18.2.2.1.3 Pneumonia

All unadjusted and adjusted Models 1, 3, and 4 analyses of pneumonia showed no significant results (Table 18-5(a,b,e–h): p>0.10 for all analyses).

Table 18-5. Analysis of Pneumonia

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***826***	***85 (10.3)***	***0.87 (0.66,1.16)***	***0.344***
	Comparison	***1,204***	***140 (11.6)***		
Officer	Ranch Hand	322	34 (10.6)	0.75 (0.48,1.17)	0.200
	Comparison	470	64 (13.6)		
Enlisted Flyer	Ranch Hand	139	19 (13.7)	1.74 (0.85,3.57)	0.129
	Comparison	180	15 (8.3)		
Enlisted Groundcrew	Ranch Hand	365	32 (8.8)	0.78 (0.50,1.22)	0.271
	Comparison	554	61 (11.0)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.87 (0.66,1.16)***	***0.354***
Officer	0.74 (0.47,1.16)	0.185
Enlisted Flyer	1.75 (0.85,3.61)	0.126
Enlisted Groundcrew	0.79 (0.50,1.24)	0.304

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	147	21 (14.3)	0.81 (0.63,1.05)	0.097
Medium	156	12 (7.7)		
High	155	13 (8.4)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
457	0.85 (0.63,1.14)	0.274

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

Table 18-5. Analysis of Pneumonia (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,168	134 (11.5)		
Background RH	361	38 (10.5)	0.93 (0.63,1.36)	0.708
Low RH	222	27 (12.2)	1.06 (0.68,1.65)	0.790
High RH	236	19 (8.1)	0.66 (0.40,1.09)	0.107
Low plus High RH	458	46 (10.0)	0.83 (0.58,1.19)	0.315

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,167		
Background RH	360	0.90 (0.61,1.33)	0.602
Low RH	221	0.98 (0.63,1.54)	0.929
High RH	236	0.74 (0.44,1.25)	0.265
Low plus High RH	457	0.85 (0.59,1.23)	0.386

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

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	269	29 (10.8)	0.91 (0.78,1.07)	0.236
Medium	270	33 (12.2)		
High	280	22 (7.9)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 18-5. Analysis of Pneumonia (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
Analysis Results for Log_2 (1987 Dioxin + 1)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
817	0.89 (0.73,1.08)	0.229

[a] Relative risk for a twofold increase in 1987 dioxin.

The unadjusted Model 2 analysis found a marginally significant relation between pneumonia and initial dioxin (Table 18-5(c): Est. RR=0.81, p=0.097). As initial dioxin increased, the prevalence of pneumonia decreased. The percentages of Ranch Hands with pneumonia in the low, medium, and high initial dioxin categories were 14.3, 7.7, and 8.4, respectively. After adjustment for covariates, the association was nonsignificant (Table 18-5(d): p=0.274).

18.2.2.2 Physical Examination Variable

18.2.2.2.1 Thorax and Lung Abnormalities

Results from the unadjusted and adjusted Models 1 through 3 analyses of thorax and lung abnormalities were nonsignificant (Table 18-6(a–f): p≥0.11 for each analysis).

Table 18-6. Analysis of Thorax and Lung Abnormalities

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***870***	***102 (11.7)***	***1.05 (0.80,1.38)***	***0.704***
	Comparison	***1,251***	***140 (11.2)***		
Officer	Ranch Hand	341	31 (9.1)	1.40 (0.84,2.33)	0.200
	Comparison	494	33 (6.7)		
Enlisted Flyer	Ranch Hand	151	29 (19.2)	1.07 (0.62,1.85)	0.810
	Comparison	187	34 (18.2)		
Enlisted Groundcrew	Ranch Hand	378	42 (11.1)	0.85 (0.57,1.27)	0.434
	Comparison	570	73 (12.8)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.97 (0.71,1.31)***	***0.821***
Officer	1.57 (0.90,2.71)	0.110
Enlisted Flyer	0.99 (0.53,1.85)	0.978
Enlisted Groundcrew	0.69 (0.44,1.09)	0.115

Table 18-6. Analysis of Thorax and Lung Abnormalities (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	22 (13.8)	1.06 (0.86,1.31)	0.573
Medium	162	23 (14.2)		
High	160	17 (10.6)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
481	1.14 (0.86,1.51)	0.366

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

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,213	137 (11.3)		
Background RH	381	39 (10.2)	0.82 (0.56,1.20)	0.304
Low RH	239	31 (13.0)	1.19 (0.79,1.82)	0.408
High RH	243	31 (12.8)	1.24 (0.82,1.89)	0.313
Low plus High RH	482	62 (12.9)	1.22 (0.88,1.68)	0.232

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 18-6. Analysis of Thorax and Lung Abnormalities (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,212		
Background RH	380	0.84 (0.55,1.28)	0.412
Low RH	238	1.01 (0.63,1.62)	0.953
High RH	243	1.01 (0.62,1.64)	0.977
Low plus High RH	481	1.01 (0.70,1.46)	0.955

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

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	288	32 (11.1)	1.03 (0.90,1.19)	0.653
Medium	287	31 (10.8)		
High	288	38 (13.2)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log_2 (1987 Dioxin + 1)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
861	1.20 (1.00,1.43)	0.054

[a] Relative risk for a twofold increase in 1987 dioxin.

The unadjusted Model 4 analysis was nonsignificant (Table 18-6(g): p=0.653). After adjusting for covariates, a marginally significant association between thorax and lung abnormalities and 1987 dioxin was revealed (Table 18-6(h): Adj. RR=1.20, p=0.054). As 1987 dioxin increased, the prevalence of thorax and lung abnormalities increased. The percentages of Ranch Hands with thorax and lung abnormalities in the low, medium, and high 1987 dioxin categories were 11.1, 10.8, and 13.2, respectively.

18.2.2.3 Laboratory Examination Variables

18.2.2.3.1 X-ray Interpretation

All unadjusted and adjusted analyses of the chest x-ray interpretation for Models 1 and 2 were nonsignificant (Table 18-7(a–d): p>0.15 for each analysis).

Table 18-7. Analysis of X-ray Interpretation

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***868***	***98 (11.3)***	***1.22 (0.92,1.62)***	***0.166***
	Comparison	***1,251***	***118 (9.4)***		
Officer	Ranch Hand	341	39 (11.4)	1.39 (0.88,2.20)	0.160
	Comparison	494	42 (8.5)		
Enlisted Flyer	Ranch Hand	151	16 (10.6)	1.19 (0.58,2.43)	0.643
	Comparison	187	17 (9.1)		
Enlisted Groundcrew	Ranch Hand	376	43 (11.4)	1.12 (0.74,1.70)	0.599
	Comparison	570	59 (10.4)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.23 (0.92,1.64)***	***0.158***
Officer	1.39 (0.87,2.20)	0.167
Enlisted Flyer	1.16 (0.56,2.39)	0.685
Enlisted Groundcrew	1.14 (0.75,1.73)	0.554

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	18 (11.3)	0.89 (0.70,1.15)	0.373
Medium	161	14 (8.7)		
High	159	11 (6.9)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 18-7. Analysis of X-ray Interpretation (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
479	0.95 (0.71,1.27)	0.730

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

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,213	116 (9.6)		
Background RH	381	53 (13.9)	1.56 (1.10,2.21)	0.013
Low RH	239	26 (10.9)	1.15 (0.73,1.80)	0.546
High RH	241	17 (7.1)	0.70 (0.41,1.20)	0.196
Low plus High RH	480	43 (9.0)	0.90 (0.62,1.31)	0.576

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,212		
Background RH	380	1.69 (1.18,2,43)	0.004
Low RH	238	1.11 (0.70,1.75)	0.657
High RH	241	0.66 (0.38,1.13)	0.127
Low plus High RH	479	0.85 (0.58,1.24)	0.406

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

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 18-7. Analysis of X-ray Interpretation (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	288	37 (12.8)	0.83 (0.71,0.97)	0.015
Medium	287	39 (13.6)		
High	286	20 (7.0)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log_2 (1987 Dioxin + 1)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
859	0.80 (0.67,0.96)	0.015

[a] Relative risk for a twofold increase in 1987 dioxin.

In the Model 3 unadjusted analysis of the x-ray interpretation, a significant difference was revealed between Ranch Hands in the background dioxin category and Comparisons (Table 18-7(e): Est. RR=1.56, p=0.013). The percentage of Ranch Hands in the background dioxin category with an x ray showing abnormalities was 13.9 percent, versus 9.6 percent of Comparisons. The same contrast was significant in the adjusted analysis (Table 18-7(f): Adj. RR=1.69, p=0.004). Unadjusted and adjusted contrasts of the low, high, and low plus high dioxin Ranch Hand categories with Comparisons were all nonsignificant (Table 18-7(e,f): p>0.12 for all analyses).

Both the unadjusted and adjusted Model 4 analyses revealed significant associations between the x-ray interpretation and 1987 dioxin (Table 18-7(g,h): Est. RR=0.83, p=0.015; Adj. RR=0.80, p=0.015, respectively). As the 1987 dioxin level increased, the prevalence of an x ray showing abnormalities decreased. The percentages of participants with an x-ray interpretation showing abnormalities in the low, medium, and high 1987 dioxin categories were 12.8, 13.6, and 7.0, respectively.

18.2.2.3.2 FVC (Percent of Predicted)

All unadjusted and adjusted analyses of the FVC were nonsignificant (Table 18-8: p>0.32 for all analyses).

Table 18-8. Analysis of FVC (Percent of Predicted)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Mean	Difference of Means (95% C.I.)	p-Value
All	***Ranch Hand***	***869***	***99.31***	***0.38 (–0.91,1.68)***	***0.564***
	Comparison	***1,249***	***98.93***		
Officer	Ranch Hand	341	100.48	0.33 (–1.73,2.39)	0.753
	Comparison	494	100.14		
Enlisted Flyer	Ranch Hand	151	99.64	0.75 (–2.45,3.96)	0.645
	Comparison	186	98.88		
Enlisted Groundcrew	Ranch Hand	377	98.14	0.24 (–1.71,2.18)	0.811
	Comparison	569	97.90		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean	Difference of Adj. Means (95% C.I.)	p-Value
All	***Ranch Hand***	***867***	***94.21***	***0.41 (–0.81,1.64)***	***0.506***
	Comparison	***1,248***	***93.79***		
Officer	Ranch Hand	340	94.31	0.56 (–1.39,2.50)	0.575
	Comparison	494	93.76		
Enlisted Flyer	Ranch Hand	151	95.01	0.56 (–2.47,3.59)	0.716
	Comparison	186	94.45		
Enlisted Groundcrew	Ranch Hand	376	93.36	0.23 (–1.61,2.07)	0.804
	Comparison	568	93.12		

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Mean	Adj. Mean[a]	R^2	Slope (Std. Error)	p-Value
Low	160	98.34	98.13	0.018	0.332 (0.491)	0.499
Medium	161	97.80	97.76			
High	160	99.44	99.68			

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean	R^2	Adj. Slope (Std. Error)	p-Value
Low	159	95.17	0.099	–0.303 (0.558)	0.588
Medium	161	94.32			
High	160	95.09			

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 18-8. Analysis of FVC (Percent of Predicted) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Mean	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)	p-Value
Comparison	1,211	99.09	99.14		
Background RH	381	100.18	99.33	0.19 (–1.50,1.88)	0.825
Low RH	238	98.07	98.34	–0.80 (–2.83,1.23)	0.439
High RH	243	98.97	99.79	0.66 (–1.36,2.67)	0.523
Low plus High RH	481	98.52	99.07	–0.06 (–1.61,1.48)	0.935

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adj. Mean	Difference of Adj. Mean vs. Comparisons (95% C.I.)	p-Value
Comparison	1,210	93.87		
Background RH	380	93.72	–0.15 (–1.80,1.50)	0.859
Low RH	237	94.29	0.42 (–1.54,2.39)	0.674
High RH	243	94.61	0.75 (–1.25,2.74)	0.465
Low plus High RH	480	94.45	0.59 (–0.92,2.09)	0.445

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	n	Mean	R^2	Slope (Std. Error)	p-Value
Low	288	100.86	0.001	–0.312 (0.338)	0.356
Medium	287	98.03			
High	287	98.86			

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 18-8. Analysis of FVC (Percent of Predicted) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean	R^2	Adjusted Slope (Std. Error)	p-Value
Low	287	94.50	0.111	0.377 (0.385)	0.329
Medium	286	94.05			
High	287	95.18			

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

18.2.2.3.3 FEV_1 (Percent of Predicted)

No significant relations were observed between group or dioxin and FEV_1 in any of the analyses (Table 18-9(a–h): p>0.13 for all analyses).

Table 18-9. Analysis of FEV_1 (Percent of Predicted)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Mean	Difference of Means (95% C.I.)	p-Value
All	***Ranch Hand***	***869***	***94.13***	***–0.15 (–1.66,1.37)***	***0.849***
	Comparison	***1,249***	***94.28***		
Officer	Ranch Hand	341	95.47	–0.18 (–2.58,2.23)	0.886
	Comparison	494	95.65		
Enlisted Flyer	Ranch Hand	151	91.09	–1.21 (–4.95,2.54)	0.527
	Comparison	186	92.30		
Enlisted Groundcrew	Ranch Hand	377	94.14	0.40 (–1.87,2.67)	0.729
	Comparison	569	93.74		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean	Difference of Adj. Means (95% C.I.)	p-Value
All	***Ranch Hand***	***867***	***90.23***	***0.17 (–1.24,1.57)***	***0.814***
	Comparison	***1,248***	***90.06***		
Officer	Ranch Hand	340	90.92	0.11 (–2.13,2.35)	0.925
	Comparison	494	90.81		
Enlisted Flyer	Ranch Hand	151	89.19	–1.27 (–4.75,2.21)	0.475
	Comparison	186	90.46		
Enlisted Groundcrew	Ranch Hand	376	90.07	0.75 (–1.36,2.87)	0.484
	Comparison	568	89.32		

Table 18-9. Analysis of FEV_1 (Percent of Predicted) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Mean	Adj. Mean[a]	R^2	Slope (Std. Error)	p-Value
Low	160	93.08	93.14	0.006	0.870 (0.581)	0.135
Medium	161	91.83	91.84			
High	160	97.27	97.20			

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean	R^2	Adj. Slope (Std. Error)	p-Value
Low	159	91.50	0.143	0.007 (0.637)	0.991
Medium	161	90.10			
High	160	93.52			

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Mean	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)	p-Value
Comparison	1,211	94.36	94.38		
Background RH	381	94.17	93.94	–0.44 (–2.46,1.57)	0.668
Low RH	238	92.82	92.89	–1.48 (–3.90,0.93)	0.229
High RH	243	95.27	95.50	1.12 (–1.28,3.53)	0.360
Low plus High RH	481	94.06	94.21	–0.17 (–2.01,1.67)	0.859

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 18-9. Analysis of FEV_1 (Percent of Predicted) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adj. Mean	Difference of Adj. Mean vs. Comparisons (95% C.I.)	p-Value
Comparison	1,210	90.03		
Background RH	380	89.32	–0.70 (–2.59,1.19)	0.469
Low RH	237	90.58	0.55 (–1.70,2.80)	0.632
High RH	243	91.19	1.16 (–1.13,3.45)	0.319
Low plus High RH	480	90.89	0.86 (–0.86,2.58)	0.328

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	n	Mean	R^2	Slope (Std. Error)	p-Value
Low	288	94.88	0.002	0.496 (0.402)	0.217
Medium	287	92.76			
High	287	94.69			

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean	R^2	Adjusted Slope (Std. Error)	p-Value
Low	287	89.98	0.161	0.652 (0.443)	0.142
Medium	286	89.99			
High	287	91.21			

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

18.2.2.3.4 Ratio of Observed FEV_1 to Observed FVC

Because of the distribution of the data, a natural logarithm transformation of 1.0 minus the ratio was used. Because of this transformation, a negative slope in Models 2 and 4 implies a positive association between dioxin and the ratio of observed FEV_1 to FVC. A negative association, which would be represented by a positive slope, is considered adverse for this variable.

Model 1 showed no significant difference between Ranch Hands and Comparisons in the mean ratio of observed FEV_1 to observed FVC (Table 18-10(a,b): $p>0.36$ for each contrast).

The Model 2 unadjusted analysis showed a significant positive association between the ratio of observed FEV_1 to observed FVC and initial dioxin (Table 18-10(c): slope=–0.026, p=0.023). The mean ratios in

the low, medium, and high initial dioxin categories were 0.759, 0.756, and 0.783, respectively. The adjusted analysis was nonsignificant (Table 18-10(d): p=0.360).

The Model 3 unadjusted and adjusted analyses showed no significant difference between any of the Ranch Hand dioxin categories and the Comparison group (Table 18-10(e,f): p>0.16 for each contrast).

The unadjusted Model 4 analysis found a significant positive association between 1987 dioxin and the ratio of observed FEV_1 to observed FVC (slope=–0.031, p<0.001). The mean ratios in the low, medium, and high 1987 dioxin categories were 0.753, 0.757, and 0.771, respectively. After adjusting for covariates, the results were nonsignificant (p=0.161).

Table 18-10. Analysis of the Ratio of Observed FEV_1 to Observed FVC

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***869***	***0.760***	***–0.003 --***	***0.366***
	Comparison	***1,249***	***0.763***		
Officer	Ranch Hand	341	0.756	–0.005 --	0.376
	Comparison	494	0.761		
Enlisted Flyer	Ranch Hand	151	0.741	–0.007 --	0.431
	Comparison	186	0.748		
Enlisted Groundcrew	Ranch Hand	377	0.772	0.001 --	0.843
	Comparison	569	0.771		

[a] Transformed from natural logarithm scale of 1.0 – ratio.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale of 1.0 – ratio.
[c] P-value is based on difference of means on natural logarithm scale of 1.0 – ratio.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***867***	***0.770***	***–0.001 --***	***0.701***
	Comparison	***1,248***	***0.771***		
Officer	Ranch Hand	340	0.771	–0.004 --	0.411
	Comparison	494	0.775		
Enlisted Flyer	Ranch Hand	151	0.764	–0.005 --	0.486
	Comparison	186	0.770		
Enlisted Groundcrew	Ranch Hand	376	0.774	0.003 --	0.532
	Comparison	568	0.771		

[a] Transformed from natural logarithm scale of 1.0 – ratio.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale of 1.0 – ratio.
[c] P-value is based on difference of means on natural logarithm scale of 1.0 – ratio.

Table 18-10. Analysis of the Ratio of Observed FEV_1 to Observed FVC (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Mean[a]	Adj. Mean[a,b]	R^2	Slope (Std. Error)[c]	p-Value
Low	160	0.757	0.759	0.053	–0.026 (0.011)	0.023
Medium	161	0.756	0.756			
High	160	0.785	0.783			

[a] Transformed from natural logarithm scale of 1.0 – ratio.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of (1.0 – ratio) versus log_2 (initial dioxin); because of this transformation, a negative slope implies a positive association between the ratio and log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	159	0.773	0.216	–0.011 (0.012)	0.360
Medium	161	0.770			
High	160	0.788			

[a] Transformed from natural logarithm scale of 1.0 – ratio.
[b] Slope and standard error based on natural logarithm of (1.0 – ratio) versus log_2 (initial dioxin); because of this transformation, a negative slope implies a positive association between the ratio and log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Mean[a]	Adj. Mean[a,b]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,211	0.763	0.763		
Background RH	381	0.753	0.757	–0.006 --	0.192
Low RH	238	0.759	0.757	–0.006 --	0.341
High RH	243	0.774	0.770	0.007 --	0.164
Low plus High RH	481	0.766	0.764	0.001 --	0.764

[a] Transformed from natural logarithm scale of 1.0 – ratio.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale of 1.0 – ratio.
[d] P-value is based on difference of means on natural logarithm scale of 1.0 – ratio.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 18-10. Analysis of the Ratio of Observed FEV_1 to Observed FVC (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	1,210	0.770		
Background RH	380	0.766	–0.004 --	0.376
Low RH	237	0.772	0.002 --	0.740
High RH	243	0.774	0.004 --	0.466
Low plus High RH	480	0.773	0.003 --	0.481

[a] Transformed from natural logarithm scale of 1.0 – ratio.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale of 1.0 – ratio.
[c] P-value is based on difference of means on natural logarithm scale of 1.0 – ratio.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	n	Mean[a]	R^2	Slope (Std. Error)[b]	p-Value
Low	288	0.753	0.018	–0.031 (0.008)	<0.001
Medium	287	0.757			
High	287	0.771			

[a] Transformed from natural logarithm scale of 1.0 – ratio.
[b] Slope and standard error based on natural logarithm of (1.0 – ratio) versus log_2 (1987 dioxin + 1); because of this transformation, a negative slope implies a positive association between the ratio and log_2 (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	287	0.767	0.218	–0.012 (0.008)	0.161
Medium	286	0.770			
High	287	0.773			

[a] Transformed from natural logarithm scale of 1.0 – ratio.
[b] Slope and standard error based on natural logarithm of (1.0 – ratio) versus log_2 (1987 dioxin + 1); because of this transformation, a negative slope implies a positive association between the ratio and log_2 (1987 dioxin+1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

18.2.2.3.5 Loss of Vital Capacity

No significant relations were observed between group or dioxin and the loss of vital capacity in Models 1 through 3 (Table 18-11(a–f): p>0.11 for each analysis).

Table 18-11. Analysis of Loss of Vital Capacity

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

Occupational Category	Group	n	Number (%) None	Mild	Moderate or Severe	Mild vs. None Est. Relative Risk (95% C.I.)	p-Value	Moderate or Severe vs. None Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***869***	***792 (91.1)***	***67 (7.7)***	***10 (1.2)***	***0.98 (0.71,1.35)***	***0.885***	***0.71 (0.33,1.53)***	***0.388***
	Comparison	***1,249***	***1,131 (90.6)***	***98 (7.8)***	***20 (1.6)***				
Officer	Ranch Hand	341	312 (91.5)	24 (7.0)	5 (1.5)	1.10 (0.63,1.90)	0.737	1.46 (0.42,5.10)	0.549
	Comparison	494	457 (92.5)	32 (6.5)	5 (1.0)				
Enlisted Flyer	Ranch Hand	151	139 (92.1)	11 (7.3)	1 (0.7)	0.72 (0.33,1.58)	0.413	0.29 (0.03,2.67)	0.277
	Comparison	186	164 (88.2)	18 (9.7)	4 (2.2)				
Enlisted Groundcrew	Ranch Hand	377	341 (90.5)	32 (8.5)	4 (1.1)	1.00 (0.62,1.59)	0.990	0.54 (0.17,1.72)	0.300
	Comparison	569	510 (89.6)	48 (8.4)	11 (1.9)				

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

Occupational Category	Mild vs. None Adj. Relative Risk (95% C.I.)	p-Value	Moderate or Severe vs. None Adj. Relative Risk (95% C.I.)	p-Value
All	***0.96 (0.69,1.35)***	***0.832***	***0.67 (0.31,1.47)***	***0.324***
Officer	1.09 (0.62,1.90)	0.768	1.42 (0.40,5.00)	0.586
Enlisted Flyer	0.68 (0.31,1.52)	0.349	0.25 (0.03,2.30)	0.220
Enlisted Groundcrew	1.00 (0.61,1.63)	0.999	0.52 (0.16,1.70)	0.279

Table 18-11. Analysis of Loss of Vital Capacity (Continued)

(c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED

Initial Dioxin Category	Initial Dioxin Category Summary Statistics Number (%)				Analysis Results for Log_2 (Initial Dioxin)[a] Mild vs. None		Moderate or Severe vs. None	
	n	None	Mild	Moderate or Severe	Est. Relative Risk (95% C.I.)[b]	p-Value	Est. Relative Risk (95% C.I.)[b]	p-Value
Low	160	146 (91.3)	12 (7.5)	2 (1.3)	0.88 (0.67,1.15)	0.345	0.73 (0.31,1.76)	0.489
Medium	161	145 (90.1)	15 (9.3)	1 (0.6)				
High	160	151 (94.4)	8 (5.0)	1 (0.6)				

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin) Mild vs. None		Moderate or Severe vs. None	
n	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value
480	0.91 (0.66,1.24)	0.539	1.02 (0.35,2.99)	0.973

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

Note: Results not adjusted for race, current cigarette smoking, and industrial chemicals exposure because of the sparse number of moderate or severe measurements.

Table 18-11. Analysis of Loss of Vital Capacity (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Number (%) None	Mild	Moderate or Severe	Mild vs. None Est. Relative Risk (95% C.I.)[ab]	p-Value	Moderate or Severe vs. None Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,211	1,096 (90.5)	97 (8.0)	18 (1.5)				
Background RH	381	344 (90.3)	31 (8.1)	6 (1.6)	1.18 (0.77,1.81)	0.456	1.27 (0.50,3.27)	0.616
Low RH	238	218 (91.6)	18 (7.6)	2 (0.8)	0.89 (0.52,1.51)	0.663	0.52 (0.12,2.28)	0.387
High RH	243	224 (92.2)	17 (7.0)	2 (0.8)	0.75 (0.43,1.29)	0.295	0.46 (0.10,2.00)	0.297
Low plus High RH	481	442 (91.9)	35 (7.3)	4 (0.8)	0.81 (0.54,1.23)	0.325	0.49 (0.16,1.46)	0.199

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Mild vs. None Adj. Relative Risk (95% C.I.)[a]	p-Value	Moderate or Severe vs. None Adj. Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,210				
Background RH	380	1.28 (0.82,1.99)	0.284	1.44 (0.54,3.81)	0.468
Low RH	237	0.71 (0.41,1.24)	0.235	0.34 (0.07,1.57)	0.165
High RH	243	0.75 (0.43,1.32)	0.325	0.47 (0.10,2.17)	0.337
Low plus High RH	480	0.73 (0.48,1.12)	0.151	0.40 (0.13,1.25)	0.115

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

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 18-11. Analysis of Loss of Vital Capacity (Continued)

(g) MODEL 4: RANCH HANDS — 1987 DIOXIN — UNADJUSTED

1987 Dioxin Category	1987 Dioxin Category Summary Statistics Number (%)				Analysis Results for Log_2 (1987 Dioxin + 1) Mild vs. None		Moderate or Severe vs. None	
	n	None	Mild	Moderate or Severe	Est. Relative Risk (95% C.I.)[a]	p-Value	Est. Relative Risk (95% C.I.)[a]	p-Value
Low	288	265 (92.0)	19 (6.6)	4 (1.4)	0.94 (0.79,1.12)	0.480	0.83 (0.53,1.31)	0.430
Medium	287	254 (88.5)	29 (10.1)	4 (1.4)				
High	287	267 (93.0)	18 (6.3)	2 (0.7)				

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS — 1987 DIOXIN — ADJUSTED

n	Analysis Results for Log_2 (1987 Dioxin + 1) Mild vs. None		Moderate or Severe vs. None	
	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value
860	0.80 (0.65,1.00)	0.046	0.87 (0.50,1.50)	0.605

[a] Relative risk for a twofold increase in 1987 dioxin.

The Model 4 unadjusted analysis of loss of vital capacity was nonsignificant (Table 18-11(g): p>0.43 for each contrast). After adjusting for covariates, a significant association between a mild loss of vital capacity and 1987 dioxin was revealed (Table 18-11(h): Adj. RR=0.80, p=0.046). The prevalence of a mild loss of vital capacity decreased as 1987 dioxin increased, after accounting for covariate effects. The percentages of participants with a mild loss of vital capacity in the low, medium, and high 1987 dioxin categories were 6.6, 10.1, and 6.3, respectively.

18.2.2.3.6 Obstructive Abnormality

The Model 1 unadjusted and adjusted analyses showed no group difference for obstructive abnormalities when combining all occupations (p>0.23 for each analysis). After stratifying by occupation, both the unadjusted and adjusted analyses revealed a significant difference between Ranch Hand and Comparison officers in the percentage of mild obstructive abnormalities (Table 18-12(a,b): Est. RR=1.38, p=0.034; Adj. RR=1.38, p=0.041, respectively). The percentage of Ranch Hand officers with mild obstructive abnormalities was higher than the percentage of Comparison officers with mild obstructive abnormalities (36.4% vs. 29.8%). No significant differences were noted for any occupation for the contrast of moderate versus no obstructive abnormalities (p>0.36 for all analyses) or for the contrast of severe versus no obstructive abnormalities (p≥0.18 for all analyses).

Table 18-12. Analysis of Obstructive Abnormality

(a1) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Number (%) None	Mild	Moderate	Severe
All	***Ranch Hand***	***869***	***528 (60.8)***	***276 (31.8)***	***51 (5.9)***	***14 (1.6)***
	Comparison	***1,249***	***790 (63.3)***	***368 (29.5)***	***75 (6.0)***	***16 (1.3)***
Officer	Ranch Hand	341	193 (56.6)	124 (36.4)	19 (5.6)	5 (1.5)
	Comparison	494	316 (64.0)	147 (29.8)	26 (5.3)	5 (1.0)
Enlisted Flyer	Ranch Hand	151	82 (54.3)	49 (32.5)	14 (9.3)	6 (4.0)
	Comparison	186	97 (52.2)	72 (38.7)	12 (6.5)	5 (2.7)
Enlisted Groundcrew	Ranch Hand	377	253 (67.1)	103 (27.3)	18 (4.8)	3 (0.8)
	Comparison	569	377 (66.3)	149 (26.2)	37 (6.5)	6 (1.1)

(a2) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Mild vs. None Est. Relative Risk (95% C.I.)	p-Value	Moderate vs. None Est. Relative Risk (95% C.I.)	p-Value	Severe vs. None Est. Relative Risk (95% C.I.)	p-Value
All	***1.12 (0.93,1.36)***	***0.237***	***1.02 (0.70,1.48)***	***0.928***	***1.31 (0.63,2.70)***	***0.467***
Officer	1.38 (1.02,1.86)	0.034	1.20 (0.64,2.22)	0.569	1.64 (0.47,5.73)	0.440
Enlisted Flyer	0.81 (0.50,1.28)	0.363	1.38 (0.60,3.15)	0.444	1.42 (0.42,4.82)	0.574
Enlisted Groundcrew	1.03 (0.77,1.39)	0.845	0.72 (0.40,1.30)	0.281	0.75 (0.18,3.00)	0.679

Table 18-12. Analysis of Obstructive Abnormality (Continued)

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

Occupational Category	Mild vs. None		Moderate vs. None		Severe vs. None	
	Est. Relative Risk (95% C.I.)	p-Value	Est. Relative Risk (95% C.I.)	p-Value	Est. Relative Risk (95% C.I.)	p-Value
All	*1.08 (0.88,1.32)*	*0.449*	*0.97 (0.66,1.44)*	*0.887*	*1.22 (0.57,2.59)*	*0.605*
Officer	1.38 (1.01,1.89)	0.041	1.21 (0.63,2.32)	0.560	1.81 (0.50,6.57)	0.366
Enlisted Flyer	0.79 (0.48,1.29)	0.345	1.36 (0.57,3.23)	0.492	1.27 (0.35,4.58)	0.715
Enlisted Groundcrew	0.96 (0.70,1.32)	0.821	0.65 (0.35,1.22)	0.180	0.69 (0.16,2.87)	0.607

(c1) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED

Initial Dioxin Category	n	Initial Dioxin Category Summary Statistics Number (%)			
		None	Mild	Moderate	Severe
Low	160	93 (58.1)	52 (32.5)	11 (6.9)	4 (2.5)
Medium	161	94 (58.4)	56 (34.8)	8 (5.0)	3 (1.9)
High	160	121 (75.6)	32 (20.0)	7 (4.4)	0 (0.0)

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(c2) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED

Analysis Results for Log_2 (Initial Dioxin)[a]					
Mild vs. None		Moderate vs. None		Severe vs. None	
Est. Relative Risk (95% C.I.)[b]	p-Value	Est. Relative Risk (95% C.I.)[b]	p-Value	Est. Relative Risk (95% C.I.)[b]	p-Value
0.79 (0.67,0.93)	0.005	0.87 (0.63,1.20)	0.393	0.53 (0.24,1.21)	0.131

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

(d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)						
	Mild vs. None		Moderate vs. None		Severe vs. None	
n	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value
480	0.86 (0.72,1.02)	0.082	0.98 (0.67,1.42)	0.902	0.63 (0.28,1.44)	0.276

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

Note: Results not adjusted for race, occupation, and industrial chemicals exposure because of the sparse number of severe obstructive abnormalities.

Table 18-12. Analysis of Obstructive Abnormality (Continued)

(e1) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Number (%)			
		None	Mild	Moderate	Severe
Comparison	1,211	767 (63.3)	356 (29.4)	73 (6.0)	15 (1.2)
Background RH	381	218 (57.2)	131 (34.4)	25 (6.6)	7 (1.8)
Low RH	238	134 (56.3)	85 (35.7)	13 (5.5)	6 (2.5)
High RH	243	174 (71.6)	55 (22.6)	13 (5.3)	1 (0.4)
Low plus High RH	481	308 (64.0)	140 (29.1)	26 (5.4)	7 (1.5)

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(e2) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	Mild vs. None		Moderate vs. None		Severe vs. None	
	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)	p-Value
Comparison						
Background RH	1.26 (0.98,1.62)	0.071	1.14 (0.70,1.85)	0.595	1.42 (0.57,3.55)	0.453
Low RH	1.38 (1.02,1.86)	0.037	1.03 (0.56,1.92)	0.915	2.37 (0.90,6.24)	0.080
High RH	0.70 (0.50,0.97)	0.031	0.82 (0.44,1.52)	0.533	0.33 (0.04,2.56)	0.291
Low plus High RH	0.98 (0.77,1.24)	0.838	0.92 (0.58,1.47)	0.731	0.88 (0.27,2.90)	0.835

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

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 18-12. Analysis of Obstructive Abnormality (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Mild vs. None		Moderate vs. None		Severe vs. None	
		Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)	p-Value
Comparison	1,210						
Background RH	380	1.21 (0.93,1.58)	0.164	1.22 (0.73,2.04)	0.440	1.64 (0.62,4.34)	0.323
Low RH	237	1.17 (0.85,1.60)	0.338	0.78 (0.40,1.52)	0.459	1.75 (0.62,4.89)	0.289
High RH	243	0.74 (0.52,1.06)	0.096	0.76 (0.39,1.49)	0.429	0.28 (0.03,2.26)	0.232
Low plus High RH	480	0.93 (0.72,1.20)	0.556	0.77 (0.46,1.28)	0.311	0.69 (0.20,2.37)	0.557

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

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g1) MODEL 4: RANCH HANDS — 1987 DIOXIN — UNADJUSTED

1987 Dioxin Category	n	1987 Dioxin Category Summary Statistics Number (%)			
		None	Mild	Moderate	Severe
Low	288	168 (58.3)	97 (33.7)	17 (5.9)	6 (2.1)
Medium	287	161 (56.1)	101 (35.2)	20 (7.0)	5 (1.7)
High	287	197 (68.6)	73 (25.4)	14 (4.9)	3 (1.0)

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(g2) MODEL 4: RANCH HANDS — 1987 DIOXIN — UNADJUSTED

Analysis Results for Log_2 (1987 Dioxin+1)					
Mild vs. None		Moderate vs. None		Severe vs. None	
Est. Relative Risk (95% C.I.)[a]	p-Value	Est. Relative Risk (95% C.I.)[a]	p-Value	Est. Relative Risk (95% C.I.)[a]	p-Value
0.83 (0.75,0.92)	<0.001	0.86 (0.70,1.05)	0.145	0.70 (0.47,1.04)	0.078

[a] Relative risk for a twofold increase in 1987 dioxin.

(h) MODEL 4: RANCH HANDS — 1987 DIOXIN — ADJUSTED

n	Analysis Results for Log_2 (1987 Dioxin+1)					
	Mild vs. None		Moderate vs. None		Severe vs. None	
	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value
860	0.91 (0.80,1.04)	0.177	0.87 (0.67,1.12)	0.269	0.78 (0.50,1.22)	0.272

[a] Relative risk for a twofold increase in 1987 dioxin.

In each of the unadjusted and adjusted Model 2 analyses, a significant or marginally significant decreased risk of mild obstructive abnormalities for increasing initial dioxin levels was revealed (Table 18-12(c,d): Est. RR=0.79, p=0.005; Adj. RR=0.86, p=0.082, respectively). The percentages of mild obstructive abnormalities in the low, medium, and high initial dioxin categories were 32.5, 34.8, and 20.0, respectively. No significant difference was seen in the moderate versus no obstructive abnormalities contrast or the severe versus no obstructive abnormalities contrast (p>0.13 for all analyses).

The unadjusted Model 3 analysis revealed three significant or marginally significant differences between Ranch Hands and Comparisons in the percentage of participants with mild abnormalities. Ranch Hands in the background dioxin category had a higher percentage of mild obstructive abnormalities than did Comparisons (Table 18-12(e): 34.4% vs. 29.4%, Est. RR=1.26, p=0.071), as did Ranch Hands in the low dioxin category (Table 18-12(e): 35.7% vs. 29.4%, Est. RR=1.38, p=0.037). Ranch Hands in the high dioxin category had a lower percentage of mild obstructive abnormalities than did Comparisons (Table 18-12(e): 22.6% vs. 29.4%, Est. RR=0.70, p=0.031). A marginally significant greater percentage of Ranch Hands in the low dioxin category had a severe obstructive abnormality than did Comparisons (Table 18-12(e): 2.5% vs. 1.2%, Est. RR=2.37, p=0.080). After adjusting for covariates, only the difference in mild obstructive abnormalities between Ranch Hands in the high dioxin category and Comparisons remained marginally significant (Table 18-12(f): Adj. RR=0.74, p=0.096). No significant difference was detected in the moderate versus no obstructive abnormalities contrast (p>0.31 for all analyses).

The unadjusted Model 4 analysis showed a significant or marginally significant decreased risk of mild and severe obstructive abnormalities with increasing 1987 dioxin levels (Table 18-12(g): Est. RR=0.83, p<0.001, for the mild versus no obstructive abnormalities contrast; Est. RR=0.70, p=0.078, for the severe versus no obstructive abnormalities contrast). The percentages of mild obstructive abnormalities in the low, medium, and high 1987 dioxin categories were 33.7, 35.2, and 25.4, respectively. The percentages of severe obstructive abnormalities in the low, medium, and high 1987 dioxin categories were 2.1, 1.7, and 1.0, respectively. After adjusting for covariates, both contrasts became nonsignificant (p>0.17 for each contrast). No significant difference was observed in the moderate versus no obstructive abnormalities contrast (p>0.14 for all analyses).

18.2.3 Longitudinal Analysis

Longitudinal analyses were conducted on the ratio of observed FEV_1 to observed FVC to examine whether changes across time differed with respect to group membership (Model 1), initial dioxin (Model 2), and categorized dioxin (Model 3). Model 4 was not examined in longitudinal analyses because 1987 dioxin, the measure of exposure in these models, changes over time and was not available for all participants for 1982 or 1997. Summary statistics are provided for reference purposes for the 1987 and 1992 examinations. This measurement was not collected for the 1985 follow-up examination.

The longitudinal analysis for the ratio of observed FEV_1 to observed FVC examined the paired difference between the measurements from 1982 and 1997. These paired differences measured the change in the ratio over time. A logarithmic transformation was applied to 1.0 minus this ratio prior to calculating the paired differences for analytic purposes. Each of the three models used in the longitudinal analysis was adjusted for age and the ratio as measured in 1982 (see Chapter 7, Statistical Methods). The analyses of Models 2 and 3 also were adjusted for body fat at the time of the blood measurement of dioxin.

18.2.3.1 Laboratory Examination Variable

18.2.3.1.1 Ratio of Observed FEV_1 to Observed FVC

The Model 1 analysis of the change in the mean ratio of observed FEV_1 to observed FVC revealed a significant difference between Ranch Hands and Comparisons when combining all occupations (Table 18-13(a): difference=–0.005, p=0.048). The Ranch Hand group had a decrease in the mean ratio of 0.057 from 1982 to 1997, whereas the Comparison group showed a decrease of 0.052. Stratifying by occupation showed a marginally significant group difference among the enlisted flyers (difference=–0.014, p=0.072). The Ranch Hand enlisted flyers showed a decrease in the mean ratio of 0.072 between 1982 and 1997, compared to a decrease of 0.058 for the Comparison enlisted flyers.

The Model 2 analysis did not reveal a significant association between the change in the ratio of observed FEV_1 to observed FVC and initial dioxin (p=0.726).

The Model 3 analysis of the change in the ratio of observed FEV_1 to observed FVC revealed a marginally significant difference between the low and high dioxin categories combined and Comparisons (Table 18-13(c): difference=–0.004, p=0.052). The low and high dioxin categories combined had a decrease in the mean ratio of 0.056 between 1982 and 1997, versus a decrease of the mean ratio of 0.052 for the Comparison category.

Table 18-13. Longitudinal Analysis of the Ratio of Observed FEV_1 to Observed FVC

(a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Mean[a]/(n) Examination 1982	1987	1992	1997	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
All	***Ranch Hand***	***0.817***	***0.818***	***0.764***	***0.760***	***–0.057***	***–0.005***	***0.048***
		(817)	***(790)***	***(795)***	***(817)***			
	Comparison	***0.816***	***0.818***	***0.765***	***0.764***	***–0.052***		
		(973)	***(948)***	***(953)***	***(973)***			
Officer	Ranch Hand	0.810	0.812	0.755	0.755	–0.055	–0.001	0.763
		(311)	(304)	(306)	(311)			
	Comparison	0.813	0.812	0.758	0.760	–0.054		
		(380)	(368)	(375)	(380)			
Enlisted Flyer	Ranch Hand	0.812	0.802	0.746	0.740	–0.072	–0.014	0.072
		(148)	(142)	(145)	(148)			
	Comparison	0.806	0.807	0.756	0.748	–0.058		
		(143)	(141)	(141)	(143)			
Enlisted Groundcrew	Ranch Hand	0.826	0.829	0.779	0.772	–0.054	–0.006	0.152
		(358)	(344)	(344)	(358)			
	Comparison	0.821	0.826	0.775	0.773	–0.048		
		(450)	(439)	(437)	(450)			

[a] Transformed from natural logarithm scale of (1 – ratio of observed FEV_1 to observed FVC).
[b] Difference between 1997 and 1982 examination means after transformation to original scale.
[c] P-value is based on analysis of natural logarithm of (1 – ratio of observed FEV_1 to observed FVC); results adjusted for natural logarithm of (1 – ratio of observed FEV_1 to observed FVC) in 1982 and age in 1997.

Note: Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations.

Table 18-13. Longitudinal Analysis of the Ratio of Observed FEV_1 to Observed FVC (Continued)

(b) MODEL 2: RANCH HANDS – INITIAL DIOXIN

Initial Dioxin Category Summary Statistics					Analysis Results for Log_2 (Initial Dioxin)[b]	
	Mean[a]/(n) Examination					
Initial Dioxin	1982	1987	1992	1997	Adjusted Slope (Std. Error)	p-Value
Low	0.816 (154)	0.815 (153)	0.759 (149)	0.757 (154)	0.003 (0.009)	0.726
Medium	0.816 (158)	0.813 (155)	0.763 (155)	0.755 (158)		
High	0.835 (153)	0.842 (148)	0.792 (150)	0.785 (153)		

[a] Transformed from natural logarithm scale of (1 – ratio of observed FEV_1 to observed FVC).
[b] Results based on difference between natural logarithm of (1 – 1997 ratio of observed FEV_1 to observed FVC) and natural logarithm of (1 – 1982 ratio of observed FEV_1 to observed FVC) versus log_2 (initial dioxin); results adjusted for percent body fat at the date of the blood measurement of dioxin, natural logarithm of (1 – 1982 ratio of observed FEV_1 to observed FVC), and age in 1997; because of the transformation used, a negative slope implies a positive association between the ratio and log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations.

Table 18-13. Longitudinal Analysis of the Ratio of Observed FEV_1 to Observed FVC (Continued)

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

Dioxin Category	Mean[a]/(n) Examination 1982	1987	1992	1997	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
Comparison	0.816 (945)	0.818 (922)	0.765 (926)	0.763 (945)	–0.052		
Background RH	0.810 (346)	0.809 (329)	0.754 (336)	0.752 (346)	–0.059	–0.007	0.486
Low RH	0.819 (229)	0.816 (226)	0.763 (222)	0.758 (229)	–0.061	–0.009	0.109
High RH	0.826 (236)	0.831 (230)	0.780 (232)	0.774 (236)	–0.052	0.000	0.161
Low plus High RH	0.822 (465)	0.823 (456)	0.772 (454)	0.766 (465)	–0.056	–0.004	0.052

[a] Transformed from natural logarithm scale of (1 – ratio of observed FEV_1 to observed FVC).
[b] Difference between 1997 and 1982 examination means after transformation to original scale.
[c] P-value is based on analysis of natural logarithm of (1 – 1997 ratio of observed FEV_1 to observed FVC); results adjusted for percent body fat at the date of the blood measurement of dioxin, natural logarithm of (1 – 1982 ratio of observed FEV_1 to observed FVC), and age in 1997.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations.

18.3 DISCUSSION

Although the presence of pulmonary disease is often apparent based on the participant's history and physical examination, confirmation of the diagnosis and quantification of the degree of pulmonary impairment usually requires collection of the laboratory data analyzed in the current chapter. In addition, because the lung is often involved secondarily in numerous infectious, inflammatory, and neoplastic disorders, the assessment of lung disease should include the type of comprehensive multi-system review conducted in these examinations and reported in other chapters.

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. Thus, all episodes of pulmonary disease were verified by medical records and only documented occurrences were analyzed.

The physical examination variables studied can provide valuable clues to the presence of pulmonary disease; however, in lacking specificity, these data have limitations 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 participant's 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, although 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. Furthermore, 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 more than 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 section, FEV_1 and FVC, are designed to measure lung volume. Height is the principal determinant of static lung volume, as measured by the vital capacity, whereas dynamic flow measurements depend more on physical strength. Accordingly, all indices require correction for height and age. Race-specific variations in spirometric indices, reflective of differences in body habitus, have been well documented and recently summarized (44). Blacks, for example, have FVC and FEV_1 values that average 12 to 15 percent less than Caucasian Americans of comparable height.

In clinical practice, it is convenient to divide respiratory disease into two broad categories: "restrictive" and "obstructive." "Restrictive" disease is characterized by reduced vital capacity as seen in interstitial fibrosis or reduced lung volume consequent to surgical resection. In "obstructive" disease, whether associated with asthma or with cigarette use, the flow-dependent index, FEV_1, is abnormally prolonged.

The analyses of the dependent variable-covariate associations confirm observations that are well established in clinical practice. Lifetime cigarette smoking history was a consistent and highly significant risk factor for the development of bronchitis and, in a dose-response pattern, associated with abnormalities in all of the laboratory indices examined. At each of the AFHS examinations, all nicotine-dependent participants were counseled on smoking cessation. Of interest, over the 15-year course of these examinations, the percentage of nicotine-dependent participants has fallen from 42 percent in 1982 to just under 20 percent in 1997. With advancing age, an increase in respiratory disease was confirmed by history and on physical examination, as was a progressive age-related reduction in the dynamic index of pulmonary function, the FEV_1 and, to a lesser extent, the vital capacity. Because spirometric indices were not corrected for race in this follow-up examination, Blacks were found to have reductions of approximately 10 percent in FVC, FEV_1, and the ratio of observed FEV_1 to observed FVC. Finally, the analyses of body fat confirmed the well recognized reduction in vital capacity and its derived indices associated with obesity.

The analyses of historical variables yielded inconsistent results. Ranch Hands were more likely than Comparisons to have had bronchitis and asthma, whereas the prevalence of pneumonia was greater in Comparisons. In none of the contrasts were the differences significant. Similar to the 1992 examinations, but of unknown cause, Ranch Hand enlisted flyers appeared to be at selective risk relative to Comparisons with respect to the history of bronchitis (27.8% vs. 19.1%). Within this occupational stratum, there are no longer any significant group differences on physical examination or by chest x ray. Further, in none of these analyses was there any relation with the body burden of dioxin.

A significantly increased risk of mild obstructive abnormality was found in Ranch Hand officers. This finding was not present in 1992. The meaning of the finding is uncertain because the risk was not significantly increased in Ranch Hand enlisted groundcrew—the subgroup with the highest dioxin levels. The relation between mild obstructive abnormality in Ranch Hand officers and indicators of herbicide exposure, such as job (pilot, navigator, nonflyer), the number of missions flown, the percentage of missions that were herbicide missions, and reported drinking of herbicide (yes, no) will be summarized in a separate report.

In none of the static and dynamic spirometric indices were any significant group differences defined, nor was there evidence for any adverse effect associated with prior dioxin exposure.

Longitudinal analyses of the ratio of observed FEV_1 to observed FVC confirms the gradual decline in this index associated with age in both the Ranch Hand and Comparison cohorts. Similar to the 1992 results, in the enlisted flyer category, Ranch Hands had a slightly greater reduction in the ratio than did Comparisons, but the difference (–0.072 vs. –0.058) is not physiologically meaningful.

In conclusion, apart from the marginally significant increase in bronchitis in enlisted flyers noted above, the historical, physical examination, and laboratory data analyzed in the current section revealed no evidence for an increase in pulmonary disease in the Ranch Hand cohort relative to Comparisons. The results also confirmed numerous dependent variable-covariate associations documented in previous AFHS examinations.

18.4 SUMMARY

18.4.1 Model 1: Group Analysis

A marginally significant difference in bronchitis was observed between Ranch Hand and Comparison enlisted flyers in unadjusted and adjusted analyses. Ranch Hand enlisted flyers had a higher prevalence of bronchitis than did Comparison enlisted flyers. Ranch Hand officers had a significantly higher prevalence of mild obstructive abnormality than did Comparison officers in both unadjusted and adjusted analyses. All other tests of the association of group and the pulmonary variables were nonsignificant. The results of the group analyses are summarized in Table 18-14.

Table 18-14. Summary of Group Analysis (Model 1) for Pulmonary Variables (Ranch Hands vs. Comparisons)

Variable	UNADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Medical Records				
Asthma (D)	NS	NS	ns	NS
Bronchitis (D)	NS	NS	NS*	NS
Pneumonia (D)	ns	ns	NS	ns
Physical Examination				
Thorax and Lung Abnormalities (D)	NS	NS	NS	ns
Laboratory				
X-ray Interpretation (D)	NS	NS	NS	NS
FVC (C)	NS	NS	NS	NS
FEV_1 (C)	ns	ns	ns	NS
Ratio of Observed FEV_1 to Observed FVC (C)[a]	ns	ns	ns	NS
Loss of Vital Capacity (D):				
Mild vs. None	ns	NS	ns	NS
Moderate or Severe vs. None	ns	NS	ns	ns
Obstructive Abnormality (D):				
Mild vs. None	NS	+0.034	ns	NS
Moderate vs. None	NS	NS	NS	ns
Severe vs. None	NS	NS	NS	ns

Note: NS or ns: Not significant ($p>0.10$).
NS*: Marginally significant ($0.05<p\leq0.10$).
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥ 1.00 for discrete analysis.
[a]Difference of means negative considered adverse for this variable.

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

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or differences of means nonnegative for continuous analysis. A lowercase "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

Variable	ADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Medical Records				
Asthma (D)	NS	NS	ns	NS
Bronchitis (D)	NS	NS	NS*	NS
Pneumonia (D)	ns	ns	NS	ns
Physical Examination				
Thorax and Lung Abnormalities (D)	ns	NS	ns	ns
Laboratory				
X-ray Interpretation (D)	NS	NS	NS	NS
FVC (C)	NS	NS	NS	NS
FEV_1 (C)	NS	NS	ns	NS
Ratio of Observed FEV_1 to Observed FVC (C)[a]	ns	ns	ns	NS

Table 18-14. Summary of Group Analysis (Model 1) for Pulmonary Variables (Ranch Hands vs. Comparisons) (Continued)

Variable	ADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Loss of Vital Capacity (D):				
Mild vs. None	ns	NS	ns	NS
Moderate or Severe vs. None	ns	NS	ns	ns
Obstructive Abnormality (D):				
Mild vs. None	NS	+0.041	ns	ns
Moderate vs. None	ns	NS	NS	ns
Severe vs. None	NS	NS	NS	ns

Note: NS or ns: Not significant ($p>0.10$).
NS*: Marginally significant ($0.05<p\leq0.10$).
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥ 1.00 for discrete analysis.
[a]Difference of means negative considered adverse for this variable.

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

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or differences of means nonnegative for continuous analysis. A lowercase "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

18.4.2 Model 2: Initial Dioxin Analysis

The results of the tests of association between the pulmonary variables and initial dioxin are summarized in Table 18-15. For the unadjusted analysis of pneumonia, a significant decrease in pneumonia was found as initial dioxin increased. After covariate adjustment, the association was no longer significant. The ratio of the observed FEV_1 to the observed FVC significantly increased as initial dioxin increased, but this association was also nonsignificant after adjustment for covariates. The prevalence of a mild obstructive abnormality significantly decreased as initial dioxin increased in the unadjusted analysis. This association was marginally significant after adjustment for covariates. All other tests of association with initial dioxin were nonsignificant.

Table 18-15. Summary of Initial Dioxin Analysis (Model 2) for Pulmonary Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Medical Records		
Asthma (D)	NS	NS
Bronchitis (D)	NS	NS
Pneumonia (D)	ns*	ns
Physical Examination		
Thorax and Lung Abnormalities	NS	NS
Laboratory		
X-ray Interpretation (D)	ns	ns
FVC (C)	NS	ns
FEV_1 (C)	NS	NS

Table 18-15. Summary of Initial Dioxin Analyses (Model 2) for Pulmonary Variables (Ranch Hands Only) (Continued)

Variable	Unadjusted	Adjusted
Ratio of Observed FEV_1 to Observed FVC (C)[a]	–0.023	ns
Loss of Vital Capacity (D):		
Mild vs. None	ns	ns
Moderate or Severe vs. None	ns	NS
Obstructive Abnormality (D):		
Mild vs. None	–0.005	ns*
Moderate vs. None	ns	ns
Severe vs. None	ns	ns

Note: NS or ns: Not significant ($p>0.10$).
ns*: Marginally significant ($0.05<p\leq0.10$).
C: Continuous analysis.
D: Discrete analysis.
–: Relative risk <1.00 for discrete analysis; slope negative for continuous analysis.
[a] Positive slope considered adverse for this variable; a negative slope implies an increase in the ratio because of the data transformation used.

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

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

18.4.3 Model 3: Categorized Dioxin Analysis

The results of the categorized dioxin analysis of the pulmonary variables are summarized in Table 18-16. Ranch Hands in the background dioxin category showed a marginally significant increase in bronchitis relative to Comparisons in the adjusted analysis. For the unadjusted and adjusted analyses of the x-ray interpretation, the background Ranch Hands exhibited a significantly higher percentage of abnormalities on the x ray than Comparisons. Unadjusted analyses revealed a higher prevalence of a mild obstructive abnormality for Ranch Hands in the background and low dioxin categories than for Comparisons. These differences between Ranch Hands and Comparisons became nonsignificant after adjustment for covariates. Ranch Hands in the high dioxin category had a significantly smaller prevalence of a mild obstructive abnormality than did Comparisons without adjustment for covariates. The prevalence was marginally significant after adjustment for covariates. Unadjusted analyses revealed a marginally higher prevalence of a severe obstructive abnormality between Ranch Hands in the low dioxin category and Comparisons. This difference between Ranch Hands and Comparisons became nonsignificant after adjustment for covariates.

Table 18-16. Summary of Categorized Dioxin Analysis (Model 3) for Pulmonary Variables (Ranch Hands vs. Comparisons)

Variable	UNADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Medical Records				
Asthma (D)	NS	NS	NS	NS
Bronchitis (D)	NS	NS	NS	NS
Pneumonia (D)	ns	NS	ns	ns
Physical Examination				
Thorax and Lung Abnormalities (D)	ns	NS	NS	NS
Laboratory				
X-ray Interpretation (D)	+0.013	NS	ns	ns
FVC (C)	NS	ns	NS	ns
FEV_1 (C)	ns	ns	NS	ns
Ratio of Observed FEV_1 to Observed FVC (C)[a]	ns	ns	NS	NS
Loss of Vital Capacity (D):				
Mild vs. None	NS	ns	ns	ns
Moderate or Severe vs. None	NS	ns	ns	ns
Obstructive Abnormality (D):				
Mild vs. None	NS*	+0.037	−0.031	ns
Moderate vs. None	NS	NS	ns	ns
Severe vs. None	NS	NS*	ns	ns

Note: NS or ns: Not significant ($p>0.10$).
NS*: Marginally significant ($0.05<p\leq0.10$).
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥ 1.00 for discrete analysis.
−: Relative risk < 1.00 for discrete analysis.
[a] Difference of means negative considered adverse for this variable.

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

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or differences of means nonnegative for continuous analysis. A lowercase "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

Variable	ADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Medical Records				
Asthma (D)	NS	NS	NS	NS
Bronchitis (D)	NS*	ns	NS	NS
Pneumonia (D)	ns	ns	ns	ns
Physical Examination				
Thorax and Lung Abnormalities (D)	ns	NS	NS	NS
Laboratory				
X-ray Interpretation (D)	+0.004	NS	ns	ns

Table 18-16. Summary of Categorized Dioxin Analysis (Model 3) for Pulmonary Variables (Ranch Hands vs. Comparisons) (Continued)

Variable	ADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
FVC (C)	ns	NS	NS	NS
FEV_1 (C)	ns	NS	NS	NS
Ratio of Observed FEV_1 to Observed FVC (C)[a]	ns	NS	NS	NS
Loss of Vital Capacity (D):				
Mild vs. None	NS	ns	ns	ns
Moderate or Severe vs. None	NS	ns	ns	ns
Obstructive Abnormality (D):				
Mild vs. None	NS	NS	ns*	ns
Moderate vs. None	NS	ns	ns	ns
Severe vs. None	NS	NS	ns	ns

Note: NS or ns: Not significant ($p>0.10$).
NS* or ns*: Marginally significant ($0.05<p\leq0.10$).
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥ 1.00 for discrete analysis.
[a] Difference of means negative considered adverse for this variable

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

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or differences of means nonnegative for continuous analysis. A lowercase "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

18.4.4 Model 4: 1987 Dioxin Level Analysis

The adjusted analysis of thorax and lung abnormalities revealed a marginally significant association between the prevalence of abnormalities and 1987 dioxin. The prevalence of abnormalities increased as 1987 dioxin increased. The unadjusted and adjusted analyses of the x-ray interpretation each exhibited a significant decrease in the prevalence of an x ray with abnormalities with an increase in 1987 dioxin. The ratio of the observed FEV_1 to the observed FVC significantly increased as 1987 dioxin increased, but this association was nonsignificant after adjustment for covariates. The adjusted analysis for a mild loss of vital capacity revealed a significant decrease in the loss of vital capacity as 1987 dioxin increased. The prevalence of a mild obstructive abnormality significantly decreased as 1987 dioxin increased in the unadjusted analysis. This association was nonsignificant after adjustment for covariates. The prevalence of a severe obstructive abnormality showed a marginally significant decrease as 1987 dioxin increased, but this association was also nonsignificant after adjustment for covariates. The results for the variables described above, as well as the other pulmonary variables, are summarized in Table 18-17.

Table 18-17. Summary of 1987 Dioxin Analysis (Model 4) for Pulmonary Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Medical Records		
Asthma (D)	NS	NS
Bronchitis (D)	ns	ns
Pneumonia (D)	ns	ns
Physical Examination		
Thorax and Lung Abnormalities (D)	NS	NS*
Laboratory		
X-ray Interpretation (D)	–0.015	–0.015
FVC (C)	ns	NS
FEV_1 (C)	NS	NS
Ratio of Observed FEV_1 to Observed FVC (C)[a]	–<0.001	ns
Loss of Vital Capacity (D):		
Mild vs. None	ns	–0.046
Moderate or Severe vs. None	ns	ns
Obstructive Abnormality (D):		
Mild vs. None	–<0.001	ns
Moderate vs. None	ns	ns
Severe vs. None	ns*	ns

Note: NS or ns: Not significant ($p>0.10$).
NS* or ns*: Marginally significant ($0.05<p\leq0.10$).
C: Continuous analysis.
D: Discrete analysis.
–: Relative risk <1.00 for discrete analysis; slope negative for continuous analysis.
[a] Positive slope considered adverse for this variable; a negative slope implies an increase in the ratio because of the data transformation used.

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

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

18.5 CONCLUSION

To assess the pulmonary status for the 1997 AFHS follow-up examination, verified histories of asthma, bronchitis, and pneumonia were studied. A composite measure of thorax and lung abnormalities, as determined from the presence of asymmetrical expansion, hyperresonance, dullness, wheezes, rales, chronic obstructive pulmonary diseases, or the physician's assessment of abnormality, also was analyzed. A routine chest x ray and five measures of pulmonary function using standard spirometric techniques were analyzed.

Few significant increases in adverse pulmonary conditions were observed for Ranch Hands, and isolated and inconsistent associations between the pulmonary endpoints and increased dioxin were seen. No consistent pattern or dose-response relation was evident. Ranch Hands in the background dioxin category exhibited a significantly higher percentage of abnormalities on the chest x-ray than did Comparisons. Ranch Hand officers had a significantly higher prevalence of mild obstructive abnormality than did

Comparison officers; the corresponding contrast was not significant in 1992, and officers were not analyzed as a separate stratum in 1982, 1985, or 1987.

In summary, analysis of historical, physical examination, and laboratory data revealed no relation between dioxin levels and pulmonary disease; however, the prevalence of mild obstructive abnormalities was significantly increased in Ranch Hand officers. The meaning of this finding is unclear because the risk was not significantly increased in Ranch Hand enlisted groundcrew—the military occupation with the highest dioxin levels.

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19 CONCLUSIONS

19.1 INTRODUCTION

This section summarizes the conclusions drawn from the statistical analyses of data from the 1997 follow-up examination of the Air Force Health Study (AFHS). The 1997 follow-up examination was an extension of the baseline, 1985, 1987, and 1992 follow-up examinations. Health endpoints measured at the 1997 examination were analyzed for associations with herbicide exposure and body burden of serum dioxin and were examined longitudinally in relation to data from previous AFHS examinations. A full explanation of the study design and methodology, terminology, and interpretive considerations is provided in Chapters 1 through 8 of this report.

19.2 STUDY PERFORMANCE ASPECTS

A total of 2,121 veterans participated in the 1997 follow-up examination. Of the 1,101 eligible Ranch Hands, 870 (79.0%) participated in the 1997 follow-up examination. Participation was voluntary and consent forms were signed by the participant at the examination site. A total of 839 of the 1,151 eligible Original Comparisons (72.9%) participated. Of the 768 Replacement Comparisons eligible for the 1997 follow-up examination, 412 (53.6%) chose to attend the examination. A total of 1,251 Comparisons attended the 1997 follow-up examination. Eighty-six percent (819 of 949) of living Ranch Hands and 87 percent of living Comparisons (976 of 1,116) who were fully compliant at the baseline examination returned for the 1997 follow-up examination.

Although more Comparisons than Ranch Hands refused to participate in the 1997 follow-up examination, there were no significant differences in the reasons for refusal among the two groups. Logistics and health reasons were the most common reasons for refusal, although approximately 25 percent of noncompliant veterans were deemed hostile and a reason for refusal was not determined. Approximately 91 percent of noncompliant Original Comparisons were either replaced or required no replacement (e.g., the Original Comparison was deceased and no Replacement Comparison had been contacted previously).

Ranch Hands reported fair or poor health more often than did Comparisons. This pattern of Ranch Hands reporting poorer health has been observed since the baseline examination. In both groups, veterans who refused were more likely to report fair or poor health than those who were fully compliant. Ranch Hands reported a slightly higher use of medications, but no difference was seen in reported work loss between Ranch Hands and Comparisons.

In summary, the results of these analyses suggested that Ranch Hands may be reporting poorer health than Comparisons and that these group differences are present for both fully compliant participants and refusals. This holds true even after accounting for rank and age differences. In addition, the difference in the percentage of fully compliant participants and refusals reporting fair or poor health was similar for Ranch Hands and Comparisons.

19.3 STATISTICAL MODELS

The analysis of the 1997 follow-up examination results used four statistical models to evaluate the relation between the health status of study participants and their dioxin exposure and serum dioxin levels.

The first model specified contrasts between Ranch Hands and Comparisons using group as a proxy for herbicide exposure and did not incorporate serum dioxin measurements. The remaining three models all incorporated serum dioxin measurements in either 1987 dioxin levels or an estimate of initial exposure based on a first-order extrapolation to the time of tour of duty in Southeast Asia (SEA). The four models are summarized as follows:

- Model 1: Ranch Hands versus Comparisons, for all military occupations (officer, enlisted flyer, enlisted groundcrew) combined and for each military occupation separately

- Model 2: Estimated initial serum dioxin levels using Ranch Hand participants with greater than 10 parts per trillion (ppt) of 1987 lipid-adjusted dioxin

- Model 3: Ranch Hands categorized according to serum dioxin levels versus Comparisons with 10 ppt of 1987 lipid-adjusted dioxin or less

- Model 4: 1987 lipid-adjusted serum dioxin using Ranch Hands only.

In Model 1, the use of group and occupation as a surrogate for herbicide exposure was less subject to the possible biases based on health conditions that may occur with variation in dioxin elimination rates. An implicit underlying assumption was that Ranch Hands were exposed and Comparisons were not exposed to herbicides. Model 2 was based on initial dioxin levels that were extrapolated from lipid-adjusted dioxin measurements above background levels (10 ppt), assuming first-order kinetics and a constant dioxin elimination rate. These lipid-adjusted dioxin measurements were collected primarily at the 1987 examination and supplemented with measurements from the 1992 or 1997 examination when a 1987 measurement was not available. Model 3 was less dependent on the accuracy of the initial dioxin estimation algorithm, but all Ranch Hands with high serum dioxin levels were treated alike without emphasizing the unusually large dioxin doses received by some Ranch Hands. Model 4 was based on lipid-adjusted dioxin measurements and assumed nothing about dioxin elimination other than that Ranch Hands were exposed in Vietnam and their body burdens have decreased over time in an unspecified manner. The extrapolated initial dose and lipid-adjusted dioxin measurements may not be accurate measures of exposure if elimination rates differed among individuals.

Statistical analyses often were applied to clinical endpoints in continuous form (i.e., original measurements) as well as in discrete form (i.e., measurements grouped into categories based on abnormal levels). Analyses also were performed to account for the effects that demographic and personal characteristics (covariates) may have had on the clinical measurements. Such analyses are termed "adjusted analyses." The relation between health and the measures of exposure in the four models described above are summarized in the next section. The relation between covariates and measures of herbicide or dioxin exposure are described in Chapter 8.

Throughout this report, dioxin levels were used as measures of both exposure to dioxin itself and exposure to dioxin-contaminated herbicides, including Herbicide Orange. Direct contrasts of Ranch Hand and Comparison veterans (Model 1) address the hypothesis of health effects attributable to any herbicide exposure experienced by Ranch Hand veterans during Operation Ranch Hand. Models involving dioxin levels address the hypothesis that health effects change with the amount of exposure. Dioxin levels were used as a measure of exposure to dioxin-contaminated herbicides because it was expected that as exposure to such herbicides increased, dioxin levels should increase. The dioxin levels, therefore, served as a direct biomarker of exposure to dioxin-contaminated herbicides. No other direct measure or estimate of herbicide exposure is available to address hypothetical dose-response relations

with health. Some indirect measures, such as self-report of skin contact among enlisted groundcrew, or simply being a Ranch Hand enlisted groundcrew member, are valuable alternatives because dioxin measures suggest that enlisted groundcrew experienced the heaviest exposures. Reported skin exposure was not addressed in this report, but enlisted groundcrew status was used in Model 1. The use of dioxin as a surrogate measure of exposure to dioxin-contaminated herbicides is consistent with the goal of the study, which is to determine whether health effects exist and can be attributed to occupational exposure to Herbicide Orange.

19.4 CLINICAL RESULTS

This section provides the conclusions from the analyses of the 10 clinical areas—general health, neoplasia, neurology, psychology, gastrointestinal, cardiovascular, hematology, endocrine, immunology, and pulmonary. Tables G-1 through G-24 of Appendix G present the results of the exposure analyses for each of the four models for 257 health endpoints analyzed in the 10 clinical chapters.

19.4.1 General Health Assessment

The self-perception of health analysis revealed significant differences between Ranch Hands and Comparisons, with more Ranch Hands than Comparisons indicating their health as fair or poor. As in previous examinations, the difference was most apparent in enlisted groundcrew, who had the highest average dioxin levels. This observation also was confirmed in the categorized dioxin analysis, where Ranch Hands with the highest dioxin levels perceived their health as fair or poor more often than Comparisons. Also, among Ranch Hands, those with the higher 1987 dioxin levels reported fair or poor health more often than Ranch Hands with lower levels. These results were consistent with the 1985, 1987, and 1992 examinations. No group differences were noted in the appearance of illness or relative age, as recorded by examining physicians, nor were these variables correlated with serum dioxin levels in the Ranch Hand cohort.

The analysis of body fat indicated positive associations with dioxin levels. The results of the 1997 examination confirmed those of the 1992 examination and appear consistent with a difference in dioxin pharmacokinetics in obese versus lean individuals.

No differences in the percentages of abnormal erythrocyte sedimentation rates between Ranch Hands and Comparisons or relations between abnormal erythrocyte sedimentation rates and dioxin levels were observed during the 1997 examination. Erythrocyte sedimentation rates increased as 1987 dioxin levels increased.

Longitudinal analyses showed that Ranch Hands, particularly the two enlisted strata, had a greater percentage of abnormal erythrocyte sedimentation rates than did Comparisons during the 15 years of the study since 1982. These analyses also showed that the percentages of abnormalities increased from 1982 to 1997 as dioxin levels increased. This result was seen at the 1987 study, but not in 1992. This positive association raises the possibility of a subtle inflammatory, infectious, or occult malignant disease process related to the body burden of dioxin.

In conclusion, fair or poor self-perception of health displayed an adverse association with dioxin, but the relation with other health conditions is unknown. Increased body fat was associated with increased levels of dioxin, a finding most likely related to the pharmacokinetics of dioxin. Longitudinal analyses indicated an increased risk of an abnormal erythrocyte sedimentation rate in Ranch Hands over Comparisons in the 15 years of the AFHS, and a relation between abnormal erythrocyte sedimentation

rates and levels of dioxin during these 15 years. Other measures of general health revealed no association with levels of dioxin.

19.4.2 Malignant Neoplastic Diseases

At the end of 15 years of surveillance, Ranch Hands as a group exhibited a nonsignificant increase in the risk of malignant neoplastic disease relative to Comparisons (relative risk=1.06, 95% confidence interval: [0.80,1.41]). Military occupation contrasts were inconsistent and, therefore, not supportive of an adverse effect of herbicide or dioxin exposure on the occurrence of malignancies. Ranch Hand enlisted groundcrew, the occupation with the highest dioxin levels and, presumably, the highest herbicide exposure, exhibited a decreased prevalence (relative risk=0.78, 95% confidence interval: [0.51,1.19]). Enlisted flyers (relative risk=1.63, 95% confidence interval: [0.91,2.92]) and officers (relative risk=1.14, 95% confidence interval: [0.79,1.65]), occupations with lower dioxin levels, exhibited nonsignificant increases in the prevalence of malignant disease. The risk of malignant disease was nonsignificantly increased among Ranch Hands having the highest dioxin levels (relative risk=1.01, 95% confidence interval: [0.66,1.57]). Longitudinal analyses found no significant group differences with regard to the risk of malignancy and no pattern suggestive of an adverse relation between herbicide or dioxin exposure and the occurrence of malignant neoplastic disease.

19.4.3 Neurological Assessment

Four neurological disorders and extensive physical examination data on cranial nerve function, peripheral nerve status, and central nervous system coordination processes were analyzed in the neurological assessment. Inflammatory diseases, as verified by a medical records review, were increased in Ranch Hands relative to Comparisons in terms of both a group designation and categorized dioxin levels. However, three of the seven Ranch Hand diseases were caused by bacterial infections, suggesting that this finding is unrelated to herbicide or dioxin exposure. Peripheral disorders, as verified by a medical records review, increased in Ranch Hands as levels of 1987 dioxin increased. Neck range of motion abnormalities were increased in Ranch Hands relative to Comparisons in terms of both a group designation and categorized dioxin levels. The increase in abnormalities for Ranch Hands relative to Comparisons was noted in enlisted flyers. An increase in the risk of an abnormal muscle status was observed in Ranch Hand enlisted groundcrew. A significant association between initial dioxin and abnormalities of both visual fields and the patellar reflex was observed. Indices of polyneuropathy showed an increase in the prevalence of abnormality in Ranch Hands relative to Comparisons, and a positive association with initial dioxin, categorized dioxin, and 1987 dioxin levels.

In summary, although a common etiology in these findings is not apparent, a statistically significant increase in neurological disease appears in Ranch Hands historically, on physical examination, and as reflected in several of the composite polyneuropathy indices. Further, the associations of neck range of motion with categorized dioxin and a history of peripheral disorders with 1987 dioxin provide evidence of an association of neurological disease with elevated dioxin levels. The results of the analysis of the polyneuropathy indices also provide support of a statistical association between elevated dioxin levels and neurological disease; however, the clinical importance of this finding is uncertain.

19.4.4 Psychological Assessment

Five psychological disorders, which were verified by a medical records review, and 12 measures from the Symptom Checklist-90-Revised (SCL-90-R) inventory were examined in the psychological assessment. The SCL-90-R consisted of nine primary symptom dimensions and three broad indices of psychological

distress. In enlisted groundcrew, a significantly greater percentage of Ranch Hands than Comparisons had a history of other neuroses. All other significant results from analyses of Ranch Hands versus Comparisons showed a greater percentage of Comparisons than Ranch Hands with high SCL-90-R scores.

Associations between initial dioxin and the psychological endpoints were either nonsignificant or revealed a significant decrease in high (adverse) SCL-90-R scores as initial dioxin increased.

Differences in the history of psychological disorders and the prevalence of high SCL-90-R scores were examined between Comparisons and Ranch Hands categorized by dioxin levels. Ranch Hands in the low dioxin category and the low plus high dioxin category displayed a significantly higher occurrence of other neuroses than did Comparisons.

The relation between the 1987 dioxin levels and the psychological endpoints was examined and all results were nonsignificant.

In summary, Ranch Hand veterans exhibited a significantly increased prevalence of other neuroses among enlisted groundcrew, the military occupation with the highest dioxin levels and, presumably, the greatest herbicide exposure. Consistent increases in the prevalence of other neuroses with dioxin levels were found. No consistent relation was found between any SCL-90-R score and any measure of herbicide or dioxin exposure. The relation between other neuroses and herbicide exposure and dioxin levels will be described in greater detail in a separate report.

19.4.5 Gastrointestinal Assessment

The gastrointestinal assessment was based on eight disorders as determined from a review and verification of each participant's medical records, a physical examination determination of hepatomegaly, and 29 laboratory measurements or indices. The laboratory parameters included measurements of hepatic enzyme activity, hepatobiliary function, lipid and carbohydrate indices, and a protein profile. In addition, the presence of hepatitis and fecal occult blood was investigated.

Analyses of Ranch Hands versus Comparisons showed higher mean levels of alkaline phosphatase, α-1-antitrypsin, and haptoglobin in Ranch Hands than in Comparisons. In addition, significantly more Ranch Hands than Comparisons had high haptoglobin levels. A review of medical records showed a positive association between initial dioxin and other liver disorders. The other liver disorders condition consisted primarily of nonspecific laboratory test elevations. A significant association between initial dioxin and high levels of aspartate aminotransferase (AST) also was revealed.

Analyses of categorized dioxin revealed a significantly higher percentage of other liver disorders among Ranch Hands in the high dioxin category than among Comparisons. Higher mean levels of gamma glutamyl transferase (GGT), triglycerides, and α-1-antitrypsin were observed in Ranch Hands in the high dioxin category than in Comparisons. Ranch Hands in the high dioxin category had a greater prevalence of abnormal AST, triglyceride, and prealbumin levels than did Comparisons.

Many significant associations between the laboratory examination variables and 1987 dioxin levels were observed. In both the continuous and discrete forms, the hepatic enzymes alanine aminotransferase (ALT), AST, and GGT revealed significant, positive associations with 1987 dioxin. In addition, significant positive associations between 1987 dioxin and the ratio of cholesterol to high-density lipoprotein (HDL), triglycerides, and creatine phosphokinase were present.

In summary, the analysis of the 1997 follow-up data reflected patterns that have been observed and documented in prior examinations. Isolated group differences exist, but 1987 dioxin levels are strongly related to hepatic enzymes such as AST, ALT, and GGT, and to lipid-related health indices such as cholesterol, HDL, and triglycerides. These results are consistent with a dose-response effect and may be related to unknown subclinical effects of dioxin. Although hepatic enzymes and lipid-related indices showed an association with dioxin, there was no evidence of an increase in overt liver disease.

19.4.6 Cardiovascular Assessment

Analyses revealed that Ranch Hands had a significantly higher percentage of participants with a history of heart disease (excluding essential hypertension) than Comparisons and, in particular, among enlisted flyers. However, the risk of disease was not significantly increased in Ranch Hand enlisted groundcrew—the military occupation with the highest dioxin levels. The association between heart disease and initial dioxin showed a negative dose-response trend, with heart disease decreasing as initial dioxin increased. Furthermore, Ranch Hands in the background and low dioxin categories had more heart disease than did Comparisons, but this increase was not seen in Ranch Hands in the high dioxin category. Increases in tachycardia and other electrocardiograph (ECG) findings, such as pre-excitation, were seen for Ranch Hands in the high dioxin category, although the analyses were based on a small number of abnormalities. A significant positive association between initial dioxin and evidence of prior myocardial infarction from the ECG was observed in Ranch Hands, and a marginally significant positive association was observed between 1987 dioxin and evidence of prior myocardial infarction from the ECG. A positive association between 1987 dioxin and a history of essential hypertension also was observed in Ranch Hands. In contrast to previous AFHS examinations, no relation was found between peripheral pulse abnormalities and any measure of exposure.

In summary, in contrast to prior examinations, the current study has documented that Ranch Hands are more likely than Comparisons to have historical evidence for heart disease (excluding essential hypertension), but are no longer at greater risk for the occurrence of pulse deficits. By all other indices, the prevalence of cardiovascular disease appears similar in both cohorts. For the first time, there is evidence that levels of dioxin may be a risk factor for the development of essential hypertension and prior myocardial infarction as indicated by interpretation of the ECG. As of 1997, the verified history of essential hypertension was associated with 1987 dioxin, and the evidence of prior myocardial infarction from the ECG was associated with initial dioxin. These findings, in conjunction with the increase in the number of deaths caused by diseases of the circulatory system for Ranch Hand nonflying enlisted personnel based on the 1994 AFHS mortality update, showed associations that require further study. A biological mechanism for the relation among dioxin levels and heart disease is unknown.

19.4.7 Hematologic Assessment

Five cell count measures, six measures of absolute blood counts, a coagulation measure, and red blood cell morphology were analyzed. In the analyses of these variables, only platelet count exhibited significant dose-response associations with the levels of dioxin. Among enlisted personnel, Ranch Hands exhibited significantly higher mean platelet counts than did Comparisons. Ranch Hands in the high dioxin category also exhibited a significantly higher mean platelet count than did Comparisons. The mean differences were small and, therefore, the clinical importance of these findings is unknown. The results in the 1997 follow-up study parallel the findings of the 1987 and 1992 follow-up studies. In conclusion, apart from platelet count, there appears to be little evidence to support a relation between prior dioxin exposure and hematopoietic toxicity.

19.4.8 Endocrine Assessment

The assessment of the endocrine system yielded an extensive evaluation of thyroid, pancreatic, and gonadal function and their relation to dioxin exposure. A significantly increased risk of abnormally high thyroid stimulating hormone values was found in Ranch Hand enlisted groundcrew.

A positive association between diabetes and initial and 1987 dioxin was observed. Consistent with previous reports, the prevalence of diabetes among Ranch Hands with high dioxin levels was increased. A greater percentage of Ranch Hands than Comparisons used insulin to control their type 2 diabetes, primarily among officers and enlisted groundcrew. The percentage of Ranch Hands requiring insulin to control their type 2 diabetes increased with initial dioxin. A greater percentage of Ranch Hands in the high dioxin category required insulin to control their type 2 diabetes than did Comparisons. The percentage of Ranch Hands who treated their diabetes through diet only and the percentage who used oral hypoglycemics increased with 1987 dioxin level.

The time to diabetes onset was significantly shorter for Ranch Hands with higher initial dioxin and 1987 levels. Both fasting glucose and α-1-C hemoglobin increased in Ranch Hands as initial dioxin and 1987 dioxin increased. Increased α-1-C hemoglobin levels also were observed for Ranch Hands with high dioxin levels. The presence of fasting urinary glucose also increased with 1987 dioxin.

Although cause and effect have not been established, the results cited above provide further evidence for an association between diabetes and levels of dioxin.

19.4.9 Immunologic Assessment

The immunologic assessment was based on laboratory data on six lymphocyte cell surface markers, absolute lymphocyte counts, three quantitative immunoglobulins, and six measurements from an autoantibody panel. The six cell marker measurements were carried out on a random sample of approximately 40 percent of the participants because of the complexity of the assay and the expense of the tests.

Group analyses revealed significant findings for the analyses of CD16+56+ cell (natural killer cell) counts and for the mouse stomach kidney (MSK) smooth muscle antibody test in enlisted flyers. Among enlisted flyers, the mean CD16+56+ cell count was greater for Comparisons than for Ranch Hands, and a greater percentage of Comparisons than Ranch Hands had a smooth muscle antibody present. Negative smooth muscle antibody tests are considered to be normal. For these analyses, the magnitude of the mean differences was small and, therefore, the clinical importance of these findings is unknown.

Consistent with the previous two physical examinations, IgA increased significantly with initial dioxin, but was not significantly increased in enlisted groundcrew or the high dioxin category, and IgA did not increase significantly with 1987 dioxin. The IgA results, although significant, were small in magnitude and their clinical importance is unknown.

When comparing categorized dioxin levels between Ranch Hands and Comparisons, a significantly higher CD16+56+ cell count mean was observed among Comparisons than among Ranch Hands in the high dioxin category. Analyses revealed significant associations between 1987 dioxin levels and CD3+ cell (T cell) count, CD4+ cell (helper T cell) count, and CD3+CD4+ cell (helper T cell) count. The cell counts increased as 1987 dioxin increased.

In summary, these findings and the findings from past examinations do not provide evidence of a biologically meaningful dose-response effect for body burden of dioxin on parameters of immunologic assessment. The statistically significant relations suggest the need for continued evaluation.

19.4.10 Pulmonary Assessment

To assess pulmonary status, verified histories of asthma, bronchitis, and pneumonia were studied. A composite measure of thorax and lung abnormalities, as determined from the presence of asymmetrical expansion, hyperresonance, dullness, wheezes, rales, chronic obstructive pulmonary diseases, or the physician's assessment of abnormality, also was analyzed. A routine chest x ray and five measures of pulmonary function using standard spirometric techniques were analyzed.

Few significant increases in adverse pulmonary conditions were observed for Ranch Hands, and isolated and inconsistent associations between the pulmonary endpoints and dioxin were seen. No consistent pattern or dose-response relation was evident. Ranch Hands in the background dioxin category exhibited a significantly higher percentage of abnormalities on the chest x ray than did Comparisons. Ranch Hand officers had a significantly higher prevalence of mild obstructive abnormality than did Comparison officers; the corresponding contrast was not significant in 1992, and officers were not analyzed as a separate stratum in 1982, 1985, or 1987. The relation between mild obstructive abnormality in Ranch Hand officers and other indicators of herbicide exposure, such as job (pilot, navigator, nonflyer), the number of missions flown, the percentage of missions that were herbicide missions, and reported drinking of herbicide (yes, no) will be summarized in a separate report.

In summary, analysis of historical, physical examination, and laboratory data revealed no consistent relation between herbicide exposure or dioxin levels and pulmonary disease. The prevalence of mild obstructive abnormalities was significantly increased in Ranch Hand officers. The meaning of this finding is unclear because the risk was not significantly increased in Ranch Hand enlisted groundcrew—the military occupation with the highest dioxin levels.

19.5 INTERPRETIVE CONSIDERATIONS

Certain facts should be considered when drawing conclusions from the statistical analysis of the 1997 follow-up examination results. For example, there are often difficulties associated with multiple testing. With repeated statistical testing, the likelihood of a test indicating some artifactual association is high. But longitudinal comparisons of previous examinations may show a consistent association, supporting a non-artifactual relation. Longitudinal tests, however, of the same population clearly are not independent tests. If a chance association was present at the first physical examination, it would tend to persist in subsequent examinations. Conversely, depending on site and mode of action, the association would be expected to increase with time (if latency or other chronic effects predominate) or decrease with time (if the current dioxin level predominates in the mechanism). It is also important to note that some conditions do not appear with reasonable frequency until middle age or later. Therefore, in the early years of the study, an increased relative risk might have been masked by abnormalities too sparse for meaningful analysis.

The site and mode of action of dioxin in the body could itself either cause or obscure a relation. Receptors might be activated only after a certain dioxin threshold value had been exceeded—that is, a value exceeding the body's capability to safely store dioxin. If, on the other hand, dioxin caused a competitive inhibition of receptor actions normally stimulated by other substances, there might be a "no-threshold" effect. Depending on the nature (lipid or non-lipid) and type of function of the