

FEV₁

No difference between the Ranch Hand and Comparison groups was detected in the unadjusted analysis of FEV₁ ($p=0.336$).

The covariate tests with FEV₁ were significant for age, race, occupation, current cigarette smoking, and lifetime cigarette smoking history ($p<0.001$ for all). There was a negative correlation between FEV₁ and age ($r=-0.145$). The mean FEV₁ was lower for Blacks than nonblacks (85.3% vs. 96.3%). The results for occupation showed that the lowest mean level was in the enlisted flyer occupation category (94.0% for enlisted flyers, 94.8% for enlisted groundcrew, and 97.4% for officers). Current cigarette smoking and lifetime cigarette smoking were both negatively correlated with FEV₁ ($r=-0.183$ and $r=-0.255$, respectively).

Based on the adjusted analysis of FEV₁, no group difference was identified ($p=0.621$). Race ($p<0.001$), occupation ($p<0.001$), age-by-current cigarette smoking interaction ($p=0.001$), and current cigarette smoking-by-lifetime cigarette smoking history interaction ($p=0.006$) were significant terms in the adjusted model.

FEFmax

No group difference was revealed in the unadjusted analysis of FEFmax ($p=0.344$).

The results of the covariate tests with FEFmax showed significant associations for age, occupation, current cigarette smoking, and lifetime cigarette smoking history ($p<0.001$ for all). Negative correlations were found for age, current cigarette smoking, and lifetime cigarette smoking history ($r=-0.077$, $r=-0.239$, and $r=-0.216$, respectively). The mean FEFmax for officers, enlisted flyers, and enlisted groundcrew was 140.8 percent, 135.3 percent, and 134.7 percent, respectively.

The Ranch Hands and the Comparisons were not significantly different based on the adjusted analysis of FEFmax ($p=0.778$). There were three significant interactions involving lifetime cigarette smoking history in the model: age ($p=0.008$), occupation ($p=0.027$), and current smoking ($p=0.006$).

Ratio of Observed FEV₁ to Observed FVC

The unadjusted analysis of the ratio of observed FEV₁ to observed FVC did not identify a significant difference between the two groups ($p=0.816$).

The covariate tests with the ratio of observed FEV₁ to observed FVC showed significant associations for all five covariates: age, race, occupation, current cigarette smoking, and lifetime cigarette smoking history ($p<0.001$ for all). Based on the positive correlation between age and 1 minus the ratio ($r=0.263$), the ratio was found to decrease as age increased. The mean of the nonblacks was 0.812, as contrasted to a mean of 0.841 for Blacks. The mean of the ratio of observed FEV₁ to observed FVC was 0.808 for officers, 0.800 for enlisted flyers, and 0.823 for enlisted groundcrew. The ratio also

decreased as current cigarette smoking and lifetime cigarette smoking increased, as demonstrated by the positive correlations with 1 minus the ratio ($r=0.190$ and $r=0.260$, respectively).

The Ranch Hands and the Comparisons did not differ significantly on the ratio of observed FEV₁ to observed FVC in the adjusted analysis ($p=0.645$). The significant terms of the model were: age-by-occupation interaction ($p=0.013$), race-by-lifetime cigarette smoking history interaction ($p=0.047$), and current cigarette smoking-by-lifetime cigarette smoking history interaction ($p=0.001$).

Loss of Vital Capacity

The unadjusted analysis of loss of vital capacity was not significant ($p=0.670$), nor were the contrasts of mild versus none and of moderate/severe versus none ($p=0.664$ and $p=0.544$, respectively).

The results of the covariate tests of association with loss of vital capacity showed that age ($p<0.001$), race ($p<0.001$), current cigarette smoking ($p=0.001$), and lifetime cigarette smoking history ($p<0.001$) were significant. For each level of loss of vital capacity (none, mild, and moderate/severe), the percentage of the participants in each category of the covariate is provided in Table Q-1 of Appendix Q.

In general, the loss of vital capacity increased with age. Of the participants born in or after 1942, 93.0 percent had no loss of vital capacity, as compared to 87.7 percent for those born between 1923 and 1941 and 86.9 percent for those born in or before 1922. Mild losses of vital capacity were detected in 6.3 percent of those born in or after 1942, 9.8 percent of those born between 1923 and 1941, and 8.3 percent of those born in or before 1922. The percentage of participants with a moderate/severe loss of vital capacity increased with age (0.7% for those born in or after 1942, 2.6% for those born between 1923 and 1941, and 4.8% for those born in or before 1922).

Blacks had a higher percentage of abnormalities than nonblacks. The percentage of participants with no loss of vital capacity was lower for Blacks than nonblacks (69.3% vs. 91.2%). Of the Black participants, 24.1 percent had a mild loss of vital capacity, as compared to 7.2 percent for nonblacks. Moderate/severe losses were detected in 6.6 percent of the Blacks and 1.6 percent of the nonblacks.

For current cigarette smoking, the loss of vital capacity increased with smoking intensity. For current cigarette smoking, 93.6 percent of the nonsmokers had no loss of vital capacity, as compared to 90.3 percent of the former smokers, 86.4 percent of the moderate smokers, and 86.2 percent of the heavy smokers. Mild losses were detected in 5.6 percent of the nonsmokers, 7.9 percent of the former smokers, 10.8 percent of the moderate smokers, and 10.8 percent of the heavy smokers based on current cigarette smoking habits. Only 0.8 percent of the nonsmokers had a moderate/severe loss of vital capacity, as compared with 1.8 percent for former smokers, 2.8 percent for moderate smokers, and 3.0 percent for heavy smokers using current cigarette smoking.

The loss of vital capacity also increased with lifetime smoking intensity. Based on this covariate, 93.6 percent of the nonsmokers had no loss of vital capacity, as contrasted with 92.1 percent of the moderate smokers and 86.2 percent of the heavy smokers. The percentage of participants with a mild loss was 5.6 percent for nonsmokers, 6.6 percent for moderate smokers, and 10.9 percent for heavy smokers. Moderate/severe losses were detected in 0.8 percent of the nonsmokers, 1.3 percent of the moderate smokers, and 2.9 percent of the heavy smokers.

The overall adjusted analysis of loss of vital capacity did not detect a difference between the two groups ($p=0.679$). Group differences were also not found in the adjusted analysis of the individual contrasts ($p=0.623$ for mild vs. none and $p=0.445$ for moderate/severe vs. none). Age, race, and lifetime cigarette smoking history were significant effects in the adjusted analysis ($p<0.001$ for all).

Obstructive Abnormality

In the unadjusted analysis of obstructive abnormality, no difference between the two groups was detected for the overall analysis of the three categories ($p=0.299$), or for either the mild versus none or the moderate/severe versus none contrasts ($p=0.140$ and $p=0.694$, respectively).

The covariate tests with obstructive abnormality showed that age, occupation, current cigarette smoking, and lifetime cigarette smoking history were significant ($p<0.001$ for all). Each participant was classified as having no obstructive abnormality, a mild obstructive abnormality, or a moderate/severe obstructive abnormality. For each level of obstructive abnormality, the percentage of participants by category of the covariate is provided in tabular form in Table Q-1 of Appendix Q.

The prevalence rate of obstructive abnormality increased with age. No obstructive abnormalities were detected in 84.4 percent of those born in or after 1942, 62.4 percent of those born between 1923 and 1941, and 52.4 percent of those born in or before 1922. Of those born in or before 1922, 38.1 percent had a mild obstructive abnormality, as compared to 30.7 percent of those born between 1923 and 1941 and 14.4 percent of those born in or after 1942. The same pattern of abnormalities was demonstrated for moderate/severe obstructive abnormalities (1.1% for those born in or after 1942, 6.9% for those born between 1923 and 1941, and 9.5% for those born in or before 1922).

The occupational category with the highest level of obstructive abnormalities was the enlisted flyers. No obstructive abnormalities were detected in 75.9 percent of the enlisted groundcrew, 70.6 percent of the officers, and 60.2 percent of the enlisted flyers. Of the enlisted flyers, 32.7 percent had a mild obstructive abnormality, as compared to 25.8 percent of the officers and 19.7 percent of the enlisted groundcrew. Moderate/severe obstructive abnormalities were detected in 7.1 percent of the enlisted flyers, 4.4 percent of the enlisted groundcrew, and 3.7 percent of the officers.

The percentage of obstructive abnormalities increased with levels of current cigarette smoking. Based on current cigarette smoking habits, 9.1 percent of the nonsmokers, 25.2 percent of the former smokers, 30.0 percent of the moderate smokers, and 41.2 percent of the heavy smokers had a mild

obstructive abnormality. The percentages of moderate/severe obstructive abnormalities were 1.0, 5.0, 5.4, and 8.9 for nonsmokers, former smokers, moderate smokers, and heavy smokers, respectively. No obstructive abnormalities were detected in 90.0 percent of the nonsmokers, 69.9 percent of the former smokers, 64.6 percent of the moderate smokers, and 49.9 percent of the heavy smokers.

The percentage of obstructive abnormalities was also found to increase based on lifetime cigarette smoking history. For lifetime cigarette smoking, 9.2 percent and 1.0 percent of the nonsmokers had mild and moderate/severe obstructive abnormalities, respectively, as contrasted with corresponding percentages of 21.5 and 4.1 for moderate smokers and 34.9 and 7.1 for heavy smokers. Only 58.0 percent of the heavy smokers had no obstructive abnormality, as compared to 74.4 percent of the moderate smokers and 89.8 percent of the nonsmokers.

The adjusted analysis of obstructive abnormality for the overall test, mild versus none, and moderate/severe versus none did not detect a difference between the Ranch Hands and the Comparisons ($p=0.389$, $p=0.175$, and $p=0.610$, respectively). The significant covariates were age ($p<0.001$), occupation ($p=0.011$), and lifetime cigarette smoking history ($p<0.001$).

Exposure Index Analysis

The results of the unadjusted and adjusted exposure index analyses are presented in Tables 20-9 and 20-10, respectively. A summary of the exposure index-by-covariate interactions is provided in Table 20-11; Table Q-3 of Appendix Q contains the detailed results of the interactions involving exposure index. The final interpretation of these exposure index data must await the reanalysis of the clinical data using the results of the serum dioxin assay. The report is expected in 1991.

Questionnaire Variables

Asthma

The results showed a significant difference in history of asthma for the overall test of officers ($p=0.045$) based on the unadjusted analysis and a borderline significant difference based on the adjusted analysis ($p=0.088$). Of the officers, 9.2 percent of the low exposure category reported having asthma, as contrasted with 3.2 percent of the officers in the medium and in the high exposure categories. All of the contrasts for the officers were borderline significant. Based on the unadjusted results, the estimated relative risk for both the medium versus low and high versus low contrasts was 0.33 (95% C.I.: [0.10,1.05] and $p=0.084$ for medium vs. low; 95% C.I.: [0.10,1.04] and $p=0.081$ for high vs. low). The adjusted relative risk from the adjusted analysis was 0.35 for both of the contrasts (95% C.I.: [0.11, 1.13] and $p=0.079$ for medium versus low; 95% C.I.: [0.11,1.14] and $p=0.082$ for high vs. low). Since the highest percentage of participants who reported having had asthma within the officer cohort was for the low exposure category, these results do not suggest a dose-response relationship.

The unadjusted and adjusted analyses for the enlisted flyers and enlisted groundcrew did not identify any significant results.

TABLE 20-9.

Unadjusted Exposure Index for Pulmonary Variables by Occupation

Variable	Occupation	Statistic	Exposure Index						Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
			Low		Medium		High				
Asthma	Officer	n	130		124		125		Overall		0.045
		Number/%									
		Yes	12	9.2%	4	3.2%	4	3.2%	M vs. L	0.33 (0.10,1.05)	0.084
	Enlisted Flyer	No	118	90.8%	120	96.8%	121	96.8%	H vs. L	0.33 (0.10,1.04)	0.081
		n	55		63		53		Overall		0.795
		Number/%									
	Enlisted Groundcrew	Yes	2	3.6%	4	6.3%	3	5.7%	M vs. L	1.80 (0.32,10.21)	0.812
		No	53	96.4%	59	93.7%	50	94.3%	H vs. L	1.59 (0.26,9.92)	0.964
		n	147		158		140		Overall		0.320
	Enlisted Groundcrew	Number/%									
		Yes	6	4.1%	13	8.2%	10	7.1%	M vs. L	2.11 (0.78,5.70)	0.206
		No	141	95.9%	145	91.8%	130	92.9%	H vs. L	1.81 (0.64,5.11)	0.384
Bronchitis	Officer	n	130		123		125		Overall		0.594
		Number/%									
		Yes	30	23.1%	22	17.9%	26	20.8%	M vs. L	0.73 (0.39,1.34)	0.386
	Enlisted Flyer	No	100	76.9%	101	82.1%	99	79.2%	H vs. L	0.88 (0.48,1.59)	0.774
		n	55		63		53		Overall		0.003
		Number/%									
	Enlisted Groundcrew	Yes	18	32.7%	5	7.9%	10	18.9%	M vs. L	0.18 (0.06,0.52)	0.001
		No	37	67.3%	58	92.1%	43	81.1%	H vs. L	0.48 (0.20,1.16)	0.154
		n	147		158		140		Overall		0.699
	Enlisted Groundcrew	Number/%									
		Yes	24	16.3%	25	15.8%	27	19.3%	M vs. L	0.96 (0.52,1.78)	0.999
		No	123	83.7%	133	84.2%	113	80.7%	H vs. L	1.23 (0.67,2.25)	0.616

TABLE 20-9. (continued)

Unadjusted Exposure Index for Pulmonary Variables by Occupation

Variable	Occupation	Statistic	Exposure Index						Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
			Low		Medium		High				
Pleurisy	Officer	n	130		124		124		Overall		0.142
		Number/%									
		Yes	8	6.2%	10	8.1%	3	2.4%	M vs. L	1.34 (0.51,3.51)	0.728
		No	122	93.9%	114	91.9%	121	97.6%	H vs. L	0.38 (0.10,1.46)	0.248
	Enlisted Flyer	n	55		63		53		Overall		0.807
		Number/%									
		Yes	3	5.5%	3	4.8%	4	7.5%	M vs. L	0.87 (0.17,4.48)	0.999
		No	52	94.5%	60	95.2%	49	92.5%	H vs. L	1.42 (0.30,6.65)	0.958
	Enlisted Groundcrew	n	146		158		140		Overall		0.356
		Number/%									
		Yes	13	8.9%	9	5.7%	7	5.0%	M vs. L	0.62 (0.26,1.49)	0.392
		No	133	91.1%	149	94.3%	133	95.0%	H vs. L	0.54 (0.21,1.39)	0.288
Pneumonia	Officer	n	130		124		125		Overall		0.628
		Number/%									
		Yes	27	20.8%	25	20.2%	31	24.8%	M vs. L	0.96 (0.52,1.77)	0.999
		No	103	79.2%	99	79.8%	94	75.2%	H vs. L	1.26 (0.70,2.26)	0.536
	Enlisted Flyer	n	55		63		53		Overall		0.439
		Number/%									
		Yes	13	23.6%	14	22.2%	17	32.1%	M vs. L	0.92 (0.39,2.18)	0.999
		No	42	76.4%	49	77.8%	36	67.9%	H vs. L	1.53 (0.65,3.56)	0.446
	Enlisted Groundcrew	n	147		158		140		Overall		0.503
		Number/%									
		Yes	35	23.8%	29	18.4%	29	20.7%	M vs. L	0.72 (0.41,1.25)	0.304
		No	112	76.2%	129	81.6%	111	79.3%	H vs. L	0.84 (0.48,1.46)	0.626

TABLE 20-9. (continued)

Unadjusted Exposure Index for Pulmonary Variables by Occupation

Variable	Occupation	Statistic	Exposure Index						Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value	
			Low		Medium		High					
Tuberculosis	Officer	n	130		124		125		Overall		0.362	
		Number/%										
		Yes	1	0.8%	0	0.0%	2	1.6%	M vs. L	— ^a	0.999	
		No	129	99.2%	124	100.0%	123	98.4%	H vs. L	2.10 (0.19,23.43)	0.970	
		Enlisted Flyer	n	55		63		53		Overall		0.105
			Number/%									
	Yes		0	0.0%	0	0.0%	2	3.8%	M vs. L	— ^a	— ^a	
		No	55	100.0%	63	100.0%	51	96.2%	H vs. L	— ^a	0.476	
		Enlisted Groundcrew	n	147		158		140		Overall		0.206
			Number/%									
	Yes		0	0.0%	3	1.9%	1	0.7%	M vs. L	— ^a	0.276	
		No	147	100.0%	155	98.1%	139	99.3%	H vs. L	— ^a	0.976	
Thorax and Lung Abnormalities		n	130		124		125		Overall		0.235	
		Number/%										
	Yes	9	6.9%	7	5.6%	3	2.4%	M vs. L	0.80 (0.29,2.23)	0.874		
	No	121	93.1%	117	94.4%	122	97.6%	H vs. L	0.33 (0.09,1.25)	0.156		
	Enlisted Flyer	n	55		63		53		Overall		0.440	
		Number/%										
Yes		11	20.0%	9	14.3%	6	11.3%	M vs. L	0.67 (0.25,1.75)	0.562		
	No	44	80.0%	54	85.7%	47	88.7%	H vs. L	0.51 (0.17,1.50)	0.330		
	Enlisted Groundcrew	n	147		158		140		Overall		0.491	
		Number/%										
Yes		8	5.4%	9	5.7%	12	8.6%	M vs. L	1.05 (0.39,2.80)	0.999		
	No	139	94.6%	149	94.3%	128	91.4%	H vs. L	1.63 (0.65,4.11)	0.418		

TABLE 20-9. (continued)

Unadjusted Exposure Index for Pulmonary Variables by Occupation

Variable	Occupation	Statistic	Exposure Index						Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value	
			Low		Medium		High					
Asymmetric Expansion	Officer	n	130		124		125		Overall		__ ^a	
		Number/%										
		Yes	0	0.0%	0	0.0%	0	0.0%	M vs. L	__ ^a	__ ^a	
		No	130	100.0%	124	100.0%	125	100.0%	H vs. L	__ ^a	__ ^a	
		Enlisted Flyer	n	55		63		53		Overall		__ ^a
			Number/%									
	Yes		0	0.0%	0	0.0%	0	0.0%	M vs. L	__ ^a	__ ^a	
		No	55	100.0%	63	100.0%	53	100.0%	H vs. L	__ ^a	__ ^a	
		Enlisted Groundcrew	n	147		158		140		Overall		__ ^a
			Number/%									
	Yes		0	0.0%	0	0.0%	0	0.0%	M vs. L	__ ^a	__ ^a	
		No	147	100.0%	158	100.0%	140	100.0%	H vs. L	__ ^a	__ ^a	
Hyper-resonance		Officer	n	130		124		125		Overall		0.391
			Number/%									
	Yes		4	3.1%	2	1.6%	1	0.8%	M vs. L	0.52 (0.09,2.87)	0.728	
	No	126	96.9%	122	98.4%	124	99.2%	H vs. L	0.25 (0.03,2.31)	0.396		
	Enlisted Flyer	n	55		63		53		Overall		0.329	
		Number/%										
Yes		8	14.5%	4	6.3%	5	9.4%	M vs. L	0.40 (0.11,1.40)	0.244		
	No	47	85.5%	59	93.7%	48	90.6%	H vs. L	0.61 (0.19,2.01)	0.606		
	Enlisted Groundcrew	n	147		158		140		Overall		0.331	
		Number/%										
Yes		6	4.1%	3	1.9%	7	5.0%	M vs. L	0.46 (0.11,1.85)	0.432		
	No	141	95.9%	155	98.1%	133	95.0%	H vs. L	1.24 (0.41,3.78)	0.928		

TABLE 20-9. (continued)

Unadjusted Exposure Index for Pulmonary Variables by Occupation

Variable	Occupation	Statistic	Exposure Index						Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
			Low		Medium		High				
Dullness	Officer	n	130		124		125		Overall		__ ^a
		Number/%									
		Yes	0	0.0%	0	0.0%	0	0.0%	M vs. L	__ ^a	__ ^a
		No	130	100.0%	124	100.0%	125	100.0%	H vs. L	__ ^a	__ ^a
	Enlisted Flyer	n	55		63		53		Overall		0.422
		Number/%									
		Yes	0	0.0%	1	1.6%	0	0.0%	M vs. L	__ ^a	0.999
		No	55	100.0%	62	98.4%	53	100.0%	H vs. L	__ ^a	__ ^a
Enlisted Groundcrew	n	147		158		140		Overall		0.362	
	Number/%										
	Yes	1	0.7%	0	0.0%	0	0.0%	M vs. L	__ ^a	0.964	
	No	146	99.3%	158	100.0%	140	100.0%	H vs. L	__ ^a	0.999	
Wheezes	Officer	n	130		124		125		Overall		0.368
		Number/%									
		Yes	4	3.1%	4	3.2%	1	0.8%	M vs. L	1.05 (0.26,4.29)	0.999
		No	126	96.9%	120	96.8%	124	99.2%	H vs. L	0.25 (0.03,2.31)	0.396
	Enlisted Flyer	n	55		63		53		Overall		0.498
		Number/%									
		Yes	3	5.5%	4	6.3%	1	1.9%	M vs. L	1.18 (0.25,5.50)	0.999
		No	52	94.5%	59	93.7%	52	98.1%	H vs. L	0.33 (0.03,3.31)	0.646
Enlisted Groundcrew	n	147		158		140		Overall		0.855	
	Number/%										
	Yes	4	2.7%	4	2.5%	5	3.6%	M vs. L	0.93 (0.23,3.78)	0.999	
	No	143	97.3%	154	97.5%	135	96.4%	H vs. L	1.32 (0.35,5.04)	0.940	

TABLE 20-9. (continued)

Unadjusted Exposure Index for Pulmonary Variables by Occupation

Variable	Occupation	Statistic	Exposure Index						Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value	
			Low		Medium		High					
Rales	Officer	n	130		124		125		Overall		0.383	
		Number/%										
		Yes	2	1.5%	1	0.8%	0	0.0%	M vs. L	0.52 (0.05,5.81)	0.999	
		No	128	98.5%	123	99.2%	125	100.0%	H vs. L	— ^a	0.518	
		Enlisted Flyer	n	55		63		53		Overall		0.815
			Number/%									
	Yes		3	5.5%	2	3.2%	2	3.8%	M vs. L	0.57 (0.09,3.53)	0.872	
		No	52	94.5%	61	96.8%	51	96.2%	H vs. L	0.68 (0.11,4.24)	0.999	
		Enlisted Groundcrew	n	147		158		140		Overall		0.724
			Number/%									
	Yes		1	0.7%	1	0.6%	2	1.4%	M vs. L	0.93 (0.06,15.00)	0.999	
		No	146	99.3%	157	99.4%	138	98.6%	H vs. L	2.12 (0.19,23.60)	0.964	
X-Ray Interpretation		n	130		124		124		Overall		0.489	
		Number/%										
	Abnormal	6	4.6%	4	3.2%	8	6.5%	M vs. L	0.69 (0.19,2.50)	0.808		
	Normal	124	95.4%	120	96.8%	116	93.5%	H vs. L	1.43 (0.48,4.23)	0.714		
	Enlisted Flyer	n	55		63		53		Overall		0.294	
		Number/%										
Abnormal		2	3.6%	6	9.5%	2	3.8%	M vs. L	2.79 (0.54,14.43)	0.370		
	Normal	53	96.4%	57	90.5%	51	96.2%	H vs. L	1.04 (0.14,7.66)	0.999		
	Enlisted Groundcrew	n	146		157		139		Overall		0.811	
		Number/%										
Abnormal		7	4.8%	8	5.1%	5	3.6%	M vs. L	1.07 (0.38,3.02)	0.999		
	Normal	139	95.2%	149	94.9%	134	96.4%	H vs. L	0.74 (0.23,2.39)	0.838		

TABLE 20-9. (continued)

Unadjusted Exposure Index for Pulmonary Variables by Occupation

Variable	Occupation	Statistic	Exposure Index			Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
			Low	Medium	High			
FVC	Officer	n	129	124	125	Overall		0.647
		Mean	99.0	97.4	98.3	M vs. L	--	0.366
		95% C.I.	(96.4, 101.6)	(95.1, 99.8)	(96.1, 100.6)	H vs. L	--	0.690
	Enlisted Flyer	n	54	63	53	Overall		0.241
		Mean	98.8	95.1	95.5	M vs. L	--	0.115
		95% C.I.	(95.1, 102.5)	(92.4, 97.9)	(92.0, 99.0)	H vs. L	--	0.205
	Enlisted Groundcrew	n	147	158	140	Overall		0.629
		Mean	94.7	95.8	94.5	M vs. L	--	0.466
		95% C.I.	(92.7, 96.7)	(93.6, 98.0)	(92.4, 96.5)	H vs. L	--	0.874
FEV ₁	Officer	n	129	124	125	Overall		0.340
		Mean	99.9	97.1	99.5	M vs. L	--	0.183
		95% C.I.	(96.8, 103.1)	(94.5, 99.8)	(96.9, 102.1)	H vs. L	--	0.815
	Enlisted Flyer	n	54	63	53	Overall		0.832
		Mean	94.1	94.7	96.0	M vs. L	--	0.826
		95% C.I.	(89.0, 99.1)	(91.1, 98.4)	(91.8, 100.1)	H vs. L	--	0.572
	Enlisted Groundcrew	n	147	158	140	Overall		0.174
		Mean	97.7	97.8	94.8	M vs. L	--	0.961
		95% C.I.	(95.3, 100.2)	(95.3, 100.4)	(92.2, 97.3)	H vs. L	--	0.103

TABLE 20-9. (continued)

Unadjusted Exposure Index for Pulmonary Variables by Occupation

Variable	Occupation	Statistic	Exposure Index			Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
			Low	Medium	High			
FEV ₂	Officer	n	129	124	125	Overall		0.453
		Mean	98.1	95.8	97.6	M vs. L	--	0.247
		95% C.I.	(95.2,101.0)	(93.4,98.3)	(95.2,99.9)	H vs. L	--	0.784
	Enlisted Flyer	n	54	63	53	Overall		0.974
		Mean	94.1	93.6	94.2	M vs. L	--	0.849
		95% C.I.	(89.9,98.4)	(90.4,96.8)	(90.3,98.0)	H vs. L	--	0.994
	Enlisted Groundcrew	n	147	158	140	Overall		0.339
		Mean	94.9	95.4	93.1	M vs. L	--	0.780
		95% C.I.	(92.7,97.1)	(93.0,97.8)	(90.8,95.3)	H vs. L	--	0.249
FEV ₃	Officer	n	129	124	125	Overall		0.540
		Mean	97.9	95.9	97.2	M vs. L	--	0.296
		95% C.I.	(95.0,100.7)	(93.5,98.3)	(95.0,99.5)	H vs. L	--	0.730
	Enlisted Flyer	n	54	63	53	Overall		0.863
		Mean	95.1	93.7	94.1	M vs. L	--	0.597
		95% C.I.	(91.1,99.0)	(90.7,96.8)	(90.4,97.8)	H vs. L	--	0.723
	Enlisted Groundcrew	n	147	158	140	Overall		0.427
		Mean	94.5	95.2	93.2	M vs. L	--	0.641
		95% C.I.	(92.3,96.6)	(92.9,97.5)	(91.0,95.3)	H vs. L	--	0.396

TABLE 20-9. (continued)

Unadjusted Exposure Index for Pulmonary Variables by Occupation

Variable	Occupation	Statistic	Exposure Index			Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
			Low	Medium	High			
FEF _{max}	Officer	n	129	124	125	Overall		0.781
		Mean	141.2	140.1	142.3	M vs. L	--	0.724
		95% C.I.	(137.0, 145.4)	(135.6, 144.6)	(138.3, 146.3)	H vs. L	--	0.723
	Enlisted Flyer	n	54	63	53	Overall		0.134
		Mean	128.3	136.7	137.5	M vs. L	--	0.113
		95% C.I.	(120.2, 136.5)	(130.2, 143.2)	(131.7, 143.4)	H vs. L	--	0.076
	Enlisted Groundcrew	n	147	158	140	Overall		0.164
		Mean	136.1	133.5	130.7	M vs. L	--	0.325
		95% C.I.	(132.2, 140.0)	(129.9, 137.0)	(126.6, 134.9)	H vs. L	--	0.064
Ratio of Observed FEV ₁ to Observed FVC	Officer	n	129	124	125	Overall		0.226
		Mean ^b	0.810	0.799	0.812	M vs. L	--	0.176
		95% C.I. ^b	(0.799, 0.821)	(0.788, 0.810)	(0.801, 0.823)	H vs. L	--	0.780
	Enlisted Flyer	n	54	63	53	Overall		0.037
		Mean ^b	0.772	0.805	0.810	M vs. L	--	0.043
		95% C.I. ^b	(0.746, 0.796)	(0.784, 0.824)	(0.791, 0.827)	H vs. L	--	0.016
	Enlisted Groundcrew	n	147	158	140	Overall		0.047
		Mean ^b	0.831	0.828	0.813	M vs. L	--	0.654
		95% C.I. ^b	(0.822, 0.839)	(0.818, 0.837)	(0.801, 0.825)	H vs. L	--	0.020

TABLE 20-9. (continued)

Unadjusted Exposure Index for Pulmonary Variables by Occupation

Variable	Occupation	Statistic	Exposure Index						Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
			Low		Medium		High				
Loss of Vital Capacity	Officer	n	129		124		125		Overall		0.147
		Number/%									
		None	117	90.7%	110	88.7%	115	92.0%	M vs. L ^c	1.82 (0.69,4.80)	0.322
		Mild	7	5.4%	12	9.7%	10	8.0%	H vs. L ^c	1.45 (0.54,3.95)	0.628
		Mod./Sev.	5	3.9%	2	1.6%	0	0.0%	M vs. L ^d	0.43 (0.08,2.24)	0.520
									H vs. L ^d	— ^a	0.069
	Enlisted Flyer	n	54		63		53		Overall		0.582
		Number/%									
		None	50	92.6%	57	90.5%	48	90.6%	M vs. L ^c	1.75 (0.42,7.38)	0.678
		Mild	3	5.6%	6	9.5%	5	9.4%	H vs. L ^c	1.74 (0.39,7.67)	0.716
		Mod./Sev.	1	1.9%	0	0.0%	0	0.0%	M vs. L ^d	— ^a	0.944
									H vs. L ^d	— ^a	0.999
	Enlisted Groundcrew	n	147		158		140		Overall		0.590
		Number/%									
		None	129	87.8%	138	87.3%	123	87.9%	M vs. L ^c	0.87 (0.39,1.92)	0.882
		Mild	14	9.5%	13	8.2%	15	10.7%	H vs. L ^c	1.12 (0.52,2.43)	0.918
		Mod./Sev.	4	2.7%	7	4.4%	2	1.4%	M vs. L ^d	1.64 (0.47,5.72)	0.644
									H vs. L ^d	0.52 (0.09,2.92)	0.744

TABLE 20-9. (continued)

Unadjusted Exposure Index for Pulmonary Variables by Occupation

Variable	Occupation	Statistic	Exposure Index						Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
			Low		Medium		High				
Obstructive Abnormality	Officer	n	129		124		125		Overall		0.109
		Number/%									
		None	96	74.4%	76	61.3%	82	65.6%	M vs. L ^c	2.09 (1.18,3.70)	0.016
		Mild	26	20.2%	43	34.7%	39	31.2%	H vs. L ^c	1.76 (0.99,3.13)	0.075
		Mod./Sev.	7	5.4%	5	4.0%	4	3.2%	M vs. L ^d	0.90 (0.28,2.96)	0.999
									H vs. L ^d	0.67 (0.19,2.37)	0.760
	Enlisted Flyer	n	54		63		53		Overall		0.265
		Number/%									
		None	25	46.3%	40	63.5%	34	64.2%	M vs. L ^c	0.46 (0.21,1.03)	0.089
		Mild	23	42.6%	17	27.0%	16	30.2%	H vs. L ^c	0.51 (0.23,1.16)	0.160
		Mod./Sev.	6	11.1%	6	9.5%	3	5.7%	M vs. L ^d	0.63 (0.18,2.15)	0.660
									H vs. L ^d	0.37 (0.08,1.61)	0.316
	Enlisted Groundcrew	n	147		158		140		Overall		0.096
		Number/%									
		None	117	79.6%	126	79.4%	95	67.9%	M vs. L ^c	1.00 (0.55,1.80)	0.999
		Mild	26	17.7%	28	17.7%	37	26.4%	H vs. L ^c	1.75 (0.99,3.10)	0.072
		Mod./Sev.	4	2.7%	4	2.5%	8	5.7%	M vs. L ^d	0.93 (0.23,3.80)	0.999
									H vs. L ^d	2.46 (0.72,8.43)	0.238

—^aEstimated relative risk/confidence interval/p-value not given due to cells with zero frequency.

—Estimated relative risk not applicable for continuous analysis of a variable.

^bTransformed from natural logarithm (1-X) scale.

^cMild contrasted with none.

^dModerate/severe contrasted with none.

TABLE 20-10.

Adjusted Exposure Index for Pulmonary Variables by Occupation

Variable	Occupation	Statistic	Exposure Index			Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value
			Low	Medium	High			
Asthma	Officer	n	130	124	125	Overall		0.088
						M vs. L	0.35 (0.11,1.13)	0.079
						H vs. L	0.35 (0.11,1.14)	0.082
	Enlisted Flyer	n	55	63	53	Overall		0.788
						M vs. L	1.85 (0.31,11.14)	0.501
						H vs. L	1.38 (0.21,8.85)	0.736
	Enlisted Groundcrew	n	147	158	140	Overall		0.326
						M vs. L	2.07 (0.75,5.71)	0.162
						H vs. L	1.82 (0.63,5.21)	0.267
Bronchitis	Officer	n	130	123	125	Overall		0.609
						M vs. L	0.73 (0.39,1.37)	0.327
						H vs. L	0.90 (0.49,1.65)	0.732
	Enlisted Flyer	n	55	63	53	Overall		0.003
						M vs. L	0.18 (0.06,0.53)	0.002
						H vs. L	0.47 (0.19,1.17)	0.104
	Enlisted Groundcrew	n	147	158	140	Overall		0.662
						M vs. L	0.89 (0.48,1.67)	0.716
						H vs. L	1.18 (0.64,2.20)	0.594

TABLE 20-10. (continued)

Adjusted Exposure Index for Pulmonary Variables by Occupation

Variable	Occupation	Statistic	Exposure Index			Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value
			Low	Medium	High			
Pleurisy	Officer	n	130	124	124	Overall		0.121
						M vs. L	1.20 (0.45,3.23)	0.714
						H vs. L	0.35 (0.09,1.37)	0.131
	Enlisted Flyer	n	55	63	53	Overall		0.822
						M vs. L	0.97 (0.18,5.10)	0.973
						H vs. L	1.52 (0.31,7.41)	0.601
	Enlisted Groundcrew	n	146	158	140	Overall		0.340**
						M vs. L	0.64 (0.26,1.58)**	0.338**
						H vs. L	0.50 (0.19,1.32)**	0.163**
Pneumonia	Officer	n	130	124	125	Overall		0.563**
						M vs. L	0.83 (0.44,1.56)**	0.567**
						H vs. L	1.16 (0.64,2.11)**	0.630**
	Enlisted Flyer	n	55	63	53	Overall		0.429**
						M vs. L	1.06 (0.44,2.59)**	0.893**
						H vs. L	1.70 (0.70,4.12)**	0.240**
	Enlisted Groundcrew	n	147	158	140	Overall		0.468
						M vs. L	0.72 (0.41,1.27)	0.256
						H vs. L	0.75 (0.42,1.34)	0.333

TABLE 20-10. (continued)

Adjusted Exposure Index for Pulmonary Variables by Occupation

Variable	Occupation	Statistic	Exposure Index			Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value
			Low	Medium	High			
Thorax and Lung Abnormalities	Officer	n	130	124	125	Overall		0.067
						M vs. L	0.73 (0.25,2.19)	0.578
						H vs. L	0.20 (0.04,0.93)	0.040
	Enlisted Flyer	n	55	63	53	Overall		0.725
						M vs. L	0.77 (0.27,2.19)	0.619
						H vs. L	0.63 (0.20,2.00)	0.434
	Enlisted Groundcrew	n	147	158	140	Overall		0.602
						M vs. L	1.55 (0.54,4.42)	0.417
						H vs. L	1.58 (0.59,4.26)	0.361
Hyper-resonance	Officer	n	130	124	125	Overall		0.139**
						M vs. L	0.33 (0.05,2.20)**	0.254**
						H vs. L	0.10 (0.01,1.60)**	0.104**
	Enlisted Flyer	n	55	63	53	Overall		0.530
						M vs. L	0.49 (0.13,1.93)	0.310
						H vs. L	0.96 (0.26,3.57)	0.956
	Enlisted Groundcrew	n	147	158	140	Overall		0.828**
						M vs. L	0.75 (0.17,3.35)**	0.707**
						H vs. L	1.17 (0.34,4.00)**	0.799**

TABLE 20-10. (continued)

Adjusted Exposure Index for Pulmonary Variables by Occupation

Variable	Occupation	Statistic	Exposure Index			Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value
			Low	Medium	High			
Wheezes	Officer	n	130	124	125	Overall		0.104
						M vs. L	0.93 (0.21,4.20)	0.928
						H vs. L	0.10 (0.01,1.71)	0.111
	Enlisted Flyer	n	55	63	53	Overall		0.613
						M vs. L	1.26 (0.25,6.40)	0.783
						H vs. L	0.44 (0.04,4.66)	0.492
	Enlisted Groundcrew	n	147	158	140	Overall		0.733**
						M vs. L	1.80 (0.37,8.74)**	0.467**
						H vs. L	1.58 (0.36,6.88)**	0.546**
Rales	Officer	n	130	124	125	Overall		0.237
						M vs. L	0.44 (0.04,5.15)	0.511
						H vs. L	---	---
	Enlisted Flyer	n	55	63	53	Overall		0.865
						M vs. L	0.71 (0.10,5.24)	0.734
						H vs. L	0.58 (0.08,4.40)	0.603
	Enlisted Groundcrew	n	147	158	140	Overall		0.979
						M vs. L	1.35 (0.06,29.41)	0.849
						H vs. L	1.27 (0.08,19.11)	0.865

TABLE 20-10. (continued)

Adjusted Exposure Index for Pulmonary Variables by Occupation

Variable	Occupation	Statistic	Exposure Index			Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value
			Low	Medium	High			
X-Ray Interpretation	Officer	n	130	124	124	Overall		0.395
						M vs. L	0.51 (0.13,1.98)	0.329
						H vs. L	1.17 (0.38,3.61)	0.783
	Enlisted Flyer	n	55	63	53	Overall		0.309
						M vs. L	3.09 (0.53,18.11)	0.211
						H vs. L	1.11 (0.13,9.31)	0.920
	Enlisted Groundcrew	n	146	157	139	Overall		0.687
						M vs. L	1.21 (0.41,3.56)	0.724
						H vs. L	0.73 (0.22,2.41)	0.606
FVC	Officer	n	129	124	125	Overall		0.884
		Adj. Mean	91.0	90.8	91.6	M vs. L	--	0.902
		95% C.I.	(85.7,96.3)	(85.6,96.0)	(86.3,96.9)	H vs. L	--	0.725
	Enlisted Flyer	n	54	63	53	Overall		0.258
		Adj. Mean	93.6	90.4	90.1	M vs. L	--	0.157
		95% C.I.	(88.3,98.9)	(85.5,95.2)	(85.0,95.3)	H vs. L	--	0.147
	Enlisted Groundcrew	n	147	158	140	Overall		0.998**
		Adj. Mean**	90.4	90.3	90.3	M vs. L	--	0.960**
		95% C.I.**	(87.9,92.9)	(87.8,92.8)	(87.7,92.9)	H vs. L	--	0.951**

TABLE 20-10. (continued)

Adjusted Exposure Index for Pulmonary Variables by Occupation

Variable	Occupation	Statistic	Exposure Index			Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value
			Low	Medium	High			
FEV ₁	Officer	n	129	124	125	Overall		0.464
		Adj. Mean	92.4	91.4	93.7	M vs. L	--	0.595
		95% C.I.	(86.4, 98.4)	(85.5, 97.2)	(87.7, 99.6)	H vs. L	--	0.485
	Enlisted Flyer	n	54	63	53	Overall		0.925
		Adj. Mean	88.7	89.1	89.8	M vs. L	--	0.885
		95% C.I.	(82.0, 95.3)	(83.0, 95.1)	(83.4, 96.3)	H vs. L	--	0.697
	Enlisted Groundcrew	n	147	158	140	Overall		0.322**
		Adj. Mean**	94.1	92.4	91.5	M vs. L	--	0.319**
		95% C.I.**	(91.1, 97.0)	(89.4, 95.4)	(88.4, 94.6)	H vs. L	--	0.141**
FEV ₂	Officer	n	129	124	125	Overall		0.622
		Adj. Mean	89.8	89.3	90.9	M vs. L	--	0.747
		95% C.I.	(84.3, 95.4)	(83.9, 94.7)	(85.5, 96.4)	H vs. L	--	0.528
	Enlisted Flyer	n	54	63	53	Overall		0.974
		Adj. Mean	88.5	88.0	88.0	M vs. L	--	0.844
		95% C.I.	(82.7, 94.3)	(82.7, 93.3)	(82.3, 93.6)	H vs. L	--	0.840
	Enlisted Groundcrew	n	147	158	140	Overall		0.595**
		Adj. Mean**	90.9	89.9	89.4	M vs. L	--	0.499**
		95% C.I.**	(88.2, 93.6)	(87.2, 92.6)	(86.6, 92.2)	H vs. L	--	0.319**

TABLE 20-10. (continued)

Adjusted Exposure Index for Pulmonary Variables by Occupation

Variable	Occupation	Statistic	Exposure Index			Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value
			Low	Medium	High			
FEV ₃	Officer	n	129	124	125	Overall		0.745
		Adj. Mean	89.2	89.0	90.2	M vs. L	--	0.903
		95% C.I.	(83.9,94.6)	(83.8,94.3)	(84.9,95.5)	H vs. L	--	0.554
	Enlisted Flyer	n	54	63	53	Overall		0.827
		Adj. Mean	89.5	88.3	88.1	M vs. L	--	0.619
		95% C.I.	(83.9,95.0)	(83.3,93.3)	(82.7,93.4)	H vs. L	--	0.571
	Enlisted Groundcrew	n	147	158	140	Overall		0.778**
		Adj. Mean**	90.4	89.7	89.3	M vs. L	--	0.630**
		95% C.I.**	(87.7,93.0)	(87.0,92.3)	(86.6,92.1)	H vs. L	--	0.491**
FEF _{max}	Officer	n	129	124	125	Overall		0.637**
		Adj. Mean**	136.4	136.4	138.8	M vs. L	--	0.982**
		95% C.I.**	(126.9, 145.9)	(127.1, 145.7)	(129.4, 148.3)	H vs. L	--	0.406**
	Enlisted Flyer	n	54	63	53	Overall		0.238
		Adj. Mean	129.9	136.4	137.2	M vs. L	--	0.155
		95% C.I.	(119.2, 140.6)	(126.7, 146.2)	(126.8, 147.6)	H vs. L	--	0.128
	Enlisted Groundcrew	n	147	158	140	Overall		0.164**
		Adj. Mean**	138.0	133.8	133.4	M vs. L	--	0.116**
		95% C.I.**	(133.3, 142.7)	(129.1, 138.6)	(128.5, 138.3)	H vs. L	--	0.088**

TABLE 20-10. (continued)

Adjusted Exposure Index for Pulmonary Variables by Occupation

Variable	Occupation	Statistic	Exposure Index			Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value
			Low	Medium	High			
Ratio of Observed FEV ₁ to Observed FVC	Officer	n	129	124	125	Overall		0.203
		Adj. Mean ^b	0.818	0.812	0.825	M vs. L	--	0.445
		95% C.I. ^b	(0.793, 0.840)	(0.787, 0.834)	(0.802, 0.846)	H vs. L	--	0.313
	Enlisted Flyer	n	54	63	53	Overall		0.071
		Adj. Mean ^b	0.774	0.800	0.807	M vs. L	--	0.078
		95% C.I. ^b	(0.734, 0.807)	(0.768, 0.827)	(0.774, 0.835)	H vs. L	--	0.030
	Enlisted Groundcrew	n	147	158	140	Overall		0.113
		Adj. Mean ^b	0.838	0.830	0.824	M vs. L	--	0.208
		95% C.I. ^b	(0.827, 0.849)	(0.818, 0.841)	(0.811, 0.836)	H vs. L	--	0.038

TABLE 20-10. (continued)

Adjusted Exposure Index for Pulmonary Variables by Occupation

Variable	Occupation	Statistic	Exposure Index			Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value
			Low	Medium	High			
Loss of Vital Capacity	Officer	n	130	124	124	Overall		0.272
						M vs. L ^c	1.41 (0.56, 3.57)	0.465
						H vs. L ^c	1.04 (0.40, 2.69)	0.943
						M vs. L ^d	0.45 (0.12, 1.73)	0.244
						H vs. L ^d	-- ^a	-- ^a
	Enlisted Flyer	n	55	63	53	Overall		0.895
						M vs. L ^c	1.26 (0.36, 4.43)	0.716
						H vs. L ^c	1.33 (0.37, 4.82)	0.663
						M vs. L ^d	0.41 (0.05, 3.20)	0.392
						H vs. L ^d	-- ^a	-- ^a
	Enlisted Groundcrew	n	146	157	139	Overall		0.406
						M vs. L ^c	1.11 (0.51, 2.41)	0.800
						H vs. L ^c	1.12 (0.53, 2.38)	0.764
						M vs. L ^d	2.19 (0.70, 6.90)	0.181
						H vs. L ^d	0.65 (0.17, 2.55)	0.541

TABLE 20-10. (continued)

Adjusted Exposure Index for Pulmonary Variables by Occupation

Variable	Occupation	Statistic	Exposure Index			Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value
			Low	Medium	High			
Obstructive Abnormality	Officer	n	130	124	124	Overall		0.341
						M vs. L ^c	1.71 (0.94, 3.13)	0.080
						H vs. L ^c	1.34 (0.73, 2.47)	0.342
						M vs. L ^d	0.72 (0.24, 2.18)	0.566
						H vs. L ^d	0.61 (0.19, 1.89)	0.388
	Enlisted Flyer	n	55	63	53	Overall		0.274
						M vs. L ^c	0.45 (0.20, 1.01)	0.054
						H vs. L ^c	0.53 (0.23, 1.19)	0.124
						M vs. L ^d	0.61 (0.19, 1.91)	0.397
						H vs. L ^d	0.42 (0.12, 1.52)	0.186
	Enlisted Groundcrew	n	146	157	139	Overall		0.378
						M vs. L ^c	1.23 (0.67, 2.26)	0.503
						H vs. L ^c	1.67 (0.93, 2.99)	0.085
						M vs. L ^d	1.78 (0.50, 6.28)	0.372
						H vs. L ^d	2.11 (0.69, 6.50)	0.192

**Group-by-covariate interaction ($0.01 < p < 0.05$)--mean, confidence interval, and p-value derived from a model fitted after deletion of this interaction.

--^aAdjusted relative risk/confidence interval/p-value not given due to a cell with zero frequency.

--Adjusted relative risk not applicable for continuous analysis of a variable.

^bTransformed from natural logarithm (1-X) scale.

^cMild contrasted with none.

^dModerate/severe contrasted with none.

TABLE 20-11.

**Summary of Exposure Index-by-Covariate Interactions
From Adjusted Analyses for Pulmonary Variables***

Variable	Occupation	Covariate	p-Value
Pleurisy	Enlisted Groundcrew	Current Cigarette Smoking	0.031
		Lifetime Cigarette Smoking History	0.045
Pneumonia	Officer	Lifetime Cigarette Smoking History	0.048
Pneumonia	Enlisted Flyer	Race	0.017
Hyperresonance	Officer	Lifetime Cigarette Smoking History	0.028
Hyperresonance	Enlisted Groundcrew	Age	0.033
Wheezes	Enlisted Groundcrew	Age	0.014
FVC	Enlisted Groundcrew	Lifetime Cigarette Smoking History	0.012
FEV ₁	Enlisted Groundcrew	Lifetime Cigarette Smoking History	0.038
FEV ₂	Enlisted Groundcrew	Lifetime Cigarette Smoking History	0.022
FEV ₃	Enlisted Groundcrew	Lifetime Cigarette Smoking History	0.019
FEFmax	Officer	Lifetime Cigarette Smoking History	0.049
PEFmax	Enlisted Groundcrew	Race	0.016

*Refer to Table Q-3 for a further investigation of these interactions.

Bronchitis

The unadjusted analyses of bronchitis revealed no significant differences among the exposure categories for officers and enlisted groundcrew. These results were supported by the adjusted analyses.

Based on the unadjusted analysis, a significant difference was detected for the enlisted flyers ($p=0.003$). For the enlisted flyer cohort, 32.7 percent of the low exposure category reported having had bronchitis, as contrasted with 7.9 percent and 18.9 percent of the medium and high exposure categories, respectively. The medium versus low contrast was significant (Est. RR: 0.18, 95% C.I.: [0.06,0.52], $p=0.001$). The same pattern was found in the adjusted analysis. The overall test for enlisted flyers was significant in the adjusted analysis ($p=0.003$). Based on the adjusted analysis of the contrasts, the Ranch Hands in the medium exposure category were significantly different than those in the low exposure category for bronchitis (Adj. RR: 0.18, 95% C.I.: [0.06,0.53], $p=0.001$). These results are opposite of an expected herbicide effect and do not support a dose-response relationship.

Pleurisy

There were no significant differences detected in the unadjusted exposure index analyses of pleurisy. These results were supported by the adjusted analyses for the officer and enlisted flyer cohorts.

In the enlisted groundcrew cohort, the interactions involving exposure index were significant for current cigarette smoking and lifetime cigarette smoking history ($p=0.031$ and $p=0.045$, respectively). When the interactions were investigated by stratifying by current and lifetime cigarette smoking, there were sparse numbers of participants reporting an occurrence of pleurisy in many of the strata. The overall test for the former smokers who were classified as moderate lifetime smokers was borderline significant ($p=0.063$). Of the enlisted groundcrew in this stratum, 17.6 percent of those in the low exposure category reported having had pleurisy, as contrasted to 0.0 percent and 5.3 percent in the medium and high exposure categories, respectively. The medium versus low and high versus low contrasts were not significant. There were no significant differences in the enlisted groundcrew cohort in the adjusted analysis without the interactions involving exposure index in the model.

Pneumonia

No significant differences in the occurrence of pneumonia among the exposure categories were identified in the unadjusted analyses. In the adjusted analysis of the officer cohort, there was a significant exposure index-by-lifetime cigarette smoking history interaction ($p=0.048$). After stratifying by lifetime cigarette smoking, there were no significant differences identified. For the enlisted flyer cohort, there was a

significant exposure index-by-race interaction ($p=0.017$). No significant differences were identified for nonblacks. One Black enlisted flyer in the low exposure category reported an occurrence of pneumonia ($p=0.018$). No other participants in this category reported pneumonia. The medium versus low and high versus low exposure contrasts for the Black enlisted flyers were not significant. Without the significant interactions in the models, no differences were detected for either the officer or enlisted flyer cohorts. There were also no significant differences found in the enlisted groundcrew cohort based on the adjusted analyses.

Tuberculosis

Based on the unadjusted analyses, there were no significant differences found for tuberculosis. Due to the low number of Ranch Hands who reported having had tuberculosis, adjusted exposure index analyses were not conducted.

Physical Examination Variables

Thorax and Lung Abnormalities

The unadjusted exposure index analyses of thorax and lung abnormalities did not reveal any significant differences. The adjusted analyses supported this finding for the enlisted flyer and enlisted groundcrew cohorts. For the officer cohort, the overall result of the adjusted analysis was borderline significant ($p=0.067$). For the officers, the percentage of abnormalities was 6.9, 5.6, and 2.4 for the low, medium, and high exposure categories, respectively. In the adjusted analysis, the high versus low contrast was significant (Adj. RR: 0.20, 95% C.I.: [0.04, 0.93], $p=0.040$). Since the percentage of abnormalities decreased as exposure increased, the results do not suggest a dose-response relationship.

Asymmetric Expansion

There were no Ranch Hands with an asymmetric expansion. Thus, no exposure index analyses for this variable were performed.

Hyperresonance

No significant differences were detected in the unadjusted analyses of hyperresonance. Based on the adjusted analyses, there were no differences found for the enlisted flyer cohort. In the officer cohort, there was a significant exposure index-by-lifetime cigarette smoking history interaction ($p=0.028$); stratifying by the lifetime cigarette smoking history categories revealed no significant differences. The exposure index-by-age interaction was significant in the adjusted analysis of the enlisted groundcrew cohort ($p=0.033$); however, no differences were found after stratifying by age. Without the significant interactions in the models, there were no significant differences detected for either the officer or enlisted groundcrew cohorts.

Dullness

Only two Ranch Hands had dullness on examination of the lungs: one enlisted flyer in the medium exposure category and one enlisted groundcrew in the low exposure category. No significant differences were identified in unadjusted analyses. Due to the small number of occurrences of dullness, no adjusted analyses were performed on this variable.

Wheezes

In the unadjusted analyses, there were no significant differences detected. This finding was supported by the results of the adjusted analyses for the officer and enlisted flyer cohorts. For the enlisted groundcrew cohort, there was a significant exposure index-by-age interaction ($p=0.014$). No significant differences were identified after stratifying by age. Without the interaction in the adjusted model, no difference among the exposure categories was revealed.

Rales

In the unadjusted and adjusted exposure index analyses of rales, no significant differences were identified.

X-Ray Interpretation

The results of the unadjusted and adjusted analyses of x-ray abnormalities did not reveal any significant differences.

Laboratory Examination Variables

FVC

There was no evidence of a significant dose-response relationship based on the unadjusted analyses of FVC. The results of the adjusted analyses were consistent with the unadjusted results for the officer and enlisted flyer cohorts.

For the enlisted groundcrew, there was a significant exposure index-by-lifetime cigarette smoking history interaction ($p=0.012$). After stratifying by lifetime cigarette smoking history, one contrast, medium versus low, was borderline significant for nonsmokers ($p=0.084$). The adjusted mean of the nonsmokers in the medium exposure category within the enlisted groundcrew cohort was 88.6 percent, as contrasted to an adjusted mean of 93.5 percent for the low exposure category; the adjusted mean of the high exposure category was 90.1 percent. No significant difference was detected in the enlisted groundcrew cohort based on an analysis without the exposure index-by-lifetime cigarette smoking history interaction.

FEV₁

No significant dose-response relationship for FEV₁ was detected in the unadjusted exposure index analyses. This finding was supported by the adjusted results for the officer and enlisted flyer cohorts.

In the enlisted groundcrew cohort there was a significant exposure index-by-lifetime cigarette smoking history interaction ($p=0.038$). Stratifying by this covariate identified one borderline significant contrast: high versus low exposure for the moderate lifetime smokers ($p=0.079$). The adjusted mean of the high exposure category within that stratum was 89.1 percent, as contrasted to an adjusted mean of 94.8 percent for the low exposure category. The adjusted mean of the medium exposure category for the same stratum was 92.4 percent. Without the exposure index-by-covariate interaction, no significant difference was detected.

FEV₂

The unadjusted analyses of FEV₂ failed to detect any significant dose-response relationships. Similarly, in the adjusted analyses, no significant differences were found for the officer and enlisted flyer cohorts. In the enlisted groundcrew cohort, there was a significant interaction involving exposure index for lifetime cigarette smoking history ($p=0.022$). Investigation of the interaction by stratifying did not reveal any significant contrasts. Without the exposure index-by-covariate interaction in the model, no difference within the enlisted groundcrew cohort was found.

FEV₃

For the three occupational cohorts, no significant dose-response relationships were identified in the unadjusted analyses of FEV₃. The adjusted analyses also did not reveal any significant differences for the officer and enlisted flyer cohorts.

Within the enlisted groundcrew cohort, the exposure index-by-lifetime cigarette smoking history interaction was significant ($p=0.019$). As with FEV₁ and FEV₂, FEV₃ adjusted means decreased as exposure increased for the moderate lifetime smoker strata. Further investigation of the interaction by stratifying by the covariate did not identify any significant differences, however. Without the interaction in the model, no significant dose-response relationship was revealed.

FEFmax

For the officer cohort, no significant differences were detected in the unadjusted analyses of FEFmax. In the adjusted analyses, there was a significant exposure index-by-lifetime cigarette smoking history interaction ($p=0.049$). One borderline significant contrast, high versus low exposure within the heavy smokers, was found ($p=0.057$). The adjusted mean of the high exposure category was 139.9 percent, as contrasted to an adjusted mean of 130.8 percent for the low exposure category within the officers classified as

heavy lifetime cigarette smokers. This finding was opposite of an expected herbicide effect and did not support an increasing dose-response relationship. The corresponding adjusted mean for the medium exposure category was 129.4 percent. Without the interaction in the model, no significant difference was found.

In the unadjusted analyses of the enlisted flyer cohort, the high versus low exposure contrast was borderline significant ($p=0.076$). The means of the low, medium, and high exposure categories for the enlisted flyer cohort were 128.3 percent, 136.7 percent, and 137.5 percent, respectively. No significant differences were detected in the adjusted analyses of this cohort.

In the enlisted groundcrew cohort, the unadjusted analyses revealed a borderline difference between the high and low exposure categories (136.1% for low vs. 130.7% for high, $p=0.064$; 133.5% for medium). In the adjusted analyses, there was a significant exposure index-by-race interaction ($p=0.016$). Stratifying by race, the high versus low exposure contrasts were significant for both Blacks and nonblacks ($p=0.028$ and $p=0.012$, respectively). The medium versus low exposure contrasts for nonblack enlisted groundcrew were borderline significant ($p=0.066$). The adjusted means of the low, medium, and high exposure categories for Black enlisted groundcrew were 130.6 percent, 134.2 percent, and 149.9 percent, respectively. For the nonblack enlisted groundcrew, the adjusted means were 137.2 percent, 132.1 percent, and 130.0 percent for the low, medium, and high exposure categories, respectively. Without the significant interaction in the model, the high versus low exposure contrast was borderline significant (adjusted means: 138.0% for low, 133.8% for medium, and 133.4% for high; $p=0.088$).

Ratio of Observed FEV₁ to Observed FVC

In the unadjusted and adjusted exposure index analyses of the officer cohort, no significant dose-response relationship was identified for the ratio of observed FEV₁ to observed FVC.

The means of the enlisted flyer cohort for the low, medium, and high exposure categories were 0.772, 0.805, and 0.810, respectively. In the unadjusted analysis, the overall, medium versus low, and high versus low contrasts were significant ($p=0.037$, $p=0.043$, and $p=0.016$, respectively). In the adjusted analysis, the high versus low contrast was significant ($p=0.030$), and the overall and medium versus low contrasts were borderline significant ($p=0.071$ and $p=0.078$, respectively). The adjusted means for the low, medium, and high exposure categories were 0.774, 0.800, and 0.807, respectively.

For the enlisted groundcrew cohort, the unadjusted analysis revealed that the overall and the high versus low exposure contrasts were significant ($p=0.047$ and $p=0.020$, respectively). The means of the enlisted groundcrew cohort for the low, medium, and high exposure categories were 0.831, 0.828, and 0.813, respectively. Based on the adjusted analysis, the high versus low exposure contrast was significant ($p=0.038$). The adjusted means were 0.838, 0.830, and 0.824 for the low, medium, and high exposure categories, respectively.

Loss of Vital Capacity

In the exposure index analyses for loss of vital capacity, there are three exposure categories and three categories of loss of vital capacity (none, mild, and moderate/severe). Consequently, an overall assessment of these nine categories was made, as well as four individual contrasts for each occupational stratum. In particular, medium versus low and high versus low exposure contrasts were examined for both the mild versus none and the moderate/severe versus none loss of vital capacity categories.

In the high versus low exposure contrast for the officer cohort, a borderline significant difference was detected for the moderate/severe loss of vital capacity versus none contrast based on the unadjusted analysis ($p=0.069$). Five officers in the low exposure category had a moderate or severe loss of vital capacity, as compared to zero officers in the high exposure category with a moderate or severe loss of vital capacity. There were 117 officers with no loss of vital capacity in the low exposure category, as compared to 115 in the high exposure category.

Neither the unadjusted nor adjusted analyses revealed any significant differences among the exposure categories for enlisted flyers or enlisted groundcrew.

Obstructive Abnormality

As with loss of vital capacity, obstructive abnormality was also classified as none, mild, or moderate/severe. For the unadjusted exposure index analyses of the officer cohort, significant or borderline significant differences were found for both the medium versus low ($p=0.016$) and the high versus low ($p=0.075$) exposure contrasts for mild versus none obstructive abnormality. The estimated relative risk for the medium versus low contrast was 2.09 (95% C.I.: [1.18, 3.70]) and 1.76 for the high versus low contrast (95% C.I.: [0.99, 3.13]). The medium versus low contrast was borderline significant in the adjusted analysis (Adj. RR: 1.71, 95% C.I.: [0.94, 3.13], $p=0.080$).

In the unadjusted analysis of the medium versus low exposure contrast for the enlisted flyer cohort, a borderline significant difference was detected for the mild versus none obstructive abnormality contrast (Est. RR: 0.46, 95% C.I.: [0.21, 1.03], $p=0.089$). A borderline significant difference was also found in the adjusted analysis (Adj. RR: 0.45, 95% C.I.: [0.20, 1.01], $p=0.054$).

For the enlisted groundcrew cohort, a borderline significant difference was detected in the overall assessment based on the unadjusted analysis ($p=0.096$). In the high versus low exposure contrast, a borderline significant difference was found for the mild versus none obstructive abnormality contrast (Est. RR: 1.75, 95% C.I.: [0.99, 3.10], $p=0.072$). This contrast was also borderline significant based on the adjusted analysis (Adj. RR: 1.67, 95% C.I.: [0.93, 2.99], $p=0.085$). These results were suggestive of a dose-response relationship, although no other contrasts were significant.

TABLE 20-12.

Longitudinal Analysis of Ratio of Observed FEV₁ to Observed FVC:
A Contrast of 1982 Baseline and 1987 Followup Examination Means

Examination	Group Means*		p-Value (Equality of Differences)
	Ranch Hand	Comparison	
1982 Baseline	0.813	0.815	0.789
1987 Followup	0.814	0.815	

*Means transformed from the natural logarithm (1-X) scale; hypothesis test performed on the natural logarithm (1-X) scale.

Note: Summary statistics for the 1982 Baseline and the 1987 followup are based on 942 Ranch Hands and 1,110 Comparisons who participated in the 1982 Baseline and the 1987 followup examinations. Two Comparisons were excluded from the analysis due to ratios greater than 1.0 at the 1982 Baseline examination.

Longitudinal Analysis

The ratio of observed FEV₁ to observed FVC was investigated for the longitudinal analysis of the pulmonary function. Results, summarized in Table 20-12, showed that the group difference did not change significantly between the 1982 Baseline and the 1987 followup examination (p=0.789).

Mortality Data

Based on the 31 December 1987 mortality data, there were 22 deaths (0.05/1,000 person-years) from respiratory conditions in the Comparison group and none in the Ranch Hand group. There were 1,261 Ranch Hands and 19,101 Comparisons in this mortality analysis.

DISCUSSION

While the presence of pulmonary disease is often evident based on a careful history and physical examination, definitive diagnosis usually requires the collection of data from a number of other sources. The standard radiographic examination of the chest and pulmonary function studies are routinely ordered and were included as variables in the Air Force Health Study examination. In addition, because the lung is often involved secondarily in numerous infectious, inflammatory, and neoplastic disorders, the assessment of pulmonary disease should include the type of comprehensive multisystem review conducted in this examination cycle 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 frequently misinterpreted 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. A positive purified protein derivative skin test, indicative of subclinical tuberculous infection, may be erroneously interpreted and reported as prior active infection. "Pneumonia" and "pneumonitis" are often confused by patients in relating the medical history.

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

In view of the limitations of the history and physical examination noted above, added emphasis is placed on screening laboratory data in the diagnosis of respiratory disease. The chest x ray, when normal, is highly reliable in excluding pulmonary parenchymal disease, though several exceptions must be recognized. Solitary lesions less than 6 millimeters, miliary granulomatous infection, and early interstitial disease, among others, may be present but not detectable radiographically. On the other hand, the chest x ray may reveal an early occult malignancy in an asymptomatic patient and thus afford an opportunity for cure.

Spirometry has been used as a clinical tool to measure static lung volumes and to detect respiratory disease for over a century. Dynamic indices, relating changes in lung volume to time, were first developed over 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, with proper coaching, to eliciting the full cooperation of the patient. In any longitudinal study emphasis must be placed on the use of identical techniques to ensure comparability of data.

In broad terms, the spirometric indices evaluated in this chapter are designed to measure lung volume (vital capacity) and respiratory air flow (FEV). Static lung volume is principally determined by height and is independent of weight, while dynamic volume measurements depend in part on physical strength. Accordingly, all indices require correction for age and gender. Further, as confirmed in the present study, normal values for Whites cannot be applied to other ethnic groups.

In clinical practice, respiratory disease can be divided into two broad categories. "Restrictive" disease is characterized by reduced vital capacity as seen in interstitial fibrosis or reduced lung volume after surgical resection. In "obstructive" airways disease, usually emphysema associated with cigarette use, there is abnormal prolongation of the flow-dependent indices (FEV_1 , FEV_2 , FEV_3 , and FEF_{max}).

With few exceptions, the dependent variable-covariate associations found in the statistical analyses, confirm observations that are well established in clinical practice. With advancing age, an increased incidence of respiratory disease would be expected and was confirmed by history, on physical examination, and in the laboratory. The age-related decline in vital capacity is considered "physiologic" over time and will occur independent of acquired pulmonary disease.

The cause of the increased incidence of bronchitis and pneumonia in nonblacks is uncertain and cannot be explained on the basis of any previously established genetic or ethnic susceptibility. Differential access and use of medical care may play a role. In contrast, Blacks were found to be at detriment by all spirometric indices.

In the exposure index analyses, the ratio of FEV_1 to FVC revealed similar trends in the enlisted flyer and enlisted groundcrew cohorts. Although the data may reflect some herbicide-related health detriment, two confounding variables must be taken into consideration. As an index reflective of obstructive airways disease, the FEV_1 will diminish with increased cigarette smoking over time. Secondly, as an effort-dependent index, the FVC is subject to performance bias and requires a fully compliant participant in order to be valid. Even in those studies considered technically adequate, the self-perception of prior herbicide exposure could introduce subtle bias sufficient to affect the results. It will be important to reexamine the FEV_1/FVC ratio data when the body burden of herbicide can be defined more objectively by serum levels.

As expected, current and lifetime cigarette use were associated with significant abnormalities in all variables examined. Enlisted participants, with greater lifetime and current cigarette exposure, were at detriment relative to officers.

Finally, though limited to a single variable, the longitudinal analysis revealed no significant difference in the Ranch Hands versus the Comparisons. These observations will be greatly strengthened by longitudinal analysis of the spirometric variables in future examination cycles.

In summary, data collected in the pulmonary assessment provide a valid reflection of lung function in the population under study. There was a similar incidence of respiratory disease and similar respiratory function in the Ranch Hand and Comparison groups.

SUMMARY

The 1987 pulmonary assessment was based on five questionnaire variables, seven variables from the physical examination, and eight laboratory variables. The results of the Ranch Hand and Comparison contrasts are summarized in Table 20-13.

The five questionnaire variables were based on self-reported data for the occurrence of the following conditions: asthma, bronchitis, pleurisy, pneumonia, and tuberculosis. There were no differences identified between the Ranch Hands and the Comparisons based on the unadjusted analyses. The results

TABLE 20-13.

**Overall Summary Results of Unadjusted and Adjusted
Group Contrast Analyses of Pulmonary Variables**

Variable	Type of Analysis	Unadjusted	Adjusted	Direction of Results
<u>Questionnaire</u>				
Asthma	D	NS	NS	
Bronchitis	D	NS	NS	
Pleurisy	D	NS	NS	
Pneumonia	D	NS	****	
Tuberculosis	D	NS	--	
<u>Physical Examination</u>				
Thorax and Lung Abnormalities	D	0.020	NS*	RH>C
Asymmetric Expansion	D	NS	--	
Hyperresonance	D	NS*	** (NS)	RH>C
Dullness	D	NS	--	
Wheezes	D	NS	NS	
Rales	D	NS	NS	
X-Ray Interpretation	D	NS	** (NS)	
<u>Laboratory</u>				
FVC	C	NS	NS	
FEV ₁	C	NS	** (NS)	
FEV ₂	C	NS	** (NS)	
FEV ₃	C	NS	NS	
FEFmax	C	NS	NS	
Ratio of Observed FEV ₁ to Observed FVC	C	NS	NS	
Loss of Vital Capacity	D	NS	NS	
Obstructive Abnormality	D	NS	NS	

D: Discrete analysis performed.

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

****: Group-by-covariate interaction ($p < 0.01$); refer to Table Q-2 for a detailed description of this interaction.

--Analysis not performed.

NS*: Borderline significant ($0.05 < p < 0.10$).

RH>C: Higher prevalence rate in Ranch Hands than in Comparisons.

** (NS): Group-by-covariate interaction ($0.01 < p \leq 0.05$); not significant when interaction is deleted; refer to Table Q-2 for a detailed description of this interaction.

C: Continuous analysis performed.

of the adjusted analyses supported this finding for asthma, bronchitis, and pleurisy. Due to the low number of participants reporting tuberculosis, no adjusted analysis was conducted. In the adjusted analysis of pneumonia, there was a significant interaction between group and lifetime cigarette smoking history ($p=0.004$). Stratifying by the covariate showed that a significantly higher percentage of Comparisons in the heavy cigarette smoking category reported pneumonia than heavy smoking Ranch Hands ($p=0.005$).

The physical examination variables of the pulmonary assessment were: thorax and lung abnormalities, asymmetric expansion, hyperresonance, dullness, wheezes, rales, and x-ray interpretation.

The Ranch Hands had significantly more thorax and lung abnormalities than the Comparisons based on the unadjusted analysis ($p=0.020$). After adjusting for age, occupation, current cigarette smoking, and lifetime cigarette smoking history, the difference was borderline significant ($p=0.072$).

There was only one participant--a Comparison--with asymmetric expansion. No significant difference was detected in the unadjusted analysis, and due to the low number of participants with this condition, no adjusted analysis was conducted.

The unadjusted analysis of hyperresonance showed a borderline difference between the two groups with a higher prevalence rate among the Ranch Hands ($p=0.100$). In the adjusted analysis, there was a significant group-by-occupation interaction ($p=0.017$). Stratifying by occupation revealed that the Ranch Hand enlisted flyers had a significantly higher rate of hyperresonance than the Comparison enlisted flyers ($p=0.006$). Without the group-by-occupation interaction in the model, no difference between the two groups was detected.

There was a total of three participants diagnosed with dullness of the lungs: two Ranch Hands and one Comparison. No difference was found in the unadjusted analysis. Due to the low prevalence rate of dullness, no adjusted analysis was performed.

Neither the unadjusted nor adjusted analyses for wheezes and rales detected a difference between the Ranch Hands and the Comparisons.

No significant difference between the two groups was identified based on the unadjusted analysis of x-ray abnormalities. In the adjusted analysis, there was a significant group-by-race interaction ($p=0.023$). Exploring the interaction by stratifying on race showed a borderline significant difference between the Black Ranch Hands and the Black Comparisons, with the Ranch Hands having more x-ray abnormalities ($p=0.068$). Without the interaction in the model, no significant difference was found.

The eight laboratory variables of the pulmonary assessment were: FVC, FEV_1 , FEV_2 , FEV_3 , FEFmax, ratio of observed FEV_1 to observed FVC, loss of vital capacity, and obstructive abnormality. For six of the eight variables, no significant difference was detected between the Ranch Hands and the Comparisons in both the unadjusted and adjusted analyses. These six variables were: FVC, FEV_3 , FEFmax, ratio of observed FEV_1 to observed FVC, loss of vital capacity, and obstructive abnormality.

No significant difference was identified in the unadjusted analysis of FEV_1 . This result was supported by the adjusted analysis without the significant group-by-age interaction ($p=0.037$). When the interaction was explored, the Ranch Hands born between 1923 and 1941 were found to have a significantly lower adjusted mean than the Comparisons in the same age category ($p=0.022$). However, the Ranch Hands who were born in or before 1922 had a marginally higher adjusted mean than the Comparisons in that category ($p=0.081$).

The results of the analyses of FEV_2 were similar to the results of FEV_1 . No difference between the two groups was detected based on the unadjusted analysis. In the adjusted analysis, there was a significant interaction between group and age ($p=0.042$). Of the participants born between 1923 and 1941, the Ranch Hands had a significantly lower adjusted mean FEV_2 than the Comparisons ($p=0.017$). Among the participants who were born in or before 1922, a borderline significant group difference was found with the adjusted mean of the Comparisons being lower than the adjusted mean of the Ranch Hands ($p=0.070$).

Although the results were primarily not significant or borderline significant, the relative risk was greater than 1 or the mean of the Ranch Hands was less favorable than the mean of the Comparisons in 17 of the 20 unadjusted analyses. In general, this pattern was repeated in the adjusted analyses, where the models were adjusted for the effects of cigarette smoking; again, however, the results were primarily not significant. Trends such as these are discussed in Chapter 21.

Longitudinal analyses showed no changes over time between groups for the ratio of observed FEV_1 to observed FVC. The exposure index analyses detected significant results suggestive of a dose-response relationship infrequently, and no pattern in the results emerged. Exposure index-by-covariate interactions observed were primarily with the two smoking covariates.

In conclusion, 14 variables demonstrated nonsignificant results in both unadjusted and adjusted Ranch Hand versus Comparison group contrasts. Two variables exhibited a significant or borderline significant result affecting the Ranch Hands in either the unadjusted or adjusted analyses. The Ranch Hands had more thorax and lung abnormalities than the Comparisons based on the unadjusted analysis; after adjustment for age and current cigarette smoking, the difference was borderline significant. A borderline significant difference in hyperresonance was found in the unadjusted analysis, and a group-by-occupation interaction was present in the adjusted analysis. Four additional variables were nonsignificant in unadjusted analyses with a group-by-covariate interaction present in the adjusted analyses. Of the five interactions, two variables showed a significant detriment to the Ranch Hands, one a significant detriment to the Comparisons, and two variables demonstrated mixed results; that is, significant or borderline significant results were present for both Ranch Hands and Comparisons, depending on which covariate stratum was examined. Without the group-by-covariate interactions in the final model, no significant effects due to group were seen. Although the pulmonary health of the two groups was reasonably comparable, assessment of the pulmonary function should be included in the future examinations.

CHAPTER 20

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CHAPTER 21

INTERPRETIVE CONSIDERATIONS

INTRODUCTION

Careful consideration of bias, interactions, consistency, multiple testing, dose-response patterns and the exposure index, trends, power limitations, strength of association, and biologic credibility is essential to the interpretation of these data. Problems inherent in the evaluation of negative results and the summarization of these data should also be considered.

BIAS

At the 1987 followup examination, 995 of 1,188 eligible Ranch Hands (84%) and 1,299 of 1,729 eligible Comparisons (75%) were fully compliant. Therefore, differential compliance and the potential for compliance bias existed. The subcohorts of fully compliant participants have remained fairly stable across study examinations. The percentages of those who were fully compliant at the 1987 followup examination and at the Baseline examination were similar across groups (92% of Ranch Hands and 93% of Comparisons). Detailed analyses of available data indicate that those who participated did not differ from those who refused and these contrasts did not change with group membership. Thus, it is concluded that there is no detectable compliance bias in this study and this form of bias is excluded as an explanation of the results.

Information bias, represented by the possible overreporting of disease symptoms, was precluded by medical record verification of major disease conditions. The possibility still exists that Ranch Hand conditions may be more verifiable because they might tend to be seen by physicians more often than Comparisons; this would be revealed by group differences in the quantity and content of medical records. Since there is currently no way to quantify these aspects, this potential bias remains unexplored. Information bias due to errors in the data base introduced via data entry or machine error is negligible. All laboratory results were subject to strict quality control procedures and medical coding data were completely verified by medical record review. The misclassifications of a Ranch Hand by race and 13 participants by verified history of diabetes are inconsequential, as shown by repeated analyses of data with these mistakes corrected.

Misclassification bias is a definite possibility with regard to the classification of Ranch Hands according to the calculated dioxin exposure index. Recent, and as yet unpublished, serum dioxin assay results suggest that there is no relationship between current dioxin levels and the calculated index. Current dioxin levels are, however, strongly associated with occupation, with enlisted groundcrew having the highest and officers having the lowest levels; enlisted flyers have current dioxin levels lower than enlisted groundcrew and higher than the officers. Thirty percent of the flying officers and 76 percent of enlisted groundcrew have levels above background (10 ppt). Thus, the exposure index analyses presented in this and

previous reports may be biased toward finding no effect. The actual extent of this bias will be fully described in another report after all assay results are available.

Since 12 percent of assayed Ranch Hands (n=848) have current dioxin levels below 4 ppt, the approximate Comparison median (n=384), the group contrasts in this report may also be biased toward finding no effect. With 12 percent of Ranch Hands misclassified as exposed, a true relative risk of 2.0 would be estimated as approximately 1.1 and would thus be missed (assuming a disease prevalence of 5% in the Comparison group, equal sample sizes of 1,000 in each group, and a population probability of exposure of 2%). It is possible, however, that Ranch Hands having background levels today may have actually been exposed but their body burdens have decayed to the current level. If this is the case, there would be no misclassification bias regarding the group contrasts. Both cases will be addressed in a reanalysis of these data with the dioxin assay serving as the measure of exposure.

ADJUSTMENTS FOR COVARIATES AND INTERACTIONS

The matched design together with extensive covariate adjustments were implemented to preclude the possibility of confounding. Lack of adjustment for a confounder could hide an otherwise significant group difference or reveal a spurious difference. Adjusted and unadjusted results were presented to reveal the effect modification of the covariates. The presence of significant interactions with group, that is, a significant difference in the relative risk with levels of a covariate, precluded the presentation of an overall adjusted relative risk and, instead, a stratified analysis was conducted to describe the interaction. When the p-value was between 0.01 and 0.05, the data were analyzed with and without the interaction. If an interaction was significant at the 0.01 level or less, the analysis was stopped with a description of the corresponding stratified analysis. The large number of dependent variables in this study (approximately 300) and covariates produced many significant interactions, all of which were listed and summarized in each clinical chapter. Review of these interactions within and across clinical areas revealed no overall patterns. Additionally, since occupation is currently the best correlate with current dioxin levels, a difference in relative risk with levels of occupation (with relative risk among enlisted ground personnel being greater than the relative risk among officers) would support a dose-response effect. The lack of such an interaction would argue against a dose-response effect.

CONSISTENCY

Ideally, an adverse health effect in Ranch Hands attributable to herbicide or dioxin exposure would be revealed by internally and externally consistent findings. A finding would be regarded as internally consistent if it did not contradict prior information, other findings, or medical knowledge. For example, the finding of significantly increased femoral pulse abnormalities is not consistent with the lack of increased posterior tibial pulse abnormalities in Ranch Hands. Further, the lack of interaction with occupation is not consistent with known patterns of dioxin levels in Ranch Hands. A finding would be externally consistent if it had been previously

established either in theory or empirically as related to exposure. The observed excess of basal cell carcinoma in Ranch Hands is externally inconsistent since there is no prior evidence that basal cell carcinoma is related to dioxin or herbicide exposure. It is also internally inconsistent because there is no evidence that basal cell carcinoma relative risk is greater among enlisted ground personnel than the relative risk among officers.

MULTIPLE TESTING

The lack of a predefined medical endpoint has necessitated the consideration of literally hundreds of dependent variables. Each dependent variable is analyzed many different ways to accommodate covariate information and different statistical models. In the hypothetical case that Ranch Hand physical health is the same as that of the Comparisons, about 5 percent of the many statistical tests of hypotheses shown in this report should be expected to detect a group difference (produce p-values less than 0.05). The observation of significant results due to multiple testing, even when there is no group difference, is known as the multiple testing artifact and is common in large studies. Unfortunately, there is no statistical procedure available to distinguish between those statistically significant results that arise due to the multiple testing artifact and those that may be due to a bona fide herbicide effect. Instead, the authors have relied on reasoned consideration of strength of association, consistency, dose-response patterns, and biologic credibility to weigh and interpret the findings.

DOSE-RESPONSE PATTERNS AND THE EXPOSURE INDEX

Ideally, a dose-response effect would be revealed by a regression of disease prevalence on exposure. The most obvious effect would be represented by an increasing trend in disease prevalence from a low rate among Ranch Hands with low exposure to a high rate among Ranch Hands with a high exposure. A dose-response effect may be expected to occur regardless of the presence or absence of a group difference.

Epidemiologic studies of health effects after environmental or occupational exposure to toxic chemicals or substances have generally relied upon indirect measures of exposure, termed exposure indices, to assess dose-response. For example, Lee and Fraumeni¹ studied respiratory cancer mortality in Montana smelter miners exposed to airborne arsenic trioxide and sulfur dioxide. The exposure index for an individual miner was simply the number of years of employment. With it, a statistically significant dose-response effect was demonstrated. In the aborted Centers for Disease Control (CDC) study of health effects in U.S. Army troops potentially exposed to Agent Orange in Vietnam, study investigators derived several exposure indices in terms of troop locations, known half-lives of dioxin in soil and on plant leaves, and the dates and spray paths of Ranch Hand aircraft. The study was canceled after their exposure indices failed to correlate with current dioxin levels in assay study subjects. In the Air Force Health Study (AFHS), each Ranch Hand's dioxin exposure was metricized as the product of the gallons of herbicide sprayed during his tour and the dioxin concentration of that herbicide divided by the number of Ranch Hands in his job category during his tour. This exposure index has so far failed to reveal consistent dose-response effects and is not correlated with current dioxin body burden in Ranch Hands. It has also failed to correlate with the extrapolated Vietnam dioxin dose in Ranch Hands assuming first order kinetics and a half-life in humans of 7.1 years.²

The AFHS exposure index was based on the best information available during the design phase of this study. The gallons sprayed, dioxin concentrations, and personnel figures are considered accurate. The index is based on the logic that exposure should increase with increased spraying or if fewer men in an occupational category became available to do the work. Similarly, it was reasoned that exposure should decrease as spraying decreased or as more men became available to do the work. The validity of this index is limited, however, since the gallons sprayed and personnel figures are not specific to an individual Ranch Hand's assigned base in Vietnam or to his specific daily work schedule. The AFHS exposure index is probably more accurate than the indices attempted by the CDC because the Ranch Hands were much closer to the herbicide than the Army and recorded troop locations were somewhat inaccurate for the individual soldier. Indirect exposure indices based on work history and demographic information have demonstrated significant dose-response effects in studies of long-term occupational exposure with moderate to high relative risks. Such indices have failed to demonstrate significant effects or have failed to correlate with direct measures of exposure, such as the dioxin assay, when exposures are short in duration, are of less than industrial intensity, or when the relative risk is small.

Fortunately, the development of the serum dioxin assay and its application to Ranch Hands and Comparisons will obviate the concern about the calculated exposure index.

TRENDS

An assessment of consistent and meaningful trends is an essential element of the interpretation of any large study with multiple endpoints, clinical areas, and covariates. However, caution must be exercised in the interpretation of trends.

Increased abnormalities or adverse means for the Ranch Hands across medically related variables within a clinical area might indicate an exposure effect. In this case, it is important to note that there is moderate to strong correlation between endpoints. Hence, the strength of the group differences must also be considered in assessing the extent of the suspected exposure effect.

Based on preliminary results, current dioxin levels are strongly associated with occupation. Thus, strong, statistically significant differences between groups in means or percent abnormalities for different occupations (i.e., group-by-occupation interactions) would be indicative of a dose-response effect. In this situation, one would expect to see a steadily increasing relative risk or difference between means as occupational exposure increased (i.e., officers less than enlisted flyers less than enlisted groundcrew). Under these assumptions, significant group-by-occupation interactions would be expected for clinical endpoints affected by dioxin exposure. The lack of a significant interaction with occupation could be due to the absence of a true effect, or the power limitations of the statistical test for interactions.

An increasing trend in differences between groups in means or disease rates with levels of a covariate (other than occupation) could also indicate an exposure effect. For example, an increased relative risk for hepatic disease with increased levels of alcohol consumption could be due to an indirect causal relationship between exposure and hepatic disease through alcohol consumption. In assessing potential indirect causal relationships, it is important to consider the strength of the group differences and consistency of both the results with related endpoints and findings over time (i.e., 1982 Baseline, 1985 followup, 1987 followup examinations).

Based on the calculated exposure index, increasing trends in Ranch Hand disease rates with increasing levels of exposure within occupational category would be expected in the presence of an exposure effect. However, preliminary results of serum dioxin assays of the Ranch Hands indicate that the calculated exposure index is not a good measure of actual dioxin exposure. Thus, the results of the exposure index analysis should be interpreted with caution.

POWER LIMITATIONS

The fixed size of the Ranch Hand cohort limits the ability of this study to detect group differences. This limitation is most obvious with regard to specific types of cancer, such as soft tissue sarcoma and non-Hodgkin's lymphoma, which are so rare that fewer than one case is expected in each group and, therefore, this study has virtually no statistical power to detect low to moderate group differences regarding them. On the other hand, these sample sizes are sufficient to detect very small mean shifts in the continuously distributed variables. For example, with regard to IgG, this study has approximately 90 percent power to detect a mean shift of 1 percent. The detection of significant mean shifts without a corresponding indication of increased Ranch Hands abnormalities or disease is considered to be of little importance or an artifact of multiple testing. This study has good power to detect relative risks of 2.0 or more with respect to diseases occurring at prevalences of at least 5 percent in the Comparison group, such as heart disease and basal cell carcinoma.

In an attempt to overcome the lack of power to detect group differences for specific types of systemic cancer, all types of systemic cancer were combined into a single variable. It is still possible, however, that an increased risk could exist for a particular rare type of cancer and that increased risk would be missed in this study.

STRENGTH OF ASSOCIATION

Ideally, an adverse effect, if it exists, would be revealed by a strong association between group and a disease condition, that is, by a statistically significant relative risk greater than 2.0. Statistically significant relative risks less than 2.0 are considered of less importance than larger risks because relative risks less than 2.0 can easily arise due to unperceived bias or confounding; relative risks greater than 5.0 are less subject to this concern. Statistically significant relative risks greater than 5.0 were not found in this study.

BIOLOGIC CREDIBILITY

The assessment of biologic credibility requires consideration of the question: In biologic terms, is it understood how the exposure under study could produce the effect of interest? While lack of biologic credibility or even a contradiction of biologic knowledge can sometimes lead to dismissal of a significant result as spurious, the failure to perceive a mechanism may reflect only ignorance of the state of nature. On the other hand, it has proven all too easy to propose credible biological mechanisms relating most exposures to most cancers. Thus, while pertinent, the response to this question is not especially convincing one way or the other.

INTERPRETATION OF NEGATIVE RESULTS

In 1985, Bross presented minimal sample size criteria for proof of safety and for proof of hazard in studies of environmental and occupational exposures. His work is directed at rectifying widespread misconceptions about proof of safety that are prevalent in Government agencies, in the medical and scientific establishments, and in other groups involved in public health and safety. He cites the erroneous notion that failure to obtain statistically significant results in an epidemiologic study warrants a claim of safety, such as in Environmental Protection Agency interpretations of Love Canal data. His work concludes that it is far more difficult to provide a valid scientific proof of safety than to provide a corresponding proof of hazard. He shows that the quantity of data required for a valid assurance of safety is 30 times greater than that required for a valid proof of hazard. In fact, the size of the sample needed so far exceeds what is ordinarily available in epidemiologic studies, that assurances of safety given on the basis of such studies have no scientific validity. Bross' work was later refined and extended by Millard. Michalek has recently applied Bross' methods to demonstrate that the AFHS is large enough to demonstrate hazard (for disease prevalences on the order of 5%), but not large enough to prove safety.

SUMMARIZATION OF RESULTS

Many readers will attempt to tally statistically significant results across clinical areas and study cycles. A study of this scope having a multitude of endpoints and no prescribed strength of association to declare an effect meaningful demands, and at the same time defies, meaningful summary tabulation. Such summaries are misleading because they ignore correlations between the endpoints, correlations between study cycle results, and the nonquantifiable medical importance of each endpoint. In fact, many endpoints are redundant (e.g., psychological scales, indices developed from combining multiple variables) in an effort not to "miss" anything. Additionally, such tabulations combine endpoints that are not medically comparable. For example, sense of smell is of less medical importance than the presence of malignant neoplasm. Statisticians attempt to summarize multidimensional repeated measures data with growth curve analyses; these methods have not been applied in this study because they apply only to continuously distributed data, do not account for medical importance, and reduce the data "too much."

Nevertheless, given the lack of adequate summary statistics, the tally of significant results will occur. Such summaries can be misleading and must be carefully interpreted.

OTHER ANALYTICAL STRATEGIES

The analytical plan for this report was written before Ranch Hand 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) results became available. Other analyses, such as restriction to enlisted groundcrew, were not carried out, although such analyses appear now to be well motivated in view of the TCDD concentrations in that occupation. The analytical strategy for this and previous reports was conceived during protocol development with no knowledge of the relative exposures of the three occupational categories of Ranch Hands. At that time, some investigators speculated that the enlisted flyers were the most heavily exposed to TCDD. The accomplishment of within occupational strata analyses at this time would constitute another attempt, as was our inspection of group-by-occupation interactions, to use occupation as a surrogate for TCDD exposure. The next report, already in progress, will show the results of analyses of all health conditions against current TCDD concentrations in Ranch Hands. Current health in Ranch Hands will also be assessed relative to the extrapolated Vietnam TCDD dose using a first-order kinetic assumption. Additionally, Ranch Hands having high current TCDD concentrations will be contrasted with Comparisons having background TCDD levels. Therefore, continued analysis of these data without accounting for TCDD concentrations is not warranted.

CONCLUSION

The interpretation of the AFHS requires careful consideration of potential biases, interactions, consistency of results, the multiple testing artifact, dose-response patterns and the exposure index, trends, power limitations, strength of association, and biologic credibility. Additionally, any assurances of safety drawn from these data are not scientifically valid and should be avoided. The AFHS is large enough to establish hazard (for disease prevalences on the order of 5%), but is not large enough to establish safety. Simple tabulations of positive results can be misleading.

CHAPTER 21

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CHAPTER 22

CONCLUSIONS

INTRODUCTION

This chapter summarizes the conclusions drawn from the statistical analyses that have been conducted on the Air Force Health Study data base. The 1987 followup was the logical extension of the 1982 Baseline and the 1985 followup, building upon the strengths of the previous studies and utilizing the data collected at the Baseline, 1985 followup, and 1987 followup. The high level of participation that characterized the Baseline and 1985 studies was maintained through the 1987 followup.

STUDY PERFORMANCE ASPECTS

Of the 2,919 study subjects who were eligible to attend the 1987 followup, 2,853, or 97.7 percent, were located and asked to participate in the 1987 followup. Participation in the 1987 followup was high. In total, 2,294 study subjects (995 Ranch Hands and 1,299 Comparisons) were fully compliant. This represented compliance rates of 84 percent and 75 percent for Ranch Hands and Comparisons, respectively. Of the living study subjects who were fully compliant at Baseline, 92.2 percent of the Ranch Hands and 93.2 percent of the Comparisons returned to participate in the 1987 examination. Of the 2,853 invited study subjects, 531 (171 Ranch Hands and 360 Comparisons) refused to participate. One Ranch Hand and 27 Comparisons (all new to the study) agreed to complete the Baseline questionnaire, but failed to attend the physical examination and were thus partially compliant.

Study participation was analyzed to assess the potential for compliance bias. The negative findings suggested that there has been no change in the way new and replacement Comparisons self-selected for entry into the 1987 followup from the Baseline and 1985 studies. Based on analysis of telephone interview data, there appeared to be little selection bias due to non-participation.

POPULATION CHARACTERISTICS

Overall, the Ranch Hands and Comparisons had similar personal characteristics and lifestyle habits. No significant differences were found in age, race, occupation, education, current military status, and individual income. Although current and lifetime alcohol use were similar for the two groups, significantly more Comparisons than Ranch Hands reported that they drank wine both at the time of the physical examination and during their lifetimes; however, the current and lifetime wine consumption means were similar for both groups. Ranch Hands smoked significantly more cigarettes per day than the Comparisons at the time of the physical examination, but there was no difference between the groups on lifetime cigarette smoking, current cigar and pipe smoking, and recent and past marijuana smoking habits. In general, risk-taking behavior of the Ranch Hands and Comparisons was comparable.

In addition to the characteristics and habits summarized above, analyses were conducted to detect group differences on all other variables that were candidate covariates in the adjusted analyses of clinical endpoints. In general, the groups were similar for these variables as well.

PATTERNS OF RESULTS

The conclusions reached in this report were carefully considered using the criteria of consistency, specificity, coherence, strength, and plausibility as they apply to the interpretation of group differences. To form an overall assessment, patterns of results that emerged from the clinical evaluations were examined. Few significant group differences were noted for the proportion of abnormalities. In general, the positive associations did not aggregate in the clinical areas of prime concern; some of the statistically significant group differences noted at Baseline or at the 1985 followup examination have disappeared and only a few new associations have emerged. The longitudinal analyses were primarily negative. The unadjusted results have been concordant with the adjusted results, both in terms of the magnitude and statistical significance of the group differences. Associations between the covariates and the dependent variables generally behaved as expected. No consistent pattern of group-by-covariate interactions emerged, and the exposure index analyses were generally not significant and did not support a dose-response relationship. Dose-response relationships were not emphasized in reaching final conclusions because of the acknowledged limitations of the calculated exposure index used in this report. Dioxin body burden levels will be analyzed in a subsequent report and will provide a more valid indicator of the level of exposure.

CLINICAL ASPECTS

This section provides the conclusions from the analyses of the 12 clinical areas. The results for the dichotomous and continuous variables are summarized in Appendix R.

General Health

General health in the Ranch Hand and Comparison groups was assessed by five measures (self-perception of health, appearance of illness or distress, relative age, percent body fat, and the erythrocyte sedimentation rate). There were no significant group differences, either unadjusted or adjusted for covariates (age, race, occupation, and, in the case of self-perception of health and sedimentation rate, personality type), nor any significant group-by-covariate interactions for self-perception of health, appearance of illness or distress, relative age, or percent body fat. There was little difference in the geometric mean values of erythrocyte sedimentation rate in the two groups, but the Ranch Hand group had a significantly higher percentage of individuals with an abnormal sedimentation rate (>20 mm/hr) than the Comparisons. However, only three participants (two Ranch Hands and one Comparison) were found to have rates in excess of 100 mm/hr. One participant (a Comparison) proved to have lung cancer and died in early 1989. For neither of the two Ranch Hands was a diagnosis established during the course of the

1987 followup. Exposure index analyses did not detect any consistent dose-response relationships. Longitudinal analyses revealed a similar decline in both groups over time in the percentage of individuals reporting their health as fair or poor. For sedimentation rate, there was a significant difference between groups in the change from Baseline to the 1987 followup examination, with a relatively greater number of Ranch Hands than Comparisons shifting from normal at Baseline to abnormal at the followup examination. The clinical meaning of this observation is unknown.

Malignancy

The unadjusted analysis of all verified neoplasms indicated that the proportion of Ranch Hands with neoplasms was significantly greater than that of the Comparisons. After including suspected neoplasms with verified neoplasms, the Ranch Hand proportion was marginally greater than the Comparison proportion. The majority of malignant neoplasms observed in the Ranch Hands were basal cell carcinomas, a nonlife-threatening form of cancer. When the analysis was performed only on skin neoplasms for nonblack participants, significantly more Ranch Hands had skin neoplasms than did the Comparisons for both the verified and the verified and suspected diagnoses. A significantly greater proportion of Ranch Hands had verified malignant skin neoplasms than did the Comparisons. Given the presence of a neoplasm, a marginally significant higher proportion of Ranch Hands had skin neoplasms than did the Comparisons.

No significant group differences were found in the analyses of systemic neoplasms by number, behavior (malignant, benign, uncertain, or unspecified), or by location and site. Thus, the increase in overall malignancy was due to elevated relative risks for skin cancer and basal cell carcinoma. Also, given the presence of any systemic neoplasm, Ranch Hands and Comparisons did not differ significantly for malignant systemic neoplasms. The number of soft tissue sarcomas and non-Hodgkin's lymphomas were comparable in the two groups.

For unadjusted analyses of verified basal cell carcinoma, a borderline significant group difference was found. The unadjusted analysis of the verified and suspected basal cell carcinomas was not significant. After adjustment for covariates was performed, the group contrast was statistically significant for verified basal cell carcinoma and borderline significant for the verified and suspected diagnoses. Ranch Hands and Comparisons differed significantly on the frequency of participants with zero, one, or multiple verified basal cell carcinomas. Also, the Ranch Hands had a significantly higher percentage of participants with multiple verified basal cell carcinomas than did the Comparisons.

Sun exposure-related malignant skin neoplasms also exhibited group differences. Approximately 90 percent of the participants with sun exposure-related malignant neoplasms had basal cell carcinomas. For the unadjusted analysis, the group contrast was significant for the verified diagnoses and borderline significant for the combination of verified and suspected sun exposure-related malignant skin neoplasms. For the adjusted analyses of these neoplasms, the Ranch Hands and Comparisons differed significantly for both the verified and combined diagnoses. Verified neoplasms of the upper extremities for the sun-exposure-related malignant skin neoplasms also exhibited a