TABLE 17-12. (Continued)

Analysis of Rales

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

Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.765[b]
(n=521)	≤18.6	0.0 (72)	2.3 (128)	0.0 (54)	1.22 (0.45,3.31)	0.692[c]
	>18.6	1.7 (58)	0.8 (132)	3.9 (77)	1.01 (0.51,2.03)	0.967[c]
f) Maximal						0.496[b]
(n=742)	≤18.6	1.9 (106)	0.5 (191)	2.4 (83)	0.94 (0.45,1.96)	0.864[c]
	>18.6	0.0 (79)	1.1 (179)	2.9 (104)	1.29 (0.74,2.23)	0.373[c]

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

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal			0.607[b]	AGE (p<0.001)
(n=521)	≤18.6	1.87 (0.66,5.26)	0.236[c]	
	>18.6	1.36 (0.68,2.69)	0.383[c]	
h) Maximal			0.545[b]	AGE (p<0.001)
(n=742)	≤18.6	1.19 (0.53,2.67)	0.680[c]	CSMOK (p=0.142)
	>18.6	1.59 (0.90,2.81)	0.107[c]	

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

[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).

[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 17-12. (Continued)

Analysis of Rales

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

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	786	1.7	All Categories		0.551
Unknown	345	1.2	Unknown vs. Background	0.70 (0.23,2.15)	0.531
Low	196	1.0	Low vs. Background	0.61 (0.14,2.74)	0.522
High	187	2.7	High vs. Background	1.63 (0.58,4.64)	0.357
Total	1,514				

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

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	786	All Categories		0.145	AGE (p<0.001) CSMOK (p=0.021)
Unknown	345	Unknown vs. Background	0.65 (0.21,2.06)	0.468	
Low	196	Low vs. Background	0.61 (0.13,2.79)	0.527	
High	187	High vs. Background	3.03 (1.00,9.14)	0.049	
Total	1,514				

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

p=0.448 for the minimal assumption and p=0.429 for the maximal assumption). After the models were adjusted for age, the association between initial dioxin and rales remained nonsignificant under both assumptions (Table 17-12 [c] and [d]: p=0.142 for the minimal assumption and p=0.171 for the maximal assumption).

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

The current dioxin-by-time since tour interaction was not significant for both the unadjusted minimal and maximal analyses of rales (Table 17-12 [e] and [f]: p=0.765 and p=0.496, respectively). After the model was adjusted for covariates, the current dioxin-by-time interactions remained nonsignificant for both analyses (Table 17-12 [g] and [h]: p=0.607 and p=0.545, respectively).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

No significant association was found between rales and the four current dioxin categories in the unadjusted model (Table 17-12 [i]: p=0.551).

After adjusting the model for significant covariates, the overall association between the current dioxin categories and rales remained nonsignificant (Table 17-12 [j]: p=0.145). Adjusting the model for age and current cigarette smoking did cause the contrast between the high current dioxin category and the background category to become significant (Adj. RR=3.03, 95% C.I.: [1.00,9.14], p=0.049). The percentages of rales occurrences in the four current dioxin categories (background, unknown, low, and high) were 1.7, 1.2, 1.0, and 2.7 percent.

Laboratory Examination Variables

X-Ray Interpretation

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

There was no significant association found between x-ray interpretation and initial dioxin for both cohorts in the unadjusted analysis (Table 17-13 [a] and [b]: p=0.823 for the minimal and p=0.844 for the maximal).

In the minimal analysis, no significant covariates were retained in the model, so the results remained unchanged. In the maximal analysis, the association between x-ray interpretation and initial dioxin remained nonsignificant after the model was adjusted for significant covariates (Table 17-13 [d]: p=0.642).

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

In the unadjusted analysis of x-ray interpretation, the current dioxin-by-time since tour interaction was not significant under both assumptions (Table 17-13 [e] and [f]: p=0.536 for the minimal and p=0.534 for the maximal).

Under the minimal assumption, no significant covariates were retained in the model; thus the results were unchanged. Under the maximal assumption, the current dioxin-by-time

TABLE 17-13.

Analysis of X-Ray Interpretation

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=519)	Low	129	3.1	1.04 (0.74,1.47)	0.823
	Medium	259	4.6		
	High	131	4.6		
b) Maximal (n=740)	Low	185	5.4	1.03 (0.80,1.32)	0.844
	Medium	370	3.8		
	High	185	4.3		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=519)	1.04 (0.74,1.47)	0.823	- -
d) Maximal (n=740)	1.06 (0.82,1.38)	0.642	RACE*CSMOK (p=0.014)

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

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

TABLE 17-13. (Continued)

Analysis of X-Ray Interpretation

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

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.536[b]
(n=519)	≤18.6	1.4 (71)	5.5 (128)	3.7 (54)	1.19 (0.68,2.09)	0.539[c]
	>18.6	5.2 (58)	3.8 (131)	5.2 (77)	0.95 (0.59,1.51)	0.816[c]
f) Maximal						0.534[b]
(n=740)	≤18.6	2.8 (106)	4.2 (190)	4.8 (83)	1.13 (0.76,1.68)	0.543[c]
	>18.6	6.3 (79)	3.9 (179)	4.9 (103)	0.96 (0.68,1.36)	0.803[c]

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

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal			0.536[b]	- -
(n=519)	≤18.6	1.19 (0.68,2.09)	0.539[c]	
	>18.6	0.95 (0.59,1.51)	0.816[c]	
h) Maximal			0.455[b]	RACE*CSMOK (p=0.012)
(n=740)	≤18.6	1.20 (0.80,1.79)	0.390[c]	
	>18.6	0.97 (0.68,1.39)	0.879[c]	

[a]Relative risk for a twofold increase in dioxin.
[b]Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).
[c]Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 17-13. (Continued)

Analysis of X-Ray Interpretation

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

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	784	4.7	All Categories		0.999
Unknown	343	4.7	Unknown vs. Background	0.99 (0.54,1.80)	0.968
Low	196	4.6	Low vs. Background	0.97 (0.46,2.05)	0.940
High	186	4.8	High vs. Background	1.03 (0.49,2.17)	0.945
Total	1,509				

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

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	784	All Categories		0.885	AGE (p<0.001) CSMOK (p=0.030)
Unknown	343	Unknown vs. Background	0.93 (0.51,1.71)	0.818	
Low	196	Low vs. Background	0.96 (0.45,2.05)	0.924	
High	186	High vs. Background	1.31 (0.61,2.82)	0.484	
Total	1,509				

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

since tour interaction remained nonsignificant after adjusting the model for significant covariates (Table 17-13 [h]: p=0.455).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

For the unadjusted model, no significant association was exhibited between x-ray interpretation and the four current dioxin categories (Table 17-13 [i]: p=0.999). After adjusting the model for covariates, this association remained nonsignificant (Table 17-13 [j]: p=0.885). Thus, the percentage of abnormal x-ray interpretations did not significantly differ among the four current dioxin categories.

FVC

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

The association between FVC and initial dioxin was not significant for the minimal assumption in the unadjusted analysis (Table 17-14 [a]: p=0.361). Under the maximal assumption a significant negative association was exhibited (Table 17-14 [b]: p<0.001). The means were 99.0, 95.5, and 94.8 percent for the low, medium, and high initial dioxin categories.

After adjusting for covariates, the interaction between initial dioxin and current cigarette smoking was found to be significant under the minimal assumption (Table 17-14 [c]: p=0.013). To investigate this interaction, current cigarette smoking was divided into four strata (never smoked; formerly smoked; smoked no more than 20 cigarettes per day; smoked over 20 cigarettes per day). A significant negative association between FVC and initial dioxin occurred for those Ranch Hands who never smoked (Appendix Table P-1: p=0.003). The adjusted means within this stratum were 95.4, 92.6, and 86.9 percent for the low, medium, and high classifications of initial dioxin. The association was nonsignificant within the other strata (p=0.158 for former smokers; p=0.987 for >0-20 cigarettes/day; p=0.483 for >20 cigarettes/day). The adjusted slopes of the individual smoking strata increased with a rise in the level of smoking.

With the interaction removed from the adjusted minimal analysis, the association between FVC and initial dioxin became significantly negative when age, race, current cigarette smoking, and lifetime cigarette smoking history were included in the model (Table 17-14 [c]: p=0.028). The adjusted means were 91.6, 90.4, and 88.8 percent for the low, medium, and high levels of initial dioxin. For the maximal analysis the association remained significantly negative in the adjusted model (Table 17-14 [d]: p<0.001).

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

For the unadjusted analysis of FVC, the current dioxin-by-time since tour interaction was not significant for both the minimal and the maximal assumptions (Table 17-14 [e] and [f]: p=0.386 and p=0.249). Under the maximal assumption a significant negative association between FVC and current dioxin was exhibited for those Ranch Hands whose time since tour was less than or equal to 18.6 years (Table 17-14 [f]: p=0.003). The means were 99.8, 96.5, and 93.9 percent for the low, medium, and high levels of current dioxin. For time greater than 18.6 years the association was nonsignificant (p=0.114).

TABLE 17-14.

Analysis of FVC (Percent of Predicted)

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Mean	Slope (Std. Error)[a]	p-Value
a) Minimal (n=521) (R^2=0.002)	Low	130	95.6	-0.412 (0.450)	0.361
	Medium	260	94.9		
	High	131	94.7		
b) Maximal (n=742) (R^2=0.016)	Low	185	99.0	-1.173 (0.337)	<0.001
	Medium	371	95.5		
	High	186	94.8		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Initial Dioxin	n	Adj. Mean	Adj. Slope (Std. Error)[a]	p-Value	Covariate Remarks
c) Minimal (n=521) (R^2=0.090)	Low	130	91.6**	-0.992 (0.450)**	0.028**	INIT*CSMOK (p=0.013)
	Medium	260	90.4**			AGE (p=0.004)
	High	131	88.8**			RACE (p<0.001)
						PACKYR (p=0.052)
d) Maximal (n=742) (R^2=0.124)	Low	185	93.0	-1.403 (0.326)	<0.001	RACE (p<0.001)
	Medium	371	90.9			AGE*CSMOK (p<0.001)
	High	186	88.4			CSMOK*PACKYR (p=0.049)

[a]Slope and standard error based on FVC versus log_2 dioxin.

**Log_2 (initial dioxin)-by-covariate interaction ($0.01<p\leq0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of this interaction.

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

TABLE 17-14. (Continued)

Analysis of FVC (Percent of Predicted)

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

Assumption	Time (Yrs.)	Mean/(n) Current Dioxin Low	Medium	High	Slope (Std. Error)[a]	p-Value
e) Minimal						0.386[b]
(n=521)	≤18.6	95.8	95.8	94.5	-0.771 (0.733)	0.293[c]
(R^2=0.004)		(72)	(128)	(54)		
	>18.6	93.9	95.3	93.7	0.050 (0.599)	0.933[c]
		(58)	(132)	(77)		
f) Maximal						0.249[b]
(n=742)	≤18.6	99.8	96.5	93.9	-1.537 (0.523)	0.003[c]
(R^2=0.018)		(106)	(191)	(83)		
	>18.6	98.9	94.9	93.9	-0.732 (0.462)	0.114[c]
		(79)	(179)	(104)		

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

Assumption	Time (Yrs.)	Adj. Mean/(n) Current Dioxin Low	Medium	High	Adj. Slope (Std. Error)[a]	p-Value	Covariate Remarks
g) Minimal						0.286[b]	AGE (p=0.004)
(n=521)	≤18.6	91.8	90.5	87.4	-1.655 (0.732)	0.024[c]	RACE (p<0.001)
(R^2=0.078)		(72)	(128)	(54)			PACKYR (p=0.003)
	>18.6	90.5	91.1	88.2	-0.677 (0.597)	0.257[c]	
		(58)	(132)	(77)			
h) Maximal						0.255[b]	RACE (p<0.001)
(n=742)	≤18.6	93.6	91.2	86.9	-1.924 (0.506)	<0.001[c]	AGE*CSMOK
(R^2=0.127)		(106)	(191)	(83)			(p<0.001)
	>18.6	94.0	90.6	87.9	-1.169 (0.448)	0.009[c]	CSMOK*PACKYR
		(79)	(179)	(104)			(p=0.049)

[a]Slope and standard error based on FVC versus log_2 dioxin.

[b]Test of significance for homogeneity of slopes (current dioxin continuous, time categorized).

[c]Test of significance for slope equal to 0 (current dioxin continuous, time categorized).

Note: Minimal--Low: ≤10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: ≤9-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 17-14. (Continued)

Analysis of FVC (Percent of Predicted)

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

Current Dioxin Category	n	Mean	Contrast	Difference of Means (95% C.I.)	p-Value
Background	786	97.5	All Categories		<0.001
Unknown	344	99.1	Unknown vs. Background	1.5 (0.2,3.2)	0.075
Low	196	96.0	Low vs. Background	-1.6 (-3.6,0.5)	0.141
High	187	93.9	High vs. Background	-3.6 (-5.7,-1.5)	0.001
Total	1,513		(R^2=0.013)		

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

Current Dioxin Category	n	Adj. Mean	Contrast	Difference of Adj. Means (95% C.I.)	p-Value	Covariate Remarks
Background	786	91.7**	All Categories		<0.001**	DXCAT*CSMOK (p=0.018)
Unknown	344	93.2**	Unknown vs. Background	1.6 (0.0,3.2)**	0.054**	AGE (p=0.025)
Low	196	90.4**	Low vs. Background	-1.3 (-3.3,0.7)**	0.194**	RACE (p<0.001)
High	187	87.4**	High vs. Background	-4.3 (-6.3,-2.2)**	<0.001**	PACKYR (p<0.001)
Total	1,513		(R^2=0.118)			

**Categorized current dioxin-by-covariate interaction ($0.01<p\leq0.05$); adjusted mean, confidence interval, and p-value derived from a model fitted after deletion of this interaction.

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

The current dioxin-by-time since tour interaction was also found to be nonsignificant for both assumptions when the model was adjusted for significant covariates (Table 17-14 [g] and [h]: p=0.286, minimal and p=0.255, maximal). However, a negative association between FVC and current dioxin was significant under the minimal assumption for time less than or equal to 18.6 years when age, race, and lifetime cigarette smoking history were included in the model (Table 17-14 [g]: p=0.024). The adjusted means in this stratum were 91.8, 90.5, and 87.5 percent for the low, medium, and high levels of current dioxin. For time greater than 18.6 years the association remained nonsignificant (p=0.257).

Under the maximal assumption, the significant covariates retained in the model were race, the age-by-current cigarette smoking interaction, and the current cigarette smoking-by-lifetime cigarette smoking history interaction. A significant negative association between FVC and current dioxin was then exhibited for both time strata (Table 17-14 [h]: p<0.001 for time≤18.6 and p=0.009 for time>18.6). For time less than or equal to 18.6 years, the adjusted means were 93.6, 91.2, and 86.9 percent for the low, medium, and high current dioxin levels, and were 94.0, 90.6, and 87.9 percent for time greater than 18.6 years.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

A significant association between FVC and the four current dioxin categories was exhibited in the unadjusted model (Table 17-14 [i]: p<0.001). Therefore, there was a significant difference in the mean FVC among the current dioxin categories. The means were 97.5, 99.1, 96.0, and 93.9 percent for the background, unknown, low, and high categories. The mean for the unknown category was higher than the mean for the background category, but the difference was only marginally significant (p=0.075). The low dioxin category had a lower mean than the background category, but the difference was not significant (p=0.141). Finally, the mean for the high dioxin category was significantly lower than the mean for the background category (p=0.001).

After the model was adjusted for covariates, a significant interaction between categorized current dioxin and current cigarette smoking was exhibited (Table 17-14 [j]: p=0.018). To examine this interaction current cigarette smoking was categorized into four strata: those who never smoked, those who formerly smoked, those who smoked no more than 20 cigarettes per day, and those who smoked over 20 cigarettes per day. For those who never smoked, there was a significant association between FVC and the four current dioxin categories (Appendix Table P-1: p<0.001). The adjusted means were 92.4, 95.2, 92.1, and 85.9 percent for the background, unknown, low, and high current dioxin categories. The unknown category had a marginally greater mean than the background category (p=0.072); the difference between the low and background categories was not significant (p=0.867); and the high category had a significantly lower mean than the background category (p<0.001).

For those who formerly smoked, the association between FVC and the four current dioxin categories was also significant (Appendix Table P-1: p=0.005). The adjusted means for the four categories were 93.0, 94.1, 92.4, and 87.4 percent. The mean for the high category was significantly lower than the mean for the background category (p=0.001), but the other two contrasts involving the background category were not significant (unknown versus background: p=0.400; low versus background: p=0.746).

For those who smoked no more than 20 cigarettes per day, the association between FVC and the four current dioxin categories was only marginally significant (Appendix Table P-1: p=0.094). The adjusted means in this stratum were 91.4, 91.8, 87.5, and 87.0 percent for the four current dioxin categories. The low and high current dioxin groups both had marginally lower means than the background group (low versus background: p=0.077; high versus background: p=0.067). The difference between the unknown and background groups was nonsignificant (p=0.830).

For those who smoked over 20 cigarettes per day, the association between FVC and the four current dioxin categories was not significant (Appendix Table P-1: p=0.591).

When the categorized current dioxin-by-current cigarette smoking interaction was removed from the model, the association between FVC and the current dioxin categories remained significant (Table 17-14 [j]: p<0.001). The pattern in the means of the current dioxin categories also remained the same as in the unadjusted model; i.e., the unknown category had a marginally significant higher mean than the background category (p=0.054), the low group was not significantly different from the background group (p=0.194), and the high group had a significantly lower mean than the background group (p<0.001).

FEV_1

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

The association between FEV_1 and initial dioxin was found not to be significant under the minimal assumption in the unadjusted analysis (Table 17-15 [a]: p=0.681). The association was also nonsignificant for the maximal assumption (Table 17-15 [b]: p=0.216).

When the model was adjusted for covariates, a significant interaction between initial dioxin and current cigarette smoking was exhibited for the minimal cohort (Table 17-15 [c]: p=0.029). Within the stratum containing the Ranch Hands who never smoked, a significant negative association was found between FEV_1 and initial dioxin (Appendix Table P-1: p=0.023). The adjusted FEV_1 means for the low, medium, and high levels of initial dioxin were 100.3, 96.8, and 92.7 percent. The association was nonsignificant within the other strata (p=0.372 for former smokers; p=0.552 for >0-20 cigarettes/day; p=0.243 for >20 cigarettes/day). However, the slopes for the strata consisting of Ranch Hands who currently do not smoke (never smoked and former smokers) were negative, and the slopes for the strata consisting of those who currently do smoke (>0-20 cigarettes/day and >20 cigarettes/day) were positive.

For the minimal cohort the association between FEV_1 and initial dioxin remained non-significant when the initial dioxin-by-current cigarette smoking interaction was removed (Table 17-15 [c]: p=0.304). For the maximal cohort, however, a significant negative association was present when the model was adjusted for race, age-by-current cigarette smoking, and current cigarette smoking-by-lifetime cigarette smoking history (Table 17-15 [d]: p=0.026). The adjusted means were 94.8, 93.1, and 92.7 percent for the low, medium, and high initial dioxin levels.

TABLE 17-15.

Analysis of FEV_1 (Percent of Predicted)

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Mean	Slope (Std. Error)[a]	p-Value
a) Minimal (n=521) (R^2<0.001)	Low	130	97.8	0.216 (0.526)	0.681
	Medium	260	95.6		
	High	131	98.5		
b) Maximal (n=742) (R^2=0.002)	Low	185	99.5	-0.493 (0.398)	0.216
	Medium	371	96.2		
	High	186	98.2		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Initial Dioxin	n	Adj. Mean	Adj. Slope (Std. Error)[a]	p-Value	Covariate Remarks
c) Minimal (n=521) (R^2=0.114)	Low	130	94.8**	-0.532 (0.518)**	0.304**	INIT*CSMOK (p=0.029)
	Medium	260	92.1**			AGE (p<0.001)
	High	131	93.1**			RACE (p<0.001)
						PACKYR (p=0.007)
d) Maximal (n=742) (R^2=0.151)	Low	185	94.8	-0.842 (0.376)	0.026	RACE (p<0.001)
	Medium	371	93.1			AGE*CSMOK (p<0.001)
	High	186	92.7			CSMOK*PACKYR (p=0.002)

[a]Slope and standard error based on FEV_1 versus log_2 dioxin.

**Log_2 (initial dioxin)-by-covariate interaction ($0.01<p\leq0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of this interaction.

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

TABLE 17-15. (Continued)

Analysis of FEV_1 (Percent of Predicted)

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

Assumption	Time (Yrs.)	Mean/(n) Current Dioxin Low	Medium	High	Slope (Std. Error)[a]	p-Value
e) Minimal						0.251[b]
(n=521)	≤18.6	98.3	96.8	98.0	-0.353 (0.856)	0.680[c]
(R^2=0.005)		(72)	(128)	(54)		
	>18.6	94.6	96.1	97.9	0.917 (0.700)	0.191[c]
		(58)	(132)	(77)		
f) Maximal						0.192[b]
(n=742)	≤18.6	100.4	97.7	97.2	-0.924 (0.617)	0.135[c]
(R^2=0.006)		(106)	(191)	(83)		
	>18.6	98.7	95.2	97.7	0.152 (0.546)	0.781[c]
		(79)	(179)	(104)		

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

Assumption	Time (Yrs.)	Adj. Mean/(n) Current Dioxin Low	Medium	High	Adj. Slope (Std. Error)[a]	p-Value	Covariate Remarks
g) Minimal						0.200[b]	AGE (p<0.001)
(n=521)	≤18.6	95.1	92.3	91.0	-1.452 (0.842)	0.085[c]	RACE (p<0.001)
(R^2=0.109)		(72)	(128)	(54)			CSMOK (p=0.008)
	>18.6	92.8	93.1	92.9	-0.101 (0.686)	0.883[c]	PACKYR (p=0.008)
		(58)	(132)	(77)			
h) Maximal						0.262[b]	RACE (p<0.001)
(n=742)	≤18.6	95.1	93.5	90.9	-1.433 (0.584)	0.014[c]	AGE*CSMOK (p<0.001)
(R^2=0.153)		(106)	(191)	(83)			CSMOK*PACKYR (p=0.002)
	>18.6	95.8	92.7	92.6	-0.575 (0.518)	0.268[c]	
		(79)	(179)	(104)			

[a]Slope and standard error based on FEV_1 versus log_2 dioxin.

[b]Test of significance for homogeneity of slopes (current dioxin continuous, time categorized).

[c]Test of significance for slope equal to 0 (current dioxin continuous, time categorized).

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 17-15. (Continued)

Analysis of FEV_1 (Percent of Predicted)

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

Current Dioxin Category	n	Mean	Contrast	Difference of Means (95% C.I.)	p-Value
Background	786	98.4	All Categories		0.321
Unknown	344	98.7	Unknown vs. Background	0.3 (-1.7,2.2)	0.795
Low	196	96.4	Low vs. Background	-2.0 (-4.5,0.4)	0.102
High	187	97.5	High vs. Background	-1.0 (-3.5,1.5)	0.449
Total	1,513		(R^2=0.002)		

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

Current Dioxin Category	n	Adj. Mean	Contrast	Difference of Adj. Means (95% C.I.)	p-Value	Covariate Remarks
Background	786	93.5**	All Categories		0.091**	DXCAT*CSMOK (p=0.039)
Unknown	344	94.1**	Unknown vs. Background	0.6 (-1.3,2.4)**	0.535**	RACE (p<0.001)
Low	196	91.9**	Low vs. Background	-1.6 (-3.9,0.6)**	0.160**	AGE*CSMOK (p=0.002)
High	187	91.3**	High vs. Background	-2.2 (-4.5,0.1)**	0.060**	CSMOK*PACKYR (p=0.003)
Total	1,513		(R^2=0.168)			

**Categorized current dioxin-by-covariate interaction ($0.01<p\leq0.05$); adjusted mean, confidence interval, and p-value derived from a model fitted after deletion of this interaction.

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

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

The current dioxin-by-time since tour interaction was not significant for both the minimal and the maximal cohorts for the unadjusted analysis of FEV_1 (Table 17-15 [e] and [f]: p=0.251 and p=0.192, respectively). Thus, there was no significant difference between the slopes in the time strata for either the minimal or the maximal assumptions.

After adjusting the model for significant covariates, the current dioxin-by-time since tour interaction remained nonsignificant for both the minimal and the maximal assumptions (Table 17-15 [g] and [h]: p=0.200 and p=0.262). Under the minimal assumption a marginally significant negative association between FEV_1 and current dioxin was exhibited for time less than or equal to 18.6 years after the model was adjusted for age, race, current cigarette smoking, and lifetime cigarette smoking history (Table 17-15 [g]: p=0.085). The adjusted means for the low, medium, and high current dioxin levels were 95.1, 92.3, and 91.0 percent. Under the maximal assumption a significant negative association was also found for time less than or equal to 18.6 years after race, age-by-current cigarette smoking, and current cigarette smoking-by-lifetime cigarette smoking history were included in this model (Table 17-15 [h]: p=0.014). The adjusted means in this stratum were 95.1, 93.5, and 90.9 percent for the low, medium, and high levels of current dioxin. For time greater than 18.6 years the association was nonsignificant under both assumptions (p=0.883 for minimal; p=0.268 for maximal).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In the unadjusted model, there was no significant difference in the FEV_1 means among all four current dioxin categories (Table 17-15 [i]: p=0.321).

In the adjusted model, the interaction between categorized current dioxin and current cigarette smoking was found to be significant (Table 17-15 [j]: p=0.039). Current cigarette smoking was then divided into four strata (never smoked; formerly smoked; smoked no more than 20 cigarettes per day; smoked over 20 cigarettes per day) and the FEV_1 means were compared among the current dioxin categories within each smoking strata. Within each of the current dioxin categories, the adjusted means tended to decrease across the smoking strata as current cigarette smoking increased.

For those who never smoked, there was a significant association between FEV_1 and the current dioxin categories (Appendix Table P-1: p=0.034). Within this stratum, the high dioxin category had a significantly lower mean than the background category (p=0.039), but the other two contrasts involving the background category were nonsignificant (unknown versus background: p=0.137; low versus background: p=0.663).

For those who formerly smoked, the association between FEV_1 and the current dioxin categories was not significant (p=0.228). However, the high current dioxin category had a significantly lower mean than the background category (p=0.043).

For those who smoked no more than 20 cigarettes per day, the overall contrast showed no significant differences among the current dioxin categories (p=0.572). For those who smoked more than 20 cigarettes per day, the association was also nonsignificant (p=0.225),

but the mean for the high dioxin category was significantly higher than the background category (p=0.046).

After removing the categorized current dioxin-by-current cigarette smoking interaction, the association between FEV_1 and the current dioxin categories became marginally significant (Table 17-15 [j]: p=0.091). The adjusted FEV_1 means were 93.5, 94.1, 91.9, and 91.3 percent for the background, unknown, low, and high categories. The mean for the high category was marginally lower than the background category (p=0.060), but the other two contrasts involving the background category were nonsignificant (unknown versus background: p=0.535; low versus background: p=0.160).

FEFmax

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

The association between FEFmax and initial dioxin in the unadjusted analysis was not significant for the minimal cohort (Table 17-16 [a]: p=0.396). A negative association was significant for the maximal cohort in the unadjusted model (Table 17-16 [b]: p=0.021). The means were 140.0, 135.5, and 135.7 percent for the low, medium, and high levels of initial dioxin.

When the model was adjusted for covariates, the association between FEFmax and initial dioxin for the minimal cohort remained nonsignificant (Table 17-16 [c]: p=0.341). The negative association between FEFmax and initial dioxin remained significant for the maximal cohort (Table 17-16 [d]: p=0.014). The adjusted means of 139.3, 136.2, and 135.1 percent decreased over the low, medium, and high levels of initial dioxin.

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

For the unadjusted analysis of FEFmax, the current dioxin-by-time since tour interaction was not significant under both the minimal and the maximal assumptions (Table 17-16 [e] and [f]: p=0.105 and p=0.160). However, for the minimal cohort there was a marginally significant negative association between FEFmax and current dioxin for time less than or equal to 18.6 years (Table 17-16 [e]: p=0.085). The means were 139.1, 134.4, and 133.9 percent for the low, medium, and high levels of current dioxin. For time greater than 18.6 years the association was nonsignificant (p=0.649). For the maximal cohort, a significant negative association was also exhibited for those Ranch Hands whose time since tour was less than or equal to 18.6 years (Table 17-16 [f]: p=0.013). The means corresponding to the low, medium, and high levels of current dioxin in this stratum were 140.8, 136.3, and 134.2 percent. For time greater than 18.6 years the association was nonsignificant (p=0.478).

After the model was adjusted for covariates (race, age-by-current cigarette smoking, and current cigarette smoking-by-lifetime cigarette smoking history), the current dioxin-by-time since tour interaction under the minimal assumption became marginally significant (Table 17-16 [g]: p=0.100). Thus, the adjusted slopes were marginally different between the two time strata. Within the time strata containing those Ranch Hands whose time since tour was less than or equal to 18.6 years, the negative association between FEFmax and current

TABLE 17-16.

Analysis of FEFmax (Percent of Predicted)

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Mean	Slope (Std. Error)[a]	p-Value
a) Minimal (n=521) (R^2=0.001)	Low	130	138.4	-0.718 (0.845)	0.396
	Medium	260	133.7		
	High	131	135.8		
b) Maximal (n=742) (R^2=0.007)	Low	185	140.0	-1.454 (0.626)	0.021
	Medium	371	135.5		
	High	186	135.7		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Initial Dioxin	n	Adj. Mean	Adj. Slope (Std. Error)[a]	p-Value	Covariate Remarks
c) Minimal (n=521) (R^2=0.081)	Low	130	141.1	-0.805 (0.845)	0.341	RACE (p=0.100)
	Medium	260	137.0			AGE*CSMOK (p=0.009)
	High	131	138.5			CSMOK*PACKYR (p=0.006)
d) Maximal (n=742) (R^2=0.099)	Low	185	139.3	-1.507 (0.611)	0.014	AGE*CSMOK (p=0.004)
	Medium	371	136.2			CSMOK*PACKYR (p=0.002)
	High	186	135.1			

[a]Slope and standard error based on FEFmax versus log_2 dioxin.

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

TABLE 17-16. (Continued)

Analysis of FEFmax (Percent of Predicted)

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

Assumption	Time (Yrs.)	Mean/(n) Current Dioxin Low	Medium	High	Slope (Std. Error)[a]	p-Value
e) Minimal						0.105[b]
(n=521)	≤18.6	139.1	134.4	133.9	-2.370 (1.374)	0.085[c]
(R^2=0.006)		(72)	(128)	(54)		
	>18.6	134.9	134.0	137.1	0.513 (1.124)	0.649[c]
		(58)	(132)	(77)		
f) Maximal						0.160[b]
(n=742)	≤18.6	140.8	136.3	134.2	-2.435 (0.972)	0.013[c]
(R^2=0.009)		(106)	(191)	(83)		
	>18.6	140.5	134.4	136.3	-0.610 (0.860)	0.478[c]
		(79)	(179)	(104)		

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

Assumption	Time (Yrs.)	Adj. Mean/(n) Current Dioxin Low	Medium	High	Adj. Slope (Std. Error)[a]	p-Value	Covariate Remarks
g) Minimal						0.100[b]	RACE (p=0.112)
(n=521)	≤18.6	142.3	137.3	136.3	-2.560 (1.374)	0.063[c]	AGE*CSMOK
(R^2=0.086)		(72)	(128)	(54)			(p=0.007)
	>18.6	138.1	137.3	139.8	0.269 (1.120)	0.810[c]	CSMOK*PACKYR
		(58)	(132)	(77)			(p=0.005)
h) Maximal						0.283[b]	AGE*CSMOK
(n=742)	≤18.6	139.4	136.2	133.4	-2.460 (0.948)	0.010[c]	(p=0.005)
(R^2=0.102)		(106)	(191)	(83)			CSMOK*PACKYR
	>18.6	141.6	135.5	135.6	-1.125 (0.841)	0.181[c]	(p=0.002)
		(79)	(179)	(104)			

[a]Slope and standard error based on FEFmax versus log_2 dioxin.

[b]Test of significance for homogeneity of slopes (current dioxin continuous, time categorized).

[c]Test of significance for slope equal to 0 (current dioxin continuous, time categorized).

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 17-16. (Continued)

Analysis of FEFmax (Percent of Predicted)

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

Current Dioxin Category	n	Mean	Contrast	Difference of Means (95% C.I.)	p-Value
Background	786	137.7	All Categories		0.077
Unknown	344	139.1	Unknown vs. Background	1.5 (-1.6,4.5)	0.347
Low	196	134.2	Low vs. Background	-3.5 (-7.2,0.2)	0.066
High	187	135.4	High vs. Background	-2.3 (-6.1,1.5)	0.228
Total	1,513		(R^2=0.005)		

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

Current Dioxin Category	n	Adj. Mean	Contrast	Difference of Adj. Means (95% C.I.)	p-Value	Covariate Remarks
Background	786	137.6	All Categories		0.026	AGE*PACKYR (p=0.026) CSMOK*PACKYR (p=0.016)
Unknown	344	139.7	Unknown vs. Background	2.1 (-0.8,5.0)	0.154	
Low	196	134.6	Low vs. Background	-3.0 (-6.6,0.6)	0.100	
High	187	134.5	High vs. Background	-3.0 (-6.7,0.6)	0.106	
Total	1,513		(R^2=0.088)			

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

dioxin remained marginally significant (p=0.063). For time greater than 18.6 years the association was positive, but remained nonsignificant (p=0.810).

Under the maximal assumption in the adjusted model, the current dioxin-by-time since tour interaction remained nonsignificant (Table 17-16 [h]: p=0.283). The negative association between FEFmax and current dioxin remained significant in the stratum for time less than or equal to 18.6 years (p=0.010), and the association in the stratum for time greater than 18.6 years remained nonsignificant (p=0.181).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In the unadjusted model, there was a marginally significant difference in the FEFmax means among the four current dioxin categories (Table 17-16 [i]: p=0.077). The means for the four categories were 137.7, 139.1, 134.2, and 135.4 percent. There was a marginally significant difference between the mean for the low category and the mean for the background category (p=0.066). However, the means for the unknown and high categories were not significantly different from the mean for the background category (unknown versus background: p=0.347; high versus background: p=0.228).

After adjusting for significant interactions (age-by-lifetime cigarette smoking history and current cigarette smoking-by-lifetime cigarette smoking history) the difference among the four current dioxin categories became significant (Table 17-16 [j]: p=0.026). The difference between the low category and the background category remained marginally significant (p=0.100), and the unknown versus background and high versus background contrasts remained nonsignificant (unknown versus background: p=0.154; high versus background: p=0.106).

Ratio of Observed FEV_1 to Observed FVC

Due to the distribution of the data, a natural logarithm of (1 - X) transformation was used. Because of this transformation, a negative slope implies a positive association between dioxin and the ratio of observed FEV_1 to observed FVC.

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Under the minimal assumption, a significant association between the ratio of observed FEV_1 to observed FVC (FEV_1/FVC) and initial dioxin was exhibited in the unadjusted analysis (Table 17-17 [a]: p=0.001). Due to the transformation used, the negative association between initial dioxin and 1 minus FEV_1/FVC resulted in an increase in the FEV_1/FVC ratio as initial dioxin increased. The mean ratios were 0.820, 0.814, and 0.839 for the low, medium, and high levels of initial dioxin. Under the maximal assumption, the association was also significant (Table 17-17 [b]: p<0.001). Based on the negative association between initial dioxin and 1 minus FEV_1/FVC, the ratio was found to increase as the initial dioxin increased. The mean ratios were 0.809, 0.810, and 0.837 for the low, medium, and high levels of initial dioxin.

After adjusting the model for significant covariates, the association between FEV_1/FVC and initial dioxin remained significant for both the minimal and the maximal cohorts (Table 17-17 [c] and [d]: p=0.022 and p<0.001).

TABLE 17-17.

Analysis of Ratio of Observed FEV_1 to Observed FVC

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Mean[a]	Slope (Std. Error)[b]	p-Value
a) Minimal	Low	130	0.820	-0.040 (0.012)	0.001
(n=521)	Medium	260	0.814		
(R^2=0.020)	High	131	0.839		
b) Maximal	Low	185	0.809	-0.040 (0.009)	<0.001
(n=742)	Medium	371	0.810		
(R^2=0.025)	High	186	0.837		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Initial Dioxin	n	Adj. Mean[a]	Adj. Slope (Std. Error)[b]	p-Value	Covariate Remarks
c) Minimal	Low	130	0.831	-0.028 (0.012)	0.022	AGE (p<0.001)
(n=521)	Medium	260	0.823			RACE (p=0.082)
(R^2=0.112)	High	131	0.843			CSMOK (p=0.004)
						PACKYR (p=0.067)
d) Maximal	Low	185	0.822	-0.030 (0.009)	<0.001	AGE (p<0.001)
(n=742)	Medium	371	0.826			RACE (p=0.004)
(R^2=0.143)	High	186	0.844			CSMOK (p<0.001)
						PACKYR (p=0.007)

[a]Transformed from natural logarithm (1 - X) scale.

[b]Slope and standard error based on natural logarithm of (1 - ratio of observed FEV_1 to observed FVC) versus log_2 dioxin.

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

TABLE 17-17. (Continued)

Analysis of Ratio of Observed FEV_1 to Observed FVC

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

Assumption	Time (Yrs.)	Mean[a]/(n) Current Dioxin Low	Medium	High	Slope (Std. Error)[b]	p-Value
e) Minimal						0.779[c]
(n=521)	≤18.6	0.821	0.818	0.839	-0.041 (0.020)	0.045[d]
(R^2=0.024)		(72)	(128)	(54)		
	>18.6	0.811	0.812	0.841	-0.048 (0.017)	0.004[d]
		(58)	(132)	(77)		
f) Maximal						0.524[c]
(n=742)	≤18.6	0.812	0.816	0.838	-0.039 (0.014)	0.005[d]
(R^2=0.034)		(106)	(191)	(83)		
	>18.6	0.797	0.807	0.838	-0.051 (0.012)	<0.001[d]
		(79)	(179)	(104)		

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

Assumption	Time (Yrs.)	Adj. Mean[a]/(n) Current Dioxin Low	Medium	High	Adj. Slope (Std. Error)[b]	p-Value	Covariate Remarks
g) Minimal						0.823[c]	AGE (p<0.001)
(n=521)	≤18.6	0.831	0.825	0.839	-0.024 (0.020)	0.224[d]	RACE (p=0.086)
(R^2=0.111)		(72)	(128)	(54)			CSMOK (p=0.004)
	>18.6	0.827	0.823	0.846	-0.030 (0.016)	0.067[d]	PACKYR (p=0.069)
		(58)	(132)	(77)			
h) Maximal						0.785[c]	AGE (p<0.001)
(n=742)	≤18.6	0.822	0.826	0.842	-0.029 (0.014)	0.034[d]	RACE (p=0.004)
(R^2=0.143)		(106)	(191)	(83)			CSMOK (p<0.001)
	>18.6	0.818	0.825	0.846	-0.034 (0.012)	0.005[d]	PACKYR (p=0.007)
		(79)	(179)	(104)			

[a]Transformed from natural logarithm (1 - X) scale.

[b]Slope and standard error based on natural logarithm of (1 - ratio of observed FEV_1 to observed FVC) versus log_2 dioxin.

[c]Test of significance for homogeneity of slopes (current dioxin continuous, time categorized).

[d]Test of significance for slope equal to 0 (current dioxin continuous, time categorized).

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 17-17. (Continued)

Analysis of Ratio of Observed FEV_1 to Observed FVC

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

Current Dioxin Category	n	Mean[a]	Contrast	Difference of Means (95% C.I.)[e]	p-Value[f]
Background	786	0.814	All Categories		<0.001
Unknown	344	0.802	Unknown vs. Background	-0.011 --	0.007
Low	196	0.810	Low vs. Background	-0.003 --	0.504
High	187	0.838	High vs. Background	0.025 --	<0.001
Total	1,513		(R^2=0.028)		

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

Current Dioxin Category	n	Adj. Mean[a]	Contrast	Difference of Adj. Means (95% C.I.)[e]	p-Value[f]	Covariate Remarks
Background	786	0.824	All Categories		<0.001	RACE (p<0.001)
						AGE*CSMOK (p=0.001)
Unknown	344	0.817	Unknown vs. Background	-0.007 --	0.042	CSMOK*PACKYR
Low	196	0.822	Low vs. Background	-0.002 --	0.623	(p=0.002)
High	187	0.841	High vs. Background	0.017 --	<0.001	
Total	1,513		(R^2=0.178)			

[a]Transformed from natural logarithm (1 - X) scale.

[e]Difference of means after transformation to original scale; confidence interval on difference of means not given because analysis was performed on natural logarithm (1 - X) scale.

[f]P-value is based on difference of means on natural logarithm (1 - X) scale.

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

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

The current dioxin-by-time since tour interaction was not significant for both assumptions in the unadjusted model of FEV_1/FVC (Table 17-17 [e] and [f]: p=0.779 for the minimal and p=0.524 for the maximal). However, under the minimal assumption a significant association between FEV_1/FVC and current dioxin was found within both time strata (Table 17-17 [e]: p=0.045 for time≤18.6 and p=0.004 for time>18.6). When time was less than or equal to 18.6 years, the mean ratios were 0.821, 0.818, and 0.839 for the low, medium, and high levels of current dioxin. When time was greater than 18.6 years, the mean ratios were 0.811, 0.812, and 0.841. Under the maximal assumption a significant association was also found within both time strata (Table 17-17 [f]: p=0.005 for time≤18.6 and p<0.001 for time>18.6). The mean ratios for this cohort were 0.812, 0.816, and 0.838 when time was less than or equal to 18.6 years, and 0.797, 0.807, and 0.838 when time was greater than 18.6 years. Due to the transformation used, the negative association between 1 minus FEV_1/FVC and current dioxin in the four strata resulted in an increasing trend in the FEV_1/FVC ratio as current dioxin increased.

The current dioxin-by-time since tour interaction remained nonsignificant for both the minimal and the maximal cohorts after the model was adjusted for covariates (Table 17-17 [g] and [h]: p=0.823 and p=0.785, respectively). For the minimal cohort, with the inclusion of age, race, current cigarette smoking, and lifetime cigarette smoking history in the model, the association between FEV_1/FVC and current dioxin became nonsignificant within the time less than or equal to 18.6 years stratum (Table 17-17 [g]: p=0.224). For time greater than 18.6 years, the association became marginally significant (Table 17-17 [g]: p=0.067). The associations within both time strata for the maximal cohort remained significant (Table 17-17 [h]: p=0.034 for time≤18.6 years and p=0.005 for time>18.6 years).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In the unadjusted model, the FEV_1/FVC means differed significantly among the four current dioxin categories (Table 17-17 [i]: p<0.001). The mean ratios were 0.814, 0.802, 0.810, and 0.838 for the background, unknown, low, and high categories. The unknown category had a significantly lower mean than the background category (p=0.007). The mean for the low category was not significantly different from the mean for the background category (p=0.504). The high category had a significantly higher mean than the background category (p<0.001).

After the model was adjusted for significant covariates, the differences among the four categories remained significant (Table 17-17 [j]: p<0.001). The mean for the unknown category remained significantly lower than the mean for the background category (p=0.042). The difference between the low and background categories remained nonsignificant (p=0.623). Also, the mean for the high category remained significantly higher than the background category (p<0.001).

Loss of Vital Capacity

Model 1: Ranch Hands - Initial Dioxin (Categorized)

In the unadjusted analysis of the minimal cohort, the overall contrast showed no significant association between the loss of vital capacity classifications and the initial dioxin

levels (Table 17-18 [a]: p=0.164). However, the risk of a moderate or severe loss of vital capacity was marginally less than 1 when contrasting the medium and low initial dioxin levels (Est. RR=0.13, 95% C.I.: [0.01,1.14], p=0.066). The percentages of a moderate or severe loss of vital capacity were 3.1, 0.4, and 2.3 percent for the low, medium, and high levels of initial dioxin. In the maximal cohort, there was a marginally significant association between the loss of vital capacity classifications and the initial dioxin levels (Table 17-18 [b]: p=0.051). For both the medium versus low and the high versus low initial dioxin contrasts there was a significant risk of a mild loss of vital capacity (medium versus low: Est. RR=1.91, 95% C.I.: [1.06,3.44], p=0.031; high versus low: Est. RR=2.03, 95% C.I.: [1.01,4.06], p=0.046). The percentages of a mild loss of vital capacity were 6.0, 11.1, and 11.5 percent for the low, medium, and high levels of initial dioxin.

When the minimal analysis was adjusted for age and race, the association between loss of vital capacity and initial dioxin became marginally significant (Table 17-18 [c]: p=0.052). The risk of a mild loss of vital capacity also became marginally significant for the high versus low initial dioxin contrast (Est. RR=2.28, 95% C.I.: [0.95,5.50], p=0.067). The risk of a moderate or severe loss of vital capacity remained marginally significant for the medium versus low contrast (Est. RR=0.18, 95% C.I.: [0.03,1.20], p=0.076).

In the maximal analysis, after adjusting the model for age, race, and lifetime cigarette smoking history, the association between loss of vital capacity and initial dioxin became significant (Table 17-18 [d]: p=0.011). The risk of a mild loss of vital capacity remained significant for both the medium versus low and the high versus low contrasts (medium versus low: Est. RR=1.83, 95% C.I.: [1.02,3.28], p=0.043; high versus low: Est. RR=2.60, 95% C.I: [1.29,5.25], p=0.008). For the low, medium, and high categories, the percentages of a mild loss of vital capacity were 6.0, 11.1, and 11.5 percent, and the percentages of a moderate or severe loss of vital capacity were 2.0, 0.4, and 2.3 percent.

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

The current dioxin-by-time since tour interaction was not significant for both the minimal and the maximal cohorts in the unadjusted analysis of loss of vital capacity (Table 17-18 [e] and [f]: p=0.512 and p=0.612, respectively). Under the minimal assumption there was no significant association between loss of vital capacity and current dioxin within each time strata (Table 17-18 [e]: p=0.334 for time≤18.6 years; p=0.866 for time>18.6 years). Under the maximal assumption there was also no significant association between loss of vital capacity and current dioxin (Table 17-18 [f]: p=0.228 for time≤18.6 years; p=0.989 for time>18.6 years). However, there was a significant risk of a mild loss of vital capacity under the high versus low current dioxin contrast for time less than or equal to 18.6 years (Est. RR=2.87, 95% C.I.: [1.03,7.94], p=0.043).

After adjusting for age and race in the minimal analysis, the current dioxin-by-time since tour interaction remained nonsignificant (Table 17-18 [g]: p=0.356) as did the association between loss of vital capacity and current dioxin (p=0.327 for time≤18.6 years; p=0.836 for time>18.6 years). However, the risk of a mild loss of vital capacity became significant under the high versus low current dioxin contrast for time less than or equal to 18.6 years (Est. RR=3.83, 95% C.I.: [1.05, 3.94], p=0.042).

TABLE 17-18.

Analysis of Loss of Vital Capacity

Ranch Hands - Initial Dioxin (Categorized) - Unadjusted

Assumption	Initial Dioxin	n	Percent None	Mild	Mod./Sev.	Initial Dioxin Contrast	Est. Relative Risk (95% C.I.)	p-Value
a) Minimal	Low	130	90.0	6.9	3.1	Overall†		0.164
(n=521)	Medium	260	88.9	10.8	0.4	M vs. L[a]	1.57 (0.72,3.45)	0.256
	High	131	86.3	11.5	2.3	H vs. L[a]	1.72 (0.73,4.10)	0.217
						M vs. L[b]	0.13 (0.01,1.14)	0.066
						H vs. L[b]	0.78 (0.17,3.54)	0.743
b) Maximal	Low	349	92.0	6.0	2.0	Overall†		0.051
(n=742)	Medium	262	88.6	11.1	0.4	M vs. L[a]	1.91 (1.06,3.44)	0.031
	High	131	86.3	11.5	2.3	H vs. L[a]	2.03 (1.01,4.06)	0.046
						M vs. L[b]	0.20 (0.02,1.62)	0.130
						H vs. L[b]	1.22 (0.31,4.80)	0.778

Ranch Hands - Initial Dioxin (Categorized) - Adjusted

Assumption	Initial Dioxin Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
c) Minimal	Overall†		0.052	AGE (p=0.012)
(n=521)	M vs. L[a]	1.66 (0.76,3.62)	0.201	RACE (p=0.016)
	H vs. L[a]	2.28 (0.95,5.50)	0.067	
	M vs. L[b]	0.18 (0.03,1.20)	0.076	
	H vs. L[b]	1.34 (0.31,5.87)	0.699	
d) Maximal	Overall†		0.011	AGE (p=0.016)
(n=742)	M vs. L[a]	1.83 (1.02,3.28)	0.043	RACE (p<0.001)
	H vs. L[a]	2.60 (1.29,5.25)	0.008	PACKYR (p=0.022)
	M vs. L[b]	0.33 (0.07,1.50)	0.150	
	H vs. L[b]	2.03 (0.59,7.00)	0.264	

[a]Mild contrasted with none.
[b]Moderate/severe contrasted with none.
†Test of independence of initial dioxin and loss of vital capacity.
Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
M vs. L: Medium initial dioxin category versus low initial dioxin category.
H vs. L: High initial dioxin category versus low initial dioxin category.

TABLE 17-18. (Continued)

Analysis of Loss of Vital Capacity

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

Assumption	Time (Yrs.)	Loss of Vital Capacity Category	Percent/(n) Current Dioxin Low	Medium	High	Current Dioxin Contrast	Est. Relative Risk (95% C.I.)	p-Value
e) Minimal						C-by-T*		0.512
(n=521)	≤18.6	None	91.7	92.2	83.3	Overall†		0.334
		Mild	5.6	7.0	13.0	M vs. L[a]	1.26 (0.37,4.25)	0.712[c]
		Mod./Sev.	2.8	0.8	3.7	H vs. L[a]	2.57 (0.71,9.29)	0.150[c]
			(72)	(128)	(54)	M vs. L[b]	0.28 (0.02,3.14)	0.302[c]
						H vs. L[b]	1.47 (0.20,10.89)	0.704[c]
	>18.6	None	82.8	87.9	88.3	Overall†		0.866
		Mild	15.5	11.4	10.4	M vs. L[a]	0.69 (0.28,1.68)	0.415[c]
		Mod./Sev.	1.7	0.8	1.3	H vs. L[a]	0.63 (0.23,1.74)	0.372[c]
			(58)	(132)	(77)	M vs. L[b]	0.41 (0.03,6.74)	0.535[c]
						H vs. L[b]	0.70 (0.04,11.54)	0.806[c]
f) Maximal						C-by-T*		0.612
(n=742)	≤18.6	None	92.9	92.2	83.3	Overall†		0.228
		Mild	5.1	7.0	13.0	M vs. L[a]	1.40 (0.55,3.56)	0.475[c]
		Mod./Sev.	2.0	0.8	3.7	H vs. L[a]	2.87 (1.03,7.94)	0.043[c]
			(198)	(128)	(54)	M vs. L[b]	0.39 (0.04,3.53)	0.402[c]
						H vs. L[b]	2.05 (0.36,11.57)	0.414[c]
	>18.6	None	88.2	87.9	88.3	Overall†		0.989
		Mild	10.5	11.4	10.4	M vs. L[a]	1.09 (0.52,2.30)	0.819[c]
		Mod./Sev.	1.3	0.8	1.3	H vs. L[a]	0.99 (0.40,2.43)	0.984[c]
			(153)	(132)	(77)	M vs. L[b]	0.58 (0.05,6.51)	0.661[c]
						H vs. L[b]	0.99 (0.09,11.16)	0.996[c]

[a]Mild contrasted with none.

[b]Moderate/severe contrasted with none.

[c]Test of significance for relative risk equal to 1 (current dioxin and time categorized).

*Test of significance of current dioxin-by-time interaction.

†Test of independence of current dioxin and loss of vital capacity within time stratum.

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
M vs. L: Medium current dioxin category versus low current dioxin category.
H vs. L: High current dioxin category versus low current dioxin category.

TABLE 17-18. (Continued)

Analysis of Loss of Vital Capacity

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

Assumption	Time (Yrs.)	Current Dioxin Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
g) Minimal		C-by-T*		0.356	AGE (p=0.015)
(n=521)	≤18.6	Overall†		0.327	RACE (p=0.005)
		M vs. L[a]	1.43 (0.44,4.69)	0.555[c]	
		H vs. L[a]	3.83 (1.05,13.94)	0.042[c]	
		M vs. L[b]	0.46 (0.05,3.94)	0.481[c]	
		H vs. L[b]	3.77 (0.52,27.25)	0.189[c]	
	>18.6	Overall†		0.836	
		M vs. L[a]	0.70 (0.29,1.71)	0.438[c]	
		H vs. L[a]	0.80 (0.29,2.22)	0.664[c]	
		M vs. L[b]	0.39 (0.04,4.35)	0.444[c]	
		H vs. L[b]	1.00 (0.09,11.03)	0.999[c]	
h) Maximal		C-by-T*		0.430	AGE (p=0.018)
(n=742)	≤18.6	Overall†		0.019	RACE (p<0.001)
		M vs. L[a]	1.48 (0.61,3.62)	0.389[c]	PACKYR (p=0.027)
		H vs. L[a]	4.44 (1.63,12.12)	0.004[c]	
		M vs. L[b]	0.69 (0.14,3.52)	0.657[c]	
		H vs. L[b]	4.52 (0.98,20.78)	0.052[c]	
	>18.6	Overall†		0.915	
		M vs. L[a]	1.10 (0.52,2.31)	0.811[c]	
		H vs. L[a]	1.32 (0.55,3.19)	0.531[c]	
		M vs. L[b]	0.63 (0.11,3.80)	0.617[c]	
		H vs. L[b]	1.62 (0.27,9.72)	0.599[c]	

[a]Mild contrasted with none.

[b]Moderate/severe contrasted with none.

[c]Test of significance for relative risk equal to 1 (current dioxin and time categorized).

*Test of significance of current dioxin-by-time interaction.

†Test of independence of current dioxin and loss of vital capacity within time stratum.

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
M vs. L: Medium current dioxin category versus low current dioxin category.
H vs. L: High current dioxin category versus low current dioxin category.

TABLE 17-18. (Continued)

Analysis of Loss of Vital Capacity

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

Current Dioxin Category	n	Percent None	Percent Mild	Percent Mod./Sev.	Contrast	Mild versus None: Est. Relative Risk (95% C.I.)	Mild versus None: p-Value	Moderate/Severe versus None: Est. Relative Risk (95% C.I.)	Moderate/Severe versus None: p-Value
Background	786	90.7	8.1	1.2					
Unknown	344	92.4	5.2	2.3	Unknown vs. Background	0.63 (0.37,1.08)	0.093	1.99 (0.76,5.21)	0.160
Low	196	89.8	9.2	1.0	Low vs. Background	1.14 (0.66,1.97)	0.639	0.90 (0.19,4.20)	0.895
High	187	87.2	11.2	1.6	High vs. Background	1.44 (0.85,2.41)	0.172	1.46 (0.39,5.47)	0.574
Total	1,513						All categories: p=0.169		

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

Current Dioxin Category	n	Contrast	Mild versus None: Adj. Relative Risk (95% C.I.)	Mild versus None: p-Value	Moderate/Severe versus None: Adj. Relative Risk (95% C.I.)	Moderate/Severe versus None: p-Value	Covariate Remarks
Background	786						AGE (p=0.010)
							RACE (p<0.001)
Unknown	344	Unknown vs. Background	0.67 (0.39,1.14)	0.142	2.23 (0.88,5.62)	0.090	PACKYR (p=0.002)
Low	196	Low vs. Background	1.17 (0.68,2.02)	0.576	1.19 (0.33,4.34)	0.792	
High	187	High vs. Background	1.76 (1.04,3.00)	0.036	2.42 (0.74,7.92)	0.143	
Total	1,513			All categories: p=0.052			

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

When the maximal analysis was adjusted for age, race, and lifetime cigarette smoking history, the current dioxin-by-time interaction remained nonsignificant (Table 17-18 [h]: p=0.430). However, the association between current dioxin and loss of vital capacity became significant for time less than or equal to 18.6 years (p=0.019). Within this time stratum there was a significant risk of a mild loss of vital capacity (Est. RR=4.44, 95% C.I.: [1.63,12.12], p=0.004) and a marginally significant risk of a moderate or severe loss of vital capacity (Est. RR=4.52, 95% C.I.: [0.98,20.78], p=0.052) under the high versus low current dioxin contrast. For time greater than 18.6 years the association between current dioxin and loss of vital capacity remained nonsignificant (p=0.915).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In the unadjusted model there was no significant association between loss of vital capacity and the four current dioxin categories (Table 17-18 [i]: p=0.169). For the unknown versus background contrast, the risk of a mild loss of vital capacity was less than 1 and marginally significant (Est. RR=0.63, 95% C.I.: [0.37,1.08], p=0.093).

When the model was adjusted for age, race, and lifetime cigarette smoking history, the association between loss of vital capacity and the four current dioxin categories became marginally significant (Table 17-18 [j]: p=0.052). The risk of a mild loss of vital capacity became significant for the high versus background contrast (Est. RR=1.76, 95% C.I.: [1.04,3.00], p=0.036), and changed to nonsignificant for the unknown versus background contrasts (p=0.142). The risk of a moderate or severe loss of vital capacity became marginally significant for the unknown versus background contrast (Est. RR=2.23, 95% C.I.: [0.88,5.62], p=0.090).

Obstructive Abnormality

Model 1: Ranch Hands - Initial Dioxin (Categorized)

There was a significant association between the obstructive abnormality classifications and the initial dioxin levels for both the minimal and the maximal cohorts in the unadjusted analysis (Table 17-19 [a] and [b]: p=0.018 and p=0.016, respectively). Both cohorts also had a risk of mild obstructive abnormalities that was significantly less than 1 for the high versus low initial dioxin contrast (Minimal: Est. RR=0.47, 95% C.I.: [0.25,0.88], p=0.019; Maximal: Est. RR=0.46, 95% C.I.: [0.27,0.78], p=0.005). The percentages of mild obstructive abnormalities were 26.2, 24.6, and 14.5 percent for the low, medium, and high levels of initial dioxin in the minimal cohort and 26.4, 25.2, and 14.5 percent in the maximal cohort.

In the adjusted minimal analysis, the association between initial dioxin and obstructive abnormalities became nonsignificant (Table 17-19 [c]: p=0.158) and the risk of mild obstructive abnormalities for the high versus low contrast became marginally significant (Est. RR=0.57, 95% C.I.: [0.30,1.10], p=0.092). The covariates that were retained in the model were age and current cigarette smoking. In the adjusted maximal analysis, the association between initial dioxin and obstructive abnormalities also became nonsignificant (Table 17-19 [d]: p=0.212). However, the risk of mild obstructive abnormalities for the high versus low contrast remained significant (Adj. RR=0.54, 95% C.I.: [0.31,0.96], p=0.035). The covariates that were retained in the maximal analysis were age, current cigarette smoking, and lifetime cigarette smoking history.

TABLE 17-19.

Analysis of Obstructive Abnormality

Ranch Hands - Initial Dioxin (Categorized) - Unadjusted

Assumption	Initial Dioxin	n	Percent None	Mild	Mod./Sev.	Initial Dioxin Contrast	Est. Relative Risk (95% C.I.)	p-Value
a) Minimal	Low	130	71.5	26.2	2.3	Overall†		0.018
(n=521)	Medium	260	70.0	24.6	5.4	M vs. L[a]	0.96 (0.59,1.56)	0.875
	High	131	84.0	14.5	1.5	H vs. L[a]	0.47 (0.25,0.88)	0.019
						M vs. L[b]	2.38 (0.67,8.49)	0.181
						H vs. L[b]	0.56 (0.09,3.45)	0.535
b) Maximal	Low	349	69.6	26.4	4.0	Overall†		0.016
(n=742)	Medium	262	69.5	25.2	5.3	M vs. L[a]	0.96 (0.66,1.39)	0.820
	High	131	84.0	14.5	1.5	H vs. L[a]	0.46 (0.27,0.78)	0.005
						M vs. L[b]	1.34 (0.62,2.87)	0.459
						H vs. L[b]	0.32 (0.07,1.41)	0.132

Ranch Hands - Initial Dioxin (Categorized) - Adjusted

Assumption	Initial Dioxin Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
c) Minimal	Overall†		0.158	AGE (p<0.001)
(n=521)	M vs. L[a]	0.94 (0.57,1.56)	0.804	CSMOK (p<0.001)
	H vs. L[a]	0.57 (0.30,1.10)	0.092	
	M vs. L[b]	2.38 (0.70,8.10)	0.167	
	H vs. L[b]	0.94 (0.17,5.17)	0.944	
d) Maximal	Overall†		0.212	AGE (p<0.001)
(n=742)	M vs. L[a]	0.87 (0.59,1.30)	0.503	CSMOK (p<0.001)
	H vs. L[a]	0.54 (0.31,0.96)	0.035	PACKYR (p=0.002)
	M vs. L[b]	1.32 (0.62,2.83)	0.473	
	H vs. L[b]	0.68 (0.19,2.41)	0.549	

[a]Mild contrasted with none.
[b]Moderate/severe contrasted with none.
†Test of independence of initial dioxin and obstructive abnormality.
Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
M vs. L: Medium initial dioxin category versus low initial dioxin category.
H vs. L: High initial dioxin category versus low initial dioxin category.

TABLE 17-19. (Continued)

Analysis of Obstructive Abnormality

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

Assumption	Time (Yrs.)	Obstructive Abnormality Category	Percent/(n) Current Dioxin Low	Medium	High	Current Dioxin Contrast	Est. Relative Risk (95% C.I.)	p-Value
e) Minimal						C-by-T*		0.844
(n=521)	≤18.6	None	72.2	74.2	83.3	Overall†		0.327
		Mild	26.4	21.1	14.8	M vs. L[a]	0.78 (0.40,1.53)	0.468[c]
		Mod./Sev.	1.4	4.7	1.9	H vs. L[a]	0.49 (0.19,1.22)	0.124[c]
			(72)	(128)	(54)	M vs. L[b]	3.29 (0.39,28.04)	0.277[c]
						H vs. L[b]	1.15 (0.07,18.96)	0.921[c]
	>18.6	None	63.8	69.7	83.1	Overall†		0.083
		Mild	31.0	25.0	15.6	M vs. L[a]	0.74 (0.37,1.47)	0.386[c]
		Mod./Sev.	5.2	5.3	1.3	H vs. L[a]	0.38 (0.17,0.89)	0.025[c]
			(58)	(132)	(77)	M vs. L[b]	0.94 (0.23,3.83)	0.929[c]
						H vs. L[b]	0.19 (0.02,1.92)	0.161[c]
f) Maximal						C-by-T*		0.977
(n=742)	≤18.6	None	70.7	74.2	83.3	Overall†		0.348
		Mild	25.8	21.1	14.8	M vs. L[a]	0.78 (0.46,1.33)	0.365[c]
		Mod./Sev.	3.5	4.7	1.9	H vs. L[a]	0.49 (0.22,1.11)	0.086[c]
			(198)	(128)	(54)	M vs. L[b]	1.26 (0.41,3.88)	0.681[c]
						H vs. L[b]	0.44 (0.05,3.71)	0.454[c]
	>18.6	None	64.7	69.7	83.1	Overall†		0.044
		Mild	30.1	25.0	15.6	M vs. L[a]	0.77 (0.45,1.31)	0.338[c]
		Mod./Sev.	5.2	5.3	1.3	H vs. L[a]	0.40 (0.20,0.82)	0.012[c]
			(153)	(132)	(77)	M vs. L[b]	0.94 (0.33,2.70)	0.913[c]
						H vs. L[b]	0.19 (0.02,1.58)	0.125[c]

[a]Mild contrasted with none.
[b]Moderate/severe contrasted with none.
[c]Test of significance for relative risk equal to 1 (current dioxin and time categorized).
*Test of significance of current dioxin-by-time interaction.
†Test of independence of current dioxin and obstructive abnormality within time stratum.
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
M vs. L: Medium current dioxin category versus low current dioxin category.
H vs. L: High current dioxin category versus low current dioxin category.

TABLE 17-19. (Continued)

Analysis of Obstructive Abnormality

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

Assumption	Time (Yrs.)	Current Dioxin Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
g) Minimal		C-by-T*		0.803	AGE (p<0.001)
(n=521)	≤18.6	Overall†		0.417	CSMOK (p<0.001)
		M vs. L[a]	0.82 (0.40,1.65)	0.571[c]	
		H vs. L[a]	0.65 (0.25,1.69)	0.375[c]	
		M vs. L[b]	3.23 (0.49,21.25)	0.222[c]	
		H vs. L[b]	2.38 (0.21,27.21)	0.486[c]	
	>18.6	Overall†		0.103	
		M vs. L[a]	0.75 (0.37,1.51)	0.414[c]	
		H vs. L[a]	0.50 (0.21,1.19)	0.117[c]	
		M vs. L[b]	0.99 (0.25,3.89)	0.990[c]	
		H vs. L[b]	0.38 (0.05,2.94)	0.357[c]	
h) Maximal		C-by-T*		0.963	AGE (p<0.001)
(n=742)	≤18.6	Overall†		0.683	CSMOK (p=0.001)
		M vs. L[a]	0.75 (0.43,1.32)	0.322[c]	PACKYR (p=0.003)
		H vs. L[a]	0.65 (0.29,1.49)	0.310[c]	
		M vs. L[b]	1.37 (0.47,3.97)	0.564[c]	
		H vs. L[b]	1.31 (0.27,6.48)	0.738[c]	
	>18.6	Overall†		0.513	
		M vs. L[a]	0.79 (0.45,1.37)	0.403[c]	
		H vs. L[a]	0.57 (0.28,1.17)	0.125[c]	
		M vs. L[b]	1.05 (0.38,2.89)	0.921[c]	
		H vs. L[b]	0.59 (0.13,2.74)	0.501[c]	

[a]Mild contrasted with none.
[b]Moderate/severe contrasted with none.
[c]Test of significance for relative risk equal to 1 (current dioxin and time categorized).
*Test of significance of current dioxin-by-time interaction.
†Test of independence of current dioxin and obstructive abnormality within time stratum.
Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
M vs. L: Medium current dioxin category versus low current dioxin category.
H vs. L: High current dioxin category versus low current dioxin category.

TABLE 17-19. (Continued)

Analysis of Obstructive Abnormality

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

Current Dioxin Category	n	Percent None	Percent Mild	Percent Mod./Sev.	Contrast	Mild versus None: Est. Relative Risk (95% C.I.)	Mild versus None: p-Value	Moderate/Severe versus None: Est. Relative Risk (95% C.I.)	Moderate/Severe versus None: p-Value
Background	786	74.1	21.4	4.6					
Unknown	344	66.3	28.8	4.9	Unknown vs. Background	1.50 (1.12,2.01)	0.006	1.20 (0.66,2.19)	0.541
Low	196	69.4	24.5	6.1	Low vs. Background	1.22 (0.84,1.77)	0.288	1.42 (0.72,2.81)	0.307
High	187	82.9	15.5	1.6	High vs. Background	0.65 (0.42,1.00)	0.050	0.31 (0.10,1.03)	0.056
Total	1,513						All categories: p=0.002		

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

Current Dioxin Category	n	Contrast	Mild versus None: Adj. Relative Risk (95% C.I.)	Mild versus None: p-Value	Moderate/Severe versus None: Adj. Relative Risk (95% C.I.)	Moderate/Severe versus None: p-Value	Covariate Remarks
Background	786						AGE (p<0.001)
							CSMOK (p<0.001)
Unknown	344	Unknown vs. Background	1.45 (1.06,1.99)	0.020	1.16 (0.63,2.12)	0.636	PACKYR (p<0.001)
Low	196	Low vs. Background	1.18 (0.79,1.75)	0.412	1.45 (0.73,2.88)	0.293	
High	187	High vs. Background	0.75 (0.48,1.19)	0.223	0.55 (0.19,1.51)	0.263	
Total	1,513			All categories: p=0.083			

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

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

The interaction between current dioxin and time since tour was not significant under both the minimal and the maximal assumptions in the unadjusted analyses of obstructive abnormality (Table 17-19 [e] and [f]: p=0.844 and p=0.977, respectively). Under the minimal assumption, there was no significant association between current dioxin and obstructive abnormalities for time less than or equal to 18.6 years (Table 17-19 [e]: p=0.327). For time greater than 18.6 years the association was marginally significant (p=0.083). The percentages of mild obstructive abnormalities were 31.0, 25.0, and 15.6 percent for the low, medium, and high categories, and the percentages of moderate or severe obstructive abnormalities were 5.2, 5.3, and 1.3 percent. Within this time stratum the risk of mild obstructive abnormalities was significantly less than 1 under the high versus low current dioxin contrast (Est. RR=0.38, 95% C.I.: [0.17,0.89], p=0.025).

Under the maximal assumption, the association between current dioxin and obstructive abnormalities was not significant for time less than or equal to 18.6 years (Table 17-19 [f]: p=0.348). However, the risk of mild obstructive abnormalities was marginally less than 1 for the high versus low contrast (Est. RR=0.49, 95% C.I.: [0.22,1.11], p=0.086). For time greater than 18.6 years, the association between current dioxin and obstructive abnormalities was significant (p=0.044). Within this stratum, the risk of mild obstructive abnormalities under the high versus low current dioxin contrast was significantly less than 1 (Est. RR=0.40, 95% C.I.: [0.20,0.82], p=0.012). The percentages of mild obstructive abnormalities were 30.1, 25.0, and 15.6 percent for the low, medium, and high categories, and the percentages of moderate or severe obstructive abnormalities were 5.2, 5.3, and 1.3 percent.

After adjusting the minimal analysis for age and current cigarette smoking, the current dioxin-by-time interaction remained nonsignificant (Table 17-19 [g]: p=0.803). The association between current dioxin and obstructive abnormalities remained nonsignificant for time less than or equal to 18.6 years (p=0.417) and became nonsignificant for time greater than 18.6 years (p=0.103). The risk of mild obstructive abnormalities under the high versus low contrast also became nonsignificant for time greater than 18.6 years (p=0.117).

In the adjusted maximal analysis, the current dioxin-by-time interaction remained nonsignificant (Table 17-19 [h]: p=0.963) and the association between current dioxin and obstructive abnormalities was nonsignificant within both time strata (p=0.683 for time$\leq$18.6 years; p=0.513 for time>18.6 years). The risk of mild obstructive abnormalities under the high versus low contrast became nonsignificant within both time strata as well (p=0.310 for time$\leq$18.6 years; p=0.125 for time>18.6 years). The covariates that were retained in the maximal analysis were age, current cigarette smoking, and lifetime cigarette smoking history.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

A significant association between obstructive abnormalities and the four current dioxin categories was exhibited in the unadjusted model (Table 17-19 [i]: p=0.002). There was a significant risk of mild obstructive abnormalities under the unknown versus background exposure contrast (Est. RR=1.50, 95% C.I.: [1.12,2.01], p=0.006). The risk of mild obstructive abnormalities was significantly less than 1 for the high versus background contrast (Est. RR=0.65, 95% C.I.: [0.42,1.00], p=0.050). Also for the high versus background contrast, the risk of moderate or severe obstructive abnormalities was marginally less than 1 (Est. RR=0.31, 95% C.I.: [0.10,1.03], p=0.056). The percentages of a mild loss of vital capacity

were 21.4, 28.8, 24.5, and 15.5 percent, and the percentages of a moderate or severe loss of vital capacity were 4.6, 4.9, 6.1, and 1.6 percent for the background, unknown, low, and high categories.

After the model was adjusted for age, current cigarette smoking, and lifetime cigarette smoking history, the association between current dioxin and obstructive abnormalities became marginally significant (Table 17-19 [j]: p=0.083). The risk of mild obstructive abnormalities for the unknown versus background contrast remained significant (Est. RR=1.45, 95% C.I.: [1.06,1.99], p=0.020), but the risks of mild and moderate or severe obstructive abnormalities for the high versus background contrast became nonsignificant (mild: p=0.223; moderate/severe: p=0.263).

Longitudinal Analysis

Laboratory Examination Variable

Ratio of Observed FEV_1 to Observed FVC

Longitudinal analyses were conducted to examine the change in FEV_1/FVC for study participants, as measured by the difference from the 1987 examination value relative to the 1982 Baseline examination value, for associations with initial dioxin in Ranch Hands, current dioxin and time since tour in Ranch Hands, and categorized current dioxin in Ranch Hands and Comparisons. For a specific longitudinal analysis of FEV_1/FVC (e.g., minimal assumption, initial dioxin analysis), the left side of each subpanel of a table provides the means and sample sizes for participants with laboratory values at each examination. The right side of each subpanel presents slopes, standard errors, and associated p-values (for models using initial dioxin or models using current dioxin and time since tour), or differences of examination mean changes, 95 percent confidence intervals, and associated p-values (for models using categorized current dioxin). The reported statistics are presented for all participants who were compliant at both the 1982 and 1987 examinations. Table 17-20 presents the results of the longitudinal analyses.

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

The longitudinal analysis of the change in FEV_1/FVC of Ranch Hands between the 1982 and 1987 examinations and initial dioxin detected a marginally significant negative slope under both the minimal and the maximal assumption (Table 17-20 [a] and [b]: p=0.093 and p=0.100). Due to the transformation used, this negative slope implies a positive association of borderline significance between the change in FEV_1/FVC, 1987 relative to 1982, and initial dioxin. Under the minimal assumption, the FEV_1/FVC means increased by 0.002 from 1982 to 1987 for the low initial dioxin category, decreased by 0.001 for the medium initial dioxin category, and increased by 0.008 for the high initial dioxin category. Similarly, under the maximal assumption, FEV_1/FVC means increased by 0.002, decreased by 0.002, and increased by 0.008 for the low, medium, and high initial dioxin categories from the 1982 examination to the 1987 examination.

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

In the longitudinal analysis of the change in FEV_1/FVC between the 1982 Baseline examination and the 1987 examination with current dioxin and time since tour, the interaction

TABLE 17-20.

Longitudinal Analysis of Ratio of Observed FEV_1 to Observed FVC

Ranch Hands - Log_2 (Initial Dioxin)

Assumption	Initial Dioxin	Mean[a]/(n) Examination 1982	Mean[a]/(n) Examination 1987	Slope (Std. Error)[b]	p-Value
a) Minimal (R^2=0.006)	Low	0.820 (124)	0.822 (124)	-0.015 (0.009)	0.093
	Medium	0.814 (255)	0.813 (255)		
	High	0.832 (125)	0.840 (125)		
b) Maximal (R^2=0.004)	Low	0.808 (171)	0.810 (171)	-0.010 (0.006)	0.100
	Medium	0.813 (359)	0.811 (359)		
	High	0.830 (179)	0.838 (179)		

[a]Transformed from natural logarithm (1 - X) scale.

[b]Slope and standard error based on difference between natural logarithm (1 - ratio of observed FEV_1 to observed FVC) from 1987 and natural logarithm (1 - ratio of observed FEV_1 to observed FVC) from 1982 versus log_2 dioxin.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.
P-values given are in reference to a contrast of 1982 and 1987 results.

TABLE 17-20. (Continued)

Longitudinal Analysis of Ratio of Observed FEV_1 to Observed FVC

Ranch Hands - Log_2 (Current Dioxin) and Time

Assumption	Time (Yrs.)	Examination	Mean[a]/(n) Current Dioxin Low	Medium	High	Slope (Std. Error)[b]	p-Value
c) Minimal							0.876[c]
(R^2=0.008)	≤18.6	1982	0.814 (69)	0.818 (125)	0.832 (52)	-0.015 (0.014)	0.304[d]
		1987	0.822 (69)	0.818 (125)	0.840 (52)		
	>18.6	1982	0.815 (55)	0.813 (130)	0.835 (73)	-0.018 (0.012)	0.135[d]
		1987	0.812 (55)	0.812 (130)	0.842 (73)		
d) Maximal							0.277[c]
(R^2=0.013)	≤18.6	1982	0.806 (95)	0.815 (185)	0.829 (80)	-0.006 (0.010)	0.524[d]
		1987	0.813 (95)	0.816 (185)	0.838 (80)		
	>18.6	1982	0.807 (76)	0.811 (173)	0.833 (100)	-0.021 (0.009)	0.018[d]
		1987	0.797 (76)	0.808 (173)	0.839 (100)		

[a]Transformed from natural logarithm (1 - X) scale.

[b]Slope and standard error based on difference between natural logarithm (1 - ratio of observed FEV_1 to observed FVC) from 1987 and natural logarithm (1 - ratio of observed FEV_1 to observed FVC) from 1982 versus log_2 dioxin.

[c]Test of significance for homogeneity of slopes (current dioxin continuous, time categorized).

[d]Test of significance for slope equal to 0 (current dioxin continuous, time categorized).

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.
P-values given are in reference to a contrast of 1982 and 1987 results.

TABLE 17-20. (Continued)

Longitudinal Analysis of Ratio of Observed FEV_1 to Observed FVC

e) Ranch Hands and Comparisons by Current Dioxin Category

Current Dioxin Category	Mean[a]/(n) Examination 1982	1987	Contrast	Difference of Examination Mean Change (95% C.I.)[e]	p-Value[f]
Background	0.814 (683)	0.815 (683)	All Categories		0.033
Unknown	0.804 (316)	0.803 (316)	Unknown vs. Background	-0.002 --	0.401
Low	0.813 (192)	0.810 (192)	Low vs. Background	-0.004 --	0.220
High	0.831 (180)	0.838 (180)	High vs. Background	0.006 --	0.032
	(R^2=0.006)				

[a]Transformed from natural logarithm (1 - X) scale.

[e]Difference of 1987 and 1982 examination mean changes after transformation to original scale; confidence interval on difference of 1987 and 1982 examination mean changes not given because analysis was performed on natural logarithm (1 - X) scale.

[f]P-value is based on difference of 1987 and 1982 examination mean changes on natural logarithm (1 - X) scale.

Note: Background (Comparisons): Current Dioxin ≤10 ppt.
Unknown (Ranch Hands): Current Dioxin ≤10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.
P-values given are in reference to a contrast of 1982 and 1987 results.

between current dioxin and time since tour was nonsignificant under both the minimal and the maximal assumptions (Table 17-20 [c] and [d]: p=0.876 and p=0.277). Thus, the association between current dioxin and the change in FEV_1/FVC (1987 relative to 1982) did not differ for the two time strata under either the minimal or the maximal assumption. However, for the maximal cohort, there was a significant negative slope for the greater than 18.6 years time stratum (Table 17-20 [d]: p=0.018). The negative slope indicates that the change in FEV_1/FVC from 1987 to 1982 increased with increasing current dioxin levels. In the greater than 18.6 years time stratum of the maximal cohort, the difference in FEV_1/FVC means between the 1987 and 1982 examinations was -0.010, -0.003, and 0.006 for the low, medium, and high current dioxin categories.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The change in FEV_1/FVC between the 1982 Baseline examination and the 1987 examination differed significantly among the four current dioxin categories (Table 17-20 [e]: p=0.033). The changes in FEV_1/FVC means (1987 relative to 1982) for the background, unknown, low, and high current dioxin categories were 0.001, -0.001, -0.003, and 0.007. The contrast of the high category versus the background category found the change in FEV_1/FVC means between 1982 and 1987 for the Ranch Hands in the high category significantly greater than the change in FEV_1/FVC means for the Comparisons in the background category (p=0.032).

DISCUSSION

While the presence of pulmonary disease is often evident based on a careful history and physical examination, definitive diagnosis usually requires the collection of data from a number of other sources. In the laboratory, the standard radiographic examination of the chest and pulmonary function studies are routinely ordered and were included as variables in the Air Force Health Study examination.

Historical information on the occurrence of pulmonary disease must be interpreted with caution in the absence of medical record verification. Many of the cardinal symptoms of lung disease, including dyspnea, chest pain, and exercise intolerance, are common to cardiovascular disease as well (particularly ischemic heart disease) and are misinterpreted frequently as to cause. Wheezing, assumed by the patient to be indicative of asthma, may in fact be reflective of hemodynamic compromise in congestive heart failure. "Pneumonia" and "pneumonitis" are often confused by patients in relating the medical history. All reported episodes of pulmonary disease were verified by medical records and only verified occurrences were analyzed.

The physical examination variables studied can provide valuable clues to the presence of pulmonary disease. In lacking specificity, however, these data are limited in confirming a diagnosis. Wheezes and hyperresonance, for example, will occur in obstructive airway disease in asthma or in emphysema secondary to cigarette use. Dullness to percussion, a finding common to many disorders, will occur in consolidation from atelectasis, infections, pleural thickening, or pleural effusion.

In view of the limitations of the history and physical examination noted above, added emphasis is placed on screening laboratory data in the diagnosis of respiratory disease. The

chest x ray, when normal, is highly reliable in excluding pulmonary parenchymal disease, though several exceptions must be recognized. Solitary lesions less than 6 millimeters, miliary granulomatous infection, and early interstitial disease, among others, may be present but not detectable radiographically. Further, it is recognized clinically that the chest x ray is not sensitive to the detection of obstructive airway disease in an early stage. On the other hand, the chest x ray may reveal an early occult malignancy in an asymptomatic patient and afford a rare opportunity for cure.

Spirometry has been used as a clinical tool to measure static lung volumes and to detect respiratory disease for over a century. Dynamic indices, relating changes in lung volume to time, were first developed more than 50 years ago and, with computerization, have been refined to a high degree of accuracy and reproducibility. To be valid, spirometry requires that particular attention be paid to technician training and to eliciting the full cooperation of the patient. In spirometry a premium is placed on using identical techniques in longitudinal studies. These factors received special emphasis in this study.

The spirometric indices evaluated in this chapter are designed to measure lung volume (FVC) and respiratory air flow (FEV). Static lung volume is principally determined by height and is independent of weight, while dynamic volume measurements depend in part on physical strength. Accordingly, all indices require correction for age and height.

Respiratory disease may be divided into two general categories in clinical practice. "Restrictive" disease is characterized by reduced vital capacity as seen in interstitial fibrosis or reduced lung volume postsurgical resection. In "obstructive" airways disease associated with cigarette use (usually chronic obstructive pulmonary disease), the flow-dependent indices of FEV_1 and FEFmax are abnormally prolonged.

With a few exceptions, statistically significant pulmonary findings in this study were limited to the laboratory indices. None of the historical variables was found to be significantly associated with the current or extrapolated initial body burden of dioxin.

With respect to the physical examination variables, there was no evidence for any increased risk related to the current body burden of dioxin. In the adjusted analysis, thorax and lung abnormalities (which was a composite of hyperresonance, dullness, wheezes, and rales) displayed an increase in relation to the extrapolated initial level of serum dioxin and a greater frequency for those Ranch Hands with the highest level of serum dioxin than for the Comparisons. An examination of the component variables showed marginally significant increases with initial dioxin for hyperresonance and dullness, a significant increase with initial dioxin for wheezes, and a nonsignificant but also positive association for rales. Similarly, Ranch Hands with the highest levels of serum dioxin were marginally greater than the Comparisons with respect to the frequency of hyperresonance and wheezes, and significantly greater for the frequency of rales. The associated adjusted relative risks for these Ranch Hands versus Comparisons contrasts ranged from 1.98 to 3.03.

Several of the laboratory indices analyzed revealed findings consistent with a dioxin effect. In the adjusted analysis, a slight decrease in FEV_1 and FEFmax was noted in the initial dioxin analysis. Though consistent with a dose-response effect, the differences were slight (i.e., FEV_1, 94.8 percent for low and 92.7 percent for high levels; FEFmax, 139.3

percent for low and 135.1 percent for high levels) and not felt to be clinically significant. A slight reduction in FVC was noted in those participants with high versus low levels of extrapolated initial serum dioxin (88.4 percent versus 93.0 percent). Regardless of time since tour, similar results were noted in relation to the current serum dioxin as well. Finally, the FVC of those Ranch Hands with the highest levels of serum dioxin was lower than that of the Comparisons (87.4 percent versus 91.7 percent). A reduction in vital capacity associated with obesity is well established in clinical practice. As noted in Chapter 6, General Health, a strong positive association was found between percent body fat and the body burden of dioxin. Accordingly, interpretation of these results must await further research into the pharmacokinetics of dioxin in lean versus obese individuals. In both the minimal and maximal cohorts, 3.1 percent and 3.2 percent of the participants had FVC values below 74 percent, the level indicating clinically relevant disease. The reduction in FVC is reflected in the only other statistically significant laboratory index, the ratio of observed FEV_1 to observed FVC that increased with the body burden of dioxin.

The historical, physical examination, and laboratory data analyzed in this chapter revealed no evidence for an increased incidence of pulmonary disease in the Ranch Hand cohort relative to the Comparisons. Analysis of four laboratory variables yielded results that were consistent with subtle dose-effects related to the body burden of dioxin. Body habitus and, more specifically, percent body fat may play a role in these associations.

SUMMARY

Five questionnaire variables, five physical examination variables, and seven laboratory variables were analyzed for associations with initial dioxin, current dioxin and time since tour, and categorized current dioxin. Tables 17-21, 17-22, and 17-23 summarize the results.

Questionnaire Variables

The five questionnaire variables that were analyzed were asthma, bronchitis, pleurisy, pneumonia, and tuberculosis. All of these conditions were restricted to disease occurring after duty in SEA.

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

The unadjusted analyses of the questionnaire variables showed no significant associations with initial dioxin.

In the adjusted analysis of asthma, under both assumptions, there was a significant interaction between initial dioxin and current cigarette smoking (minimal, $p<0.001$; maximal, $p=0.024$). Under the minimal assumption, the risk of asthma was greater than 1 but not significant for Ranch Hands with no current cigarette smoking and was of borderline significance less than 1 for those with current cigarette use (>0-20 cigarettes/day: $p=0.062$; >20 cigarettes/day: $p=0.052$). Under the maximal assumption, the risk of asthma was significantly less than 1 for Ranch Hands who smoked more than 20 cigarettes per day ($p=0.034$) and was not significant for the other strata. Without this interaction, there was no significant association between asthma and initial dioxin under the maximal assumption. In the adjusted maximal analysis of bronchitis there was a marginally significant risk of bronchitis that was

TABLE 17-21.

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

	Unadjusted		Adjusted	
Variable	Minimal	Maximal	Minimal	Maximal
Questionnaire				
Asthma (D)	ns	ns	****	** (ns)
Bronchitis (D)	ns	ns	ns	ns*
Pleurisy (D)	NS	NS	NS*	NS
Pneumonia (D)	ns	ns	ns	ns
Tuberculosis (D)	ns	ns	ns	ns
Physical Examination				
Thorax and Lung Abnormalities (D)	NS	NS	NS*	+0.022
Hyperresonance (D)	NS	NS	NS	NS*
Dullness (D)	NS	NS*	NS	NS*
Wheezes (D)	NS	NS	+0.034	+0.034
Rales (D)	NS	NS	NS	NS
Laboratory				
X-Ray Interpretation (D)	NS	NS	NS	NS
FVC[a] (C)	ns	-<0.001	** (-0.028)	-<0.001
FEV_1[a] (C)	NS	ns	** (ns)	-0.026
FEFmax[a] (C)	ns	-0.021	ns	-0.014
Ratio of Observed FEV_1 to Observed FVC[b] (C)	+0.001	+<0.001	+0.022	+<0.001
Loss of Vital Capacity (D)	NS	NS*	NS*	0.011
Obstructive Abnormality (D)	0.018	0.016	NS	NS

[a]Negative slope considered adverse for this variable.

[b]Positive association between variable and $\log_2$ (initial dioxin); however, slope is negative in analysis due to natural logarithm (1 - X) transformation; directionality of association in table is opposite of analysis slope.

C: Continuous analysis.

D: Discrete analysis.

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

-: Slope negative for continuous analysis.

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

NS*/ns*: Marginally significant ($0.05<p\leq0.10$).

** (ns): Log_2 (initial dioxin)-by-covariate interaction ($0.01<p\leq0.05$); not significant when interaction is deleted; refer to Appendix Table P-1 for a detailed description of this interaction.

TABLE 17-21. (Continued)

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

** (-0.028): Log_2 (initial dioxin)-by-covariate interaction ($0.01<p\leq0.05$); significant ($p=0.028$) when interaction is deleted; refer to Appendix Table P-1 for a detailed description of this interaction.

****: Log_2 (initial dioxin)-by-covariate interaction ($0.01<p\leq0.05$); refer to Appendix Table P-1 for a detailed description of this interaction.

Note: P-value given if $p\leq0.05$.

A capital "NS" denotes relative risk 1.00 or greater for discrete analysis or slope nonnegative for continuous analysis; a lowercase "ns" denotes relative risk less than 1.00 for discrete analysis or negative for continuous analysis; a capital "NS" for loss of vital capacity and obstructive abnormality does not imply directionality due to log-linear analysis.

TABLE 17-22.

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

	Unadjusted					
	Minimal			Maximal		
Variable	C*T	≤18.6	>18.6	C*T	≤18.6	>18.6
Questionnaire						
Asthma (D)	ns	NS	ns	ns	NS	ns
Bronchitis (D)	NS	ns	ns	NS	-0.044	ns
Pleurisy (D)	ns	NS	NS	NS	ns	NS
Pneumonia (D)	ns	ns	ns	NS	ns	ns
Tuberculosis (D)	NS	ns	ns	NS	ns	ns
Physical Examination						
Thorax and Lung Abnormalities (D)	ns	NS	ns	NS	NS	NS
Hyperresonance (D)	NS	NS	NS	NS	NS	NS
Dullness (D)	--	--	--	--	--	--
Wheezes (D)	ns	NS	NS	ns	NS	NS
Rales (D)	ns	NS	NS	NS	ns	NS
Laboratory						
X-Ray Interpretation (D)	ns	NS	ns	ns	NS	ns
FVC[a] (C)	NS	ns	NS	NS	-0.003	ns
FEV_1[a] (C)	NS	ns	NS	NS	ns	NS
FEFmax[a] (C)	NS	ns*	NS	NS	-0.013	ns
Ratio of Observed FEV_1 to Observed FVC[b] (C)	NS	+0.045	+0.004	NS	+0.005	+<0.001
Loss of Vital Capacity (D)	NS	NS	NS	NS	NS	NS
Obstructive Abnormality (D)	NS	NS	NS*	NS	NS	0.044

[a]Negative slope considered adverse for this variable.

[b]Positive association between variable and $\log_2$ (current dioxin); however, slope is negative in analysis due to natural logarithm (1 - X) transformation; directionality of association in table is opposite of analysis slope.

C: Continuous analysis.

D: Discrete analysis.

+: ≤18.6 and >18.6: Slope nonnegative for continuous analysis.

-: ≤18.6 and >18.6: Relative risk less than 1.00 for discrete analysis; slope negative for continuous analysis.

--: Analysis not performed due to sparse number of abnormalities.

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

NS*/ns*: Marginally significant ($0.05<p\leq0.10$).

TABLE 17-22. (Continued)

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

Note: P-value given if $p \leq 0.05$.
C*T: Log_2 (current dioxin)-by-time interaction hypothesis test.
≤18.6: Log_2 (current dioxin) hypothesis test for Ranch Hands with time since end of tour of 18.6 years or less.
>18.6: Log_2 (current dioxin) hypothesis test for Ranch Hands with time since end of tour greater than 18.6 years.
A capital "NS" denotes relative risk/slope for ≤18.6 category less than relative risk/slope for >18.6 category, relative risk 1.00 or greater for discrete analysis, or slope nonnegative for continuous analysis; a lowercase "ns" denotes relative risk/slope for ≤18.6 category greater than relative risk/slope for >18.6 category, relative risk less than 1.00 for discrete analysis, or slope negative for continuous analysis; a capital "NS" for loss of vital capacity and obstructive abnormality does not imply directionality due to log-linear analysis.

TABLE 17-22. (Continued)

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

	Adjusted					
	Minimal			Maximal		
Variable	C*T	≤18.6	>18.6	C*T	≤18.6	>18.6
Questionnaire						
Asthma (D)	ns	NS	ns	ns	NS	ns
Bronchitis (D)	** (NS)	** (ns*)	** (ns)	****	****	****
Pleurisy (D)	****	****	****	****	****	****
Pneumonia (D)	ns	NS	ns	NS	ns	ns
Tuberculosis (D)	NS	ns	ns	NS	ns	ns
Physical Examination						
Thorax and Lung Abnormalities (D)	** (ns)	** (NS*)	** (NS)	NS	NS	+0.030
Hyperresonance (D)	ns	NS	NS	NS	NS	+0.027
Dullness (D)	--	--	--	--	--	--
Wheezes (D)	** (ns)	** (NS*)	** (NS)	ns	NS	NS*
Rales (D)	ns	NS	NS	NS	NS	NS
Laboratory						
X-Ray Interpretation (D)	ns	NS	ns	ns	NS	ns
FVC[a] (C)	NS	-0.024	ns	NS	-<0.001	-0.009
FEV_1[a] (C)	NS	ns*	ns	NS	-0.014	ns
FEFmax[a] (C)	NS*	ns*	NS	NS	-0.010	ns
Ratio of Observed FEV_1 to Observed FVC[b] (C)	NS	NS	NS*	NS	+0.034	+0.005
Loss of Vital Capacity (D)	NS	NS	NS	NS	0.019	NS
Obstructive Abnormality (D)	NS	NS	NS	NS	NS	NS

[a]Negative slope considered adverse for this variable.

[b]Positive association between variable and $\log_2$ (current dioxin); however, slope is negative in analysis due to natural logarithm (1 - X) transformation; directionality of association in table is opposite of analysis slope.

C: Continuous analysis.

D: Discrete analysis.

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

-: ≤18.6 and >18.6: Slope negative for continuous analysis.

--: Analysis not performed due to sparse number of abnormalities.

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

NS*/ns*: Marginally significant ($0.05<p\leq0.10$).

** (NS)/** (ns): $\log_2$ (current dioxin)-by-time-by-covariate interaction ($0.01<p\leq0.05$); not significant when interaction is deleted; refer to Appendix Table P-1 for a detailed description of this interaction.

TABLE 17-22. (Continued)

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

** (NS*)/** (ns*): Log_2 (current dioxin)-by-time-by-covariate interaction ($0.01<p\leq0.05$); marginally significant when interaction is deleted; refer to Appendix Table P-1 for a detailed description of this interaction.

****: Log_2 (current dioxin)-by-time-by-covariate interaction ($p\leq0.01$); refer to Appendix Table P-1 for a detailed description of this interaction.

Note: P-value given if $p\leq0.05$.

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

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

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

A capital "NS" denotes relative risk/slope for ≤18.6 category less than relative risk/slope for >18.6 category, relative risk 1.00 or greater for discrete analysis, or slope nonnegative for continuous analysis; a lowercase "ns" denotes relative risk/slope for ≤18.6 category greater than relative risk/slope for >18.6 category, relative risk less than 1.00 for discrete analysis, or slope negative for continuous analysis; a capital "NS" for loss of vital capacity and obstructive abnormality does not imply directionality due to log-linear analysis.

TABLE 17-23.

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

Variable	All	Unadjusted: Unknown versus Background	Unadjusted: Low versus Background	Unadjusted: High versus Background
Questionnaire				
Asthma (D)	NS	+0.040	NS	NS
Bronchitis (D)	NS	NS	NS	ns
Pleurisy (D)	NS	ns	ns	NS
Pneumonia (D)	NS	ns	ns	ns
Tuberculosis (D)	NS	NS	ns	ns
Physical Examination				
Thorax and Lung Abnormalities (D)	NS	NS	NS*	NS
Hyperresonance (D)	NS	NS	NS	NS
Dullness (D)	--	--	--	--
Wheezes (D)	NS	NS	NS	NS
Rales (D)	NS	ns	ns	NS
Laboratory				
X-Ray Interpretation (D)	NS	ns	ns	NS
FVC[a] (C)	<0.001	NS*	ns	-0.001
FEV_1[a] (C)	NS	NS	ns	ns
FEFmax[a] (C)	NS*	NS	ns*	ns
Ratio of Observed FEV_1 to Observed FVC (C)	<0.001	-0.007	ns	+<0.001
Loss of Vital Capacity[b] (D)	NS	ns*	NS	NS
Loss of Vital Capacity[c] (D)		NS	ns	NS
Obstructive Abnormality[b] (D)	0.002	+0.006	NS	-0.050
Obstructive Abnormality[c] (D)		NS	NS	ns*

[a]Negative difference considered adverse for this variable.
[b]Mild contrasted with none for the last three columns.
[c]Moderate/severe contrasted with none for the last three columns.
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk 1.00 or greater for discrete analysis; difference in means nonnegative for continuous analysis.
-: Relative risk less than 1.00 for discrete analysis; difference in means negative for continuous analysis.
--: Analysis not performed due to sparse number of abnormalities.
NS/ns: Not significant ($p>0.10$).
NS*/ns*: Marginally significant ($0.05<p\leq0.10$).
Note: P-value given if $p\leq0.05$.
A capital "NS" denotes relative risk 1.00 or greater for discrete analysis or difference in means nonnegative for continuous analysis; a lowercase "ns" denotes relative risk less than 1.00 for discrete analysis or difference in means negative for continuous analysis; a capital "NS" in the first column does not imply directionality; a capital "NS" for loss of vital capacity and obstructive abnormality does not imply directionality due to log-linear analysis.