CHAPTER 17

RENAL ASSESSMENT

INTRODUCTION

Background

In humans, there is no evidence that the kidneys are target organs for 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD, or dioxin) toxicity. Although renal excretion of phenoxy herbicides (TCDD and 2,4,5-trichlorophenoxyacetic acid [2,4,5-T]) has been well established in animals (1) and humans (2,3), more recent studies indicate that it may be of secondary importance to intestinal elimination (4,5).

Several studies have focused on the renal sequelae of chlorophenol toxicity in laboratory animals. Rats exposed to dichlorophenoxyacetic acid (2,4-D) by cutaneous application were noted to have an increase in renal weight but no histologic changes despite the development of a wasting syndrome (6). In contrast, in a study of TCDD toxicity in guinea pigs, a decrease in kidney weight was noted relative to controls, and histopathologic examination revealed focal mineralization changes in the renal parenchyma (7). Renal anomalies including hydronephrosis in mice (8-10) and hamsters (11) occurred after maternal TCDD exposure at toxic levels. In one study, these effects were limited to an aryl hydrocarbon (Ah) receptor-responsive strain (10). Because the doses of phenoxy herbicides used in these experiments were extreme by any measure of reported human exposure and because routes of administrations were not comparable, the relevance of these and other animal studies to dioxin toxicity in humans is not established.

Renal and urinary tract disease have received relatively little emphasis in morbidity studies of humans exposed to phenoxy herbicides, although an isolated case of hemorrhagic cystitis occurred in a child exposed to high concentrations of TCDD in soil (12). Acute renal failure also has been reported in cases of extreme phenoxy herbicide (though not TCDD) toxicity in man, though the mechanism appears to be secondary to rhabdomyolysis rather than to a direct nephrotoxic effect (13,14).

Epidemiologic studies of populations heavily exposed to dioxin through environmental contamination have failed to document the kidney as a target organ for TCDD toxicity (15-18), and studies of veterans potentially exposed to dioxin in Southeast Asia (SEA) have yielded similar results (19). Prior Air Force Health Study (AFHS) reports, which established the body burden of TCDD by serum levels, found no significant differences in standard indices of renal function between the Ranch Hand and Comparison cohorts (20,21). On routine microscopic urinalysis, however, 10.2 percent of those participants with high (>218 ppt) calculated initial serum dioxin levels were found to have microhematuria versus 4.9 percent of those with lower levels (25 ppt to 57 ppt) (21). Though in clinical practice such hematuria is usually of benign origin, the possibility of occult TCDD-induced renal disease is raised and will bear close scrutiny in this and subsequent examination cycles.

Summary of Previous Analyses of the Air Force Health Study

1982 Baseline Study Summary Results

The 1982 Baseline examination assessed renal disease and function by questionnaire and basic laboratory testing. Based on questionnaire information, the Ranch Hand group reported significantly more kidney disease than the Comparison group ($p=0.039$), but this finding was not substantiated by laboratory test results, even when all abnormalities in blood urea nitrogen, creatinine clearance, presence of occult blood, five or more urinary white blood cells per high-power field (WBC per HPF), and the presence of urine protein were summed. The Comparison group manifested a twofold increase in proteinuria ($p=0.055$). The distributions of creatinine clearance levels were similar for the two groups, as were the means of blood urea nitrogen, urine specific gravity, and urine WBC count. Difficulty in assessing the degree and significance of hidden noncompliance to the full 24-hour urine collection made the interpretation of the creatinine clearance test results somewhat problematic. Known noncompliance to urine collection was much more frequent ($p<0.001$) in the older participants.

The validity of the renal assessment was reinforced by the demonstrated effects of the covariates of age (born in or after 1942, born before 1942) and 2-hour postprandial glucose levels (<120 mg/dl, ≥ 120 mg/dl). Blood urea nitrogen increased with age and urine specific gravity decreased ($p<0.001$ for both), while an abnormally high postprandial glucose level indicative of diabetes was associated only with an increasing urine specific gravity, as expected.

Overall, the Baseline renal assessment suggested an excess of historical kidney disease in the Ranch Hand group not corroborated by laboratory urinalysis testing.

1985 Followup Study Summary Results

A historical assessment of kidney disease and kidney stones by a review-of-systems questionnaire showed no significant differences between the Ranch Hand and Comparison groups. Current renal function was evaluated by five laboratory variables: urine protein, urine red blood cell (RBC) counts, urine WBC counts, blood urea nitrogen, and urine specific gravity. Invasive procedures were not used.

The unadjusted analysis of proteinuria showed no group differences in contrast to the Baseline findings, which showed a marginally significant increase in proteinuria in the Comparison group ($p=0.055$). The unadjusted prevalence rates for hematuria were similar for both the Ranch Hand and Comparison groups. The approximate tenfold increase in hematuria in both groups over that observed at Baseline was most likely due to different laboratory techniques (reagent-strip testing vs. microscopic observation). Similar results were found for leukocyturia. Blood urea nitrogen levels did not vary significantly by group based on the unadjusted analysis. Overall, the blood urea nitrogen results were similar to those observed at the Baseline examination.

Unadjusted urine specific gravity levels manifested marginally significant group differences ($p=0.082$). In contrast to the Baseline values, the followup urine specific gravities were lower, a finding most likely attributable to differences in laboratory methodology (falling drop method vs. multistick procedure).

In conclusion, none of the five renal assessment variables showed a significant difference between the Ranch Hand and Comparison groups by unadjusted tests. However, in the adjusted analyses, all renal measurements except reported kidney disease revealed group-by-covariate interactions. These interactions were often complex, making it impossible to reach a firm conclusion as to the presence of a group difference.

1987 Followup Study Summary Results

Without adjustments for covariates, none of the variables of reported history of kidney disease or kidney stones, urinary protein, urinary red blood cells, urinary white blood cells, blood urea nitrogen, and urine specific gravity showed a significant difference between the two groups for the 1987 examination. In general, these findings were supported by the adjusted analyses. Examination of the group-by-covariate interactions did not yield a consistent pattern to suggest renal detriment to either the Ranch Hands or the Comparisons. Lack of a group difference in the reported history of kidney disease or kidney stones (consistent with the 1985 examination results) was in contrast with the Baseline findings, in which Ranch Hands reported significantly more disease. A nonsignificant difference in the percentage of participants with urinary protein also was inconsistent with the Baseline examination when the Comparisons had a marginally significant higher prevalence rate. In the longitudinal analysis of blood urea nitrogen, no difference in the change over time was detected.

Serum Dioxin Analysis of 1987 Followup Study Summary Results

The different sets of statistical analyses performed for the renal assessment did not indicate that an association existed between the serum dioxin levels of study participants and their 1987 examination health status. No significant associations with dioxin were observed in the longitudinal analyses of blood urea nitrogen. For some adjusted analyses, diabetic class was a significant covariate in the model. Because dioxin may influence diabetic status, ancillary models without diabetic class also were examined. For the most part, deletion of diabetic class from an adjusted model had no appreciable effect on the outcome of the analysis.

Parameters for the Renal Assessment

Dependent Variables

The Renal Assessment was based on laboratory data collected at the 1992 physical examination, as well as on a verified history of kidney disease, as reported by the participant and subsequently verified by a medical records review.

Medical Records Data

In the self-administered family and personal history questionnaire, each study participant was asked whether he had ever experienced kidney trouble or kidney stones or had recurrent occurrences of kidney infections in the years prior to the 1992 physical examination. This information was subsequently verified and combined with data from previous examinations and from the physical examination. A composite variable, kidney disease, was constructed by assigning "yes" to any participant who was verified to have had at least one of the following conditions: kidney trouble, kidney stones, or kidney infections.

Participants with a pre-SEA history of one of these conditions were excluded from the analysis. No other participants were excluded for medical reasons from the analysis of this variable.

Physical Examination Data

Kidney stones (present, absent), as determined by the kidney, urethra, and bladder (KUB) x ray, were analyzed.

Laboratory Examination Data

Five renal variables were quantified by general laboratory procedures to assess nonspecific renal system function. Urinary protein and urine specific gravity were determined by accepted dipstick methods using a Clinitek 200®. Hematuria and leukocyturia were measured by high-powered microscopic examination. Serum creatinine was assayed using Baxter/Dade Paramax® equipment.

Urinary protein (absent, present), hematuria ($\leq$ 2 urinary red blood cells per high-powered field [RBC per HPF], $>$ 2 RBC per HPF), and leukocyturia ($\leq$2 urinary WBC per HPF, $>$2 WBC per HPF) were analyzed as dichotomous variables. Serum creatinine (mg/dl) and urine specific gravity were analyzed as continuous variables.

The Scripps Clinic and Research Foundation (SCRF) normal range for serum creatinine was 0.5-1.2 mg/dl, and 1.005-1.030 mg/dl for urine specific gravity. However, statistical analyses were only performed for these variables in the continuous form.

No participants were excluded for medical reasons from the analysis of these variables.

Covariates

The effects of the four covariates age, race, military occupation, and diabetic class were examined in adjusted statistical analyses of the renal data. Diabetic class was defined as diabetic (verified history of diabetes or $\geq$200 mg/dl 2-hour postprandial glucose), impaired (140 mg/dl $\leq$ 2-hour postprandial glucose $<$200 mg/dl), and normal ($<$140 mg/dl 2-hour postprandial glucose). Age was used in its continuous form for modeling purposes for all dependent variables. Age was dichotomized for clarity of presentation (e.g., interaction summaries).

Statistical Methods

Chapter 7, Statistical Methods, describes the basic statistical methods used throughout this report. Table 17-1 summarizes the statistical analyses performed for the Renal Assessment. The first part of this table describes the dependent variables and identifies the candidate covariates and the statistical methods. The second part of the table further describes the candidate covariates. Abbreviations used in the body of the table are defined at the end of the table. Table 17-2 provides the number of participants excluded for a pre-SEA history of kidney disease and the number of participants with missing dependent variable or diabetic class status data.

Analyses of data collected at the 1987 followup study indicated that dioxin was associated with military occupation. In general, enlisted personnel had higher levels of dioxin than officers, with enlisted groundcrew having higher levels than enlisted flyers. Consequently, adjustment for military occupation in statistical models using dioxin as a measure of exposure may improperly mask an actual dioxin effect. However, occupation also can be a surrogate for socioeconomic effects. Failure to adjust for occupation could overlook important risk factors related to lifestyle. If occupation was found to be significantly associated with a dependent variable in the 1992 followup analyses and was retained in the final statistical models using dioxin as a measure of exposure, the dioxin effect was evaluated in the context of two models. Analyses were performed with and without occupation in the final models to investigate whether conclusions regarding the association between the health endpoint and dioxin differed.

Diabetes also exhibited a significant positive association with dioxin in the serum dioxin analysis of the 1987 followup data. The results of similar diabetic analyses for the 1992 followup are discussed in Chapter 18, Endocrine Assessment. Consequently, clinical endpoints in the Renal Assessment may be related to dioxin due to the association between dioxin and diabetes. To investigate this possibility, the dioxin effect was evaluated in the context of two models whenever diabetic class was retained in the final model. Analyses again were performed with and without diabetic class in the model to investigate whether conclusions regarding the association between the health endpoint and dioxin differed.

The results of the analyses without occupation and diabetic class in the final adjusted model are presented in Appendix M-3 and are only discussed in the text if the level of significance differs from the original final adjusted model (significant versus nonsignificant).

Longitudinal Analysis

Longitudinal analyses were conducted on four laboratory variables (urinary red blood cell count, urinary protein, urinary white blood cell count, and urine specific gravity) to evaluate the changes between previous examinations and the 1992 followup examination. The longitudinal analyses for urinary protein investigated differences between the 1982 examination and the 1992 examination because the same measurement method was used at each examination. By contrast, the longitudinal analyses for urinary red blood cell count and urine specific gravity assessed changes between the 1985 examination and the 1992 examination because the 1982 examination employed a different measurement method than

Table 17-1.
Statistical Analyses for the Renal Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analysis
Kidney Disease	MR-V	D	Yes No	AGE,RACE,OCC, DIAB	U:LR,CS A:LR
Kidney Stones from KUB X-Ray	PE	D	Present Absent	AGE,RACE,OCC, DIAB	U:LR,CS A:LR
Urinary Protein	LAB	D	Present Absent	AGE,RACE,OCC, DIAB	U:LR,CS A:LR L:LR
Urinary Red Blood Cell Count (RBC per HPF)	LAB	D	Abnormal: >2 Normal: ≤2	AGE,RACE,OCC, DIAB	U:LR,CS A:LR L:LR
Urinary White Blood Cell Count (WBC per HPF)	LAB	D	Abnormal: >2 Normal: ≤2	AGE,RACE,OCC, DIAB	U:LR,CS A:LR L:LR
Serum Creatinine (mg/dl)	LAB	C	--	AGE,RACE,OCC, DIAB	U:GLM,TT A:GLM
Urine Specific Gravity	LAB	C	--	AGE,RACE,OCC, DIAB	U:GLM,TT A:GLM L:GLM

Covariates

Variable (Abbreviation)	Data Source	Data Form	Cutpoints
Age (AGE)	MIL	D/C	Born ≥ 1942 Born < 1942
Race (RACE)	MIL	D	Black Non-Black
Occupation (OCC)	MIL	D	Officer Enlisted Flyer Enlisted Groundcrew
Diabetic Class (DIAB)	LAB and MR-V	D	Diabetic: past history or ≥200 mg/dl 2-hr. postprandial glucose Impaired: ≥140 – ≤200 mg/dl 2-hr. postprandial glucose Normal: <140 mg/dl 2-hr. postprandial glucose

Table 17-1. (Continued)
Statistical Analyses for the Renal Assessment

Abbreviations

Data Source:	LAB	=	1992 laboratory results
	MIL	=	Air Force military records
	MR-V	=	Medical records (verified)
	PE	=	1992 physical examination
Data Form:	C	=	Continuous analysis only
	D	=	Discrete analysis only
	D/C	=	Appropriate form for analysis (either discrete or continuous)
Statistical Analyses:	U	=	Unadjusted analyses
	A	=	Adjusted analyses
	L	=	Longitudinal analyses
Statistical Methods:	CS	=	Continuity-adjusted chi-square statistic
	GLM	=	General linear models analysis
	LR	=	Logistic regression analysis
	TT	=	Two-sample t-test

Table 17-2.
Number of Participants with Missing Data for, or Excluded from, the Renal Assessment

		Group		Dioxin (Ranch Hands Only)		Categorized Dioxin	
Variable	**Variable Use**	**Ranch Hand**	**Comparison**	**Initial**	**Current**	**Ranch Hand**	**Comparison**
Urinary Protein	DEP	2	2	2	2	2	1
Urinary Red Blood Cell Count	DEP	2	2	2	2	2	1
Urinary White Blood Cell Count	DEP	2	2	2	2	2	1
Serum Creatinine	DEP	0	1	0	0	0	0
Urine Specific Gravity	DEP	2	2	2	2	2	1
Diabetic Class	COV	1	2	0	1	1	1
Pre-SEA Kidney Disease	EXC	21	30	11	21	21	22

Abbreviations: DEP = Dependent variable (missing data).
COV = Covariate (missing data).
EXC = Exclusion.

Note: 952 Ranch Hands and 1,281 Comparisons;
520 Ranch Hands for initial dioxin; 894 Ranch Hands for current dioxin;
894 Ranch Hands and 1,063 Comparisons for categorized dioxin.

One Ranch Hand missing total lipids for current dioxin.

the procedure used at subsequent examinations (reagent strip testing in 1982 vs. microscopic observation for urinary red blood cells; falling drop in 1982 vs. multistick for urine specific gravity).

The longitudinal analyses for urinary white blood cell count investigated differences between the 1985 and 1992 examinations because, even though all the examinations employed the same measurement method (microscopic observation), the cutpoint for defining an abnormality changed between the 1982 examination and subsequent examinations (>4 urinary WBC per HPF in 1982 vs. >2 urinary WBC per HPF in 1985, 1987, and 1992). See Chapter 7, Statistical Methods, for a further discussion of methods used in the longitudinal analysis.

RESULTS

Dependent Variable-Covariate Associations

Unadjusted covariate tests of association were done to examine the relationships between the dependent variables and the candidate covariates—age, race, occupation, and diabetic class. Analyses were performed on the combined Ranch Hand and Comparison group cohorts. Associations with a p-value less than 0.10 are discussed below.

Kidney disease was significantly associated with age and diabetic class (Appendix Table M-1-1: p=0.001 and p<0.001 respectively). Older participants were more likely to have a verified history of kidney disease than younger participants (18.8% of men born before 1942 vs. 13.2% of men born in or after 1942), and diabetics had a higher rate of kidney disease than subjects with normal and impaired glucose levels. The percentages of AFHS participants with a verified history of kidney disease in the normal, impaired, and diabetic categories were 14.7, 17.4, and 24.0 percent respectively.

The only covariate significantly associated with kidney stones was age (p=0.023), with older participants having a higher rate of occurrence than younger participants (3.6% vs. 1.9%).

The only covariate significantly associated with urinary protein was diabetic class (p<0.001). Diabetics were much more likely to have urinary protein abnormalities (13.9%) than were subjects with impaired glucose levels (4.8%) and subjects with normal glucose levels (2.7%).

Urinary red blood cell count was significantly associated with occupation (p=0.018) and race (p=0.007). The percentages of abnormalities for officers, enlisted flyers, and enlisted groundcrew were 1.7 percent, 2.2 percent, and 3.8 percent respectively. Blacks were more than twice as likely as non-Blacks to have urinary red blood cell count abnormalities (6.9% vs. 2.5%).

Covariate analyses for urinary white blood cell count were significant for occupation (p=0.031) and diabetic class (p=0.003). For occupation, enlisted flyers had the highest percentage of urinary white blood cell abnormalities (4.7%) followed by enlisted groundcrew

(3.1%) and officers (2.0%). For diabetic class, diabetics were more than twice as likely to have urinary white blood cell abnormalities than either subjects with impaired glucose levels or those with normal levels (5.9% of diabetics vs. 2.8% of impaired and 2.4% of normal).

Covariate analyses for serum creatinine revealed a significant association with age (p=0.004) and race (p<0.001), and a marginally significant association with diabetic class (p=0.081). Age was positively correlated with serum creatinine, and Blacks had a higher mean level of serum creatinine than non-Blacks (1.0513 mg/dl vs. 0.9692 mg/dl). Of the diabetic class categories, diabetics had the lowest mean level of serum creatinine (0.9584 mg/dl) while subjects with impaired glucose levels had the highest mean level (0.9877 mg/dl). Normal subjects had a mean level of serum creatinine of 0.9750 mg/dl.

Urine specific gravity was significantly associated with occupation (p<0.001) and diabetic class (p=0.002) and marginally associated with age (p=0.081) and race (p=0.069) in the covariate tests of association. Of the occupational categories, enlisted groundcrew had the highest mean urine specific gravity (1.0196), while the mean for both enlisted flyers and officers was 1.0182. For diabetic class, the means were 1.0186, 1.0194, and 1.0198 for the normal, impaired, and diabetic categories respectively. Age was negatively correlated with urine specific gravity (r=-0.037, p=0.081). Blacks had a higher mean urine specific gravity than non-Blacks (1.0198 vs. 1.0188).

In summary, the covariate tests of association found that older participants were more likely than younger participants to have a verified history of kidney disease, evidence at the physical examination of kidney stones, higher serum creatinine, and a lower mean urine specific gravity. Racial differences showed that Blacks were more likely than non-Blacks to have urinary red blood cell count abnormalities, a higher serum creatinine level, and a higher urine specific gravity. Of the occupational categories, enlisted groundcrew had the highest prevalence of urinary red blood cells and the highest levels of urine specific gravity, while enlisted flyers had the highest prevalence of urinary white blood cells. Associations with the diabetic class covariate found that, as expected, diabetics were more likely than nondiabetics to have a history of kidney disease, urinary protein, urinary white blood cells, a lower serum creatinine level, and a higher urine specific gravity.

Exposure Analysis

The following section presents the results of the statistical analyses of the dependent variables shown in Table 17-1. Dependent variables are grouped into three sections: those derived and verified from a review of medical records, data obtained during the 1992 physical examination, and data derived from the laboratory portion of the 1992 followup examination.

Unadjusted and adjusted analyses of six models are presented for each variable. Model 1 examines the relationship between the dependent variable and group (Ranch Hand or Comparison). Model 2 explores the relationship between the dependent variable and an extrapolated initial dioxin measure for Ranch Hands who had a 1987 dioxin measurement greater than 10 ppt. If a participant did not have a 1987 dioxin level, a 1992 level was used. A statistical adjustment for the percent of body fat at the participant's time of duty in SEA and the change in the percent of body fat from the time of duty in SEA to the date of the blood draw for dioxin is included in this model to account for body-fat-related differences in elimination rate (22). 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. These participants are added to Ranch Hands and Comparisons with current serum dioxin levels (1987, if available; 1992, if the 1987 level was not available) at or below 10 ppt to create a total of four categories. Ranch Hands with current serum dioxin levels at or below 10 ppt are referred to as the "background Ranch Hand" category. The relationship between the dependent variable in each of the three Ranch Hand categories and the dependent variable in the "Comparison" category is examined. A fourth contrast, exploring the relationship of the dependent variable in the low Ranch Hand category and the high Ranch Hand category combined, also is conducted. This combination is referred to in the text and tables as the "low plus high Ranch Hand" category. As in Model 2, a statistical adjustment is made for the percent of body fat at the participant's time of duty in SEA and the change in the percent of body fat from the time of duty in SEA to the date of the blood draw for dioxin.

Models 4, 5, and 6 examine the relationship between the dependent variable and 1987 dioxin levels in all Ranch Hands with a dioxin measurement. If a participant did not have a 1987 dioxin measurement, a 1992 measurement was utilized in determining the current dioxin level. The measure of dioxin in Model 4 is lipid-adjusted, whereas whole-weight dioxin is used in Models 5 and 6. Model 6 differs from Model 5 in that a statistical adjustment for total lipids is included in Model 6. Further details on dioxin and the modeling strategy are found in Chapters 2 and 7 respectively.

Results of investigations for group-by-covariate and dioxin-by-covariate interactions are referenced in the text, and tabular results are presented in Appendix M-2. As described previously, additional analyses were performed when occupation or diabetic class was retained in the final models for Models 2 through 6. Results excluding occupation and diabetic class from these models are tabled in Appendix M-3. Results from analyses excluding occupation and diabetic class are discussed in the text only if a meaningful change occurred (that is, changes between significant results, marginally significant results, and nonsignificant results).

Verified Medical Records Variable

Kidney Disease

The results from the Model 1 analysis did not detect a significant difference in the history of kidney disease between Ranch Hands and Comparisons (Table 17-3(a,b): $p > 0.22$ for all contrasts). The adjusted analysis accounted for diabetic class and the age-by-occupation interaction.

Similarly, Models 2 and 3 did not show kidney disease to be significantly associated with initial dioxin or categorized dioxin (Table 17-3(c-f): $p > 0.56$ for all analyses). For Model 2, the final adjusted model was the same as the unadjusted model; however, the adjusted analysis of Model 3 contained the covariates age, occupation, and diabetic class.

Table 17-3.
Analysis of Kidney Disease

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Yes**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***931***	***17.0***	***1.08 (0.86,1.36)***	***0.545***
	Comparison	***1,251***	***15.9***		
Officer	Ranch Hand	358	17.3	1.28 (0.88,1.87)	0.225
	Comparison	485	14.0		
Enlisted Flyer	Ranch Hand	158	16.5	1.12 (0.63,1.98)	0.818
	Comparison	200	15.0		
Enlisted Groundcrew	Ranch Hand	415	16.9	0.93 (0.67,1.31)	0.754
	Comparison	566	17.8		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.08 (0.86,1.36)***	***0.526***	DIAB (p=0.025) OCC*AGE (p=0.034)
Officer	1.25 (0.85,1.83)	0.256	
Enlisted Flyer	1.13 (0.64,2.00)	0.681	
Enlisted Groundcrew	0.95 (0.68,1.33)	0.752	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 17-3. (Continued)
Analysis of Kidney Disease

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	170	17.1	0.97 (0.81,1.15)	0.717
Medium	170	17.1		
High	169	17.8		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[a]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
509	0.97 (0.81,1.15)	0.717	

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

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

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 17-3. (Continued)
Analysis of Kidney Disease

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	**n**	**Percent Yes**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,041	16.0		
Background RH	364	16.2	1.07 (0.77,1.48)	0.690
Low RH	253	17.0	1.04 (0.72,1.51)	0.830
High RH	256	17.6	1.08 (0.75,1.55)	0.694
Low plus High RH	509	17.3	1.06 (0.80,1.41)	0.695

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	**n**	**Adj. Relative Risk (95% C.I.)[ac]**	**p-Value**	**Covariate Remarks**
Comparison	1,040			AGE (p<0.001) OCC (p=0.016) DIAB (p=0.030)
Background RH	363	1.11 (0.79,1.55)	0.560	
Low RH	253	1.01 (0.69,1.47)	0.960	
High RH	256	1.06 (0.72,1.54)	0.773	
Low plus High RH	509	1.03 (0.77,1.38)	0.828	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 17-3. (Continued)
Analysis of Kidney Disease

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Yes/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	15.0 (286)	18.3 (295)	17.1 (292)	1.02 (0.90,1.15)	0.729
5	14.1 (291)	19.2 (291)	17.2 (291)	1.02 (0.92,1.14)	0.685
6[c]	14.1 (291)	19.2 (291)	17.2 (291)	1.01 (0.90,1.13)	0.918

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	873	1.07 (0.94,1.21)	0.313	AGE*RACE (p=0.032)
5	873	1.06 (0.95,1.18)	0.329	AGE*RACE (p=0.033)
6[d]	873	1.05 (0.93,1.18)	0.480	AGE*RACE (p=0.034)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

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

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

For Models 4 through 6, no significant association between history of kidney disease and current dioxin was found in the unadjusted and adjusted analyses (Table 17-3(g,h): $p > 0.31$ for all analyses). Each of the adjusted analyses for Models 4 through 6 accounted for the age-by-race interaction.

Physical Examination Variable

Kidney Stones

As shown in Table 17-4(a,b), the unadjusted and adjusted analyses for Model 1 did not reveal a significant association between kidney stones and group ($p > 0.46$ for all contrasts). The final model in the adjusted analysis for Model 1 contained the covariate age.

Examination of the unadjusted results for Model 2 revealed a significant inverse relationship between initial dioxin and kidney stones (Table 17-4(c): $p=0.016$, Est. RR=0.58, 95% C.I.=[0.36, 0.94]). The percentages of participants with kidney stones in the low, medium, and high initial dioxin categories were 5.2, 2.9, and 1.7 percent respectively.

The adjusted analysis for Model 2 detected a significant initial dioxin-by-diabetic class interaction (Table 17-4(d): $p=0.016$). Appendix Table M-2-1 presents stratified results to examine this interaction. Age also was a significant covariate in the final model. After deleting the initial dioxin-by-diabetic class interaction from the final model, a marginally significant inverse relationship between initial dioxin and kidney stones was detected (Table 17-4(d): $p=0.069$, Adj. RR=0.65, 95% C.I.=[0.39, 1.07]).

The unadjusted and adjusted analyses of Model 3 did not uncover a significant association between kidney stones and categorized dioxin (Table 17-4(e,f): $p > 0.24$ for unadjusted and adjusted results). Although the prevalence rates in the three Ranch Hand categories did not differ significantly from the Comparison group prevalence rate, the percentage of abnormalities decreased from the low Ranch Hand category to the high Ranch Hand category, which was consistent with the results of Model 2. The lack of significant differences between the Ranch Hand categories and Comparison group is consistent with the results of Model 1. Age was the only significant covariate in the adjusted analysis of Model 3.

As presented in Table 17-4(g,h), none of the analyses for Models 4 through 6 uncovered a significant association between kidney stones and current dioxin ($p > 0.51$ for all analyses). Each of the adjusted analyses for Models 4 through 6 accounted for the covariate age.

Table 17-4.
Analysis of Kidney Stones

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Present**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	*Ranch Hand*	*952*	*3.0*	*1.12 (0.68,1.84)*	*0.755*
	Comparison	*1,281*	*2.7*		
Officer	Ranch Hand	367	3.3	0.91 (0.43,1.91)	0.949
	Comparison	502	3.6		
Enlisted Flyer	Ranch Hand	162	3.7	1.26 (0.40,3.99)	0.918
	Comparison	203	3.0		
Enlisted Groundcrew	Ranch Hand	423	2.6	1.37 (0.59,3.19)	0.605
	Comparison	576	1.9		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	*1.11 (0.67,1.83)*	*0.684*	AGE (p=0.004)
Officer	0.90 (0.43,1.89)	0.777	
Enlisted Flyer	1.25 (0.39,3.95)	0.709	
Enlisted Groundcrew	1.37 (0.59,3.20)	0.462	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 17-4. (Continued)
Analysis of Kidney Stones

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[a]**	
Initial Dioxin	**n**	**Percent Present**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	174	5.2	0.58 (0.36,0.94)	0.016
Medium	173	2.9		
High	173	1.7		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
	Analysis Results for Log_2 (Initial Dioxin)[c]		
n	**Adj. Relative Risk (95% C.I.)[b]**	**p-Value**	**Covariate Remarks**
520	0.65 (0.39,1.07)**	0.069**	INIT*DIAB (p=0.016) AGE (p=0.016)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

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

[c] Adjusted for percent body fat at the time of duty, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial 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; refer to Appendix Table M-2-1 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.
INIT = Log_2 (initial dioxin).

Table 17-4. (Continued)
Analysis of Kidney Stones

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	**n**	**Percent Present**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,063	2.5		
Background RH	374	2.7	1.02 (0.49,2.14)	0.957
Low RH	260	3.8	1.55 (0.74,3.25)	0.246
High RH	260	2.7	1.09 (0.47,2.54)	0.839
Low plus High RH	520	3.3	1.32 (0.71,2.46)	0.377

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	**n**	**Adj. Relative Risk (95% C.I.)[ac]**	**p-Value**	**Covariate Remarks**
Comparison	1,063			AGE (p=0.020)
Background RH	374	0.97 (0.46,2.03)	0.929	
Low RH	260	1.49 (0.71,3.14)	0.291	
High RH	260	1.23 (0.53,2.89)	0.630	
Low plus High RH	520	1.37 (0.74,2.56)	0.316	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 17-4. (Continued)
Analysis of Kidney Stones

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Present/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	2.0 (295)	5.0 (300)	2.0 (299)	0.91 (0.70,1.20)	0.510
5	1.7 (300)	5.1 (297)	2.4 (297)	0.94 (0.75,1.18)	0.613
6[c]	1.7 (299)	5.1 (297)	2.4 (297)	0.94 (0.74,1.20)	0.623

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	894	0.96 (0.72,1.27)	0.766	AGE (p=0.057)
5	894	0.98 (0.77,1.24)	0.850	AGE (p=0.053)
6[d]	893	0.98 (0.76,1.27)	0.898	AGE (p=0.052)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

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

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = $\leq$ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = $\leq$ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Laboratory Examination Variables

Urinary Protein

Table 17-5(a,b) demonstrates that group differences in the presence of urinary protein were not statistically significant ($p>0.20$ for all analyses). Covariate adjustment for the Model 1 analysis accounted for age, occupation, and diabetic class.

Analyses of Models 2 and 3 did not show initial dioxin or categorized dioxin to be significantly associated with urinary protein (Table 17-5(c-f): $p>0.15$ for all analyses). The adjusted analysis for Model 2 accounted for diabetic class, while the adjusted analysis for Model 3 contained the covariates age, occupation, and diabetic class.

Table 17-5(g,h) displays results for the current dioxin analysis of urinary protein. No statistically significant results were found in any of the unadjusted analyses for Models 4 through 6 ($p>0.36$ for each unadjusted analysis). The adjusted analyses for Models 4, 5, and 6 each had a significant current dioxin-by-diabetic class interaction (Table 17-5(h): $p=0.004$, $p=0.012$, and $p=0.011$ respectively). Appendix Table M-2-2 presents results stratified by each level of diabetic class. The relationship between dioxin and diabetes is discussed in Chapter 18, Endocrine Assessment. The age-by-race interaction was also significant in the adjusted analyses of Models 4 through 6. Current dioxin was not found to be significantly associated with urinary protein after removing the current dioxin-by-diabetic class interaction from the final adjusted models (Table 17-5(h): $p>0.53$ for all analyses).

Urinary Red Blood Cell Count

The percentage of participants with abnormal urinary red blood cell counts did not differ significantly between the Ranch Hand and Comparison groups in the Model 1 analyses (Table 17-6(a,b): $p>0.17$ for each analysis). The adjusted analysis accounted for age, race, and occupation.

No significant association was detected between initial dioxin and urinary red blood cell count in the unadjusted and adjusted analyses of Model 2 (Table 17-6(c-d): $p>0.28$ for all analyses), even though Ranch Hands in the medium category of initial dioxin had noticeably more abnormalities than Ranch Hands in the low or high categories. The percentages of abnormalities for the low, medium, and high categories of initial dioxin were 1.7, 6.9, and 3.5 respectively. Covariate adjustment in Model 2 accounted for age. By contrast, the unadjusted analysis for Model 3 found a significantly higher percentage of urinary red blood cell count abnormalities in the high Ranch Hand category (5.8%) than in the Comparison category (2.0%) (Table 17-6(e): $p=0.002$, Est. RR=3.00, 95% C.I.=[1.51, 5.93]). The unadjusted relative risk was also significant for the low plus high Ranch Hand category (Table 17-6(e): $p=0.019$, Est. RR=2.10, 95% C.I.=[1.13, 3.90]). In the low plus high category, 4.1 percent of participants had urinary red blood cell count abnormalities.

The adjusted analysis for Model 3 contained a significant categorized dioxin-by-occupation interaction (Table 17-6(f): $p=0.013$) plus two significant covariates, age and race. Appendix Table M-2-3 displays results stratified by occupation. To examine the relationship

Table 17-5.
Analysis of Urinary Protein

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Present**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***950***	***4.6***	***1.02 (0.68,1.53)***	***0.995***
	Comparison	***1,279***	***4.5***		
Officer	Ranch Hand	367	4.6	1.69 (0.82,3.48)	0.207
	Comparison	502	2.8		
Enlisted Flyer	Ranch Hand	161	3.7	0.67 (0.24,1.86)	0.603
	Comparison	202	5.4		
Enlisted Groundcrew	Ranch Hand	422	5.0	0.86 (0.49,1.51)	0.701
	Comparison	575	5.7		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.00 (0.66,1.51)***	***0.999***	AGE (p=0.006) OCC (p=0.038) DIAB (p<0.001)
Officer	1.52 (0.73,3.16)	0.263	
Enlisted Flyer	0.70 (0.25,1.96)	0.493	
Enlisted Groundcrew	0.87 (0.49,1.55)	0.634	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 17-5. (Continued)
Analysis of Urinary Protein

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Present	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	173	3.5	1.18 (0.87,1.59)	0.287
Medium	173	3.5		
High	172	5.2		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
	Analysis Results for Log_2 (Initial Dioxin)[c]		
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
518	1.14 (0.85,1.54)	0.383	DIAB (p=0.015)

[a] Adjusted for percent body fat at the time of duty and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

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

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 17-5. (Continued)
Analysis of Urinary Protein

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	**n**	**Percent Present**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,062	4.5		
Background RH	374	4.8	1.31 (0.75,2.31)	0.345
Low RH	259	3.5	0.67 (0.32,1.39)	0.280
High RH	259	4.6	0.87 (0.45,1.68)	0.677
Low plus High RH	518	4.1	0.77 (0.45,1.31)	0.334

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	**n**	**Adj. Relative Risk (95% C.I.)[ac]**	**p-Value**	**Covariate Remarks**
Comparison	1,061			AGE (p=0.062) OCC (p=0.078) DIAB (p<0.001)
Background RH	373	1.55 (0.85,2.83)	0.153	
Low RH	259	0.60 (0.28,1.28)	0.188	
High RH	259	0.76 (0.38,1.51)	0.427	
Low plus High RH	518	0.68 (0.39,1.18)	0.168	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 17-5. (Continued)
Analysis of Urinary Protein

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Present/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	4.1 (295)	5.0 (299)	4.0 (298)	1.09 (0.88,1.36)	0.417
5	4.0 (300)	4.1 (296)	5.1 (296)	1.09 (0.90,1.32)	0.361
6[c]	4.0 (299)	4.1 (296)	5.1 (296)	1.07 (0.88,1.31)	0.500

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	891	1.08 (0.85,1.36)**	0.538**	CURR*DIAB (p=0.004) AGE*RACE (p=0.018)
5	891	1.06 (0.86,1.30)**	0.576**	CURR*DIAB (p=0.012) AGE*RACE (p=0.020)
6[d]	890	1.07 (0.86,1.34)**	0.536**	CURR*DIAB (p=0.011) AGE*RACE (p=0.019)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

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

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table M-2-2 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.
CURR = Log_2 (current dioxin + 1).

Table 17-6.
Analysis of Urinary Red Blood Cell Count

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***950***	***3.3***	***1.40 (0.84,2.34)***	***0.237***
	Comparison	***1,279***	***2.3***		
Officer	Ranch Hand	367	2.5	2.08 (0.73,5.89)	0.254
	Comparison	502	1.2		
Enlisted Flyer	Ranch Hand	161	2.5	1.26 (0.31,5.12)	0.999
	Comparison	202	2.0		
Enlisted Groundcrew	Ranch Hand	422	4.3	1.24 (0.65,2.37)	0.636
	Comparison	575	3.5		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.41 (0.84,2.35)***	***0.190***	AGE (p=0.014) RACE (p=0.025) OCC (p=0.005)
Officer	2.04 (0.72,5.80)	0.179	
Enlisted Flyer	1.27 (0.31,5.17)	0.741	
Enlisted Groundcrew	1.24 (0.65,2.38)	0.518	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 17-6. (Continued)
Analysis of Urinary Red Blood Cell Count

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[a]**	
Initial Dioxin	**n**	**Percent Abnormal**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	173	1.7	1.10 (0.79,1.52)	0.582
Medium	173	6.9		
High	172	3.5		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	**Adj. Relative Risk (95% C.I.)[b]**	**p-Value**	**Covariate Remarks**
518	1.21 (0.86,1.69)	0.282	AGE (p=0.055)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

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

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 17-6. (Continued)
Analysis of Urinary Red Blood Cell Count

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,062	2.0		
Background RH	374	2.1	1.08 (0.47,2.47)	0.858
Low RH	259	2.3	1.21 (0.48,3.03)	0.688
High RH	259	5.8	3.00 (1.51,5.93)	0.002
Low plus High RH	518	4.1	2.10 (1.13,3.90)	0.019

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,062			DXCAT*OCC (p=0.013) AGE (p=0.016) RACE (p=0.006)
Background RH	374	1.17 (0.50,2.75)**	0.712**	
Low RH	259	1.10 (0.44,2.79)**	0.835**	
High RH	259	2.98 (1.45,6.14)**	0.003**	
Low plus High RH	518	1.97 (1.05,3.68)**	0.035**	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interaction ($0.01<p\leq0.05$); adjusted relative risk, confidence interval, and p-value derived from a model after deletion of this interaction; refer to Appendix Table M-2-3 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.
DXCAT = Categorized dioxin.

Table 17-6. (Continued)
Analysis of Urinary Red Blood Cell Count

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	1.7 (295)	3.3 (299)	4.7 (298)	1.18 (0.92,1.50)	0.197
5	1.7 (300)	3.4 (296)	4.7 (296)	1.16 (0.93,1.44)	0.194
6[c]	1.7 (299)	3.4 (296)	4.7 (296)	1.16 (0.92,1.46)	0.224

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	892	1.13 (0.86,1.50)**	0.384**	CURR*OCC (p=0.013)
5	892	1.12 (0.87,1.43)**	0.371**	CURR*OCC (p=0.024)
6[d]	891	1.11 (0.86,1.45)**	0.417**	CURR*OCC (p=0.019)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

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

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin +1)-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; refer to Appendix Table M-2-3 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

between categorized dioxin and urinary red blood cell count, the categorized dioxin-by-occupation interaction was removed from the adjusted analysis of Model 3. Without the interaction, the relative risk for the high Ranch Hand category remained significant after adjusting for age, race, and occupation (Table 17-6(f): $p=0.003$, Adj. RR=2.98, 95% C.I.=[1.45, 6.14]). In addition, a significant adjusted relative risk was observed for the low plus high Ranch Hand category (Table 17-6(f): $p=0.035$, Adj. RR=1.97, 95% C.I.=[1.05, 3.68]).

As shown in Table 17-6(g), the unadjusted results for Models 4 through 6 did not display a significant association between urinary red blood cell count and current dioxin ($p>0.19$ for each model). Each of the adjusted analyses for Models 4, 5, and 6 contained a significant current dioxin-by-occupation interaction (Table 17-6(h): $p=0.013$, $p=0.024$, and $p=0.019$ respectively). Appendix Table M-2-3 displays stratified results for this interaction. The current dioxin-by-occupation interaction was the only covariate in Models 4 through 6. Current dioxin was not found to be significantly associated with urinary protein when current dioxin-by-occupation was removed from the final adjusted models (Table 17-6(g,h): $p>0.37$ for each model).

Urinary White Blood Cell Count

The unadjusted and adjusted analyses of Model 1 did not find a significant difference in abnormal urinary white blood cell counts between the Ranch Hand and Comparison groups (Table 17-7(a,b): $p=0.222$ and $p=0.208$ respectively). The final model in the adjusted analysis for Model 1 contained the covariates age, occupation, and diabetic class. However, stratifying the Model 1 analyses by occupation revealed a statistically significant association between group and urinary white blood cell count for enlisted groundcrew. For the unadjusted analysis, the percentage of enlisted groundcrew Ranch Hands with abnormalities (4.5%) was significantly greater than the percentage of enlisted groundcrew Comparisons with abnormalities (2.1%) (Table 17-7(a): $p=0.047$, Est. RR=2.21, 95% C.I.=[1.06, 4.61]). The relative risk remained significant after adjusting for age, occupation, and diabetic class (Table 17-7(b): $p=0.033$, Adj. RR=2.23, 95% C.I.=[1.07, 4.67]).

The initial dioxin and categorized dioxin analyses (Models 2 and 3) for urinary white blood cell count did not uncover any statistically significant results (Table 17-7(c-f): $p>0.16$ for all analyses). For Model 2, the final model for the adjusted analysis was the same as the unadjusted model, whereas the adjusted analysis for Model 3 included the covariates age, occupation, and race.

Similar to the results of Models 2 and 3, the unadjusted and adjusted analyses for Models 4 through 6 did not detect a significant relationship between urinary white blood cell count and current dioxin (Table 17-7(g,h): $p>0.42$ for all analyses). For each of the three models, the adjusted results accounted for the covariates age and occupation.

Serum Creatinine

Examination of the unadjusted results for Model 1 revealed no significant group difference in the mean levels of serum creatinine (Table 17-8(a): $p>0.77$ for all contrasts).

Table 17-7.
Analysis of Urinary White Blood Cell Count

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Percent Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*950*	*3.5*	*1.40 (0.86,2.30)*	*0.222*
	Comparison	*1,279*	*2.5*		
Officer	Ranch Hand	367	1.9	0.96 (0.36,2.54)	0.999
	Comparison	502	2.0		
Enlisted Flyer	Ranch Hand	161	4.3	0.87 (0.32,2.35)	0.984
	Comparison	202	5.0		
Enlisted Groundcrew	Ranch Hand	422	4.5	2.21 (1.06,4.61)	0.047
	Comparison	575	2.1		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	*1.38 (0.84,2.27)*	*0.208*	AGE (p=0.015) OCC (p=0.007) DIAB (p=0.082)
Officer	0.91 (0.34,2.42)	0.850	
Enlisted Flyer	0.87 (0.32,2.36)	0.792	
Enlisted Groundcrew	2.23 (1.07,4.67)	0.033	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 17-7. (Continued)
Analysis of Urinary White Blood Cell Count

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	173	3.5	0.94 (0.66,1.34)	0.736
Medium	173	4.0		
High	172	3.5		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[a]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
518	0.94 (0.66,1.34)	0.736	

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

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

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 17-7. (Continued)
Analysis of Urinary White Blood Cell Count

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,062	2.4		
Background RH	374	2.4	1.06 (0.49,2.30)	0.887
Low RH	259	3.5	1.45 (0.67,3.16)	0.346
High RH	259	3.9	1.63 (0.77,3.45)	0.202
Low plus High RH	518	3.7	1.54 (0.84,2.83)	0.165

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	**n**	**Adj. Relative Risk (95% C.I.)[ac]**	**p-Value**	**Covariate Remarks**
Comparison	1,062			AGE (p=0.005) OCC (p=0.046) RACE (p=0.133)
Background RH	374	1.21 (0.55,2.68)	0.640	
Low RH	259	1.37 (0.62,2.99)	0.434	
High RH	259	1.47 (0.68,3.18)	0.333	
Low plus High RH	518	1.42 (0.76,2.62)	0.270	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA, and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 17-7. (Continued)
Analysis of Urinary White Blood Cell Count

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	2.4 (295)	3.0 (299)	4.0 (298)	1.08 (0.84,1.40)	0.533
5	2.3 (300)	3.0 (296)	4.1 (296)	1.06 (0.85,1.33)	0.579
6[c]	2.3 (299)	3.0 (296)	4.1 (296)	1.10 (0.87,1.40)	0.424

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	892	0.95 (0.72,1.24)	0.684	AGE (p=0.023) OCC (p=0.008)
5	892	0.95 (0.75,1.19)	0.644	AGE (p=0.023) OCC (p=0.007)
6[d]	891	0.98 (0.76,1.26)	0.881	AGE (p=0.018) OCC (p=0.008)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

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

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 17-8.
Analysis of Serum Creatinine (mg/dl)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	*Ranch Hand*	*952*	*0.9741*	*0.0005 --*	*0.943*
	Comparison	*1,280*	*0.9737*		
Officer	Ranch Hand	367	0.9792	-0.0002 --	0.981
	Comparison	502	0.9795		
Enlisted Flyer	Ranch Hand	162	0.9616	0.0044 --	0.777
	Comparison	202	0.9572		
Enlisted Groundcrew	Ranch Hand	423	0.9746	0.0002 --	0.988
	Comparison	576	0.9744		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]	Covariate Remarks[d]
All	*Ranch Hand*	*951*	*1.0031***	*0.0002 --***	*0.972***	GROUP*DIAB (p=0.006)
	Comparison	*1,279*	*1.0028***			RACE (p<0.001)
Officer	Ranch Hand	367	1.0057**	0.0010 --**	0.929**	AGE*DIAB (p=0.041)
	Comparison	502	1.0047**			OCC*DIAB (p=0.015)
Enlisted Flyer	Ranch Hand	162	0.9817**	0.0036 --**	0.831**	
	Comparison	202	0.9782**			
Enlisted Groundcrew	Ranch Hand	422	1.0235**	-0.0017 --**	0.873**	
	Comparison	575	1.0252**			

[a] Transformed from natural logarithm scale.

[b] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on natural logarithm scale.

[c] P-value is based on difference of means on natural logarithm scale.

[d] Covariates and associated p-values correspond to final model based on all participants with available data.

** Group-by-covariate interaction ($p \leq 0.05$); adjusted mean, difference of adjusted means, confidence interval, and p-value derived from a model after deletion of this interaction; refer to Appendix Table M-2-4 for further analysis of this interaction.

Table 17-8. (Continued)
Analysis of Serum Creatinine (mg/dl)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	174	1.0058	1.0063	0.005	-0.0093 (0.0066)	0.161
Medium	173	0.9564	0.9568			
High	173	0.9680	0.9670			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ad]	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
Low	174	1.0413**	0.061	-0.0086 (0.0069)**	0.214**	INIT*DIAB (p=0.017) RACE (p=0.091) AGE*DIAB (p=0.018)
Medium	173	0.9949**				
High	173	1.0030**				

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Slope and standard error based on natural logarithm of serum creatinine versus $\log_2$ (initial dioxin).

[d] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted mean, slope, standard error, and p-value derived from a model after deletion of this interaction; refer to Appendix Table M-2-4 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 17-8. (Continued)
Analysis of Serum Creatinine (mg/dl)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,063	0.9717	0.9716		
Background RH	374	0.9647	0.9676	-0.0041--	0.678
Low RH	260	0.9910	0.9894	0.0178--	0.116
High RH	260	0.9624	0.9600	-0.0116--	0.298
Low plus High RH	520	0.9766	0.9746	0.0030--	0.728

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED					
Dioxin Category	n	Adj. Mean[ae]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]	Covariate Remarks
Comparison	1,062	0.9953**			DXCAT*DIAB (p=0.002) AGE*RACE (p=0.050) AGE*DIAB (p=0.032) OCC*DIAB (p=0.018)
Background RH	373	0.9872**	-0.0081--**	0.424**	
Low RH	260	1.0095**	0.0142--**	0.217**	
High RH	260	0.9893**	-0.0060--**	0.606**	
Low plus High RH	520	1.0001**	0.0048--**	0.624**	

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA, and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on natural logarithm scale.

[d] P-value is based on difference of means on natural logarithm scale.

[e] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interaction ($p \leq 0.05$); adjusted mean, difference of adjusted means, confidence interval, and p-value derived from a model after deletion of this interaction; refer to Appendix Table M-2-4 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 17-8. (Continued)
Analysis of Serum Creatinine (mg/dl)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED						
	Current Dioxin Category Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)		
Model[b]	Low	Medium	High	R^2	Slope (Std. Error)[c]	p-Value
4	0.9679 (295)	0.9850 (300)	0.9618 (299)	<0.001	0.0011 (0.0042)	0.797
5	0.9635 (300)	0.9840 (297)	0.9674 (297)	<0.001	0.0021 (0.0036)	0.571
6[d]	0.9646 (299)	0.9840 (297)	0.9674 (297)	<0.001	0.0007 (0.0039)	0.863

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED							
	Current Dioxin Category Adjusted Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)			
Model[b]	Low	Medium	High	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
4	1.0155 (294)	1.0251 (300)	1.0080 (299)	0.035	0.0017 (0.0044)	0.697	RACE (p=0.001) AGE*DIAB (p=0.001)
5	1.0100 (299)	1.0224 (297)	1.0134 (297)	0.035	0.0027 (0.0037)	0.473	RACE (p=0.001) AGE*DIAB (p=0.001)
6[e]	1.0130 (298)	1.0227 (297)	1.0113 (297)	0.035	0.0010 (0.0040)	0.796	RACE (p=0.001) AGE*DIAB (p=0.001)

[a] Transformed from natural logarithm scale.

[b] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[c] Slope and standard error based on natural logarithm of serum creatinine versus log_2 (current dioxin + 1).

[d] Adjusted for log_2 total lipids.

[e] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

The adjusted analysis of Model 1 found a significant group-by-diabetic class interaction (Table 17-8(b): $p=0.006$). Appendix Table M-2-4 presents results stratified by each level of diabetic class. Race and the age-by-diabetic class and occupation-by-diabetic class interactions were also significant in the final model. Removing the group-by-diabetic class interaction from the adjusted model resulted in no significant association between group and serum creatinine (Table 17-8(b): $p>0.83$ for all contrasts).

The unadjusted analyses for Models 2 and 3 did not show initial dioxin or categorized dioxin to be significantly associated with serum creatinine (Table 17-8(c,e): $p>0.11$ for all analyses). However, the adjusted analysis for Model 2 revealed a significant initial dioxin-by-diabetic class interaction (Table 17-8(d): $p=0.017$). Appendix Table M-2-4 displays results stratified by diabetic class. The race covariate and the age-by-diabetic class interaction also were retained in the adjusted analysis for Model 2. No significant relationship between initial dioxin and serum creatinine was observed when initial dioxin-by-diabetic class was removed from the final adjusted model (Table 17-8(d): $p=0.214$). The categorized dioxin-by-diabetic class adjusted analysis of Model 3 (Table 17-8(f): $p=0.002$). Appendix Table M-2-4 presents results stratified by diabetic class. The interactions age-by-race, age-by-diabetic class, and occupation-by-diabetic class also were significant in the adjusted analysis of Model 3. After deleting the categorized dioxin-by-diabetic class interaction from the final model, serum creatinine was not significantly associated with current dioxin (Table 17-8(f): $p>0.21$ for all contrasts).

No significant association between current dioxin and serum creatinine was detected in the analyses of Models 4 through 6 (Table 17-8(g,h): $p>0.47$ for all analyses). Each of the three models adjusted for a race covariate and the age-by-diabetic class interaction.

Urine Specific Gravity

The Model 1 analysis did not detect a significant group difference in the mean levels of urine specific gravity (Table 17-9(a,b): $p>0.15$ for all analyses). The adjusted analysis accounted for the occupation covariate and the age-by-diabetic class interaction.

The initial and categorized dioxin results (Models 2 and 3) also were not significant (Table 17-9(c-f): $p>0.14$ for unadjusted and adjusted analyses). Model 2 had a significant initial dioxin-by-age interaction in the final adjusted model (Table 17-9(d): $p=0.024$). Appendix Table M-2-5 presents stratified results to examine this interaction. Besides the initial dioxin-by-age interaction, occupation was significant in the adjusted analysis of Model 2. After deleting the initial dioxin-by-age interaction from the final model, urine specific gravity was not significantly associated with initial dioxin (Table 17-9(d): $p=0.231$). For Model 3, covariate adjustment accounted for occupation and diabetic class.

The unadjusted results for Models 4 through 6 showed a significant positive association between current dioxin levels and urine specific gravity (Table 17-9(g): $p=0.013$, Est. slope=0.0004; $p=0.007$, Est. slope=0.0003; $p=0.027$, Est. slope=0.0003 for Models 4, 5, and 6 respectively). The adjusted results were identical to the unadjusted results for Models 4 and 5 because no covariates were retained. By contrast, the association with current dioxin became nonsignificant in Model 6 after adjusting for occupation (Table 17-9(h): $p=0.123$, Adj. slope=0.0002).

Table 17-9.
Analysis of Urine Specific Gravity

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Mean**	**Difference of Means (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***950***	***1.0187***	***-0.0002 (-0.0007,0.0003)***	***0.489***
	Comparison	***1,279***	***1.0189***		
Officer	Ranch Hand	367	1.0183	0.0002 (-0.0007,0.0010)	0.662
	Comparison	502	1.0181		
Enlisted Flyer	Ranch Hand	161	1.0177	-0.0010 (-0.0025,0.0005)	0.190
	Comparison	202	1.0187		
Enlisted Groundcrew	Ranch Hand	422	1.0195	-0.0002 (-0.0010,0.0006)	0.597
	Comparison	575	1.0197		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED						
Occupational Category	**Group**	**n**	**Adj. Mean**	**Difference of Adj. Means (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***Ranch Hand***	***949***	***1.0189***	***-0.0002 (-0.0008,0.0003)***	***0.430***	OCC ($p<0.001$) AGE*DIAB ($p=0.048$)
	Comparison	***1,278***	***1.0192***			
Officer	Ranch Hand	367	1.0187	0.0001 (-0.0007,0.0010)	0.762	
	Comparison	502	1.0186			
Enlisted Flyer	Ranch Hand	161	1.0181	-0.0010 (-0.0023,0.0004)	0.152	
	Comparison	202	1.0190			
Enlisted Groundcrew	Ranch Hand	421	1.0198	-0.0002 (-0.0010,0.0006)	0.554	
	Comparison	574	1.0200			

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 17-9. (Continued)
Analysis of Urine Specific Gravity

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[a]		
Initial Dioxin	n	Mean	Adj. Mean[a]	R^2	Slope (Std. Error)	p-Value
Low	173	1.0183	1.0184	0.028	0.0003 (0.0002)	0.142
Medium	173	1.0192	1.0192			
High	172	1.0194	1.0193			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[b]			
Initial Dioxin	n	Adj. Mean[b]	R^2	Adj. Slope (Std. Error)	p-Value	Covariate Remarks
Low	173	1.0182**	0.048	0.0003 (0.0002)**	0.231**	INIT*AGE (p=0.024) OCC (p=0.033)
Medium	173	1.0190**				
High	172	1.0189**				

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted mean, adjusted slope, standard error, and
p-value derived from a model after deletion of this interaction; refer to Appendix Table M-2-5 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 17-9. (Continued)
Analysis of Urine Specific Gravity

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED					
Dioxin Category	**n**	**Mean**	**Adj. Mean[a]**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)**	**p-Value**
Comparison	1,062	1.0189	1.0189		
Background RH	374	1.0183	1.0186	-0.0003 (-0.0011,0.0004)	0.385
Low RH	259	1.0187	1.0186	-0.0003 (-0.0011,0.0006)	0.528
High RH	259	1.0192	1.0190	0.0001 (-0.0008,0.0009)	0.852
Low plus High RH	518	1.0190	1.0188	-0.0001 (-0.0008,0.0006)	0.774

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED					
Dioxin Category	**n**	**Adj. Mean[b]**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)**	**p-Value**	**Covariate Remarks**
Comparison	1,061	1.0191			OCC (p=0.001) DIAB (p=0.132)
Background RH	373	1.0190	-0.0001 (-0.0009,0.0007)	0.820	
Low RH	259	1.0188	-0.0003 (-0.0011,0.0006)	0.549	
High RH	259	1.0188	-0.0003 (-0.0012,0.0006)	0.507	
Low plus High RH	518	1.0188	-0.0003 (-0.0010,0.0004)	0.414	

[a] Adjusted for percent body fat at the time of duty in SEA, and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 17-9. (Continued)
Analysis of Urine Specific Gravity

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED						
	Current Dioxin Category Mean/(n)			Analysis Results for Log_2 (Current Dioxin + 1)		
Model[a]	Low	Medium	High	R^2	Slope (Std. Error)	p-Value
4	1.0183 (295)	1.0185 (299)	1.0192 (298)	0.007	0.0004 (0.0001)	0.013
5	1.0180 (300)	1.0187 (296)	1.0194 (296)	0.008	0.0003 (0.0001)	0.007
6[b]	1.0180 (299)	1.0187 (296)	1.0194 (296)	0.008	0.0003 (0.0001)	0.027

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED							
	Current Dioxin Category Adjusted Mean/(n)			Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	Low	Medium	High	R^2	Adj. Slope (Std. Error)	p-Value	Covariate Remarks
4	1.0183 (295)	1.0185 (299)	1.0192 (298)	0.007	0.0004 (0.0001)	0.013	
5	1.0180 (300)	1.0187 (296)	1.0194 (296)	0.008	0.0003 (0.0001)	0.007	
6[c]	1.0180 (299)	1.0186 (296)	1.0190 (296)	0.013	0.0002 (0.0002)	0.123	OCC (p=0.135)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Adjusted for log_2 total lipids.

[c] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Longitudinal Analysis

Longitudinal analyses were conducted on four variables—urinary protein, urinary red blood cell count, urinary white blood cell count, and urine specific gravity—to examine whether changes across time differed with respect to group membership (Model 1), initial dioxin (Model 2), and categorized dioxin (Model 3). Models 4, 5, and 6 were not examined in longitudinal analyses because current dioxin, the measure of exposure in these models, changes over time and is not available for all participants for 1982, 1985, or 1992. The longitudinal analyses for urinary protein investigated the difference between the 1982 examination and the 1992 examination, because the measurement technique and abnormal cutpoint remained unchanged. Measurement procedures at the 1982 examination differed from the techniques used at subsequent examinations for urinary red blood cell count and urine specific gravity. For the detection of urinary red blood cells, microscopic observation used at the 1985, 1987, and 1992 examinations replaced reagent strip testing used during the 1982 examination; and the multistick procedure incorporated at the 1985, 1987, and 1992 examinations replaced the falling drop method used during the 1982 examination for measuring urine specific gravity. Thus, longitudinal analyses for urinary red blood cell count and urine specific gravity studied changes between the 1985 examination and the 1992 examination. The longitudinal analyses for urinary white blood cell count investigated changes between the 1985 and 1992 examinations because the abnormal cutpoint in 1982 (>4 WBC per HPF) from the Kelsey-Sebold clinic differed from the cutpoint used at the 1985, 1987, and 1992 SCRF examinations (>2 WBC per HPF).

The longitudinal analyses for the discrete variables (urinary protein, urinary red blood cell count, urinary white blood cell count) examined relative risks at the 1992 examination for participants who were classified as normal at the earlier examination. Participants considered abnormal in 1982 (or 1985, as applicable) were excluded because the focus of the analyses was on investigating the temporal effects of dioxin during the period between 1982 or 1985 and 1992. Participants considered abnormal in 1982 or 1985 were already abnormal before this period; consequently, only participants considered normal at the 1982 or 1985 examination were considered to be at risk when the effects of dioxin over time are explored. The rate of abnormalities under this restriction approximates an incidence rate between 1982 or 1985 and 1992. All three models were adjusted for age; Models 2 and 3 were also adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

The longitudinal analysis for the continuous variable, urine specific gravity, examined the paired difference between the measurements from 1985 and 1992. These paired differences measured the change in urine specific gravity over time. Each of the three models used in the longitudinal analysis were adjusted for age and urine specific gravity measured in 1985. The analyses of Models 2 and 3 were also adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

Laboratory Examination Variables

Urinary Protein

The longitudinal analysis for Model 1 did not find a significant group difference in the presence of urinary protein for participants who had an absence of urinary protein in 1982 (Table 17-10(a): $p>0.27$ for all contrasts). Similarly, the analysis of Model 3 did not detect a significant relationship between urinary protein and categorized dioxin (Table 17-10(c): $p>0.14$ for all contrasts).

By contrast, Model 2 detected a marginally significant positive association between urinary protein and initial dioxin (Table 17-10(b): p=0.065, Adj. RR=1.38, 95% C.I.=[0.98, 1.94]). Of the Ranch Hand cohort without urinary protein in 1982, 5.4 percent of the participants in the high category of initial dioxin had urinary protein at the 1992 examination, while the percentages of abnormalities in the low and medium categories were 3.0 and 2.4 percent respectively.

Urinary Red Blood Cell Count

Longitudinal analyses for urinary red blood cell count were conditioned on participants without evidence of urinary red blood cells in 1985. No statistically significant results were detected with respect to group differences, associations with initial dioxin, or associations with categorized dioxin (Table 17-11(a-c): $p>0.14$ for all analyses).

In both the Ranch Hand and Comparison cohorts, the percentage of participants with urinary red blood cells in 1982 showed a marked increase between 1982 and 1985 and a decrease between 1985 and 1992. The increase between 1982 and 1985 was most likely due to the change in measurement method. The decrease in 1992 may have resulted in part because the 1985 examination defined presence as at least one urinary red blood cell in contrast to the 1992 examination, which defined an abnormality as more than two urinary red blood cells.

Urinary White Blood Cell Count

The longitudinal analysis of Model 1 did not uncover a significant overall group difference for urinary white blood cell counts (Table 17-12(a): p=0.204). However, stratifying the Model 1 analysis by occupation revealed a marginally significant adjusted relative risk for the enlisted groundcrew (Table 17-12(a): p=0.053, Adj. RR=2.51, 95% C.I.=[0.99, 6.39]). Of enlisted groundcrew who had no evidence of urinary white blood cells at the 1985 examination, Ranch Hands were more than twice as likely than Comparisons to have urinary white blood cells at the 1992 examination (Table 17-12(a): 3.7% vs. 1.5%).

Displayed in Table 17-12(b), the results of the Model 2 analysis did not reveal a significant association between urinary white blood cell count and initial dioxin (p=0.770). The longitudinal analysis for Model 3 detected a significant relative risk for the low plus high Ranch Hand category (Table 17-12(c): p=0.028, Adj. RR=2.41, 95% C.I.=[1.10, 5.30]).

Table 17-10.
Longitudinal Analysis of Urinary Protein

a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Percent Present/(n) Examination 1982	1985	1987	1992
All	***Ranch Hand***	***1.3***	***3.1***	***4.4***	***4.5***
		(898)	***(876)***	***(867)***	***(898)***
	Comparison	***1.5***	***2.6***	***3.9***	***4.4***
		(1,062)	***(1,039)***	***(1,036)***	***(1,062)***
Officer	Ranch Hand	1.8	2.1	4.2	4.7
		(340)	(335)	(334)	(340)
	Comparison	0.7	1.0	1.8	3.0
		(403)	(395)	(391)	(403)
Enlisted Flyer	Ranch Hand	1.3	1.3	2.6	3.8
		(158)	(156)	(153)	(158)
	Comparison	1.1	3.5	5.8	5.1
		(175)	(172)	(174)	(175)
Enlisted Groundcrew	Ranch Hand	1.0	4.7	5.3	4.5
		(400)	(385)	(380)	(400)
	Comparison	2.3	3.6	4.9	5.4
		(484)	(472)	(471)	(484)

Occupational Category	Group	Absent in 1982: n in 1992	Absent in 1982: Percent Present in 1992	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	***Ranch Hand***	***886***	***4.0***	***0.99 (0.63,1.57)***	***0.977***
	Comparison	***1,046***	***4.0***		
Officer	Ranch Hand	334	4.2	1.56 (0.70,3.49)	0.279
	Comparison	400	2.8		
Enlisted Flyer	Ranch Hand	156	3.9	0.83 (0.28,2.44)	0.729
	Comparison	173	4.6		
Enlisted Groundcrew	Ranch Hand	396	3.8	0.80 (0.41,1.56)	0.510
	Comparison	473	4.9		

[a] Relative risk, confidence interval, and p-value are in reference to a contrast of 1982 and 1992 results; results adjusted for age in 1992.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations. Statistical analyses are based only on participants who had no urinary protein present in 1982 (see Chapter 7, Statistical Methods).

Table 17-10. (Continued)
Longitudinal Analysis of Urinary Protein

b) MODEL 2: RANCH HANDS — INITIAL DIOXIN				
	Percent Present/(n) Examination			
Initial Dioxin	1982	1985	1987	1992
Low	0.6 (166)	4.3 (163)	4.9 (165)	3.6 (166)
Medium	1.2 (169)	3.1 (163)	5.5 (165)	3.0 (169)
High	0.0 (167)	3.0 (165)	3.7 (161)	5.4 (167)

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
	Absent in 1982			
Initial Dioxin	n in 1992	Percent Present in 1992	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	165	3.0	1.38 (0.98,1.94)	0.065
Medium	167	2.4		
High	167	5.4		

[a] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and age in 1992.

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

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations. Statistical analyses are based only on participants who had no urinary protein present in 1982 (see Chapter 7, Statistical Methods).

Table 17-10. (Continued)
Longitudinal Analysis of Urinary Protein

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY				
	Percent Present/(n) Examination			
Dioxin Category	**1982**	**1985**	**1987**	**1992**
Comparison	1.4 (916)	2.2 (905)	4.1 (906)	4.6 (916)
Background RH	2.4 (341)	2.7 (338)	3.6 (335)	4.7 (341)
Low RH	0.8 (249)	3.3 (243)	5.3 (247)	3.6 (249)
High RH	0.4 (253)	3.6 (248)	4.1 (244)	4.4 (253)
Low plus High RH	0.6 (502)	3.5 (491)	4.7 (491)	4.0 (502)

	Absent in 1982			
Dioxin Category	**n in 1992**	**Percent Present in 1992**	**Adj. Relative Risk (95% C.I.)[ab]**	**p-Value[b]**
Comparison	903	4.2		
Background RH	333	4.2	1.16 (0.61,2.20)	0.650
Low RH	247	2.8	0.54 (0.23,1.23)	0.143
High RH	252	4.4	0.99 (0.49,2.03)	0.989
Low plus High RH	499	3.6	0.74 (0.41,1.34)	0.324

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and age in 1992.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations. Statistical analyses are based only on participants who had no urinary protein present in 1982 (see Chapter 7, Statistical Methods).

Table 17-11.
Longitudinal Analysis of Urinary Red Blood Cell Count

a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Percent Abnormal/(n) Examination 1982	1985	1987	1992
All	***Ranch Hand***	***1.4***	***17.8***	***8.6***	***3.1***
		(877)	***(912)***	***(887)***	***(912)***
	Comparison	***0.8***	***16.2***	***6.8***	***2.3***
		(1,038)	***(1,152)***	***(1,129)***	***(1,152)***
Officer	Ranch Hand	1.8	14.8	6.4	2.6
		(335)	(352)	(345)	(352)
	Comparison	0.5	13.1	5.5	0.9
		(394)	(444)	(435)	(444)
Enlisted Flyer	Ranch Hand	0.6	17.7	11.7	2.5
		(156)	(158)	(154)	(158)
	Comparison	1.2	20.1	8.1	2.1
		(172)	(189)	(186)	(189)
Enlisted Groundcrew	Ranch Hand	1.3	20.4	9.3	3.7
		(386)	(402)	(388)	(402)
	Comparison	0.9	17.5	7.5	3.5
		(472)	(519)	(508)	(519)

Occupational Category	Group	Normal in 1985: n in 1992	Normal in 1985: Percent Abnormal in 1992	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	***Ranch Hand***	***750***	***1.6***	***0.91 (0.43,1.91)***	***0.796***
	Comparison	***965***	***1.8***		
Officer	Ranch Hand	300	1.3	1.71 (0.38,7.72)	0.483
	Comparison	386	0.8		
Enlisted Flyer	Ranch Hand	130	2.3	1.16 (0.23,5.90)	0.857
	Comparison	151	2.0		
Enlisted Groundcrew	Ranch Hand	320	1.6	0.61 (0.21,1.78)	0.367
	Comparison	428	2.6		

[a] Relative risk, confidence interval, and p-value are in reference to a contrast of 1985 and 1992 results; results adjusted for age in 1992.

Note: Summary statistics for 1982 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1985, 1987, and 1992 examinations. Statistical analyses are based only on participants who had normal urinary red blood cell counts in 1985 (see Chapter 7, Statistical Methods).

Table 17-11. (Continued)
Longitudinal Analysis of Urinary Red Blood Cell Count

b) MODEL 2: RANCH HANDS — INITIAL DIOXIN				
	Percent Abnormal/(n) Examination			
Initial Dioxin	1982	1985	1987	1992
Low	0.6 (163)	12.6 (167)	7.2 (167)	1.8 (167)
Medium	4.3 (163)	19.2 (167)	12.2 (164)	7.2 (167)
High	0.6 (165)	20.1 (169)	9.2 (163)	3.0 (169)

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
	Normal in 1985			
Initial Dioxin	n in 1992	Percent Abnormal in 1992	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	146	0.7	1.26 (0.77,2.08)	0.372
Medium	135	4.4		
High	135	1.5		

[a] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and age in 1992.

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

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Summary statistics for 1982 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1985, 1987, and 1992 examinations. Statistical analyses are based only on participants who had normal urinary red blood cell counts in 1985 (see Chapter 7, Statistical Methods).

Table 17-11. (Continued)
Longitudinal Analysis of Urinary Red Blood Cell Count

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY				
	Percent Abnormal/(n) Examination			
Dioxin Category	**1982**	**1985**	**1987**	**1992**
Comparison	0.9 (904)	16.3 (997)	7.0 (987)	2.0 (997)
Background RH	0.9 (339)	16.9 (361)	7.4 (353)	2.2 (361)
Low RH	2.1 (243)	13.6 (250)	7.7 (248)	2.4 (250)
High RH	1.6 (248)	21.0 (253)	11.4 (246)	5.5 (253)
Low plus High RH	1.8 (491)	17.3 (503)	9.5 (494)	4.0 (503)

	Normal in 1985			
Dioxin Category	**n in 1992**	**Percent Abnormal in 1992**	**Adj. Relative Risk (95% C.I.)[ab]**	**p-Value[b]**
Comparison	835	1.3		
Background RH	300	1.0	0.78 (0.21,2.83)	0.703
Low RH	216	1.4	0.91 (0.24,3.40)	0.883
High RH	200	3.0	2.17 (0.76,6.19)	0.146
Low plus High RH	416	2.2	1.48 (0.60,3.70)	0.397

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and age in 1992.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Summary statistics for 1982 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1985, 1987, and 1992 examinations. Statistical analyses are based only on participants who had normal urinary red blood cell counts in 1985 (see Chapter 7, Statistical Methods).

Table 17-12.
Longitudinal Analysis of Urinary White Blood Cell Count

a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Percent Abnormal/(n) Examination 1982	1985	1987	1992
All	*Ranch Hand*	*1.5*	*10.0*	*7.1*	*3.5*
		(877)	*(912)*	*(886)*	*(912)*
	Comparison	*2.3*	*7.8*	*6.6*	*2.7*
		(1,039)	*(1,153)*	*(1,130)*	*(1,153)*
Officer	Ranch Hand	1.5	7.4	6.1	2.0
		(335)	(352)	(345)	(352)
	Comparison	1.5	5.8	7.1	2.3
		(395)	(445)	(436)	(445)
Enlisted Flyer	Ranch Hand	0.6	10.8	7.1	4.4
		(156)	(158)	(154)	(158)
	Comparison	2.3	7.4	3.8	5.3
		(172)	(189)	(186)	(189)
Enlisted Groundcrew	Ranch Hand	1.8	11.9	8.0	4.5
		(386)	(402)	(387)	(402)
	Comparison	3.0	9.6	7.3	2.1
		(472)	(519)	(508)	(519)

Occupational Category	Group	Normal in 1985: n in 1992	Normal in 1985: Percent Abnormal in 1992	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	*Ranch Hand*	*821*	*2.4*	*1.53 (0.79,2.93)*	*0.204*
	Comparison	*1,063*	*1.6*		
Officer	Ranch Hand	326	0.9	0.76 (0.18,3.23)	0.715
	Comparison	419	1.2		
Enlisted Flyer	Ranch Hand	141	2.8	0.98 (0.26,3.71)	0.976
	Comparison	175	2.9		
Enlisted Groundcrew	Ranch Hand	354	3.7	2.51 (0.99,6.39)	0.053
	Comparison	469	1.5		

[a] Relative risk, confidence interval, and p-value are in reference to a contrast of 1985 and 1992 results; results adjusted for age in 1992.

Note: Summary statistics for 1982 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1985, 1987, and 1992 examinations. Statistical analyses are based only on participants who had normal urinary white blood cell counts in 1985 (see Chapter 7, Statistical Methods).

Table 17-12. (Continued)
Longitudinal Analysis of Urinary White Blood Cell Count

b) MODEL 2: RANCH HANDS — INITIAL DIOXIN				
	Percent Abnormal/(n) Examination			
Initial Dioxin	1982	1985	1987	1992
Low	3.1 (163)	11.4 (167)	9.6 (166)	3.6 (167)
Medium	2.5 (163)	11.4 (167)	7.3 (164)	4.2 (167)
High	0.6 (165)	10.7 (169)	8.6 (163)	3.6 (169)

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
	Normal in 1985			
Initial Dioxin	n in 1992	Percent Abnormal in 1992	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	148	3.4	0.94 (0.61,1.44)	0.770
Medium	148	3.4		
High	151	2.7		

[a] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and age in 1992.

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

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Summary statistics for 1982 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1985, 1987, and 1992 examinations. Statistical analyses are based only on participants who had normal urinary white blood cell counts in 1985 (see Chapter 7, Statistical Methods).

Table 17-12. (Continued)
Longitudinal Analysis of Urinary White Blood Cell Count

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY

	Percent Abnormal/(n) Examination			
Dioxin Category	**1982**	**1985**	**1987**	**1992**
Comparison	2.4 (905)	7.6 (998)	6.6 (988)	2.4 (998)
Background RH	0.9 (339)	8.3 (361)	6.0 (353)	2.5 (361)
Low RH	2.5 (243)	11.6 (250)	8.5 (247)	3.6 (250)
High RH	1.6 (248)	10.7 (253)	8.5 (246)	4.0 (253)
Low plus High RH	2.0 (491)	11.1 (503)	8.5 (493)	3.8 (503)

	Normal in 1985			
Dioxin Category	**n in 1992**	**Percent Abnormal in 1992**	**Adj. Relative Risk (95% C.I.)[ab]**	**p-Value[b]**
Comparison	922	1.3		
Background RH	331	0.9	0.69 (0.19,2.50)	0.577
Low RH	221	3.2	2.38 (0.92,6.15)	0.074
High RH	226	3.1	2.45 (0.94,6.42)	0.068
Low plus High RH	447	3.1	2.41 (1.10,5.30)	0.028

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and age in 1992.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Summary statistics for 1982 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1985, 1987, and 1992 examinations. Statistical analyses are based only on participants who had normal urinary white blood cell counts in 1985 (see Chapter 7, Statistical Methods).

Only 1.3 percent of Comparisons with normal counts of urinary white blood cells during the 1985 examination had abnormal counts of urinary white blood cells at the 1992 examination, while 3.1 percent of Ranch Hands in the low plus high category of dioxin with normal urinary white blood cells counts in 1985 displayed abnormal urinary white blood cell counts in 1992. In addition, the low Ranch Hand category of dioxin and the high Ranch Hand category of dioxin displayed marginally significant relative risks (Table 17-12(c): $p=0.074$, Adj. RR=2.38, 95% C.I.=[0.92, 6.15]; $p=0.068$, Adj. RR=2.45, 95% C.I.=[0.94, 6.42] respectively). Examination of Ranch Hands in the low dioxin category and the high dioxin category with normal urinary white blood cell counts in 1985 revealed that the prevalence rates for abnormal urinary white blood cell counts in 1992 were similar for the two categories (3.2% and 3.1% respectively).

Similar to the urinary red blood cell count findings, the prevalence rate of urinary white blood cells increased substantially between 1982 and 1985, and decreased between 1985 and 1992 in both the Ranch Hand and Comparison groups. The difference between the 1982 and 1985 results is partly because an abnormality in 1982 was defined as >4 WBC per HPF, while in 1985 an abnormality was defined as >2 WBC per HPF.

Urine Specific Gravity

Examination of the paired difference between 1985 and 1992 for urine specific gravity did not uncover a significant group difference (Model 1 analysis, Table 17-13(a): $p>0.21$ for all contrasts). Also, the analyses of Models 2 and 3 did not find a significant association with initial dioxin or categorized dioxin (Table 17-13(b,c): $p>0.17$ for all analyses).

DISCUSSION

In clinical practice, the presence of renal or urinary tract disease can be determined with confidence based on the medical history, physical examination, and the five laboratory indices included in the current analysis.

Although subject to some day-to-day variation related to diet and state of hydration, the serum creatinine is considered a reliable index of glomerular filtration, while the integrity and concentrating ability of the renal tubular system are reflected in the urine specific gravity. In documenting the presence of red or white blood cells in significant numbers, the examination of the urinary sediment can provide valuable clues to the presence of a broad range of infectious, inflammatory, and neoplastic conditions intrinsic to the upper and lower urinary tracts.

Pertinent to the interpretation of the renal assessment data and to the covariate associations noted below is the frequent finding in ambulatory medicine of isolated abnormalities in the routine urinalysis of healthy individuals who in fact have no disease of the genitourinary system. With normal fluid balance, the healthy kidneys can excrete up to 100 mg to 150 mg of total protein in 24 hours. The qualitative dipstick test used in the current study is sensitive to protein concentrations as low as 10 mg to 15 mg per deciliter and, particularly in specimens collected after overnight fasting, will often give a trace to 1+ positive reaction in the absence of intrinsic renal disease.

Table 17-13.
Longitudinal Analysis of Urine Specific Gravity

a) MODEL 1: RANCH HANDS VS. COMPARISONS								
		Mean/(n) Examination						
Occupational Category	Group	1982	1985	1987	1992	Exam. Mean Change[a]	Difference of Exam. Mean Change	p-Value[b]
All	***Ranch Hand***	1.0190 (877)	1.0157 (912)	1.0199 (887)	1.0188 (912)	0.0030	-0.0006	0.268
	Comparison	1.0181 (1,038)	1.0153 (1,152)	1.0200 (1,129)	1.0190 (1,152)	0.0037		
Officer	***Ranch Hand***	1.0211 (335)	1.0148 (352)	1.0191 (345)	1.0184 (352)	0.0035	-0.0001	0.819
	Comparison	1.0156 (394)	1.0146 (444)	1.0189 (435)	1.0182 (444)	0.0036		
Enlisted Flyer	***Ranch Hand***	1.0132 (156)	1.0151 (158)	1.0190 (154)	1.0177 (158)	0.0027	-0.0002	0.349
	Comparison	1.0210 (172)	1.0157 (189)	1.0202 (186)	1.0185 (189)	0.0028		
Enlisted Groundcrew	***Ranch Hand***	1.0195 (386)	1.0167 (402)	1.0209 (388)	1.0195 (402)	0.0028	-0.0013	0.216
	Comparison	1.0191 (472)	1.0157 (519)	1.0209 (508)	1.0198 (519)	0.0040		

[a] Difference between 1992 and 1985 examination means.

[b] Results adjusted for urine specific gravity in 1985 and age in 1992.

Note: Summary statistics for 1982 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1985, 1987, and 1992 examinations.

Table 17-13. (Continued)
Longitudinal Analysis of Urine Specific Gravity

b) MODEL 2: RANCH HANDS — INITIAL DIOXIN						
	Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[a]	
	Mean/(n) Examination					
Initial Dioxin	1982	1985	1987	1992	Adj. Slope (Std. Error)	p-Value
Low	1.0148 (163)	1.0149 (167)	1.0199 (167)	1.0183 (167)	0.0003 (0.0002)	0.178
Medium	1.0146 (163)	1.0167 (167)	1.0203 (164)	1.0193 (167)		
High	1.0218 (165)	1.0167 (169)	1.0206 (163)	1.0196 (169)		

[a] Results based on difference between 1992 and 1985 urine specific gravity versus $\log_2$ (initial dioxin); results adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, 1985 urine specific gravity, and age in 1992.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Summary statistics for 1982 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1985, 1987, and 1992 examinations.

Table 17-13. (Continued)
Longitudinal Analysis of Urine Specific Gravity

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY							
	Mean/(n) Examination						
Dioxin Category	1982	1985	1987	1992	Exam. Mean Change[a]	Difference of Exam. Mean Change[b]	p-Value[c]
Comparison	1.0175 (904)	1.0152 (997)	1.0200 (987)	1.0190 (997)	0.0038		
Background RH	1.0214 (339)	1.0152 (361)	1.0194 (353)	1.0183 (361)	0.0032	-0.0006	0.351
Low RH	1.0124 (243)	1.0153 (250)	1.0200 (248)	1.0187 (250)	0.0035	-0.0003	0.527
High RH	1.0217 (248)	1.0169 (253)	1.0205 (246)	1.0193 (253)	0.0024	-0.0014	0.479
Low plus High RH	1.0171 (491)	1.0161 (503)	1.0203 (494)	1.0190 (503)	0.0029	-0.0008	0.386

[a] Difference between 1992 and 1985 examination means.

[b] Difference between Ranch Hand dioxin category and Comparison category.

[c] Results adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, 1985 urine specific gravity, and age in 1992.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Summary statistics for 1982 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1985, 1987, and 1992 examinations.

Similarly, on microscopic examination of the urinary sediment, it is not unusual to find a few red or white blood cells in the absence of definable neoplastic or inflammatory cause, trauma, or renal calculi. When documented as an isolated finding in the absence of symptoms or other signs, such intermittent microcyturia usually can be considered benign and safely followed over time.

In the current assessment, no significant group differences were noted in the history of urinary tract disease. Furthermore, in the Ranch Hand cohort, there was no evidence linking prior dioxin exposure or the current body burden of dioxin to the occurrence of renal disease or the presence of renal calculi detected by plain films of the abdomen.

In the analyses of laboratory data, several statistically significant associations were documented. Although the prevalence of microhematuria was similar in both groups, Ranch Hands with the highest levels of extrapolated initial dioxin had a significantly higher prevalence of microhematuria than Comparisons in both the unadjusted (5.8% vs. 2.0%, p=0.002) and adjusted (p=0.003) analyses. These results are similar to those documented in the Serum Dioxin Analysis Report, when hematuria was noted in 10.2 percent of Ranch Hands with high initial dioxin levels versus 4.9 percent of those with low exposure. Although not statistically significant, the analyses employing current serum dioxin yielded results consistent with a dose-response effect. Clinically, the finding of hematuria can signal the presence of "silent" renal calculi or neoplastic disease.

The presence of white blood cells in the urine (pyuria) can be a marker for the presence of a urinary tract infection. Though the overall history of renal disease was similar in both cohorts, those Ranch Hands most highly exposed to dioxin, the enlisted groundcrew, had twice the prevalence of pyuria as Comparisons (4.5% vs. 2.1%; p=0.047).

The analysis of urine specific gravity documented a highly significant positive association with current serum dioxin in all models, but the differences in the means are not clinically significant. Analyses of serum creatinine and proteinuria revealed no differences between the cohorts.

Dependent variable-covariate analyses revealed several associations that are well established in clinical practice. The increased occurrence of urinary tract disease in older participants would be expected with benign enlargement of the prostate, as would the more common occurrence of renal calculi. The gradual reduction in renal mass and renal plasma flow that occurs with benign nephrosclerosis is associated with age-related increases in serum creatinine and proteinuria. Blacks, at increased risk for hypertension associated with nephropathy, were found to be at increased risk for proteinuria, hematuria and elevation in the serum creatinine. Finally, in diabetics, the increased occurrence of hypertensive arteriosclerotic vascular disease and urinary tract infections related to glycosuria provide a reasonable explanation for the significant covariate associations with proteinuria, pyuria, and the history of renal disease.

With respect to the variables analyzed longitudinally, there was no evidence of any detriment related to the current body burden of dioxin. Consistent with the exposure analysis results noted above, enlisted groundcrew Ranch Hands were, by longitudinal analysis, twice as likely as enlisted groundcrew Comparisons to develop pyuria over time. Though this finding raises the possibility of a subtle inflammatory reaction, the similar prevalence of pyuria in Ranch Hands with low (3.3%) and high (3.6%) levels of serum dioxin provides evidence against a dose-response effect.

In summary, the data analyzed in the current section revealed abnormalities in five laboratory indices common in ambulatory practice. With the possible exception of hematuria noted above, there was no consistent evidence for any detriment related to current body burden of dioxin or to the estimated severity of prior exposure.

SUMMARY

Seven dependent variables were analyzed in the Renal Assessment—kidney disease, kidney stones, urinary protein, urinary red blood cell count, urinary white blood cell count, serum creatinine, and urine specific gravity. Subjects' prior history of kidney disease was verified from medical records and the presence of kidney stones by x ray was evaluated during the physical exam. The remaining five variables were measured through laboratory analysis. These seven health endpoints were analyzed for associations with group (Model 1), initial dioxin (Model 2), categorized initial dioxin (Model 3), current lipid-adjusted dioxin (Model 4), and current whole-weight dioxin (Models 5 and 6). Of the seven variables, serum creatinine and urine specific gravity were analyzed in continuous form, while the other five variables were examined in discrete form. In addition, four of the seven variables were examined longitudinally (urinary protein, urinary red blood cell count, urinary white blood cell count, and urine specific gravity). The results of the group, initial dioxin, categorized dioxin and current dioxin analyses are summarized in Tables 17-14 through 17-17. A summary of group-by-covariate and dioxin-by-covariate interactions is found in Table 17-18.

Model 1: Group Analysis

Examination of the unadjusted and adjusted results from Model 1 showed no significant overall group differences among the seven variables. However, when the analyses were stratified by occupation, a significant group difference was detected for urinary white blood cell count in the enlisted groundcrew stratum (Adj. RR=2.23, 95% C.I.=[1.07, 4.67]).

The longitudinal analysis results paralleled these findings. A significant overall group difference was not detected for each of the longitudinal variables. However, stratifying the results by occupation revealed a significant group difference within the enlisted groundcrew stratum for increases in urinary white blood cell count over time (Table 17-12(a): Adj. RR=2.69, 95% C.I.=[1.14, 6.32]). The adjusted relative risks estimated from the Model 1 analysis were based on participants without evidence of urinary white blood cells in 1982.

Model 2: Initial Dioxin Analysis

Reviewing the results of Model 2, kidney stones was the only variable that displayed a significant association with initial dioxin. The unadjusted analysis exhibited a significant decrease in kidney stones with increasing initial dioxin. This association became marginally significant after adjusting for age.

Table 17-14.
Summary of Group Analyses (Model 1) for Renal Variables
(Ranch Hands vs. Comparisons)

	UNADJUSTED			
Variable	**All**	**Officer**	**Enlisted Flyer**	**Enlisted Groundcrew**
Medical Records				
History of Kidney Disease (D)	NS	NS	NS	ns
Physical Examination				
Kidney Stones (D)	NS	ns	NS	NS
Laboratory				
Urinary Protein (D)	NS	NS	ns	ns
Urinary Red Blood Cell Count (D)	NS	NS	NS	NS
Urinary White Blood Cell Count (D)	NS	ns	ns	+0.047
Serum Creatinine (C)	NS	ns	NS	NS
Urine Specific Gravity (C)	ns	NS	ns	ns

C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥ 1.00.
NS or ns: Not significant ($p > 0.10$).
Note: P-value given if $p \leq 0.05$.
A capital "NS" denotes a relative risk of 1.00 or greater for discrete analyses or difference of means nonnegative for continuous analyses. A lower case "ns" denotes relative risk less than 1.00 for discrete analyses or difference of means negative for continuous analyses.

Table 17-14. (Continued)
Summary of Group Analyses (Model 1) for Renal Variables
(Ranch Hands vs. Comparisons)

	ADJUSTED			
Variable	**All**	**Officer**	**Enlisted Flyer**	**Enlisted Groundcrew**
Medical Records				
History of Kidney Disease (D)	NS	NS	NS	ns
Physical Examination				
Kidney Stones (D)	NS	ns	NS	NS
Laboratory				
Urinary Protein (D)	NS	NS	ns	ns
Urinary Red Blood Cell Count (D)	NS	NS	NS	NS
Urinary White Blood Cell Count (D)	NS	ns	ns	+0.033
Serum Creatinine (C)	**(NS)	**(NS)	**(NS)	**(ns)
Urine Specific Gravity (C)	ns	NS	ns	ns

C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥ 1.00.
NS or ns: Not significant ($p>0.10$).
**(NS) or **(ns): Group-by-covariate interaction ($p\leq0.05$); not significant when interaction is deleted; refer to Appendix M-2 for further analysis of this interaction.
Note: P-value given if $p\leq0.05$.
A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or difference of means nonnegative for continuous analysis; a lower case "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

Table 17-15.
Summary of Initial Dioxin Analyses (Model 2) for Renal Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Medical Records		
History of Kidney Disease (D)	ns	ns
Physical Examination		
Kidney Stones (D)	-0.016	**(ns*)
Laboratory		
Urinary Protein (D)	NS	NS
Urinary Red Blood Cell Count (D)	NS	NS
Urinary White Blood Cell Count (D)	ns	ns
Serum Creatinine (C)	ns	**(ns)
Urine Specific Gravity (C)	NS	**(NS)

C: Continuous analysis.
D: Discrete analysis.
-: Relative risk < 1.00.
NS or ns: Not significant ($p>0.10$).
ns*: Marginally significant ($0.05<p\leq0.10$).
**(NS) or **(ns): Log_2 (initial dioxin)-by-covariate interaction ($p\leq0.05$); not significant when interaction is deleted; refer to Appendix M-2 for further analysis of this interaction.
**(ns*): Log_2 (initial dioxin)-by-covariate interaction ($p\leq0.05$); marginally significant when interaction is deleted; refer to Appendix M-2 for further analysis of this interaction.
Note: P-value given if $p\leq0.05$.
A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or nonnegative slope for continuous analysis; a lowercase "ns" denotes relative risk less than 1.00 for discrete analysis or negative slope for continuous analysis.

Table 17-16.
Summary of Categorized Dioxin Analyses (Model 3) for Renal Variables (Ranch Hands vs. Comparisons)

	UNADJUSTED			
Variable	**Background Ranch Hands vs. Comparisons**	**Low Ranch Hands vs. Comparisons**	**High Ranch Hands vs. Comparisons**	**Low plus High Ranch Hands vs. Comparisons**
Medical Records				
History of Kidney Disease (D)	NS	NS	NS	NS
Physical Examination				
Kidney Stones (D)	NS	NS	NS	NS
Laboratory				
Urinary Protein (D)	NS	ns	ns	ns
Urinary Red Blood Cell Count (D)	NS	NS	+0.002	+0.019
Urinary White Blood Cell Count (D)	NS	NS	NS	NS
Serum Creatinine (C)	ns	NS	ns	NS
Urine Specific Gravity (C)	ns	ns	NS	ns

C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥ 1.00.
NS or ns: Not significant ($p>0.10$).
Note: P-value given if $p \leq 0.05$.
A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or difference of means nonnegative for continuous analysis; a lower case "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

Table 17-16. (Continued)
Summary of Categorized Dioxin Analyses (Model 3) for Renal Variables
(Ranch Hands vs. Comparisons)

	ADJUSTED			
Variable	**Background Ranch Hands vs. Comparisons**	**Low Ranch Hands vs. Comparisons**	**High Ranch Hands vs. Comparisons**	**Low plus High Ranch Hands vs. Comparisons**
Medical Records				
History of Kidney Disease (D)	NS	NS	NS	NS
Physical Examination				
Kidney Stones (D)	ns	NS	NS	NS
Laboratory				
Urinary Protein (D)	NS	ns	ns	ns
Urinary Red Blood Cell Count (D)	**(NS)	**(NS)	**(+0.003)	**(+0.035)
Urinary White Blood Cell Count (D)	NS	NS	NS	NS
Serum Creatinine (C)	**(ns)	**(NS)	**(ns)	**(NS)
Urine Specific Gravity (C)	ns	ns	ns	ns

C: Continuous analysis.
D: Discrete analysis.
+: Relative risk $\geq$ 1.00.
NS or ns: Not significant ($p > 0.10$).
**(NS) or **(ns): Categorized dioxin-by-covariate interaction ($p \leq 0.05$); not significant when interaction is deleted; refer to Appendix M-2 for further analysis of this interaction.
**(...): Categorized dioxin-by-covariate interaction ($p \leq 0.05$); significant when interaction is deleted and p-value is given in parentheses; refer to Appendix M-2 for further analysis of this interaction.
Note: P-value given if $p \leq 0.05$.
A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or difference of means nonnegative for continuous analysis; a lower case "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

Table 17-17.
Summary of Current Dioxin Analyses (Models 4, 5, and 6) for Renal Variables (Ranch Hands Only)

	UNADJUSTED		
Variable	**Model 4: Lipid-Adjusted Current Dioxin**	**Model 5: Whole-Weight Current Dioxin**	**Model 6: Whole-Weight Current Dioxin Adjusted for Total Lipids**
Medical Records			
History of Kidney Disease (D)	NS	NS	NS
Physical Examination			
Kidney Stones (D)	ns	ns	ns
Laboratory			
Urinary Protein (D)	NS	NS	NS
Urinary Red Blood Cell Count (D)	NS	NS	NS
Urinary White Blood Cell Count (D)	NS	NS	NS
Serum Creatinine (C)	NS	NS	NS
Urine Specific Gravity (C)	+0.013	+0.007	+0.027

C: Continuous analysis.
D: Discrete analysis.
+: Slope nonnegative.
NS or ns: Not significant.
Note: P-value given if $p \leq 0.05$.
A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or nonnegative slope for continuous analysis; a lower case "ns" denotes relative risk less than 1.00 for discrete analysis or negative slope for continuous analysis.

Table 17-17. (Continued)
Summary of Current Dioxin Analyses (Models 4, 5, and 6) for Renal Variables (Ranch Hands Only)

	ADJUSTED		
Variable	**Model 4: Lipid-Adjusted Current Dioxin**	**Model 5: Whole-Weight Current Dioxin**	**Model 6: Whole-Weight Current Dioxin Adjusted for Total Lipids**
Medical Records			
History of Kidney Disease (D)	NS	NS	NS
Physical Examination			
Kidney Stones (D)	ns	ns	ns
Laboratory			
Urinary Protein (D)	**(NS)	**(NS)	**(NS)
Urinary Red Blood Cell Count (D)	**(NS)	**(NS)	**(NS)
Urinary White Blood Cell Count (D)	ns	ns	ns
Serum Creatinine (C)	NS	NS	NS
Urine Specific Gravity (C)	+0.013	+0.007	NS

C: Continuous analysis.
D: Discrete analysis.
+: Slope nonnegative.
NS or ns: Not significant.
**(NS): Log_2 (current dioxin + 1)-by-covariate interaction ($p \leq 0.05$); not significant when interaction is deleted; refer to Appendix M-2 for further analysis of this interaction.
Note: P-value given if $p \leq 0.05$.
A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or nonnegative slope for continuous analysis; a lower case "ns" denotes relative risk less than 1.00 for discrete analysis or negative slope for continuous analysis.

Table 17-18.
Summary of Group-by-Covariate and Dioxin-by-Covariate Interactions from Analyses of Renal Variables

Model	Variable	Covariate
1[a]	Serum Creatinine	Diabetic Class
2[b]	Kidney Stones	Diabetic Class
	Serum Creatinine	Diabetic Class
	Urine Specific Gravity	Age
3[c]	Urinary Red Blood Cell Count	Occupation
	Serum Creatinine	Diabetic Class
4[d]	Urinary Protein	Diabetic Class
	Urinary Red Blood Cell Count	Occupation
5[e]	Urinary Protein	Diabetic Class
	Urinary Red Blood Cell Count	Occupation
6[f]	Urinary Protein	Diabetic Class
	Urinary Red Blood Cell Count	Occupation

[a] Group Analysis (Ranch Hands vs. Comparisons).
[b] Ranch Hand—Log_2 (Initial Dioxin).
[c] Categorized Dioxin.
[d] Ranch Hand—Log_2 (Current Lipid-Adjusted Dioxin + 1).
[e] Ranch Hand—Log_2 (Current Whole-Weight Dioxin + 1).
[f] Ranch Hand—Log_2 (Current Whole-Weight Dioxin + 1) Adjusted for Total Lipids.

The longitudinal analyses of urinary protein revealed a marginally significant positive association with initial dioxin; results for the other variables analyzed longitudinally were not significant.

Model 3: Categorized Dioxin Analysis

For Model 3, urinary red blood cell count was the only variable to display a significant association with categorized dioxin. A significant difference was observed between the high Ranch Hand and Comparison categories in both the unadjusted and adjusted analyses (Adj. RR=2.98, 95% C.I.=[1.45, 6.14]). Also, both analyses detected a significant relative risk for the low plus high Ranch Hand category (Adj. RR=1.97, 95% C.I.=[1.05, 3.68]). The Model 3 longitudinal analyses were not significant.

Models 4, 5, and 6: Current Dioxin Analysis

Urine specific gravity was the only variable in the analyses of Models 4 through 6 to display a significant association with current dioxin. The unadjusted analyses of Models 4 through 6 revealed a significant positive association with current dioxin. The adjusted analyses for Models 4 and 5 were identical to the unadjusted analyses because no covariates were retained in the final models. By contrast, the adjusted Model 6 analysis kept occupation in the final model causing the relationship between urine specific gravity and current dioxin to become nonsignificant.

CONCLUSION

The analysis of the seven renal health endpoints revealed isolated statistically significant findings, but did not reveal consistent evidence for any detriment related to group membership, estimated initial dioxin exposure, or current serum dioxin levels. One finding that deserves scrutiny in future examination cycles is the higher prevalence of urinary red blood cells (microhematuria) for Ranch Hands in the high initial dioxin category relative to the Comparison group. This is consistent with the significant positive dose-response relationship between microhematuria and initial dioxin levels (Ranch Hands only) noted in the results of the 1987 examination. However, none of the other 1992 exposure analysis results were statistically significant for urinary red blood cell count, and the longitudinal analyses indicate that the prevalence of microhematuria has decreased in the Ranch Hand cohort at each of the last two cycles. Clinically, the detection of urinary red blood cells may signal the presence of silent renal calculi or neoplastic disease. The analyses of kidney stones did not support the presence of silent renal calculi. Neoplastic disease is discussed in Chapter 10, Neoplasia.

CHAPTER 17
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