r), or means ($\bar{x}$). If a covariate is discrete in Models 1 and 3, the percentage of participants (Ranch Hands and Comparisons for Model 1 and Comparisons and background, low, and high Ranch Hands for Model 3) in each of the covariate categories is shown. If a covariate is continuous, the mean of the covariate is given for each exposure category.

Because the measure of dioxin is in a continuous form for Model 2, 3, 5, and 6 analyses, if a covariate is continuous, a correlation coefficient between initial dioxin and the covariate is provided. If a covariate is discrete, dioxin means for each of the covariate categories are displayed. Consistent with the methodology used in each of the clinical chapters (Chapters 9 through 20), these means are transformed from the logarithmic (base 2) scale for initial dioxin in Model 2, and from the ($\log_2$ (X+1)) scale for current dioxin in Models 4, 5, and 6.

The p-values used in these tables measure the association of the relationship with a covariate. A smaller p-value corresponds to a greater degree of association. The p-value referred to for Model 1 refers to the strength of the association between a covariate and group, and the p-value for Model 2 refers to the strength of the association between a covariate and initial dioxin in Ranch Hands. The Model 3 p-value describes the strength of association between a covariate and categorized dioxin, as described above. The p-values for Models 4, 5, and 6 quantify the strength of the association between a covariate and current dioxin, whether it be lipid-adjusted in Model 4 or whole-weight adjusted in Models 5 and 6.

MATCHING DEMOGRAPHIC VARIABLES (AGE, RACE, AND MILITARY OCCUPATION)

The variables age, race, and military occupation were used in the design of the Air Force Health Study (AFHS) to match Ranch Hand participants with Comparisons and thus reduce the association between these variables and group status. However, it was not possible to eliminate the association of these variables with serum dioxin in Models 2 through 6 through the study design. Results of tests of association between age, race, and occupation and the five estimates of dioxin exposure are given in Table 8-1.

Examining the association between age, in both its continuous and discrete forms, and dioxin revealed highly significant relationships in the analyses of Models 2 through 6 ($p<0.001$ for each model, both continuous and discrete). In the Model 3 analysis, the mean ages in the Comparison, background Ranch Hand, low Ranch Hand, and high Ranch Hand categories are 53.8, 54.8, 55.3, and 51.2 years respectively. Older Ranch Hands tended to have lower dioxin levels in analyses of Models 2, 4, 5 and 6. In the Model 3 analysis, a significant difference in the percentage of younger participants (born in or after 1942) was seen among Comparisons (42.7%), background Ranch Hands (34.2%), low Ranch Hands (32.7%), and high Ranch Hands (59.2%). The relationship between age and dioxin in Models 2 through 6 is most likely due to the relationship between dioxin and military occupation, as discussed below (Ranch Hand enlisted groundcrew, the occupational category with the greatest risk of exposure, tended to be younger than Ranch Hand officers and enlisted flyers).

Similar to the correlation between age and dioxin, a highly significant association was found between military occupation and dioxin in analyses using Models 2, 3, 4, 5, and 6 ($p<0.001$ for each model). In Models 2, 4, 5, and 6, the mean dioxin levels were lowest among officers, followed by enlisted flyers and enlisted groundcrew. In the Model 3 analysis, a significant difference between the percentage of officers, enlisted flyers, and enlisted groundcrew was seen among Comparisons (38.5%, 16.3%, and 45.3%), background Ranch Hands (63.1%, 10.7%, and 26.2%), low Ranch Hands (39.6%, 21.2%, and 39.2%), and high Ranch Hands (3.5%, 21.2%, and 75.4%).

Table 8-1.
Associations Between Matching Demographic Variables (Age, Race, and Military Occupation) and Estimates of Dioxin Exposure

Covariate	Covariate Category	Model 1		Model 2
		Ranch Hand	Comparison	Initial Dioxin (ppt)
Age (years) (Continuous)	--	n=952 $\bar{x}$=53.8	n=1,281 $\bar{x}$=53.6	n=520 r=-0.264
		p=0.533		p<0.001
Age (Discrete)		n=952	n=1,281	
	Born ≥ 1942	41.6%	43.7%	$\bar{x}$=220.94 (n=239)
	Born < 1942	58.4%	56.3%	$\bar{x}$=130.78 (n=281)
		p=0.338		p<0.001
Race		n=952	n=1,281	
	Black	5.9%	5.9%	$\bar{x}$=126.21 (n=36)
	Non-Black	94.1%	94.1%	$\bar{x}$=169.88 (n=484)
		p=0.999		p=0.062
Occupation		n=952	n=1,281	
	Officer	38.6%	39.2%	$\bar{x}$=77.18 (n=112)
	Enlisted Flyer	17.0%	15.8%	$\bar{x}$=156.01 (n=110)
	Enlisted Groundcrew	44.4%	45.0%	$\bar{x}$=227.51 (n=298)
		p=0.760		p<0.001

Table 8-1. (Continued)
Associations Between Matching Demographic Variables (Age, Race, and Military Occupation) and Estimates of Dioxin Exposure

		Model 3			
Covariate	**Covariate Category**	**Comparison**	**Background Ranch Hand**	**Low Ranch Hand**	**High Ranch Hand**
Age (years) (Continuous)	--	n=1,063 $\bar{x}$=53.8	n=374 $\bar{x}$=54.8	n=260 $\bar{x}$=55.3	n=260 $\bar{x}$=51.2
			p<0.001		
Age (Discrete)		n=1,063	n=374	n=260	n=260
	Born ≥ 1942	42.7%	34.2%	32.7%	59.2%
	Born < 1942	57.3%	65.8%	67.3%	40.8%
			p<0.001		
Race		n=1,063	n=374	n=260	n=260
	Black	5.2%	4.0%	8.9%	5.0%
	Non-Black	94.8%	96.0%	91.2%	95.0%
			p=0.054		
Occupation		n=1,063	n=374	n=260	n=260
	Officer	38.5%	63.1%	39.6%	3.5%
	Enlisted Flyer	16.3%	10.7%	21.2%	21.2%
	Enlisted Groundcrew	45.3%	26.2%	39.2%	75.4%
			p<0.001		

Table 8-1. (Continued)
Associations Between Matching Demographic Variables (Age, Race, and Military Occupation) and Estimates of Dioxin Exposure

Covariate	Covariate Category	Model 4: Lipid-Adjusted Current Dioxin (ppt)	Models 5 and 6: Whole-Weight Current Dioxin (ppq)
Age (years) (Continuous)	--	n=894 r=-0.214 p<0.001	n=894 r=-0.186 p<0.001
Age (Discrete)	Born ≥ 1942 Born < 1942	$\bar{x}$=19.63 (n=367) $\bar{x}$=11.74 (n=527) p<0.001	$\bar{x}$=111.05 (n=367) $\bar{x}$=68.01 (n=527) p<0.001
Race	Black Non-Black	$\bar{x}$=14.71 (n=51) $\bar{x}$=14.52 (n=843) p=0.934	$\bar{x}$=79.98 (n=51) $\bar{x}$=83.40 (n=843) p=0.808
Occupation	Officer Enlisted Flyer Enlisted Groundcrew	$\bar{x}$=7.47 (n=348) $\bar{x}$=17.24 (n=150) $\bar{x}$=23.91 (n=396) p<0.001	$\bar{x}$=42.14 (n=348) $\bar{x}$=100.73 (n=150) $\bar{x}$=140.07 (n=396) p<0.001

Note: Means for discrete covariates are transformed from the logarithmic (base 2) scale for initial dioxin in Model 2, and from the ($\log_2$ (X+1)) scale for current dioxin in Models 4, 5, and 6.

No significant ($p \leq 0.05$) associations were observed between race and the five estimates of dioxin exposure.

TIME OF DUTY IN SOUTHEAST ASIA CHARACTERISTICS

Results of tests of association between variables related to the participants' time of duty in Southeast Asia (SEA) and the estimates of dioxin exposure are presented in Table 8-2. Model 1 analysis showed a highly significant association between the number of days in combat and group ($p < 0.001$). The mean number of days in combat for the Ranch Hands was 452.5 days and 210.3 days for the Comparisons. The Model 3 analysis revealed a significant relationship between categorized dioxin and the number of days in combat ($p < 0.001$), due to the inherent difference between Ranch Hands and Comparisons. The mean number of days in combat in the Comparison, background Ranch Hand, low Ranch Hand, and high Ranch Hand categories are 203.9, 445.9, 454.0, and 458.7 days respectively.

Stratifying the number of days a participant spent in combat into fewer than or equal to 360 days and more than 360 days revealed significant relationships with group in Model 1 ($p < 0.001$) and dioxin in Model 3 ($p < 0.001$), Model 4 ($p = 0.001$), and Models 5 and 6 ($p = 0.002$). A significant difference between the percentage of participants who were in combat fewer than 360 days was seen between Ranch Hands (14.0%) and Comparisons (76.7%). In Model 3, a significant difference between the percentage of participants who were in combat less than 360 days was seen among Comparisons (77.4%), background Ranch Hands (18.2%), low Ranch Hands (11.2%), and high Ranch Hands (10.4%). The mean current dioxin levels in Models 4, 5, and 6 were higher for participants who were in combat more than 360 days. However, the association with initial dioxin in Model 2 was not statistically significant, which may be due to the restricted sample size of participants with greater than 10 ppt lipid-adjusted current dioxin, and thus, decreased statistical power.

No significant ($p \leq 0.05$) associations were observed between the occurrence of acne in reference to duty in SEA (Pre- & Post-SEA, Post-SEA) or presence of pre-SEA acne (yes, no) and the five estimates of dioxin exposure.

ALCOHOL CONSUMPTION

Results of tests of association between alcohol consumption and the estimates of dioxin exposure are shown in Table 8-3. Statistically significant associations were found between current wine use in its continuous form and dioxin for Model 1 ($p = 0.025$), Model 3 ($p = 0.001$), Model 4 ($p = 0.002$), and Models 5 and 6 ($p = 0.001$). The mean current wine use was 0.13 drinks per day for Ranch Hands and 0.10 drinks per day for Comparisons. In Model 3, the mean drinks of wine per day in the Comparison, background Ranch Hands, low Ranch Hands, and high Ranch Hands categories are 0.10, 0.17, 0.14, and 0.07 respectively. The drinks of wine per day increased as the current dioxin levels decreased in Model 4 and Models 5 and 6. This association may be due to occupation, because officers are more likely to drink wine than are enlisted personnel ($p < 0.001$).

Table 8-2.
Associations Between Time of Duty in Southeast Asia Characteristics and Estimates of Dioxin Exposure

Covariate	Covariate Category	Model 1		Model 2
		Ranch Hand	Comparison	Initial Dioxin (ppt)
Combat Service (number of days) (Continuous)	--	n=952 $\bar{x}$=452.5	n=1,281 $\bar{x}$=210.3	n=520 r=0.071
		p<0.001		p=0.108
Combat Service (number of days) (Discrete)		n=952	n=1,281	
	0-360 days	14.0%	76.7%	$\bar{x}$=160.26 (n=56)
	>360 days	86.0%	23.3%	$\bar{x}$=167.18 (n=464)
		p<0.001		p=0.746
Time Reference of Acne to Southeast Asia		n=826	n=1,083	
	Pre & Post	89.2%	88.2%	$\bar{x}$=180.83 (n=47)
	Post	10.8%	11.8%	$\bar{x}$=163.17 (n=401)
		p=0.523		p=0.472
Presence of Pre-SEA Acne		n=952	n=1,281	
	Yes	90.2%	89.7%	$\bar{x}$=180.62 (n=50)
	No	9.8%	10.3%	$\bar{x}$=164.98 (n=470)
		p=0.730		p=0.509

Table 8-2. (Continued)
Associations Between Time of Duty in Southeast Asia Characteristics and Estimates of Dioxin Exposure

		Model 3			
Covariate	**Covariate Category**	**Comparison**	**Background Ranch Hand**	**Low Ranch Hand**	**High Ranch Hand**
Combat Service (number of days) (Continuous)	--	n=1,063 $\bar{x}$=203.9	n=374 $\bar{x}$=445.9	n=260 $\bar{x}$=454.0	n=260 $\bar{x}$=458.7
			p<0.001		
Combat Service (number of days) (Discrete)		n=1,063	n=374	n=260	n=260
	0-360 days	77.4%	18.2%	11.2%	10.4%
	>360 days	22.6%	81.8%	88.8%	89.6%
			p<0.001		
Time Reference of Acne to Southeast Asia		n=911	n=329	n=227	n=221
	Pre & Post	12.4%	10.9%	9.3%	11.8%
	Post	87.6%	89.1%	90.7%	88.2%
			p=0.585		
Presence of Pre-SEA Acne		n=1,063	n=374	n=260	n=260
	No	89.0%	90.1%	91.2%	89.6%
	Yes	11.0%	9.9%	8.8%	10.4%
			p=0.755		

Table 8-2. (Continued)
Associations Between Time of Duty in Southeast Asia Characteristics and Estimates of Dioxin Exposure

		Model 4	Models 5 and 6
Covariate	**Covariate Category**	**Lipid-Adjusted Current Dioxin (ppt)**	**Whole-Weight Current Dioxin (ppq)**
Combat Service (number of days) (Continuous)	--	n=894 r=0.069 p=0.042	n=894 r=0.064 p=0.056
Combat Service (number of days) (Discrete)	0-360 Days >360 Days	$\bar{x}$=10.61 (n=124) $\bar{x}$=15.28 (n=770) p=0.001	$\bar{x}$=60.74 (n=124) $\bar{x}$=87.52 (n=770) p=0.002
Time Reference of Acne to SEA	Pre & Post Post	$\bar{x}$=14.46 (n=83) $\bar{x}$=14.39 (n=694) p=0.970	$\bar{x}$=80.62 (n=83) $\bar{x}$=82.80 (n=694) p=0.847
Presence of Pre-SEA Acne	No Yes	$\bar{x}$=14.52 (n=807) $\bar{x}$=14.64 (n=87) p=0.946	$\bar{x}$=83.3 (n=807) $\bar{x}$=81.9 (n=87) p=0.899

Note: Means for discrete covariates are transformed from the logarithmic (base 2) scale for initial dioxin in Model 2, and from the ($\log_2$ (X+1)) scale for current dioxin in Models 4, 5, and 6.

Table 8-3.
Associations Between Alcohol Consumption and Estimates of Dioxin Exposure

Covariate	Covariate Category	Model 1: Ranch Hand	Model 1: Comparison	Model 2: Initial Dioxin (ppt)
Current Alcohol Use (drinks/day) (Continuous)	--	n=942 $\bar{x}$=0.73	n=1,263 $\bar{x}$=0.75	n=513 r=-0.034
		p=0.738		p=0.445
Current Alcohol Use (drinks/day) (Discrete)		n=942	n=1,263	
	0-1	78.5%	79.7%	$\bar{x}$=172.24 (n=407)
	>1-4	19.5%	17.2%	$\bar{x}$=144.56 (n=98)
	>4	2.0%	3.2%	$\bar{x}$=153.15 (n=8)
		p=0.110		p=0.234
Lifetime Alcohol History (drink-years) (Continuous)	--	n=930 $\bar{x}$=33.91	n=1,260 $\bar{x}$=32.71	n=507 r=0.042
		p=0.573		p=0.341
Lifetime Alcohol History (drink-years) (Discrete)		n=930	n=1,260	
	0	6.8%	5.6%	$\bar{x}$=217.27 (n=39)
	>0-40	68.0%	68.3%	$\bar{x}$=162.11 (n=335)
	>40	25.3%	26.1%	$\bar{x}$=162.56 (n=133)
		p=0.525		p=0.166
Current Wine Use (drinks/day) (Continuous)	--	n=941 $\bar{x}$=0.13	n=1,263 $\bar{x}$=0.10	n=513 r=-0.071
		p=0.025		p=0.108
Current Wine Use (drinks/day) (Discrete)		n=941	n=1,263	
	0	46.0%	42.4%	$\bar{x}$=193.19 (n=254)
	>0	54.0%	57.6%	$\bar{x}$=143.51 (n=259)
		p=0.096		p<0.001
Lifetime Wine History (wine-years) (Continuous)	--	n=933 $\bar{x}$=2.92	n=1,260 $\bar{x}$=2.50	n=509 r=-0.165
		p=0.235		p<0.001
Lifetime Wine History (wine-years) (Discrete)		n=933	n=1,260	
	0	33.8%	29.0%	$\bar{x}$=206.21 (n=186)
	>0	66.2%	71.0%	$\bar{x}$=147.27 (n=323)
		p=0.019		p<0.001

Table 8-3. (Continued)
Associations Between Alcohol Consumption and Estimates of Dioxin Exposure

Covariate	Covariate Category	Model 3			
		Comparison	Background Ranch Hand	Low Ranch Hand	High Ranch Hand
Current Alcohol Use (drinks/day) (Continuous)	--	n=1,047 $\bar{x}$=0.77	n=372 $\bar{x}$=0.75	n=257 $\bar{x}$=0.71	n=256 $\bar{x}$=0.68
			p=0.759		
Current Alcohol Use (drinks/day) (Discrete)		n=1,047	n=372	n=257	n=256
	0-1	79.4%	77.2%	76.7%	82.0%
	>1-4	17.2%	20.4%	22.2%	16.0%
	>4	3.4%	2.4%	1.2%	2.0%
			p=0.124		
Lifetime Alcohol History (drink-years) (Continuous)	--	n=1,045 $\bar{x}$=33.66	n=367 $\bar{x}$=31.61	n=254 $\bar{x}$=33.08	n=253 $\bar{x}$=35.88
			p=0.768		
Lifetime Alcohol History (drink-years) (Discrete)		n=1,045	n=367	n=254	n=253
	0	5.2%	5.4%	5.9%	9.5%
	>0-40	67.9%	71.1%	66.9%	65.2%
	>40	26.9%	23.4%	27.2%	25.3%
			p=0.180		
Current Wine Use (drinks/day) (Continuous)	--	n=1,047 $\bar{x}$=0.10	n=371 $\bar{x}$=0.17	n=257 $\bar{x}$=0.14	n=256 $\bar{x}$=0.07
			p=0.001		
Current Wine Use (drinks/day) (Discrete)		n=1,047	n=371	n=257	n=256
	0	41.7%	40.7%	45.1%	53.9%
	>0	58.3%	59.3%	54.9%	46.1%
			p=0.003		
Lifetime Wine History (drink-years) (Continuous)	--	n=1,045 $\bar{x}$=2.60	n=368 $\bar{x}$=3.69	n=254 $\bar{x}$=3.62	n=255 $\bar{x}$=1.31
			p=0.003		
Lifetime Wine History (wine-years) (Discrete)		n=1,045	n=368	n=254	n=255
	0	28.1%	29.9%	32.7%	40.4%
	>0	71.9%	70.1%	67.3%	59.6%
			p=0.002		

Table 8-3. (Continued)
Associations Between Alcohol Consumption and Estimates of Dioxin Exposure

Covariate	Covariate Category	Model 4 Lipid-Adjusted Current Dioxin (ppt)	Models 5 and 6 Whole-Weight Current Dioxin (ppq)
Current Alcohol Use (drinks/day) (Continuous)	--	n=885 r=-0.021 p=0.534	n=885 r=-0.007 p=0.842
Current Alcohol Use (drinks/day) (Discrete)	0-1	$\bar{x}$=14.84 (n=694)	$\bar{x}$=84.44 (n=694)
	>1-4	$\bar{x}$=13.38 (n=174)	$\bar{x}$=78.49 (n=174)
	>4	$\bar{x}$=11.71 (n=17)	$\bar{x}$=69.49 (n=17)
		p=0.381	p=0.639
Lifetime Alcohol History (drink-years) (Continuous)	--	n=874 r=0.032 p=0.348	n=874 r=0.031 p=0.362
Lifetime Alcohol History (drink-years) (Discrete)	0	$\bar{x}$=18.40 (n=59)	$\bar{x}$=102.17 (n=59)
	>0-40	$\bar{x}$=13.98 (n=596)	$\bar{x}$=80.32 (n=596)
	>40	$\bar{x}$=14.75 (n=219)	$\bar{x}$=84.41 (n=219)
		p=0.166	p=0.324
Current Wine Use (drinks/day) (Continuous)	--	n=884 r=-0.105 p=0.002	n=884 r=-0.114 p=0.001
Current Wine Use (drinks/day) (Discrete)	0	$\bar{x}$=16.72 (n=405)	$\bar{x}$=95.98 (n=405)
	>0	$\bar{x}$=12.82 (n=479)	$\bar{x}$=73.34 (n=479)
		p<0.001	p=0.001
Lifetime Wine Use (wine-years) (Continuous)	--	n=877 r=-0.102 p=0.003	n=877 r=-0.110 p=0.001
Lifetime Wine Use (wine-years) (Discrete)	0	$\bar{x}$=17.23 (n=296)	$\bar{x}$=98.03 (n=296)
	>0	$\bar{x}$=13.25 (n=581)	$\bar{x}$=76.12 (n=581)
		p=0.001	p=0.003

Note: Means for discrete covariates are transformed from the logarithmic (base 2) scale for initial dioxin in Model 2, and from the ($\log_2$ (X+1)) scale for current dioxin in Models 4, 5, and 6.

The examination of current wine use, when stratified into categories of those who do not currently drink wine and those who currently drink wine, showed a significant association with dioxin in Model 2 ($p<0.001$), Model 3 ($p=0.003$), Model 4 ($p<0.001$), and Models 5 and 6 ($p=0.001$). In Model 3, a significant difference between the percentage of participants who do not drink wine was seen among Comparisons (41.7%), background Ranch Hands (40.7%), low Ranch Hands (45.1%), and high Ranch Hands (53.9%). In Models 2, 4, 5, and 6, the mean dioxin levels are higher for participants who do not currently drink wine.

Lifetime wine history in its continuous form showed significant inverse associations with dioxin in Model 2 ($p<0.001$), Model 3 ($p=0.003$), Model 4 ($p=0.003$), and Models 5 and 6 ($p=0.001$). The mean wine-years in the Comparison, background Ranch Hands, low Ranch Hands, and high Ranch Hands categories for Model 3 are 2.60, 3.69, 3.62, and 1.31 respectively. In Models 2, 4, 5, and 6, wine consumption increased as dioxin levels decreased.

Stratifying participants into those who have never consumed wine and those who have showed a significant relationship between lifetime wine history and group in Model 1 analysis ($p=0.019$). A significant difference between the percentage of participants who have never had wine was seen between Ranch Hands (33.8%) and Comparisons (29.0%). Additionally, significant relationships between lifetime wine history and dioxin were revealed in analyses of Model 2 ($p<0.001$), Model 3 ($p=0.002$), Model 4 ($p=0.001$), and Models 5 and 6 ($p=0.003$). In Models 2, 4, 5, and 6, the mean dioxin levels were lower for those participants who had consumed wine in the past than for those who had not. In the Model 3 analysis, a significant difference between the percentage of participants who have never had wine was seen among Comparisons (28.1%), background Ranch Hands (29.9%), low Ranch Hands (32.7%), and high Ranch Hands (40.4%).

No significant ($p \leq 0.05$) associations were observed between alcohol (beer, wine, and liquor combined) consumption and the five estimates of dioxin exposure.

CIGARETTE SMOKING HISTORY

No significant ($p \leq 0.05$) associations were observed between either current or lifetime cigarette smoking and the five estimates of dioxin exposure. Results of tests of association between cigarette smoking and the estimates of dioxin exposure are given in Table 8-4.

EXPOSURE TO CARCINOGENS

Results of tests of association between reported exposure to asbestos, ionizing radiation, industrial chemicals, herbicides, insecticides, and degreasing chemicals and the estimates of dioxin exposure are presented in Table 8-5. These variables were constructed based on responses given by participants and were intended to capture post-SEA exposures to these suspected carcinogens.

Table 8-4.
Associations Between Cigarette Smoking and Estimates of Dioxin Exposure

Covariate	Covariate Category	Model 1		Model 2
		Ranch Hand	Comparison	Initial Dioxin (ppt)
Current Cigarette Smoking (cigarettes/day) (Continuous)	--	n=952 $\bar{x}$=6.07	n=1,279 $\bar{x}$=5.42	n=520 r=0.050
		p=0.205		p=0.258
Current Cigarette Smoking (cigarettes/day) (Discrete)		n=952	n=1,279	
	0-Never Smoked	27.0%	27.8%	$\bar{x}$=174.72 (n=139)
	0-Former Smoker	46.0%	48.4%	$\bar{x}$=154.06 (n=239)
	0-20	16.7%	14.9%	$\bar{x}$=181.29 (n=88)
	>20	10.3%	8.9%	$\bar{x}$=179.75 (n=54)
		p=0.399		p=0.362
Lifetime Cigarette Smoking History (pack-years) (Continuous)	--	n=951 $\bar{x}$=14.78	n=1,279 $\bar{x}$=14.19	n=520 r=-0.058
		p=0.476		p=0.185
Lifetime Cigarette Smoking History (pack-years) (Discrete)		n=951	n=1,279	
	0	27.0%	27.8%	$\bar{x}$=174.72 (n=139)
	>0-10	31.3%	30.0%	$\bar{x}$=182.38 (n=162)
	>10	41.6%	42.2%	$\bar{x}$=150.79 (n=219)
		p=0.796		p=0.105

Table 8-4. (Continued)
Associations Between Cigarette Smoking and Estimates of Dioxin Exposure

Covariate	Covariate Category	Model 3			
		Comparison	Background Ranch Hand	Low Ranch Hand	High Ranch Hand
Current Cigarette Smoking (cigarettes/day) (Continuous)	--	n=1,061 $\bar{x}$=5.44	n=374 $\bar{x}$=6.18	n=260 $\bar{x}$=5.13	n=260 $\bar{x}$=6.62
			p=0.373		
Current Cigarette Smoking (cigarettes/day) (Discrete)		n=1,061	n=374	n=260	n=260
	0-Never Smoked	26.6%	29.1%	27.7%	25.8%
	0-Former Smoker	50.0%	45.5%	48.5%	43.5%
	0-20	14.3%	15.8%	15.0%	18.8%
	>20	9.1%	9.6%	8.8%	11.9%
			p=0.526		
Lifetime Cigarette Smoking History (pack-years) (Continuous)	--	n=1,061 $\bar{x}$=14.31	n=373 $\bar{x}$=14.48	n=260 $\bar{x}$=15.84	n=260 $\bar{x}$=13.96
			p=0.674		
Lifetime Cigarette Smoking History (pack-years) (Discrete)		n=1,061	n=373	n=260	n=260
	0	26.6%	29.2%	27.7%	25.8%
	>0-10	30.5%	29.2%	26.5%	35.8%
	>10	42.9%	41.6%	45.8%	38.5%
			p=0.359		

Table 8-4. (Continued)
Associations Between Cigarette Smoking and Estimates of Dioxin Exposure

Covariate	Covariate Category	Model 4	Models 5 and 6
		Lipid-Adjusted Current Dioxin (ppt)	Whole-Weight Current Dioxin (ppq)
Current Cigarette Smoking (cigarettes/ day) (Continuous)	--	n=894 r=-0.015 p=0.665	n=894 r=-0.011 p=0.744
Current Cigarette Smoking (cigarettes/ day) (Discrete)	0-Never Smoked 0-Former Smoker >0-20 >20	$\bar{x}$=15.00 (n=248) $\bar{x}$=14.08 (n=409) $\bar{x}$=15.03 (n=147) $\bar{x}$=14.52 (n=90) p=0.873	$\bar{x}$=83.15 (n=248) $\bar{x}$=81.89 (n=409) $\bar{x}$=86.49 (n=147) $\bar{x}$=84.10 (n=90) p=0.972
Lifetime Cigarette Smoking History (pack-years) (Continuous)	--	n=893 r=-0.051 p=0.129	n=893 r=-0.041 p=0.226
Lifetime Cigarette Smoking History (pack-years) (Discrete)	0 >0-10 >10	$\bar{x}$=15.00 (n=248) $\bar{x}$=15.47 (n=271) $\bar{x}$=13.62 (n=374) p=0.293	$\bar{x}$=83.15 (n=248) $\bar{x}$=87.46 (n=271) $\bar{x}$=80.41 (n=374) p=0.677

Note: Means for discrete covariates are transformed from the logarithmic (base 2) scale for initial dioxin in Model 2, and from the ($\log_2 (X+1)$) scale for current dioxin in Models 4, 5, and 6.

Table 8-5.
Associations Between Exposure to Carcinogens and Estimates of Dioxin Exposure

Covariate	Covariate Category	Model 1: Ranch Hand	Model 1: Comparison	Model 2: Initial Dioxin (ppt)
Asbestos Exposure		n=952	n=1,281	
	No	73.6%	71.5%	$\bar{x}$=164.33 (n=379)
	Yes	26.4%	28.5%	$\bar{x}$=172.19 (n=141)
		p=0.287		p=0.607
Ionizing Radiation		n=952	n=1,281	
Exposure	No	78.7%	73.1%	$\bar{x}$=172.43 (n=408)
	Yes	21.3%	26.9%	$\bar{x}$=146.25 (n=112)
		p=0.003		p=0.094
Industrial Chemical		n=952	n=1,281	
Exposure	No	42.0%	40.7%	$\bar{x}$=142.86 (n=187)
	Yes	58.0%	59.3%	$\bar{x}$=181.32 (n=333)
		p=0.577		p=0.005
Herbicide		n=952	n=1,281	
Exposure	No	5.1%	61.7%	$\bar{x}$=191.21 (n=21)
	Yes	94.9%	38.3%	$\bar{x}$=165.45 (n=499)
		p<0.001		p=0.481
Insecticide		n=952	n=1,281	
Exposure	No	23.6%	37.3%	$\bar{x}$=190.80 (n=119)
	Yes	76.4%	62.7%	$\bar{x}$=159.81 (n=401)
		p<0.001		p=0.065
Degreasing		n=952	n=1,281	
Chemical Exposure	No	37.0%	36.9%	$\bar{x}$=133.37 (n=148)
	Yes	63.0%	63.1%	$\bar{x}$=181.75 (n=372)
		p=0.999		p=0.001

Table 8-5. (Continued)
Associations Between Exposure to Carcinogens and Estimates of Dioxin Exposure

		Model 3			
Covariate	Covariate Category	Comparison	Background Ranch Hand	Low Ranch Hand	High Ranch Hand
Asbestos Exposure		n=1,063	n=374	n=260	n=260
	No	71.8%	73.8%	73.1%	72.7%
	Yes	28.2%	26.2%	26.9%	27.3%
			p=0.887		
Ionizing Radiation		n=1,063	n=374	n=260	n=260
Exposure	No	72.7%	78.3%	74.6%	82.3%
	Yes	27.3%	21.7%	25.4%	17.7%
			p=0.006		
Industrial Chemical		n=1,063	n=374	n=260	n=260
Exposure	No	40.5%	51.3%	41.2%	30.8%
	Yes	59.5%	48.7%	58.8%	69.2%
			p<0.001		
Herbicide Exposure		n=1,063	n=374	n=260	n=260
	No	61.8%	6.1%	3.5%	4.6%
	Yes	38.2%	93.9%	96.5%	95.4%
			p<0.001		
Insecticide		n=1,063	n=374	n=260	n=260
Exposure	No	37.3%	24.6%	19.6%	26.2%
	Yes	62.7%	75.4%	80.4%	73.8%
			p<0.001		
Degreasing		n=1,063	n=374	n=260	n=260
Chemical Exposure	No	35.3%	48.7%	36.9%	20.0%
	Yes	64.7%	51.3%	63.1%	80.0%
			p<0.001		

Table 8-5. (Continued)
Associations Between Exposure to Carcinogens and Estimates of Dioxin Exposure

		Model 4	Models 5 and 6
Covariate	Covariate Category	Lipid-Adjusted Current Dioxin (ppt)	Whole-Weight Current Dioxin (ppq)
Asbestos Exposure	No	$\bar{x}$=14.28 (n=655)	$\bar{x}$=82.09 (n=655)
	Yes	$\bar{x}$=15.26 (n=239)	$\bar{x}$=86.31 (n=239)
		p=0.416	p=0.578
Ionizing Radiation Exposure	No	$\bar{x}$=14.99 (n=701)	$\bar{x}$=86.87 (n=701)
	Yes	$\bar{x}$=12.96 (n=193)	$\bar{x}$=71.13 (n=193)
		p=0.098	p=0.039
Industrial Chemical Exposure	No	$\bar{x}$=11.65 (n=379)	$\bar{x}$=66.13 (n=379)
	Yes	$\bar{x}$=17.06 (n=515)	$\bar{x}$=98.48 (n=515)
		p<0.001	p<0.001
Herbicide Exposure	No	$\bar{x}$=11.78 (n=44)	$\bar{x}$=66.29 (n=44)
	Yes	$\bar{x}$=14.69 (n=850)	$\bar{x}$=84.19 (n=850)
		p=0.191	p=0.196
Insecticide Exposure	No	$\bar{x}$=14.94 (n=211)	$\bar{x}$=85.58 (n=211)
	Yes	$\bar{x}$=14.41 (n=683)	$\bar{x}$=82.48 (n=683)
		p=0.668	p=0.695
Degreasing Chemical Exposure	No	$\bar{x}$=10.37 (n=330)	$\bar{x}$=57.80 (n=330)
	Yes	$\bar{x}$=17.64 (n=564)	$\bar{x}$=102.88 (n=564)
		p<0.001	p<0.001

Note: Means for discrete covariates are transformed from the logarithmic (base 2) scale for initial dioxin in Model 2, and from the ($\log_2$ (X+1)) scale for current dioxin in Models 4, 5, and 6.

The Model 1 analysis showed a highly significant association between group and exposure to ionizing radiation ($p=0.003$). A significant difference between the percentage of participants who have never been exposed to ionizing radiation was seen between Ranch Hands (78.7%) and Comparisons (73.1%). In Model 3, a significant difference in the percentage of participants who have never been exposed to ionizing radiation was seen among Comparisons (72.7%), background Ranch Hands (78.3%), low Ranch Hands (74.6%), and high Ranch Hands (82.3%) ($p=0.006$). A significant association existed for Models 5 and 6 between current dioxin and exposure to ionizing radiation ($p=0.039$). The mean current whole-weight dioxin level was greater for those who had never been exposed to ionizing radiation than for those who were exposed.

The association between industrial chemical exposure and dioxin was highly significant in the analysis of Models 2 through 6 ($p=0.005$ for Model 2 and $p<0.001$ for Models 3 through 6). Participants who were exposed to industrial chemicals had higher mean dioxin levels in Models 2, 4, 5, and 6 than those participants who were not exposed. In Model 3, a significant difference in the percentage of participants who were not exposed to industrial chemicals was seen among Comparisons (40.5%), background Ranch Hands (51.3%), low Ranch Hands (41.2%), and high Ranch Hands (30.8%).

As expected, a highly significant association between group and reported exposure to herbicides was revealed in Model 1 ($p<0.001$). A significant difference between the percentage of participants who have never been exposed to herbicides was seen between Ranch Hands (5.1%) and Comparisons (61.7%). A highly significant association between categorized dioxin and exposure to herbicides also was revealed in Model 3 ($p<0.001$), due to the inherent difference between Ranch Hands and Comparisons. A significant difference between the percentage of participants not exposed to herbicides was seen among Comparisons (61.8%), background Ranch Hands (6.1%), low Ranch Hands (3.5%), and high Ranch Hands (4.6%).

Highly significant associations were shown between insecticide exposure and group in Model 1 ($p<0.001$), as well as between insecticide exposure and categorized dioxin in Model 3 ($p<0.001$). In Model 1, 23.6 percent of Ranch Hands and 37.3 percent of Comparisons were never exposed to insecticides. In Model 3, the percentage of participants not exposed to insecticides was 37.3 among Comparisons, 24.6 among background Ranch Hands, 19.6 among low Ranch Hands, and 26.2 among high Ranch Hands.

The association between reported degreasing chemical exposure and dioxin was highly significant in the analysis of Models 2 through 6 ($p\leq0.001$ for each model). The mean dioxin level increased with exposure to degreasing chemicals in Models 2, 4, 5, and 6. In Model 3, a significant difference between the percentage of participants who have not been exposed to degreasing chemicals was seen among Comparisons (35.3%), background Ranch Hands (48.7%), low Ranch Hands (36.9%), and high Ranch Hands (20.0%).

No significant ($p\leq0.05$) associations were observed between asbestos exposure and the five estimates of dioxin exposure.

HEALTH VARIABLES

Results of tests of association between numerous measures related to a participant's health and the five estimates of dioxin exposure are presented in Table 8-6. Caloric intake in its continuous form was shown to be significantly associated with categorized dioxin in Model 3 ($p=0.018$). The mean caloric intake in the Comparison, background Ranch Hand, low Ranch Hand, and high Ranch Hand categories are 1,944.3 kcal/day; 2,046.9 kcal/day; 1,879.3 kcal/day; and 1,885.5 kcal/day respectively.

Statistically significant associations were found between body fat and dioxin for Model 2 ($p=0.015$), Model 3 ($p<0.001$), Model 4 ($p<0.001$), and Models 5 and 6 ($p<0.001$). In Model 3, the mean percent body fat in the Comparison, background Ranch Hands, low Ranch Hands, and high Ranch Hands categories was 22.63, 20.87, 23.27, and 23.83 respectively. Body fat increased as dioxin levels increased in Models 2 and 4, and Models 5 and 6. The examination of body fat when dichotomized into lean or normal ($\leq$25 percent body fat) and obese (>25 percent body fat) showed a significant association with dioxin in Models 3 through 6 ($p<0.001$ for each model). In Model 3, a significant difference in the percentage of participants considered lean or normal was seen among Comparisons (73.7%), background Ranch Hands (85.8%), low Ranch Hands (69.6%), and high Ranch Hands (64.2%). The mean current dioxin levels were higher for the obese participants in Models 4 through 6.

Serum insulin in its continuous form showed a significant association with dioxin in Models 3 through 6 ($p\leq0.001$ for each model). Model 3 revealed mean serum insulin levels of 97.57 mIU/ml for Comparisons, 87.98 mIU/ml for background Ranch Hands, 108.46 mIU/ml for low Ranch Hands, and 119.46 mIU/ml for high Ranch Hands. In Models 4 through 6, serum insulin levels increased as current dioxin levels increased. When stratified into either less than or equal to 56 mIU/ml or greater than 56 mIU/ml, serum insulin showed significant associations with dioxin in Model 3 ($p=0.033$), Model 4 ($p=0.005$), and Models 5 and 6 ($p<0.001$). In Model 3, a significant difference between the percentage of participants with serum insulin less than or equal to 56 mIU/ml was seen among Comparisons (42.5%), background Ranch Hands (50.5%), low Ranch Hands (42.7%), and high Ranch Hands (40.8%). The mean current dioxin levels were higher for participants with serum insulin greater than 56 mIU/ml in Models 4 through 6.

Analysis of cholesterol in both its continuous and discrete forms revealed highly significant positive associations with current dioxin in Models 5 and 6 ($p<0.001$ for cholesterol continuous; $p=0.003$ when cholesterol discrete). Cholesterol increased as the level of dioxin increased.

High-density lipoprotein (HDL) cholesterol showed highly significant associations in Model 2 ($p=0.006$), Model 3 ($p<0.001$), Model 4 ($p<0.001$), and Models 5 and 6 ($p<0.001$). HDL cholesterol levels decreased as the mean dioxin levels increased for Models 2, 4, 5, and 6. Model 3 revealed mean HDL cholesterol levels of 42.02 mg/dl for the Comparisons, 43.89 mg/dl for background Ranch Hands, 42.31 mg/dl for low Ranch Hands, and 39.52 mg/dl for high Ranch Hands. Stratifying participants into either less than or equal to 35 mg/dl or greater than 35 mg/dl, revealed significant associations between

Table 8-6.
Associations Between Health Variables and Estimates of Dioxin Exposure

Covariate	Covariate Category	Model 1		Model 2
		Ranch Hand	Comparison	Initial Dioxin (ppt)
Caloric Intake (kcal/day) (Continuous)	--	n=950 $\bar{x}$=1,956.4	n=1,279 $\bar{x}$=1,952.7	n=518 r=-0.002
		p=0.912		p=0.957
Caloric Intake (kcal/day) (Discrete)		n=950	n=1,279	
	≤ 2000	58.8%	59.7%	$\bar{x}$=167.04 (n=324)
	> 2000	41.2%	40.3%	$\bar{x}$=163.51 (n=194)
		p=0.731		p=0.798
Body Fat (percent) (Continuous)	--	n=952 $\bar{x}$=22.41	n=1,281 $\bar{x}$=22.55	n=520 r=0.106
		p=0.529		p=0.015
Body Fat (percent) (Discrete)		n=952	n=1,281	
	Lean or Normal	74.6%	74.4%	$\bar{x}$=157.50 (n=348)
	Obese	25.4%	25.6%	$\bar{x}$=186.06 (n=172)
		p=0.960		p=0.052
Serum Insulin (mIU/ml) (Continuous)	--	n=952 $\bar{x}$=103.00	n=1,279 $\bar{x}$=97.51	n=520 r=0.059
		p=0.204		p=0.181
Serum Insulin (mIU/ml) (Discrete)		n=952	n=1,279	
	0-56	45.2%	43.5%	$\bar{x}$=164.02 (n=217)
	>56	54.8%	56.5%	$\bar{x}$=168.17 (n=303)
		p=0.450		p=0.761
Cholesterol (mg/dl) (Continuous)	--	n=952 $\bar{x}$=218.61	n=1,280 $\bar{x}$=218.30	n=520 r=0.052
		p=0.849		p=0.233
Cholesterol (mg/dl) (Discrete)		n=952	n=1,280	
	0-200	32.9%	32.0%	$\bar{x}$=155.28 (n=170)
	200-239	38.0%	41.6%	$\bar{x}$=176.67 (n=194)
	>239	29.1%	26.5%	$\bar{x}$=166.62 (n=156)
		p=0.202		p=0.412

Table 8-6. (Continued)
Associations Between Health Variables and Estimates of Dioxin Exposure

Covariate	Covariate Category	Model 1: Ranch Hand	Model 1: Comparison	Model 2: Initial Dioxin (ppt)
HDL Cholesterol (mg/dl) (Continuous)	--	n=938	n=1,268	n=511
		$\bar{x}$=42.06	$\bar{x}$=42.19	r=-0.120
		p=0.778		p=0.006
HDL Cholesterol (mg/dl) (Discrete)		n=938	n=1,268	
	0-35	28.3%	23.8%	$\bar{x}$=176.02 (n=158)
	>35	71.7%	76.2%	$\bar{x}$=161.21 (n=353)
		p=0.021		p=0.320
Cholesterol-HDL Cholesterol Ratio (Continuous)	--	n=938	n=1,268	n=511
		$\bar{x}$=5.52	$\bar{x}$=5.45	r=0.127
		p=0.302		p=0.004
Cholesterol-HDL Cholesterol Ratio (Discrete)		n=938	n=1,268	
	0-5	41.3%	43.5%	$\bar{x}$=148.47 (n=188)
	>5	58.7%	56.5%	$\bar{x}$=176.56 (n=323)
		p=0.305		p=0.040
Physical Activity Index		n=952	n=1,279	
	Sedentary	57.6%	56.1%	$\bar{x}$=183.44 (n=313)
	Moderate	17.8%	18.5%	$\bar{x}$=145.91 (n=92)
	Very Active	24.7%	25.3%	$\bar{x}$=141.85 (n=115)
		p=0.791		p=0.012
Diabetic Class[a]		n=951	n=1,279	
	Normal	72.3%	75.4%	$\bar{x}$=159.44 (n=348)
	Impaired	12.5%	10.3%	$\bar{x}$=187.46 (n=74)
	Diabetic	15.1%	14.2%	$\bar{x}$=177.12 (n=98)
		p=0.187		p=0.296
Diabetic Severity[b]		n=144	n=182	
	No Treatment	54.2%	61.0%	$\bar{x}$=152.18 (n=48)
	Diet Only	21.5%	18.7%	$\bar{x}$=170.64 (n=23)
	Oral Hypoglycemic	12.5%	13.2%	$\bar{x}$=303.03 (n=18)
	Insulin Dependent	11.8%	7.1%	$\bar{x}$=149.55 (n=9)
		p=0.407		p=0.103

Table 8-6. (Continued)
Associations Between Health Variables and Estimates of Dioxin Exposure

Covariate	Covariate Category	Model 1: Ranch Hand	Model 1: Comparison	Model 2: Initial Dioxin (ppt)
Family History of		n=934	n=1,263	
Diabetes	No	77.1%	75.5%	$\bar{x}$=159.42 (n=386)
	Yes	22.9%	24.5%	$\bar{x}$=187.84 (n=122)
		p=0.427		p=0.086
Family History of		n=939	n=1,267	
Heart Disease	No	40.8%	43.5%	$\bar{x}$=168.14 (n=222)
	Yes	59.2%	56.5%	$\bar{x}$=165.58 (n=290)
		p=0.220		p=0.853
Family History of		n=917	n=1,250	
Heart Disease	No	89.9%	88.7%	$\bar{x}$=162.86 (n=453)
Before Age 45	Yes	10.1%	11.3%	$\bar{x}$=202.22 (n=45)
		p=0.439		p=0.135
Currently Taking		n=952	n=1,281	
Blood Pressure	No	78.9%	80.6%	$\bar{x}$=167.05 (n=410)
Medication	Yes	21.1%	19.4%	$\bar{x}$=164.11 (n=110)
		p=0.333		p=0.858

Table 8-6. (Continued)
Associations Between Health Variables and Estimates of Dioxin Exposure

Covariate	Covariate Category	Model 3: Comparison	Model 3: Background Ranch Hand	Model 3: Low Ranch Hand	Model 3: High Ranch Hand
Caloric Intake (kcal/day) (Continuous)	--	n=1,061 $\bar{x}$=1,944.3	n=374 $\bar{x}$=2,046.9	n=260 $\bar{x}$=1,879.3	n=258 $\bar{x}$=1,885.5
			p=0.018		
Caloric Intake (kcal/day) (Discrete)		n=1,061	n=374	n=260	n=258
	≤2000	59.3%	54.8%	62.3%	62.8%
	>2000	40.7%	45.2%	37.7%	37.2%
			p=0.145		
Body Fat (percent) (Continuous)	--	n=1,063 $\bar{x}$=22.63	n=374 $\bar{x}$=20.87	n=260 $\bar{x}$=23.27	n=260 $\bar{x}$=23.83
			p<0.001		
Body Fat (percent) (Discrete)		n=1,063	n=374	n=260	n=260
	Lean or Normal	73.7%	85.8%	69.6%	64.2%
	Obese	26.3%	14.2%	30.4%	35.8%
			p<0.001		
Serum Insulin (mIU/ml) (Continuous)	--	n=1,062 $\bar{x}$=97.57	n=374 $\bar{x}$=87.98	n=260 $\bar{x}$=108.46	n=260 $\bar{x}$=119.46
			p=0.001		
Serum Insulin (mIU/ml) (Discrete)		n=1,062	n=374	n=260	n=260
	0-56	42.5%	50.5%	42.7%	40.8%
	>56	57.5%	49.5%	57.3%	59.2%
			p=0.033		
Cholesterol (mg/dl) (Continuous)	--	n=1,063 $\bar{x}$=217.74	n=374 $\bar{x}$=217.37	n=260 $\bar{x}$=217.70	n=260 $\bar{x}$=221.38
			p=0.533		
Cholesterol (mg/dl) (Discrete)		n=1,063	n=374	n=260	n=260
	0-200	31.7%	33.2%	35.0%	30.4%
	200-239	42.0%	39.0%	35.4%	39.2%
	>239	26.3%	27.8%	29.6%	30.4%
			p=0.504		

Table 8-6. (Continued)
Associations Between Health Variables and Estimates of Dioxin Exposure

Covariate	Covariate Category	Model 3: Comparison	Model 3: Background Ranch Hand	Model 3: Low Ranch Hand	Model 3: High Ranch Hand
HDL Cholesterol (mg/dl) (Continuous)	--	n=1,053 $\bar{x}$=42.02	n=370 $\bar{x}$=43.89	n=256 $\bar{x}$=42.31	n=255 $\bar{x}$=39.52
			p<0.001		
HDL Cholesterol (mg/dl) (Discrete)		n=1,053	n=370	n=256	n=255
	0-35	24.4%	23.8%	29.3%	32.5%
	>35	75.6%	76.2%	70.7%	67.5%
			p=0.024		
Cholesterol-HDL Cholesterol Ratio (Continuous)	--	n=1,053 $\bar{x}$=5.45	n=370 $\bar{x}$=5.31	n=256 $\bar{x}$=5.46	n=255 $\bar{x}$=5.85
			p<0.001		
Cholesterol-HDL Cholesterol Ratio (Discrete)		n=1,053	n=370	n=256	n=255
	0-5	42.9%	47.3%	41.8%	31.8%
	>5	57.1%	52.7%	58.2%	68.2%
			p=0.001		
Physical Activity Index		n=1,061	n=374	n=260	n=260
	Sedentary	55.6%	53.5%	55.0%	65.4%
	Moderate	18.6%	19.0%	20.0%	15.4%
	Very Active	25.8%	27.5%	25.0%	19.2%
			p=0.092		
Diabetic Class[a]		n=1,062	n=373	n=260	n=260
	Normal	75.5%	79.9%	67.7%	66.2%
	Impaired	10.3%	8.8%	12.7%	15.8%
	Diabetic	14.2%	11.3%	19.6%	18.1%
			p=0.001		
Diabetic Severity[b]		n=151	n=42	n=51	n=47
	No Treatment	57.0%	61.9%	54.9%	42.6%
	Diet Only	21.2%	19.1%	23.5%	23.4%
	Oral Hypoglycemic	13.3%	0.0%	11.8%	25.5%
	Insulin Dependent	8.6%	19.1%	9.8%	8.5%
			p=0.050		

Table 8-6. (Continued)
Associations Between Health Variables and Estimates of Dioxin Exposure

		Model 3			
Covariate	**Covariate Category**	**Comparison**	**Background Ranch Hand**	**Low Ranch Hand**	**High Ranch Hand**
Family History of		n=1,048	n=368	n=254	n=254
Diabetes	No	75.2%	79.1%	76.8%	75.2%
	Yes	24.8%	20.9%	23.2%	24.8%
			p=0.485		
Family History of		n=1,051	n=369	n=255	n=257
Heart Disease	No	43.6%	37.9%	44.7%	42.0%
	Yes	56.4%	62.1%	55.3%	58.0%
			p=0.244		
Family History of		n=1,035	n=361	n=249	n=249
Heart Disease	No	88.2%	88.6%	94.0%	88.0%
Before Age 45	Yes	11.8%	11.4%	6.0%	12.0%
			p=0.063		
Currently Taking		n=1,063	n=374	n=260	n=260
Blood Pressure	No	80.3%	79.9%	79.2%	78.5%
Medication	Yes	19.7%	20.1%	20.8%	21.5%
			p=0.911		

Table 8-6. (Continued)
Associations Between Health Variables and Estimates of Dioxin Exposure

Covariate	Covariate Category	Model 4: Lipid-Adjusted Current Dioxin (ppt)	Models 5 and 6: Whole-Weight Current Dioxin (ppq)
Caloric Intake (kcal/day) (Continuous)	--	n=892 r=-0.062 p=0.064	n=892 r=-0.055 p=0.101
Caloric Intake (kcal/day) (Discrete)	≤2000 >2000	$\bar{x}$=15.21 (n=529) $\bar{x}$=13.46 (n=363) p=0.095	$\bar{x}$=86.69 (n=529) $\bar{x}$=77.45 (n=363) p=0.164
Body Fat (percent) (Continuous)	--	n=894 r=0.284 p<0.001	n=894 r=0.296 p<0.001
Body Fat (percent) (Discrete)	Lean or Normal Obese	$\bar{x}$=12.68 (n=669) $\bar{x}$=21.66 (n=225) p<0.001	$\bar{x}$=71.35 (n=669) $\bar{x}$=131.20 (n=225) p<0.001
Serum Insulin (mIU/ml) (Continuous)	--	n=894 r=0.134 p<0.001	n=894 r=0.153 p<0.001
Serum Insulin (mIU/ml) (Discrete)	0-56 >56	$\bar{x}$=12.98 (n=406) $\bar{x}$=15.95 (n=488) p=0.005	$\bar{x}$=71.00 (n=406) $\bar{x}$=94.92 (n=488) p<0.001
Cholesterol (mg/dl) (Continuous)	--	n=894 r=0.052 p=0.123	n=894 r=0.142 p<0.001
Cholesterol (mg/dl) (Discrete)	0-200 200-239 >239	$\bar{x}$=13.74 (n=294) $\bar{x}$=14.73 (n=340) $\bar{x}$=15.21 (n=260) p=0.521	$\bar{x}$=69.89 (n=294) $\bar{x}$=84.58 (n=340) $\bar{x}$=99.14 (n=260) p=0.003

Table 8-6. (Continued)
Associations Between Health Variables and Estimates of Dioxin Exposure

Covariate	Covariate Category	Model 4: Lipid-Adjusted Current Dioxin (ppt)	Models 5 and 6: Whole-Weight Current Dioxin (ppq)
HDL Cholesterol (mg/dl) (Continuous)	--	n=881 r=-0.157	n=881 r=-0.171
		p<0.001	p<0.001
HDL Cholesterol (mg/dl) (Discrete)	0-35	x̄=16.86 (n=246)	x̄=101.25 (n=246)
	>35	x̄=13.59 (n=635)	x̄=75.48 (n=635)
		p=0.008	p=0.001
Cholesterol-HDL Cholesterol Ratio (Continuous)	--	n=881 r=0.145	n=881 r=0.211
		p<0.001	p<0.001
Cholesterol-HDL Cholesterol Ratio (Discrete)	0-5	x̄=12.34 (n=363)	x̄=63.74 (n=363)
	>5	x̄=16.11 (n=518)	x̄=97.67 (n=518)
		p<0.001	p<0.001
Physical Activity Index	Sedentary	x̄=15.93 (n=513)	x̄=91.67 (n=513)
	Moderate	x̄=13.68 (n=163)	x̄=78.27 (n=163)
	Very Active	x̄=12.23 (n=218)	x̄=69.30 (n=218)
		p=0.008	p=0.011
Diabetic Class[a]	Normal	x̄=13.18 (n=646)	x̄=73.55 (n=646)
	Impaired	x̄=19.31 (n=107)	x̄=117.54 (n=107)
	Diabetic	x̄=18.41 (n=140)	x̄=113.81 (n=140)
		p<0.001	p<0.001
Diabetic Severity[b]	No Treatment	x̄=16.04 (n=74)	x̄=96.76 (n=74)
	Diet Only	x̄=20.52 (n=31)	x̄=142.30 (n=31)
	Oral Hypoglycemic	x̄=49.76 (n=18)	x̄=325.16 (n=18)
	Insulin Dependent	x̄=9.25 (n=17)	x̄=50.08 (n=17)
		p<0.001	p<0.001

Table 8-6. (Continued)
Associations Between Health Variables and Estimates of Dioxin Exposure

Covariate	Covariate Category	Model 4: Lipid-Adjusted Current Dioxin (ppt)	Models 5 and 6: Whole-Weight Current Dioxin (ppq)
Family History of Diabetes	No	$\bar{x}$=13.87 (n=677)	$\bar{x}$=78.65 (n=677)
	Yes	$\bar{x}$=16.60 (n=199)	$\bar{x}$=97.80 (n=199)
		p=0.038	p=0.023
Family History of Heart Disease	No	$\bar{x}$=15.39 (n=362)	$\bar{x}$=88.05 (n=362)
	Yes	$\bar{x}$=13.96 (n=519)	$\bar{x}$=79.90 (n=519)
		p=0.187	p=0.234
Family History of Heart Disease Before Age 45	No	$\bar{x}$=14.60 (n=773)	$\bar{x}$=83.31 (n=773)
	Yes	$\bar{x}$=13.17 (n=86)	$\bar{x}$=75.82 (n=86)
		p=0.404	p=0.489
Currently Taking Blood Pressure Medication	No	$\bar{x}$=14.36 (n=709)	$\bar{x}$=80.80 (n=709)
	Yes	$\bar{x}$=15.20 (n=185)	$\bar{x}$=93.08 (n=185)
		p=0.522	p=0.150

[a] Diabetic Class: Normal: <140 mg/dl 2-hour postprandial glucose.
Impaired: ≥140-<200 mg/dl 2-hour postprandial glucose.
Diabetic: Verified past history of diabetes or ≥200 mg/dl 2-hour postprandial glucose.

[b] Diabetic severity analyzed only for participants classified as diabetic.

Note: Means for discrete covariates are transformed from the logarithmic (base 2) scale for initial dioxin in Model 2, and from the ($\log_2 (X+1)$) scale for current dioxin in Models 4, 5, and 6.

group in Model 1 (p=0.021) and dioxin in Model 3 (p=0.024), Model 4 (p=0.008), and Models 5 and 6 (p=0.001) and HDL cholesterol. A significant difference between the percentage of participants in the lower HDL cholesterol category was seen between Ranch Hands (28.3%) and Comparisons (23.8%) in Model 1. In Model 3, a significant difference between the percentage of participants with lower HDL cholesterol levels was seen among Comparisons (24.4%), background Ranch Hands (23.8%), low Ranch Hands (29.3%), and high Ranch Hands (32.5%). The mean current dioxin levels were lower for participants with HDL cholesterol levels greater than 35 mg/dl in Models 4 through 6.

Statistically significant associations were found between the cholesterol-HDL ratio and dioxin for Model 2 (p=0.004), Model 3 (p<0.001), Model 4 (p<0.001), and Models 5 and 6 (p<0.001). As dioxin levels increased, the cholesterol-HDL cholesterol ratio increased in Models 2, 4, 5, and 6. In Model 3, the mean cholesterol-HDL cholesterol ratio in the Comparison, background Ranch Hand, low Ranch Hand, and high Ranch Hand categories was 5.45, 5.31, 5.46, and 5.85 respectively. Dichotomizing the cholesterol-HDL cholesterol ratio into less than or equal to five and greater than five revealed significant associations for Model 2 (p=0.040), Model 3 (p=0.001), Model 4 (p<0.001), and Models 5 and 6 (p<0.001). The mean dioxin levels were higher for participants with cholesterol-HDL cholesterol ratios greater than 5 in Models 2, 4, 5, and 6. In Model 3, a significant difference between the percentage of participants with a ratio less than five was seen among Comparisons (42.9%), background Ranch Hands (47.3%), low Ranch Hands (41.8%), and high Ranch Hands (31.8%).

The examination of the physical activity index showed a significant association with dioxin in Model 2 (p=0.012), Model 4 (p=0.008), and Models 5 and 6 (p=0.011). In each of these models, the mean dioxin levels were smaller as activity levels progressed from sedentary to moderate activity to very active. This relationship between the physical activity index and dioxin is most likely due to the relationship between dioxin and body fat, as discussed above.

A highly significant association between dioxin and diabetic class was revealed in Models 3 through 6 (p≤0.001). In Model 3, a significant difference between the percentage of participants classified as normal, impaired, and diabetic was seen among Comparisons (75.5%, 10.3%, and 14.2%), background Ranch Hands (79.9%, 8.8%, and 11.3%), low Ranch Hands (67.7%, 12.7%, and 19.6%), and high Ranch Hands (66.2%, 15.8%, and 18.1%). In Models 4 through 6, participants classified as impaired or diabetic had higher mean current dioxin levels than participants classified as normal. This relationship between diabetic class and dioxin also may be due to the association between dioxin and body fat.

Examining the association between diabetic severity and dioxin in diabetics revealed significant relationships in the analysis of Model 3 (p=0.050), Model 4 (p<0.001), and Models 5 and 6 (p<0.001). In Model 3, a significant difference between the percentage of participants with no treatment for diabetes, treatment through diet only, oral hypoglycemic, and insulin dependent was seen among Comparisons (57.0%, 21.2%, 13.3%, and 8.6%), background Ranch Hands (61.9%, 19.1%, 0.0%, and 19.1%), low Ranch Hands (54.9%, 23.5%, 11.8%, and 9.8%), and high Ranch Hands (42.6%, 23.4%, 25.5%, and 8.2%). In Models 4, 5, and 6, the mean current dioxin level was highest for the oral hypoglycemic participants followed by participants treating diabetes through diet only, participants with no treatment, and insulin dependent participants.

The analysis of family history of diabetes revealed significant associations with current dioxin in Models 4 ($p=0.038$) and Models 5 and 6 ($p=0.023$). In each model, the mean current dioxin level was higher for participants with a family history of diabetes, which may be due to the association between dioxin and body fat.

No significant ($p \leq 0.05$) associations were observed between family history of heart disease, family history of heart disease before age 45, or current use of blood pressure medication and any of the five estimates of dioxin exposure.

SUN-EXPOSURE VARIABLES

Results of tests of association between a participant's reaction to sun exposure and the estimates of dioxin exposure are shown in Table 8-7. These statistics are based on non-Black participants only, because the sun-exposure covariates were used in adjusted analyses of skin neoplasms only, and Blacks were excluded from the skin neoplasm analyses.

Model 2 showed a significant relationship between initial dioxin and hair color ($p=0.038$). The mean initial dioxin level was highest for participants with dark brown hair followed by black, light brown, blonde, and red hair colors.

The analysis of a participant's skin reaction to the sun after repeated exposure revealed a significant association with current dioxin in Models 5 and 6 ($p=0.034$). The mean current dioxin level was highest for participants who tan dark brown followed by participants who tan moderately, participants who tan mildly, and those who freckle but do not tan.

Analysis of average lifetime residential latitude revealed significant associations with group in Model 1 ($p=0.001$) and dioxin in Model 2 ($p=0.029$) and Model 3 ($p=0.005$). In Model 1, a significant difference between the percentage of participants living in areas less than 37 degrees latitude was seen between Ranch Hands (44.6%) and Comparisons (51.9%). In Model 2, the mean initial dioxin levels were greater for participants living south of 37 degrees latitude. In Model 3, a significant difference between the percentage of participants living south of 37 degrees latitude was seen among Comparisons (51.4%), background Ranch Hands (44.7%), low Ranch Hands (40.0%), and high Ranch Hands (45.3%).

No significant ($p \leq 0.05$) associations were observed between the five estimates of dioxin exposure and skin color, eye color, reaction of skin to sun after at least 2 hours, or a composite sun-reaction index.

OTHER MISCELLANEOUS COVARIATES

Results of tests of association between other miscellaneous covariates and the estimates of dioxin exposure are shown in Table 8-8. Examining the association between current total household income in both its continuous and discrete forms and dioxin revealed highly significant relationships in the analysis of Models 2 through 6 ($p<0.001$ for each model both

Table 8-7.
Associations Between Sun-Exposure Variables and Estimates of Dioxin Exposure (Non-Blacks Only)

Covariate	Covariate Category	Model 1: Ranch Hand	Model 1: Comparison	Model 2: Initial Dioxin
Skin Color		n=895	n=1,202	
	Dark	0.0%	0.1%	(n=0)
	Medium	4.1%	2.8%	$\bar{x}$=153.73 (n=21)
	Pale	17.3%	17.6%	$\bar{x}$=168.36 (n=72)
	Dark Peach	55.2%	57.7%	$\bar{x}$=176.44 (n=285)
	Pale Peach	23.4%	21.9%	$\bar{x}$=157.46 (n=106)
		p=0.311		p=0.701
Hair Color		n=896	n=1,202	
	Black	18.5%	22.2%	$\bar{x}$=173.21 (n=90)
	Dark Brown	48.9%	47.4%	$\bar{x}$=189.93 (n=239)
	Light Brown	27.1%	24.7%	$\bar{x}$=144.13 (n=128)
	Blonde	4.9%	4.6%	$\bar{x}$=134.17 (n=24)
	Red	0.6%	1.0%	$\bar{x}$=96.56 (n=3)
	Bald	0.0%	0.1%	(n=0)
		p=0.231		p=0.038
Eye Color		n=896	n=1,200	
	Brown	28.7%	30.9%	$\bar{x}$=188.50 (n=149)
	Hazel	23.3%	20.4%	$\bar{x}$=155.34 (n=112)
	Green	5.1%	5.6%	$\bar{x}$=166.24 (n=28)
	Gray	4.7%	4.2%	$\bar{x}$=154.11 (n=23)
	Blue	38.2%	38.9%	$\bar{x}$=167.31 (n=172)
		p=0.487		p=0.526
Reaction of Skin to Sun After at Least Two Hours		n=895	n=1,203	
	No Reaction	37.8%	39.0%	$\bar{x}$=164.25 (n=191)
	Becomes Red	41.1%	39.1%	$\bar{x}$=170.34 (n=193)
	Burns	12.9%	15.7%	$\bar{x}$=204.62 (n=60)
	Painfully Burns	8.3%	6.2%	$\bar{x}$=150.85 (n=39)
		p=0.085		p=0.352
Reaction of Skin to Sun After Repeated Exposure		n=892	n=1,199	
	Tans Dark Brown	29.5%	28.7%	$\bar{x}$=164.62 (n=152)
	Tans Moderately	51.6%	51.5%	$\bar{x}$=172.24 (n=244)
	Tans Mildly	16.8%	17.8%	$\bar{x}$=181.98 (n=77)
	Freckles-No Tan	2.1%	2.1%	$\bar{x}$=91.69 (n=8)
		p=0.944		p=0.244

Table 8-7. (Continued)
Associations Between Sun-Exposure Variables and Estimates of Dioxin Exposure (Non-Blacks Only)

Covariate	Covariate Category	Model 1 Ranch Hand	Model 1 Comparison	Model 2 Initial Dioxin
Composite Sun-Reaction Index[a]		n=895	n=1,204	
	High	8.9%	7.6%	$\bar{x}$=152.71 (n=41)
	Medium	20.2%	23.7%	$\bar{x}$=194.10 (n=97)
	Low	70.8%	68.8%	$\bar{x}$=166.01 (n=345)
		p=0.119		p=0.256
Average Lifetime Residential Latitude		n=893	n=1,187	
	< 37°	44.6%	51.9%	$\bar{x}$=189.57 (n=206)
	≥ 37°	55.4%	48.1%	$\bar{x}$=157.26 (n=276)
		p=0.001		p=0.029

Table 8-7. (Continued)
Associations Between Sun-Exposure Variables and Estimates of Dioxin Exposure (Non-Blacks Only)

Covariate	Covariate Category	Model 3: Comparison	Model 3: Background Ranch Hand	Model 3: Low Ranch Hand	Model 3: High Ranch Hand
Skin Color		n=1,008	n=358	n=237	n=247
	Dark	0.1%	0.0%	0.0%	0.0%
	Medium	2.8%	3.9%	4.2%	4.5%
	Pale	17.7%	18.7%	13.1%	16.6%
	Dark Peach	56.7%	52.0%	59.5%	58.3%
	Pale Peach	22.8%	25.4%	23.2%	20.7%
			p=0.628		
Hair Color		n=1,008	n=359	n=237	n=247
	Black	20.8%	17.8%	17.3%	19.8%
	Dark Brown	48.5%	47.4%	44.3%	54.3%
	Light Brown	24.5%	29.5%	31.2%	21.9%
	Blonde	5.0%	4.7%	6.3%	3.6%
	Red	1.1%	0.6%	0.8%	0.4%
	Bald	0.1%	0.0%	0.0%	0.0%
			p=0.411		
Eye Color		n=1,006	n=359	n=237	n=247
	Brown	29.6%	26.5%	27.4%	34.0%
	Hazel	20.6%	24.2%	23.6%	22.7%
	Green	5.7%	5.0%	5.1%	6.5%
	Gray	4.0%	4.5%	4.6%	4.9%
	Blue	40.2%	39.8%	39.2%	32.0%
			p=0.617		
Reaction of Skin to Sun After at Least 2 Hours		n=1,005	n=359	n=236	n=247
	No Reaction	38.5%	33.7%	38.1%	40.9%
	Becomes Red	39.7%	43.7%	40.7%	39.3%
	Burns	15.3%	13.4%	11.4%	13.4%
	Painfully Burns	6.5%	9.2%	9.8%	6.5%
			p=0.293		
Reaction of Skin to Sun After Repeated Exposure		n=1,002	n=358	n=235	n=246
	Tans Dark Brown	28.6%	25.7%	30.6%	32.5%
	Tans Moderately	51.6%	53.6%	50.6%	50.8%
	Tans Mildly	17.4%	17.9%	15.7%	16.3%
	Freckles-No Tan	2.4%	2.8%	3.0%	0.4%
			p=0.506		

Table 8-7. (Continued)
Associations Between Sun-Exposure Variables and Estimates of Dioxin Exposure (Non-Blacks Only)

		Model 3			
Covariate	**Covariate Category**	**Comparison**	**Background Ranch Hand**	**Low Ranch Hand**	**High Ranch Hand**
Composite Sun-Reaction Index[a]		n=1,006	n=359	n=236	n=247
	High	8.1%	10.0%	10.2%	6.9%
	Medium	23.5%	20.6%	19.1%	21.1%
	Low	68.5%	69.4%	70.8%	72.1%
			p=0.484		
Average Lifetime Residential Latitude		n=997	n=358	n=235	n=247
	< 37°	51.4%	44.7%	40.0%	45.3%
	≥ 37°	48.6%	55.3%	60.0%	54.7%
			p=0.005		

Table 8-7. (Continued)
Associations Between Sun-Exposure Variables and Estimates of Dioxin Exposure (Non-Blacks Only)

		Model 4	Models 5 and 6
Covariate	Covariate Category	Lipid-Adjusted Current Dioxin	Whole-Weight Current Dioxin
Skin Color	Dark	(n=0)	(n=0)
	Medium	$\bar{x}$=13.60 (n=35)	$\bar{x}$=75.41 (n=35)
	Pale	$\bar{x}$=13.37 (n=139)	$\bar{x}$=75.51 (n=139)
	Dark Peach	$\bar{x}$=15.61 (n=471)	$\bar{x}$=91.97 (n=471)
	Pale Peach	$\bar{x}$=13.11 (n=197)	$\bar{x}$=72.24 (n=197)
		p=0.194	p=0.070
Hair Color	Black	$\bar{x}$=15.14 (n=154)	$\bar{x}$=87.15 (n=154)
	Dark Brown	$\bar{x}$=15.60 (n=409)	$\bar{x}$=89.87 (n=409)
	Light Brown	$\bar{x}$=12.84 (n=234)	$\bar{x}$=74.10 (n=234)
	Blonde	$\bar{x}$=12.53 (n=41)	$\bar{x}$=67.88 (n=41)
	Red	$\bar{x}$=11.52 (n=5)	$\bar{x}$=64.98 (n=5)
	Bald	(n=0)	(n=0)
		p=0.205	p=0.247
Eye Color	Brown	$\bar{x}$=16.81 (n=244)	$\bar{x}$=100.14 (n=244)
	Hazel	$\bar{x}$=13.41 (n=199)	$\bar{x}$=76.22 (n=199)
	Green	$\bar{x}$=14.83 (n=46)	$\bar{x}$=79.96 (n=46)
	Gray	$\bar{x}$=14.38 (n=39)	$\bar{x}$=88.39 (n=39)
	Blue	$\bar{x}$=13.60 (n=315)	$\bar{x}$=76.53 (n=315)
		p=0.156	p=0.076
Reaction of Skin to Sun After at Least Two Hours	No Reaction	$\bar{x}$=15.52 (n=312)	$\bar{x}$=90.46 (n=312)
	Becomes Red	$\bar{x}$=13.90 (n=350)	$\bar{x}$=79.31 (n=350)
	Burns	$\bar{x}$=15.25 (n=108)	$\bar{x}$=86.57 (n=108)
	Painfully Burns	$\bar{x}$=12.46 (n=72)	$\bar{x}$=70.31 (n=72)
		p=0.344	p=0.313
Reaction of Skin to Sun After Repeated Exposure	Tans Dark Brown	$\bar{x}$=15.54 (n=244)	$\bar{x}$=88.00 (n=244)
	Tans Moderately	$\bar{x}$=14.61 (n=436)	$\bar{x}$=85.09 (n=436)
	Tans Mildly	$\bar{x}$=13.50 (n=141)	$\bar{x}$=77.34 (n=141)
	Freckles-No Tan	$\bar{x}$=7.57 (n=18)	$\bar{x}$=38.05 (n=18)
		p=0.053	p=0.034

Table 8-7. (Continued)
Associations Between Sun-Exposure Variables and Estimates of Dioxin Exposure (Non-Blacks Only)

Covariate	Covariate Category	Model 4: Lipid-Adjusted Current Dioxin	Models 5 and 6: Whole-Weight Current Dioxin
Composite Sun-Reaction Index[a]	High	$\bar{x}$=12.32 (n=77)	$\bar{x}$=69.83 (n=77)
	Medium	$\bar{x}$=15.01 (n=171)	$\bar{x}$=86.31 (n=171)
	Low	$\bar{x}$=14.69 (n=594)	$\bar{x}$=84.43 (n=594)
		p=0.380	p=0.395
Average Lifetime Residential Latitude	< 37°	$\bar{x}$=15.11 (n=366)	$\bar{x}$=87.37 (n=366)
	≥ 37°	$\bar{x}$=14.09 (n=474)	$\bar{x}$=80.46 (n=474)
		p=0.357	p=0.328

[a] Composite sun reaction index (from reaction of skin after at least 2 hours and reaction of skin after repeated exposure):

High: Burns painfully, freckles with no tan, or both.
Medium: Burns, tans mildly, or both.
Low: All other reactions.

Note: Means for discrete covariates are transformed from the logarithmic (base 2) scale for initial dioxin in Model 2, and from the ($\log_2$ (X+1)) scale for current dioxin in Models 4, 5, and 6.

Table 8-8.
Associations Between Other Miscellaneous Covariates and Estimates of Dioxin Exposure

Covariate	Covariate Category	Model 1		Model 2
		Ranch Hand	Comparison	Initial Dioxin
Current Total Household Income (Continuous)	--	n=941 x̄=$60,550	n=1,263 x̄=$59,293	n=516 r=-0.222
		p=0.268		p<0.001
Current Total Household Income (Discrete)		n=941	n=1,263	
	≤$55,000	47.2%	50.3%	x̄=199.15 (n=275)
	>$55,000	52.8%	49.7%	x̄=137.19 (n=241)
		p=0.163		p<0.001
Personality Type		n=951	n=1,280	
	A	44.1%	41.8%	x̄=153.97 (n=215)
	B	55.9%	58.2%	x̄=176.32 (n=304)
		p=0.305		p=0.099
Education		n=952	n=1,281	
	College	50.6%	53.1%	x̄=138.46 (n=208)
	High School	49.4%	46.9%	x̄=188.14 (n=312)
		p=0.269		p<0.001
Current Employment Status		n=952	n=1,279	
	No	22.7%	21.1%	x̄=136.59 (n=111)
	Yes	77.3%	78.9%	x̄=175.59 (n=409)
		p=0.400		p=0.011
Current Marital Status		n=952	n=1,279	
	Not Married	13.8%	14.9%	x̄=161.02 (n=76)
	Married	86.2%	85.1%	x̄=167.37 (n=444)
		p=0.504		p=0.735
Current Parental Status (child less than 18 years old)		n=952	n=1,281	
	No	75.9%	72.1%	x̄=155.12 (n=382)
	Yes	24.1%	27.9%	x̄=202.20 (n=138)
		p=0.048		p=0.004

Table 8-8. (Continued)
Associations Between Other Miscellaneous Covariates and Estimates of Dioxin Exposure

Covariate	Covariate Category	Model 1 Ranch Hand	Model 1 Comparison	Model 2 Initial Dioxin
Worked with		n=952	n=1,279	
Vibrating Power	No	75.6%	79.4%	$\bar{x}$=162.76 (n=375)
Equipment or	Yes	24.4%	20.6%	$\bar{x}$=176.28 (n=145)
Tools				
		p=0.037		p=0.376
Composite		n=952	n=1,279	
Exposure to Heavy	No	84.6%	84.4%	$\bar{x}$=163.26 (n=427)
Metals	Yes	15.4%	15.6%	$\bar{x}$=181.75 (n=93)
		p=0.986		p=0.309

Table 8-8. (Continued)
Associations Between Other Miscellaneous Covariates and Estimates of Dioxin Exposure

Covariate	Covariate Category	Model 3: Comparison	Model 3: Background Ranch Hand	Model 3: Low Ranch Hand	Model 3: High Ranch Hand
Current Total Household Income (Continuous)	--	n=1,048 $\bar{x}$=\$60,000	n=367 $\bar{x}$=\$67,800	n=256 $\bar{x}$=\$61,328	n=260 $\bar{x}$=\$50,346
			p<0.001		
Current Total Household Income (Discrete)		n=1,048	n=367	n=256	n=260
	≤\$55,000	49.3%	37.9%	42.6%	63.8%
	>\$55,000	50.7%	62.1%	57.4%	36.2%
			p<0.001		
Personality Type		n=1,062	n=374	n=259	n=260
	A	41.9%	46.8%	44.4%	38.5%
	B	58.1%	53.2%	55.6%	61.5%
			p=0.168		
Education		n=1,063	n=374	n=260	n=260
	College	53.2%	66.6%	49.6%	30.4%
	High School	46.8%	33.4%	50.4%	69.6%
			p<0.001		
Current Employment Status		n=1,061	n=374	n=260	n=260
	No	19.4%	24.3%	26.2%	16.5%
	Yes	80.6%	75.7%	73.8%	83.5%
			p=0.010		
Current Marital Status		n=1,061	n=374	n=260	n=260
	Not Married	13.7%	11.8%	13.8%	15.4%
	Married	86.3%	88.2%	86.2%	84.6%
			p=0.616		
Current Parental Status (child less than 18 years old)		n=1,063	n=374	n=260	n=260
	No	72.6%	79.4%	79.6%	67.3%
	Yes	27.4%	20.6%	20.4%	32.7%
			p=0.001		

Table 8-8. (Continued)
Associations Between Other Miscellaneous Covariates and Estimates of Dioxin Exposure

		Model 3			
Covariate	**Covariate Category**	**Comparison**	**Background Ranch Hand**	**Low Ranch Hand**	**High Ranch Hand**
Worked With		n=1,061	n=374	n=260	n=260
Vibrating Power	No	80.0%	80.5%	73.8%	70.4%
Equipment or Tools	Yes	20.0%	19.5%	26.2%	29.6%
			p=0.002		
Composite		n=1,061	n=374	n=260	n=260
Exposure to Heavy	No	84.2%	88.5%	82.7%	81.5%
Metals	Yes	15.8%	11.5%	17.3%	18.5%
			p=0.071		

Table 8-8. (Continued)
Associations Between Other Miscellaneous Covariates and Estimates of Dioxin Exposure

Covariate	Covariate Category	Model 4: Lipid-Adjusted Current Dioxin	Models 5 and 6: Whole-Weight Current Dioxin
Current Total Household Income (Continuous)	--	n=883 r=-0.253	n=883 r=-0.240
		p<0.001	p<0.001
Current Total Household Income (Discrete)	≤$55,000 >$55,000	$\bar{x}$=18.37 (n=414) $\bar{x}$=12.00 (n=469)	$\bar{x}$=107.12 (n=414) $\bar{x}$=68.03 (n=469)
		p<0.001	p<0.001
Personality Type	A B	$\bar{x}$=13.34 (n=390) $\bar{x}$=15.53 (n=503)	$\bar{x}$=76.76 (n=390) $\bar{x}$=88.57 (n=503)
		p=0.037	p=0.075
Education	College High School	$\bar{x}$=11.10 (n=457) $\bar{x}$=19.17 (n=437)	$\bar{x}$=62.73 (n=457) $\bar{x}$=111.68 (n=437)
		p<0.001	p<0.001
Current Employment Status	No Yes	$\bar{x}$=12.21 (n=202) $\bar{x}$=15.28 (n=692)	$\bar{x}$=69.22 (n=202) $\bar{x}$=87.78 (n=692)
		p=0.010	p=0.013
Current Marital Status	Not Married Married	$\bar{x}$=14.69 (n=120) $\bar{x}$=14.51 (n=774)	$\bar{x}$=84.95 (n=120) $\bar{x}$=82.93 (n=774)
		p=0.907	p=0.837
Current Parental Status (child less than 18 years old)	No Yes	$\bar{x}$=13.48 (n=679) $\bar{x}$=18.40 (n=215)	$\bar{x}$=77.16 (n=679) $\bar{x}$=105.51 (n=215)
		p<0.001	p<0.001

Table 8-8. (Continued)
Associations Between Other Miscellaneous Covariates and Estimates of Dioxin Exposure

		Model 4	Models 5 and 6
Covariate	**Covariate Category**	**Lipid-Adjusted Current Dioxin**	**Whole-Weight Current Dioxin**
Worked With Vibrating Power Equipment or Tools	No	$\bar{x}$=13.82 (n=676)	$\bar{x}$=79.25 (n=676)
	Yes	$\bar{x}$=16.97 (n=218)	$\bar{x}$=96.75 (n=218)
		p=0.014	p=0.032
Composite Exposure to Heavy Metals	No	$\bar{x}$=13.98 (n=758)	$\bar{x}$=80.00 (n=758)
	Yes	$\bar{x}$=18.02 (n=136)	$\bar{x}$=103.53 (n=136)
		p=0.011	p=0.020

Note: Means for discrete covariates are transformed from the logarithmic (base 2) scale for initial dioxin in Model 2, and from the ($\log_2$ (X+1)) scale for current dioxin in Models 4, 5, and 6.

continuous and discrete). Current income was greater for those participants with lower dioxin levels in Models 2, 4, 5, and 6. In Model 3, a significant difference in the percentage of participants with an income less than or equal to $55,000 per year was observed for Comparisons (49.3%), background Ranch Hands (37.9%), low Ranch Hands (42.6%), and high Ranch Hands (63.8%). This relationship between current total household income and dioxin may be due to the association between dioxin and occupation, as discussed previously (officers tended to have higher current total household incomes than enlisted personnel).

Model 4 revealed a significant association between current lipid-adjusted dioxin and personality type ($p=0.037$). Participants with personality Type A had a lower mean current dioxin level than participants with personality Type B.

A significant relationship between education and dioxin was revealed for Models 2 through 6 ($p<0.001$ for each model). The mean dioxin levels in Models 2, 4, 5, and 6 were lower for participants with a college education than for participants with a high school education. In Model 3, a significant difference between the percentage of participants with a college education was seen among Comparisons (53.2%), background Ranch Hands (66.6%), low Ranch Hands (49.6%), and high Ranch Hands (30.4%). The relationship between education and dioxin in Models 2 through 6 is most likely due to the relationship between dioxin and military occupation, as discussed previously (a greater percentage of officers were college-educated, as compared to enlisted personnel).

Statistically significant associations were found between current employment status and dioxin for Model 2 ($p=0.011$), Model 3 ($p=0.010$), Model 4 ($p=0.010$), and Models 5 and 6 ($p=0.013$). In Models 2, 4, 5, and 6, participants who were currently employed had higher dioxin levels than those not currently employed (this group would contain retired participants as well). In Model 3, a significant difference between the percentage of participants not currently employed was seen among Comparisons (19.4%), background Ranch Hands (24.3%), low Ranch Hands (26.2%), and high Ranch Hands (16.5%).

Current parental status (having a child less than 18 years old: yes, no) was shown to have a significant relationship to group in Model 1 ($p=0.048$) and dioxin in Model 2 ($p=0.004$), Model 3 ($p=0.001$), Model 4 ($p<0.001$), and Models 5 and 6 ($p<0.001$). In Models 2, 4, 5, and 6, participants with children under the age of 18 had higher mean dioxin levels. In Model 1, a significant difference between the percentage of participants with no children under the age of 18 was seen between Ranch Hands (75.9%) and Comparisons (72.1%). In Model 3, a significant difference between the percentage of participants with no children under the age of 18 also was seen among Comparisons (72.6%), background Ranch Hands (79.4%), low Ranch Hands (79.6%), and high Ranch Hands (67.3%).

The analysis of participants who reported having worked with vibrating power equipment or tools for 30 days or more revealed a significant relationship with group in Model 1 ($p=0.037$) and dioxin in Model 3 ($p=0.002$), Model 4 ($p=0.014$), and Models 5 and 6 ($p=0.032$). A significant difference between the percentage of participants who had not worked with vibrating power equipment was seen between Ranch Hands (75.6%) and Comparisons (79.4%) in Model 1. In Models 4, 5, and 6, participants who had worked with vibrating power equipment or tools had higher mean dioxin levels. In Model 3, a significant difference between the percentage of participants who had not worked with vibrating power equipment was seen among Comparisons (80.0%), background Ranch Hands (80.5%), low Ranch Hands (73.8%), and high Ranch Hands (70.4%).

Testing the association between exposure to heavy metals (worked for 30 days or more with lead, mercury, chromium, nickel, copper, cadmium, manganese, arsenic, selenium, or molybdenum) and dioxin showed significant positive relationships in the analysis of Models 4 ($p=0.011$) and Models 5 and 6 ($p=0.020$). Participants who have been exposed to heavy metals had higher mean current dioxin levels than those participants who were not exposed.

No significant ($p \leq 0.05$) associations were observed between current marital status and the five estimates of dioxin exposure.

SUMMARY

The purpose of this chapter is to determine if the covariates used throughout this report are associated with the five estimates of dioxin exposure and, therefore, could potentially be confounding variables in subsequent statistical analyses in this report. However, the associations between covariates and the estimates of dioxin exposure were not adjusted for known and suspected confounders and, therefore, the results should not be interpreted as indicating causal relationships between dioxin exposure and covariate levels.

The demographic variables of age, race, and occupation were used as matching variables in the original study design. As expected, there were no significant differences between Ranch Hands and Comparisons for these three variables. As exhibited in previous study analyses, dioxin was significantly associated with military occupation. Officers had the lowest levels, followed by enlisted flyers and enlisted groundcrew. Because the Ranch Hand enlisted groundcrew tended to be younger on average than the Ranch Hand officers and enlisted flyers, a strong negative association also was seen between dioxin levels and age. Race was not significantly associated with dioxin.

Ranch Hands tended to serve in combat longer than Comparisons. This relationship is explained by the fact that the Ranch Hands were stationed in combat for their entire time of duty in SEA, whereas the Comparisons conducted missions in combat areas and then returned to a station outside of the combat zone. Also, approximately 25 percent of Comparisons did not serve in combat at all and approximately 80 percent of them served in combat less than 1 year. Positive associations were seen between dioxin and days in combat within the Ranch Hand cohort, indicating that Ranch Hands who had longer times of duty in Vietnam have the higher levels of dioxin. No significant associations were observed between the presence of post-SEA acne and group or dioxin.

Ranch Hands have higher levels of current wine use than Comparisons. Within the Ranch Hand cohort, participants with lower dioxin levels have greater amounts of wine consumption. This association also may be due to occupation because officers are more likely to drink wine than are enlisted personnel ($p<0.001$). No significant associations were seen between total current alcohol use or lifetime alcohol history and group or dioxin. No significant associations were observed between either current cigarette smoking or lifetime cigarette smoking history and group or dioxin.

The percentage of Comparisons exposed to ionizing radiation was larger than the percentage of Ranch Hands exposed. However, a greater percentage of Ranch Hands were exposed to herbicides and insecticides. Questions were posed to the participants to capture post-SEA exposure to possible carcinogens. However the data appear to indicate that the participants may have included SEA exposures as well. Within the Ranch Hand cohort, higher dioxin levels were seen for those participants exposed to industrial chemicals and degreasing chemicals. No significant associations were observed between group or dioxin and asbestos exposure. Again, the significant associations between dioxin and industrial chemical exposure and between dioxin and degreasing chemical exposure may be related to occupation. A smaller percentage of Ranch Hand officers tended to be exposed to industrial chemicals and degreasing chemicals than Ranch Hand enlisted personnel.

The significant associations between dioxin and health measurements, such as HDL cholesterol and the cholesterol-HDL cholesterol ratio, can be partially explained by confounding with body fat. Higher body fat measurements correspond to higher dioxin levels, lower levels of HDL cholesterol, and higher cholesterol-HDL cholesterol ratio measurements. Also, higher body fat is more likely to occur with sedentary lifestyles.

Of covariates related to sun exposure or reaction to sun exposure, non-Black Ranch Hands with darker hair tended to have higher levels of initial dioxin than those with lighter-colored hair. Higher levels of current dioxin were seen in non-Black Ranch Hands who tanned easier. The relationship between dioxin and hair color also may be related to occupation, in that a greater percentage of Ranch Hand officers had light brown hair than did Ranch Hand enlisted personnel. Conversely, a larger percentage of Ranch Hand enlisted personnel had dark brown hair than did Ranch Hand officers. A larger percentage of Ranch Hands lived in latitudes farther from the equator than did Comparisons. However, within the Ranch Hand cohort, higher levels of initial dioxin were seen for those participants who live in more southerly latitudes. No other significant associations were observed with the other sun-exposure or reaction to sun exposure covariates.

The relationships between dioxin and current total household income, education, current employment status, and having a child less than 18 years old also may directly or indirectly relate to occupation and age. Officers currently make more money than enlisted personnel, and officers have the lowest dioxin levels; consequently, there is a negative association between income and dioxin. A larger percentage of Ranch Hand officers tended to be college graduates than enlisted personnel, and consequently college graduates have lower dioxin levels than high school graduates. More Ranch Hand enlisted groundcrew than Ranch Hand officers or enlisted flyers are currently employed, which may be due to their age, income, and level of education. More Ranch Hand enlisted groundcrew than officers or enlisted flyers have children under the age of 18, and participants with children under the age of 18 have higher dioxin levels.

CONCLUSION

The purpose of this chapter is to determine if the covariates used throughout this report are associated with the five estimates of dioxin exposure and, therefore, could potentially be confounding variables in subsequent statistical analyses in this report. However, the associations between covariates and the estimates of dioxin exposure were not adjusted for known and suspected confounders, and therefore, the results should not be interpreted as indicating causal relationships between dioxin exposure and covariate levels.

In general, the Ranch Hand and Comparison groups are similar for a number of the covariates. However, notable exceptions include duration of combat service, reported herbicide exposure, and HDL cholesterol. Ranch Hands tended to serve in combat longer than Comparisons, because Ranch Hands were stationed in combat areas for their entire time of duty in SEA, whereas Comparisons conducted missions in combat zones and then returned to a station outside of combat areas. A greater percentage of Ranch Hands than Comparisons reported herbicide exposure. A possible explanation for this association between group and herbicide exposure may have been the tendency of Ranch Hands to report their exposure to dioxin during their time of duty in SEA. The questionnaire had been structured to capture post-SEA exposure only. The relationship between group and HDL cholesterol is not quite as clear. The group means are not significantly different, but the percentage of Ranch Hand participants considered abnormal (less than 35 mg/dl) is significantly greater than the percentage of Comparisons considered abnormal. The analysis of HDL cholesterol as an endpoint is discussed in Chapter 13, Gastrointestinal Assessment.

Most of the significant associations between dioxin and the covariates in the Ranch Hand group can be attributed to, or partially explained by, the effects of occupation, age, or body fat. Of the three occupational cohorts, enlisted groundcrew have the highest levels of current and initial dioxin. Adjusted analyses in the clinical chapters (Chapters 9 through 20) fully account for group, age, body fat, and other potential confounders to further investigate significant associations between covariates and dioxin. The reader is referred to these chapters for a more complete assessment of the effect of dioxin on the relevant medical endpoints.