TABLE 10-8. (continued)

Unadjusted Analysis of Basal Cell Carcinoma and Sun Exposure-Related Malignant Neoplasms on the Ear, Face, Head, and Neck or Other Sites by Occupation (Nonblacks Only)

Cell Type (Status)	Occupation	Statistic	Group: Ranch Hand		Group: Comparison		Contrast	Est. Relative Risk (95% C.I.)	p-Value
Sun Exposure-Related Malignant Skin Neoplasms (Verified and Suspected)	Officer	n	372		488				
		Number/%							
		Ear, Face, Head, and Neck	34	9.1%	30	6.1%	Overall		0.127
		Other Sites	13	3.5%	11	2.3%	EFHN vs. None	1.56 (0.94,2.60)	0.115
		No Cancer	325	87.4%	447	91.6%	Other vs. None	1.63 (0.72,3.67)	0.332
	Enlisted Flyer	n	163		196				
		Number/%							
		Ear, Face, Head, and Neck	11	6.7%	13	6.6%	Overall		0.283
		Other Sites	7	4.3%	3	1.5%	EFHN vs. None	1.05 (0.46,2.41)	0.999
		No Cancer	145	89.0%	180	91.8%	Other vs. None	2.90 (0.74,11.40)	0.206
	Enlisted Groundcrew	n	403		535				
		Number/%							
		Ear, Face, Head, and Neck	16	4.0%	23	4.3%	Overall		0.916
		Other Sites	8	2.0%	9	1.7%	EFHN vs. None	0.92 (0.48,1.77)	0.946
		No Cancer	379	94.0%	503	94.0%	Other vs. None	1.18 (0.45,3.09)	0.920

Abbreviation: EFHN — Ear, Face, Head, and Neck.

For the verified sun exposure-related malignant skin neoplasms, as shown in Table 10-8, the Ranch Hand and Comparison officers displayed a borderline significant difference between their relative frequencies (p=0.078). Ranch Hand frequencies exceeded Comparison frequencies for sun exposure-related malignant skin neoplasms on the ear, face, head, and neck (9.1% vs. 5.9%) and other sites (3.5% vs. 2.1%). The relative frequencies of sun exposure-related malignant skin neoplasms on the ear, face, head, and neck versus no malignant neoplasm were borderline significantly different (p=0.088) for the Ranch Hand and Comparison officers, with an estimated relative risk of 1.62 (95% C.I.: [0.97, 2.71]). For the set of verified sun exposure-related malignant skin neoplasms, neither the enlisted flyers nor the enlisted groundcrew exhibited a significant group difference (p=0.284 and p=0.845, respectively). For each occupation, Ranch Hands and Comparisons did not differ significantly on their relative frequencies of verified and suspected sun exposure-related malignant skin neoplasms (officers: p=0.127; enlisted flyers: p=0.283; enlisted groundcrew: p=0.916).

Conditional Analyses

For Ranch Hands with any verified neoplasm, 74.1 percent (157/212) had a verified skin neoplasm; in contrast, the corresponding percentage for the Comparisons was 66.4 percent (156/235). The difference in these proportions was borderline significant (p=0.095). When suspected neoplasms were included, the Ranch Hand percentage was 73.5 percent (158/215) and the Comparison percentage was 66.0 percent (163/247). These two percentages were borderline significantly different (p=0.100).

Fifty-eight percent (91/157) of the Ranch Hands with any verified skin neoplasm had a verified malignant skin neoplasm. The analogous percentage for the Comparisons was 56.4 percent (88/156). These percentages were not significantly different (p=0.870). The inclusion of suspected neoplasms with the verified neoplasms resulted in a Ranch Hand percentage of 58.2 percent (92/158) and a Comparison percentage of 57.7 percent (94/163). Again, these percentages were not significantly different (p=0.999).

For Ranch Hands having a verified malignant skin neoplasm, 85.7 percent (78/91) had a verified basal cell carcinoma. For Comparisons having a verified malignant skin neoplasm, 86.4 percent (76/88) had a verified basal cell carcinoma. The group percentages were not significantly different (p=0.999). For Ranch Hands with a verified or suspected malignant skin neoplasm, 85.9 percent (79/92) had a verified or suspected basal cell carcinoma. For Comparisons with a verified or suspected malignant skin neoplasm, 86.2 percent (81/94) had a verified or suspected basal cell carcinoma. These percentages also were not significantly different (p=0.999).

For Ranch Hands with a verified basal cell carcinoma, 76.9 percent (60/78) had basal cell carcinoma of the ear, face, head, neck, or upper extremities, and 80.3 percent of the Comparisons (61/76) had basal cell carcinoma at these sites. The difference between these percentages was not significant (p=0.758). Corresponding percentages after including suspected basal cell carcinomas were 75.9 percent (60/79) for the Ranch Hands versus 75.3 percent (61/81) for the Comparisons. These percentages also were not significantly different (p=0.999).

For Ranch Hands with verified sun exposure-related malignant skin neoplasms, 76.1 percent (67/88) had these neoplasms on the ear, face, head, neck, or upper extremities, compared to 77.4 percent (65/84) for the Comparisons. These percentages were not significantly different (p=0.990). Combining the verified with the suspected sun exposure-related malignant skin neoplasms resulted in the following percentages for the specified sites of interest: 75.3 percent (67/89) for the Ranch Hands versus 73.0 percent (65/89) for the Comparisons. Again, these percentages were not significantly different (p=0.864).

Multiple Basal Cell Carcinoma

For verified basal cell carcinoma, the Ranch Hand and Comparison groups were compared on the numbers of men having zero, one, or more than one basal cell carcinoma (Comparisons: 1,143, 61, and 15, respectively; Ranch Hands: 860, 54, and 24, respectively). The Ranch Hand and Comparison groups differed significantly (p=0.050), with the Ranch Hands having higher relative frequencies than the Comparisons for one basal cell carcinoma (5.8% vs. 5.0%) and more than one basal cell carcinoma (2.6% vs. 1.2%), and a lower relative frequency than the Comparisons for zero basal cell carcinoma (91.7% vs. 93.8%). Comparing the relative frequencies for those participants with zero basal cell carcinomas versus one verified basal cell carcinoma indicated no difference between the Ranch Hands and the Comparisons (p=0.452). However, the relative frequency for Ranch Hands with zero basal cell carcinomas versus more than one verified basal cell carcinoma was significantly different from that of the Comparisons (p=0.032). This contrast had an estimated relative risk of 2.13 (95% C.I.: [1.11,4.08]).

Analogous comparisons were made for the combined set of verified and suspected basal cell carcinomas. The Ranch Hand and Comparison groups did not differ (p=0.115) on their distributions of participants having zero, one, or multiple verified or suspected basal cell carcinomas (Comparisons: 1,138 [93.4%], 64 [5.3%], and 17 [1.4%], respectively; Ranch Hands: 859 [91.6%], 55 [5.9%], and 24 [2.6%], respectively). For this combined set of malignant neoplasms, the relative frequencies for those participants having zero basal cell carcinomas versus one basal cell carcinoma were not significantly different (p=0.554) between groups; however, the relative frequencies for Ranch Hands and Comparisons with zero basal cell carcinomas versus multiple basal cell carcinomas was marginally significant (p=0.069), with an estimated relative risk of 1.87 (95% C.I.: [1.00,3.50]).

Basal Cell Carcinoma (Covariate Associations)

The presence of basal cell carcinoma was evaluated for association with previously specified covariates using the pooled group data. Basal cell carcinoma was examined for covariate associations based on verified basal cell carcinoma only, and combining verified and suspected basal cell carcinomas. Table G-1 of Appendix G contains the covariate associations for these malignant skin neoplasms.

Age displayed a significant covariate association with the presence of verified basal cell carcinoma (p<0.001). The younger participants (born in or

after 1942) had lower relative frequencies of verified basal cell carcinoma (3.7%) than participants born between 1923 and 1941 (9.5%) or in or before 1922 (9.5%). Age was also strongly associated with the set of verified and suspected basal cell carcinomas ($p<0.001$).

For verified basal cell carcinoma, occupation exhibited a significant covariate association ($p=0.015$). The relative frequency of verified basal cell carcinoma was highest among the officers (8.7%), slightly lower for the enlisted flyers (8.1%), and lowest among the enlisted groundcrew (5.3%). For the set of verified and suspected basal cell carcinomas, occupation was also significant ($p=0.014$).

Average lifetime residential latitude also exhibited significant covariate relationships with the presence of basal carcinoma ($p=0.010$ for the verified set; $p=0.006$ for the verified and suspected set). For participants with an average lifetime residential latitude below 37 degrees, 8.7 percent had a verified basal cell carcinoma, compared to 5.8 percent for participants with average lifetime residential latitudes at or above 37 degrees. Average lifetime residential latitude has also been identified as a possible confounding variable because it is associated with group as well as basal cell carcinoma (i.e., 57.4% of the nonblack Ranch Hands had average lifetime residential latitudes at or above 37 degrees, whereas the nonblack Comparisons were almost equally divided above and below an average lifetime residential latitude of 37 degrees; see Chapter 2). Because of the confounding effect of the latitude variable, an analysis was performed to evaluate this variable for misclassification or bias. Similar to analyses performed for the 1985 followup study, total residential years and chronologic age were evaluated for underreporting and overreporting. No significant group difference was found between total residential years and chronologic age ($p=0.912$).

Ionizing radiation exposure also displayed a significant association with basal cell carcinoma ($p=0.048$ for the verified set; $p=0.026$ for the verified and suspected set). For participants exposed to ionizing radiation, 9.3 percent had a verified basal cell carcinoma, compared to 6.5 percent of the participants not exposed to ionizing radiation.

For ethnic background, there was a borderline significant association for the set of verified basal cell carcinomas ($p=0.092$). For the ethnic group categories defined in Table 10-1, the following percentages of participants with verified basal cell carcinoma were obtained: 7.9 percent for group A, 6.1 percent for Group B, 1.7 percent for Group C, and 0.0 percent for groups D and E.

A marginally significant association was found between skin color and verified and suspected basal cell carcinoma ($p=0.075$). For the skin color categories listed in Table 10-1, percentages of participants with verified and suspected basal cell carcinoma were determined for the following skin tones: 0.0 percent for dark; 2.7 percent for medium; 4.6 percent for pale; 8.2 percent for dark peach; and 8.4 percent for pale peach.

Significant associations were found between hair color and basal cell carcinoma ($p=0.013$ for verified; $p=0.006$ for verified and suspected). Percentages of participants with verified basal carcinoma were determined for the following hair colors: 7.0 percent for black; 5.5 percent for dark brown; 9.2 percent for light brown; 10.4 percent for blonde; and 18.8 percent for red.

Assuming several preceding episodes of sun exposure, the covariate assessing skin reaction after at least 2 hours sun exposure exhibited a significant association with basal cell carcinoma ($p<0.001$ for verified; $p<0.001$ for verified and suspected). For participants having no reaction, 4.1 percent had a verified basal carcinoma; for those that became red, 7.4 percent had a verified basal cell carcinoma; for participants that burned, 14.1 percent had a verified basal cell carcinoma; and for those that burned painfully, 9.3 percent had a verified basal cell carcinoma.

Skin reaction after repeated sun exposure displayed a significant covariate association with both the verified, and the verified and suspected, basal cell carcinomas ($p<0.001$ for both sets). For participants that tanned deep brown, 4.5 percent had a verified basal cell carcinoma; for those that tanned moderately, 7.5 percent had a verified basal cell carcinoma; for those that tanned mildly, 9.1 percent had a verified basal cell carcinoma; and for those that had freckles with no tan, 23.4 percent had a verified basal cell carcinoma.

For the composite sun reaction index, there was a significant association with both the verified, and the verified and suspected, basal cell carcinomas ($p<0.001$ for both sets). For those participants having a low composite sun reaction index, 5.5 percent had a verified basal cell carcinoma; for participants with a medium sun reaction index, 11.2 percent had a verified basal cell carcinoma; and for those having a high composite sun reaction index, 11.9 percent had a verified basal cell carcinoma.

Basal Cell Carcinoma (Adjusted Group Contrast Analyses)

As described in the preceding paragraphs, a number of the covariates and host factors were found to be associated with the presence of basal cell carcinoma. In addition, the host factors of hair color, skin color, and ethnic background were implicitly related to the reaction of the skin to the sun. Because of these multiple relationships and because a reduced set of covariates was needed for the adjusted analyses, two main effects statistical models of basal cell carcinoma on selected covariates were implemented. The first model included the following covariates and host factors: occupation, age, skin reaction after at least 2 hours of sun exposure (assuming several preceding episodes), skin reaction after repeated sun exposure, skin color, ethnic background, hair color, ionizing radiation exposure, and average lifetime residential latitude. A second main effects model was used in which the two individual skin reaction variables were replaced by the composite skin reaction index. To simplify the models, the original categories for skin color, hair color, and ethnic background were dichotomized as follows: peach versus not peach for skin color, black or dark brown hair versus other hair colors, and ethnic background group A (English, Welsh, Scottish, or Irish) or group B (Scandanavian, German, Polish, Russian, other Slavic, Jewish, or French) versus the other ethnic groups. The frequencies for the noncollapsed categories of these covariates are described in Table G-1 of Appendix G.

Appendix Table G-2 summarizes the results of the two modeling strategies. Log likelihood values were compared and the model including the individual skin reaction variables (model 1) was chosen. Upon completion of the stepwise procedures to reduce this model, the individual skin reaction variables were

retained along with occupation, age, ethnic background, ionizing radiation exposure, and average lifetime residential latitude as covariates for the adjusted group contrast analyses.

The adjusted analysis results for basal cell carcinoma are presented in Table 10-9. For the verified set of basal cell carcinomas, the significant group difference ($p=0.030$) had an adjusted relative risk of 1.46 (95% C.I.: [1.04,2.06]). For this set of neoplasms, skin reaction after repeated sun exposure and average lifetime residential latitude were significant covariates in the model ($p=0.011$ and $p=0.007$, respectively). In addition, there was a significant age-by-ethnic background interaction ($p=0.037$) and a significant ionizing radiation-by-skin reaction after at least 2 hours sun exposure interaction ($p=0.045$). For the set of verified and suspected basal cell carcinomas, a borderline significant group difference ($p=0.053$) had an adjusted relative risk of 1.39 (95% C.I.: [1.00,1.95]). Skin reaction after at least 2 hours sun exposure ($p<0.001$), skin reaction after repeated sun exposure ($p=0.015$), average lifetime residential latitude ($p=0.006$), ionizing radiation exposure ($p=0.043$), and an age-by-ethnic background interaction ($p=0.036$) were significant terms in the adjusted model.

Sun Exposure-Related Malignant Skin Neoplasms (Covariate Associations)

The presence of sun exposure-related malignant skin neoplasms was evaluated for association with previously specified covariates using the pooled group data. These skin neoplasms were examined for covariate associations based on verified sun exposure-related malignant neoplasms only, and combining verified and suspected sun exposure-related malignant neoplasms. Table G-1 of Appendix G contains the covariate associations with these sun exposure-related malignant skin neoplasms.

Age displayed a significant covariate association with the presence of verified sun exposure-related malignant skin neoplasms ($p<0.001$). The younger participants (born in or after 1942) had lower relative frequencies of verified sun exposure-related malignant skin neoplasms (4.2%) than participants born between 1923 and 1941 (10.4%) or in or before 1922 (13.1%). Age was also strongly associated with the set of verified and suspected sun exposure-related malignant skin neoplasms ($p<0.001$).

For verified sun exposure-related malignant skin neoplasms, occupation exhibited a significant association ($p=0.003$). The relative frequency of verified sun exposure-related malignant skin neoplasms was highest among the officers (10.0%), slightly lower for the enlisted flyers (8.9%), and lowest among the enlisted groundcrew (5.8%). For the set of verified and suspected sun exposure-related malignant skin neoplasms, occupation was also significantly associated ($p=0.003$).

Average lifetime residential latitude displayed significant covariate relationships with the presence of sun exposure-related malignant skin neoplasms ($p=0.012$ for the verified set; $p=0.008$ for the verified and suspected set). For participants with an average lifetime residential latitude below 37 degrees, 9.6 percent had a verified sun exposure-related malignant skin neoplasm, compared to 6.6 percent for participants with average lifetime residential latitudes at or above 37 degrees.

TABLE 10-9.

Adjusted Analysis for Basal Cell Carcinoma and Sun Exposure-Related Malignant Skin Neoplasms by Group (Nonblacks Only)

Cell Type (Status)	Statistic	Group		Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
		Ranch Hand	Comparison			
Basal Cell Carcinoma (Verified)	n	912	1,184	1.46 (1.04,2.06)	0.030	SUNREPEAT (p=0.011) LAT (p=0.007) AGE*ETHBACK (p=0.037) SUN2HR*RAD (p=0.045)
Basal Cell Carcinoma (Verified and Suspected)	n	912	1,184	1.39 (1.00,1.95)	0.053	SUN2HR (p<0.001) SUNREPEAT (p=0.015) LAT (p=0.006) RAD (p=0.043) AGE*ETHBACK (p=0.036)
Sun Exposure-Related Malignant Skin Neoplasms (Verified)	n	912	1,184	1.48 (1.07,2.04)	0.019	SUN2HR (p<0.001) SUNREPEAT (p=0.002) LAT (p=0.010) AGE*ETHBACK (p=0.032)
Sun Exposure-Related Malignant Skin Neoplasms (Verified and Suspected)	n	912	1,184	1.39 (1.01,1.91)	0.044	SUNREPEAT (p=0.002) AGE*ETHBACK (p=0.028) SUN2HR*LAT (p=0.019)

For asbestos exposure, there was a borderline significant covariate association with the presence of verified sun exposure-related malignant skin neoplasms ($p=0.078$). However, the covariate association was inversely related to asbestos exposure. For participants exposed to asbestos, 6.1 percent had a verified sun exposure-related malignant skin neoplasm, compared to 8.6 percent for those not exposed to asbestos.

Ionizing radiation exposure also displayed covariate associations with sun exposure-related malignant skin neoplasms ($p=0.044$ for the verified set; $p=0.024$ for the verified and suspected set). For participants exposed to ionizing radiation, 10.2 percent had a verified sun exposure-related malignant skin neoplasm, compared to 7.3 percent of the participants not exposed to ionizing radiation.

Self-reported herbicide exposure exhibited a borderline significant covariate relationship with the verified and suspected sun exposure-related malignant skin neoplasms ($p=0.098$). For participants reporting herbicide exposure, 9.1 percent had a sun exposure-related malignant skin neoplasm, compared to 7.0 percent not reporting herbicide exposure.

For ethnic background, there were significant covariate associations with the presence of sun exposure-related malignant skin neoplasms ($p=0.032$ for the verified set; $p=0.045$ for the verified and suspected set). For the ethnic group categories, the following percentages of participants with verified sun exposure-related malignant skin neoplasms were obtained: 9.0 percent for group A; 6.3 percent for Group B; 1.7 percent for Group C; and 0.0 percent for groups D and E.

A marginally significant association was found between skin color and verified and suspected sun exposure-related malignant skin neoplasms ($p=0.088$). Percentages of participants with verified and suspected sun exposure-related malignant skin neoplasms were determined for the following skin tones: 0.0 percent for dark; 2.7 percent for medium; 5.7 percent for pale; 8.8 percent for dark peach; and 9.6 percent for pale peach.

Significant associations were found between hair color and sun exposure-related malignant skin neoplasms ($p=0.003$ for verified; $p=0.001$ for verified and suspected). Percentages of participants with verified sun exposure-related malignant skin neoplasms were determined for the following hair colors: 7.7 percent for black; 6.0 percent for dark brown; 10.8 percent for light brown; 11.3 percent for blonde; and 18.8 percent for red.

For skin reaction to sun exposure after at least 2 hours (assuming several preceding episodes of sun exposure), significant associations were found for sun exposure-related malignant skin neoplasms ($p<0.001$ for verified; $p<0.001$ for verified and suspected). For participants having no reaction, 4.7 percent had a verified sun exposure-related malignant skin neoplasm; for those that became red, 8.4 percent had a verified sun exposure-related malignant skin neoplasm; for participants that burned, 15.5 percent had this type of neoplasm; and for those that burned painfully, 9.3 percent had a verified sun exposure-related malignant skin neoplasm.

Skin reaction after repeated sun exposure displayed a significant covariate association with both the verified, and the verified and suspected,

sun exposure-related malignant skin neoplasms ($p<0.001$ for both sets). For participants who tanned deep brown, 5.1 percent had a verified sun exposure-related malignant skin neoplasm; for those who tanned moderately, 8.2 percent had a verified sun exposure-related malignant skin neoplasm; for those who tanned mildly, 10.7 percent had this form of neoplasm; and for those who had freckles with no tan, 27.7 percent had this type of malignant condition.

For the composite sun reaction index, there were significant covariate associations for both the verified, and the verified and suspected, sun exposure-related malignant skin neoplasms ($p<0.001$ for both sets). For those participants having a low composite sun reaction index, 6.2 percent had a verified sun exposure-related malignant skin neoplasm; for participants with a medium sun reaction index, 12.4 percent had a verified sun exposure-related malignant skin neoplasm; and for those having a high composite sun reaction index, 13.1 percent had a verified sun exposure-related malignant skin neoplasm.

Sun Exposure-Related Malignant Skin Neoplasms (Adjusted Group Contrast Analyses)

The adjusted analysis results for sun exposure-related malignant neoplasms are presented in Table 10-9. For the set of verified sun exposure-related malignant skin neoplasms, the adjusted contrast of the Ranch Hands and Comparisons was significant ($p=0.019$), with an adjusted relative risk of 1.48 (95% C.I.: [1.07,2.04]). For the adjusted model, the significant covariates were skin reaction after at least 2 hours exposure ($p<0.001$) and repeated sun exposure ($p=0.002$), and average lifetime residential latitude ($p=0.010$). The age-by-ethnic background interaction was again significant ($p=0.032$). For the combined set of verified and suspected sun exposure-related malignant skin neoplasms, the significant adjusted group contrast ($p=0.044$) had an adjusted relative risk of 1.39 (95% C.I.: [1.01,1.91]). For this analysis, repeated sun exposure was a significant covariate ($p=0.002$); there was a significant age-by-ethnic background interaction ($p=0.028$) and a significant interaction between the covariates for skin reaction after at least 2 hours sun exposure and average lifetime residential latitude ($p=0.019$).

Systemic Neoplasms

Ranch Hands and Comparisons were compared on their relative frequencies of systemic neoplasms for the following three groups of analyses: behavior; malignant neoplasms by location/site; and malignant systemic neoplasms conditioned on the presence of any systemic neoplasm. For malignant systemic neoplasms, covariate associations and adjusted group analysis were performed.

Behavior

Table 10-10 displays the distribution of Ranch Hands and Comparisons having malignant systemic neoplasms, benign systemic neoplasms, systemic neoplasms of uncertain behavior or unspecified nature, and all systemic neoplasms. Results are presented for verified systemic neoplasms and for verified and suspected systemic neoplasms.

TABLE 10-10.

Unadjusted Analysis for Systemic Neoplasms by Behavior, Status, and Group

Behavior (Status)	Statistic	Group: Ranch Hand		Group: Comparison		Est. Relative Risk (95% C.I.)	p-Value
Malignant (Verified)	n	995		1,299			
	Number/%						
	Yes	21	2.1%	21	1.6%	1.31 (0.71,2.42)	0.472
	No	974	97.9%	1,278	98.4%		
Malignant (Verified and Suspected)	n	995		1,299			
	Number/%						
	Yes	21	2.1%	23	1.8%	1.20 (0.66,2.17)	0.660
	No	974	97.9%	1,276	98.2%		
Benign (Verified)	n	995		1,299			
	Number/%						
	Yes	55	5.5%	69	5.3%	1.04 (0.73,1.50)	0.892
	No	940	94.5%	1,230	94.7%		
Benign (Verified and Suspected)	n	995		1,299			
	Number/%						
	Yes	55	5.5%	71	5.5%	1.01 (0.71,1.45)	0.999
	No	940	94.5%	1,228	94.5%		
Uncertain Behavior or Unspecified Nature (Verified)	n	995		1,299			
	Number/%						
	Yes	5	0.5%	8	0.6%	0.82 (0.27,2.50)	0.948
	No	990	99.5%	1,291	99.4%		

TABLE 10-10. (continued)

Unadjusted Analysis for Systemic Neoplasms by Behavior, Status, and Group

Behavior (Status)	Statistic	Group				Est. Relative Risk (95% C.I.)	p-Value
		Ranch Hand		Comparison			
Uncertain Behavior or Unspecified Nature (Verified and Suspected)	n	995		1,299			
	Number/%						
	Yes	7	0.7%	11	0.9%	0.83 (0.32,2.15)	0.892
	No	988	99.3%	1,288	99.1%		
All (Verified)	n	995		1,299			
	Number/%						
	Yes	80	8.0%	97	7.5%	1.08 (0.80,1.48)	0.666
	No	915	92.0%	1,202	92.5%		
All (Verified and Suspected)	n	995		1,299			
	Number/%						
	Yes	82	8.2%	104	8.0%	1.03 (0.76,1.40)	0.896
	No	913	91.8%	1,195	92.0%		

For malignant systemic neoplasms, Ranch Hands and Comparisons were not significantly different for the unadjusted analyses (p=0.472 for verified; p=0.660 for verified and suspected). Ranch Hands and Comparisons also did not differ significantly for the unadjusted analyses of benign systemic neoplasms (p=0.892 for verified; p=0.999 for verified and suspected). The Ranch Hand and Comparison unadjusted group contrasts for systemic neoplasms of uncertain behavior or unspecified nature were not significant (p=0.948 for verified; p=0.892 for verified and suspected).

The unadjusted analysis comparing Ranch Hands and Comparisons for all systemic neoplasms (malignant, benign, and uncertain behavior or unspecified nature) also did not exhibit a significant group difference (p=0.666 for verified; p=0.896 for verified and suspected).

Malignant Neoplasms by Location/Site

Table 10-11 summarizes the distributions of Ranch Hands and Comparisons having malignant systemic neoplasms by location/site. The statistical power for detecting group differences on the frequency of systemic neoplasms at specified sites is low. Results are presented both for verified, and verified and suspected, systemic neoplasms when appropriate. The results presented in Table 10-11 incorporate corrections to the 1985 followup data that were made after additional medical records were obtained (see Table 10-9 on page 10-26 and Table 10-17 on page 10-44 of the 1985 followup report). In the 1985 followup report, one Ranch Hand was counted as having a verified malignant systemic neoplasm of the eye. This was actually a skin neoplasm of the eyelid. The 1985 followup report also counted one Ranch Hand and one Comparison with verified malignant systemic neoplasms of ill-defined sites; both of these were subsequently verified as skin neoplasms. In addition, two Ranch Hands, instead of three Ranch Hands, had verified systemic testicular cancer. At the 1987 followup, an additional Ranch Hand was diagnosed as having testicular cancer, bringing the Ranch Hand total back to three cases (see Table 10-11). Also in the 1985 followup report (Table 10-9), one of the Ranch Hand bronchus and lung suspected systemic neoplasms should have been included in the Comparison group.

For verified malignant systemic neoplasms of the oral cavity, pharynx, and larynx, the unadjusted analysis comparing Ranch Hands and Comparisons was not significant (p=0.440). Ranch Hands and Comparisons did not differ significantly for the unadjusted analysis comparing the distributions of participants having verified malignant systemic neoplasms of the thyroid (p=0.999). For the unadjusted group contrast of verified, and verified and suspected, malignant systemic neoplasms of the bronchus and lung, there were no significant differences (p=0.999 and p=0.999, respectively).

For verified malignant systemic neoplasms of the colon and rectum, the distributions of Ranch Hands and Comparisons were not significantly different (p=0.836). The unadjusted group contrast comparing the distributions of Ranch Hands and Comparisons for verified malignant systemic neoplasms of the kidney and bladder was not significant (p=0.460). The unadjusted group contrast for Ranch Hands and Comparisons were not significant for verified malignant systemic neoplasms of the prostate, testicles, or penis (p=0.698, 0.162, and 0.999, respectively). For malignant systemic neoplasms of ill-defined sites, Ranch Hands and Comparisons did not differ significantly for the verified and

TABLE 10-11.

Unadjusted Analysis for Malignant Systemic Neoplasms by Location/Site, Status, and Group

Location/Site (Status)	Statistic	Group: Ranch Hand		Group: Comparison		Est. Relative Risk (95% C.I.)	p-Value
Oral Cavity, Pharynx, and Larynx (Verified*)	n	995		1,299			
	Number/%						
	Yes	3	0.3%	1	0.1%	3.93 (0.41,37.79)	0.440
	No	992	97.7%	1,298	99.9%		
Thyroid (Verified*)	n	995		1,299			
	Number/%						
	Yes	0	0.0%	1	0.1%	--[a]	0.999
	No	995	100.0%	1,298	99.9%		
Bronchus and Lung (Verified)	n	995		1,299			
	Number/%						
	Yes	3	0.3%	3	0.2%	1.31 (0.26,6.49)	0.999
	No	992	99.7%	1,296	99.8%		
Bronchus and Lung (Verified and Suspected)	n	995		1,299			
	Number/%						
	Yes	3	0.3%	4	0.3%	0.98 (0.22,4.39)	0.999
	No	992	99.7%	1,295	99.7%		
Colon and Rectum (Verified*)	n	995		1,299			
	Number/%						
	Yes	1	0.1%	3	0.2%	0.44 (0.05,4.18)	0.836
	No	994	99.9%	1,296	99.8%		

TABLE 10-11. (continued)

Unadjusted Analysis for Malignant Systemic Neoplasms by Location/Site, Status, and Group

Location/Site (Status)	Statistic	Group: Ranch Hand	Group: Comparison	Est. Relative Risk (95% C.I.)	p-Value
Kidney and Bladder (Verified*)	n	995	1,299		
	Number/%				
	Yes	5 0.5%	3 0.2%	2.18 (0.52,9.15)	0.460
	No	990 99.5%	1,296 99.8%		
Prostate (Verified*)	n	995	1,299		
	Number/%				
	Yes	2 0.2%	5 0.4%	0.52 (0.10,2.69)	0.698
	No	993 99.8%	1,294 99.6%		
Testicles (Verified*)	n	995	1,299		
	Number/%				
	Yes	3 0.3%	0 0.0%	--[a]	0.162
	No	992 99.7%	1,299 100.0%		
Hodgkin's Disease (Verified*)	n	995	1,299		
	Number/%				
	Yes	0 0.0%	1 0.1%	--[a]	0.999
	No	995 100.0%	1,298 99.9%		
Ill-Defined Sites (Verified and Suspected**)	n	995	1,299		
	Number/%				
	Yes	0 0.0%	1 0.1%	--[a]	0.999
	No	995 100.0%	1,298 99.9%		

TABLE 10-11. (continued)

Unadjusted Analysis for Malignant Systemic Neoplasms by Location/Site, Status, and Group

Location/Site (Status)	Statistic	Group: Ranch Hand	Group: Comparison	Est. Relative Risk (95% C.I.)	p-Value
Thymus and Mediastinum (Verified*)	n	995	1,299		
	Number/%				
	Yes	2 0.2%	0 0.0%	--[a]	0.376
	No	993 99.8%	1,299 100.0%		
Head, Face, and Neck (Verified*)	n	995	1,299		
	Number/%				
	Yes	0 0.0%	1 0.1%	--[a]	0.999
	No	995 100.0%	1,298 99.9%		
Brain (Verified*)	n	995	1,299		
	Number/%				
	Yes	0 0.0%	1 0.1%	--[a]	0.999
	No	995 100.0%	1,298 99.9%		
Other Malignant Neoplasms of Lymphoid and Histiocytic Tissue (Verified*)	n	995	1,299		
	Number/%				
	Yes	2 0.2%	1 0.1%	2.61 (0.24,28.87)	0.802
	No	993 99.8%	1,298 99.9%		
Leukemia (Verified*)	n	995	1,299		
	Number/%				
	Yes	1 0.1%	0 0.0%	--[a]	0.868
	No	994 99.9%	1,299 100.0%		

TABLE 10-11. (continued)

Unadjusted Analysis for Malignant Systemic Neoplasms by Location/Site, Status, and Group

Location/Site (Status)	Statistic	Group: Ranch Hand		Group: Comparison		Est. Relative Risk (95% C.I.)	p-Value
Carcinoma In Situ of Penis (Verified*)	n	995		1,299			
	Number/%						
	Yes	0	0.0%	1	0.1%	--[a]	0.999
	No	995	100.0%	1,298	99.9%		
Carcinoma In Situ of Other Specified Sites (Verified*)	n	995		1,299			
	Number/%						
	Yes	1	0.1%	0	0.0%	--[a]	0.868
	No	994	99.9%	1,299	100.0%		

*No suspected malignant neoplasms; therefore, verified and suspected same as verified.

--[a]Estimated relative risk/confidence interval/p-value not given due to cell with zero frequency.

**No verified malignant neoplasms.

suspected neoplasms (p=0.999). The distribution of Ranch Hands having verified malignant systemic neoplasms of the thymus and mediastinum was not significantly different from that of the Comparisons (p=0.376).

For the head, face, and neck, Ranch Hands and Comparisons did not differ with respect to the occurrence of verified malignant systemic neoplasms (p=0.999). The Comparison had a verified fibrosarcoma of the neck. Ranch Hands and Comparisons did not differ significantly on their relative frequencies of verified malignant systemic neoplasms of the brain (p=0.999).

For the verified set of other malignant neoplasms of lymphoid and histiocytic tissue, Ranch Hands did not differ significantly from the Comparisons (p=0.802). One Ranch Hand had a verified NHL. For verified leukemia and Hodgkin's Disease, the unadjusted group contrasts of Ranch Hands versus Comparisons were not significant (p=0.868 and 0.999, respectively).

For verified carcinoma in situ of other and unspecified sites, the unadjusted group contrast was not significant (p=0.868).

Conditional Analyses

For participants with any verified systemic neoplasm (malignant, benign, uncertain behavior, or unspecified nature), 26.3 percent (21/80) of the Ranch Hands had malignant systemic neoplasms, compared to 21.6 percent (21/97) for the Comparison group. These percentages were not significantly different (p=0.590). Combining the verified and suspected systemic neoplasms, the corresponding Ranch Hand and Comparison percentages were 25.6 percent (21/82) and 22.1 percent (23/104), respectively. These percentages also were not statistically different (p=0.700).

Malignant Systemic Neoplasms (Covariate Associations)

All covariates described in Table 10-1 were investigated for associations with malignant systemic neoplasms, except average lifetime residential latitude and the host factors of ethnic background, skin color, hair color, eye color, and skin reactions to sun exposure. As noted previously, race was included among the candidate covariates for the malignant systemic neoplasms. Appendix Table G-1 contains the results of the covariate association analyses.

Age displayed significant covariate associations for both the verified malignant systemic neoplasms ($p<0.001$) and the verified and suspected malignant systemic neoplasms ($p<0.001$). For both sets, the relative frequency of malignant systemic neoplasms increased with age. Participants born in or after 1942 had lower relative frequencies of verified malignant systemic neoplasms (0.7%) than participants born between 1923 and 1941 (2.2%) or in or before 1922 (8.3%).

Occupation exhibited marginally significant associations with malignant systemic neoplasms (p=0.075 for verified; p=0.060 for verified and suspected). For verified malignant systemic neoplasms, the officers had the highest relative frequency (2.6%), followed by the enlisted flyers (1.6%), and then the enlisted groundcrew (1.3%).

Lifetime alcohol history displayed significant associations with malignant systemic neoplasms (p=0.041 for verified; p=0.010 for verified and suspected). For verified malignant systemic neoplasms, the relative frequency was highest for participants with more than 40 drink-years (0 drink-years: 1.5%; over 0 drink-years and not exceeding 40 drink-years: 1.4%; over 40 drink-years: 3.1%).

Although lifetime cigarette smoking history (p=0.198 for verified; p=0.208 for verified and suspected) and race (p=0.546 for verified; p=0.500 for verified and suspected) did not display significant associations with malignant systemic neoplasms, these covariates were also included in the adjusted systemic analyses because for some types of systemic neoplasms these covariates are known risk factors. Other covariates used for the adjusted analyses were: age, occupation, and lifetime alcohol history.

Malignant Systemic Neoplasms (Adjusted Group Contrast Analyses)

The adjusted analysis results for malignant systemic neoplasms are presented in Table 10-12. The Ranch Hand and Comparison groups did not differ for either the verified set of malignant systemic neoplasms (p=0.525) or the verified and suspected set of malignant systemic neoplasms (p=0.731). For verified malignant systemic neoplasms, age and lifetime alcohol history were significant covariates (p<0.001 and p=0.010, respectively). Similarly, for the verified and suspected malignant systemic neoplasms, age and lifetime alcohol history were significant covariates in the model (p<0.001 and p=0.006, respectively).

Skin and Systemic Neoplasms

Unadjusted analyses were performed for the combined set of all skin and all systemic neoplasms. For these analyses all 2,294 participants were used (i.e., Black participants were not excluded). For the verified skin and verified systemic neoplasms presented in Table 10-13, the Ranch Hand and Comparison groups differed significantly (p=0.032), with an estimated relative risk of 1.26 (95% C.I.: [1.03,1.54]). The relative frequencies for the combined set of verified skin and verified systemic neoplasms were 22.5 percent for the Ranch Hands and 18.8 percent for the Comparisons. For the verified and suspected set of skin and systemic neoplasms, the Ranch Hand and Comparison group contrast was borderline significant (p=0.079), with an estimated relative risk of 1.20 (95% C.I.: [0.98,1.47]). The relative frequencies of verified and suspected skin and systemic neoplasms for Ranch Hands and Comparisons were 22.8 percent and 19.7 percent, respectively.

Table 10-13 also presents unadjusted analyses comparing Ranch Hands and Comparisons on the frequency of nonverifiable skin and systemic neoplasms. The Ranch Hand and Comparison group contrast was not significant (p=0.744), indicating that the frequency of unverified reports of malignancy did not differ in the two groups.

TABLE 10-12.

Adjusted Analysis for Malignant Systemic Neoplasms by Status and Group

Variable (Status)	Statistic	Group		Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
		Ranch Hand	Comparison			
Malignant Systemic Neoplasms (Verified)	n	985	1,296	1.23 (0.66,2.29)	0.525	AGE (p<0.001) DRKYR (p=0.010)
Malignant Systemic Neoplasms (Verified and Suspected)	n	985	1,296	1.11 (0.60,2.06)	0.731	AGE (p<0.001) DRKYR (p=0.006)

TABLE 10-13.

Unadjusted Analysis for Verified, Suspected, and Nonverifiable Skin and Systemic Neoplasms by Group

Variable	Statistic	Group				Est. Relative Risk (95% C.I.)	p-Value
		Ranch Hand		Comparison			
All Skin and Systemic (Verified)	n	995		1,299			
	Number/%						
	Yes	224	22.5%	244	18.8%	1.26 (1.03,1.54)	0.032
	No	771	77.5%	1,055	81.2%		
All Skin and Systemic (Verified and Suspected)	n	995		1,299			
	Number/%						
	Yes	227	22.8%	256	19.7%	1.20 (0.98,1.47)	0.079
	No	768	77.2%	1,043	80.3%		
Nonverifiable Neoplasm	n	995		1,299			
	Number/%						
	Yes	23	2.3%	34	2.6%	--	0.744
	No	972	97.7%	1,265	97.4%		

--Relative risk and associated confidence interval not appropriate.

Exposure Index Analysis

Table 10-14 summarizes, within each occupational stratum, the unadjusted results comparing the relative frequencies of basal cell carcinoma, sun exposure-related malignant skin neoplasms, and malignant systemic neoplasms in the Ranch Hand group across exposure categories. For basal cell carcinoma, sun exposure-related malignant skin neoplasms, and malignant systemic neoplasms, Table 10-15 summarizes by occupation the adjusted exposure index analyses for the Ranch Hands. The covariates, in addition to exposure index, included in the adjusted analysis models for basal cell carcinoma and sun exposure-related malignant skin neoplasms were age, skin reaction after at least 2 hours sun exposure (assuming several preceding episodes of sun exposure) and after repeated sun exposure, ethnic background, average lifetime residential latitude, and ionizing radiation exposure. The covariates, in addition to exposure index, included in the adjusted analysis models for malignant systemic neoplasms were age, race, lifetime cigarette smoking history, and lifetime alcohol history. Models investigated also included the exposure index-by-covariate interaction terms.

The final interpretation of the 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.

Skin Neoplasms

Basal Cell Carcinoma

For the unadjusted analysis of the enlisted flyers presented in Table 10-14, the frequencies of verified basal cell carcinoma were borderline significant across the three exposure levels ($p=0.067$). However, the relative frequency was highest in the low exposure group. For this set of neoplasms, the contrast of the Ranch Hand frequency for the medium exposure group to the frequency for the low exposure group was also marginally significant ($p=0.088$). The medium versus low exposure contrast had an estimated relative risk of 0.27 (95% C.I.: [0.07,1.05]). For officers and for enlisted groundcrew, the relative frequencies of verified basal cell carcinoma did not differ significantly across exposure categories. For unadjusted analyses on the set of verified and suspected basal cell carcinomas, the difference for the enlisted flyers across the three exposure levels was more pronounced ($p=0.031$). However, the low exposure group again had the higher frequency of basal cell carcinomas. The contrast of the Ranch Hand enlisted flyers in the medium and low exposure categories was significant ($p=0.050$), with an estimated relative risk of 0.24 (95% C.I.: [0.06,0.91]). The corresponding contrast for the high and low exposure categories was borderline significant ($p=0.098$) with an estimated relative risk of 0.28 (95% C.I.: [0.07,1.09]). No significant differences were found for officers or enlisted groundcrew on the relative frequency of verified and suspected basal cell carcinoma across the exposure index categories.

Table 10-15 shows that for the Ranch Hand officers and enlisted groundcrew, there were no significant differences among the exposure levels for either the verified basal cell carcinomas or the verified and suspected

TABLE 10-14.

Unadjusted Exposure Index for Malignancy Variables by Occupation

Variable	Occupation	Statistic	Exposure Index						Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
			Low		Medium		High				
Basal Cell Carcinoma (Verified)[a]	Officer	n	128		121		123		Overall		0.556
		Number/%									
		Yes	11	8.6%	15	12.4%	15	12.2%	M vs. L	1.51 (0.66,3.42)	0.440
		No	117	91.4%	106	87.6%	108	87.8%	H vs. L	1.48 (0.65,3.36)	0.466
	Enlisted Flyer	n	54		59		50		Overall		0.067
		Number/%									
		Yes	9	16.7%	3	5.1%	3	6.0%	M vs. L	0.27 (0.07,1.05)	0.088
		No	45	83.3%	56	94.9%	47	94.0%	H vs. L	0.32 (0.08,1.26)	0.160
	Enlisted Groundcrew	n	131		144		128		Overall		0.615
		Number/%									
		Yes	9	6.9%	6	4.2%	7	5.5%	M vs. L	0.59 (0.20,1.70)	0.472
		No	122	93.1%	138	95.8%	121	94.5%	H vs. L	0.78 (0.28,2.17)	0.834
Basal Cell Carcinoma (Verified and Suspected)[a]	Officer	n	128		121		123		Overall		0.556
		Number/%									
		Yes	11	8.6%	15	12.4%	15	12.2%	M vs. L	1.51 (0.66,3.42)	0.440
		No	117	91.4%	106	87.6%	108	87.8%	H vs. L	1.48 (0.65,3.36)	0.466
	Enlisted Flyer	n	54		59		50		Overall		0.031
		Number/%									
		Yes	10	18.5%	3	5.1%	3	6.0%	M vs. L	0.24 (0.06,0.91)	0.050
		No	44	81.5%	56	94.9%	47	94.0%	H vs. L	0.28 (0.07,1.09)	0.098
	Enlisted Groundcrew	n	131		144		128		Overall		0.615
		Number/%									
		Yes	9	6.9%	6	4.2%	7	5.5%	M vs. L	0.59 (0.20,1.70)	0.472
		No	122	93.1%	138	95.8%	121	94.5%	H vs. L	0.78 (0.28,2.17)	0.834

TABLE 10-14. (continued)

Unadjusted Exposure Index for Malignancy Variables by Occupation

Variable	Occupation	Statistic	Exposure Index: Low		Exposure Index: Medium		Exposure Index: High		Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
Sun Exposure-Related Malignant Skin Neoplasms (Verified)[a]	Officer	n	128		121		123		Overall		0.636
		Number/%									
		Yes	14	10.9%	18	14.9%	15	12.2%	M vs. L	1.42 (0.67,3.01)	0.460
		No	114	89.1%	103	85.1%	108	87.8%	H vs. L	1.13 (0.52,2.45)	0.908
	Enlisted Flyer	n	54		59		50		Overall		0.059
		Number/%									
		Yes	10	18.5%	4	6.8%	3	6.0%	M vs. L	0.32 (0.09,1.09)	0.106
		No	44	81.5%	55	93.2%	47	94.0%	H vs. L	0.28 (0.07,1.09)	0.098
	Enlisted Groundcrew	n	131		144		128		Overall		0.865
		Number/%									
		Yes	9	6.9%	8	5.6%	7	5.5%	M vs. L	0.80 (0.30,2.13)	0.838
		No	122	93.1%	136	94.4%	121	94.5%	H vs. L	0.78 (0.28,2.17)	0.834
Sun Exposure-Related Malignant Skin Neoplasms (Verified and Suspected)[a]	Officer	n	128		121		123		Overall		0.636
		Number/%									
		Yes	14	10.9%	18	14.9%	15	12.2%	M vs. L	1.42 (0.67,3.01)	0.460
		No	114	89.1%	103	85.1%	108	87.8%	H vs. L	1.13 (0.52,2.45)	0.908
	Enlisted Flyer	n	54		59		50		Overall		0.028
		Number/%									
		Yes	11	20.4%	4	6.8%	3	6.0%	M vs. L	0.28 (0.09,0.96)	0.062
		No	43	79.6%	55	93.2%	47	94.0%	H vs. L	0.25 (0.07,0.96)	0.060
	Enlisted Groundcrew	n	131		144		128		Overall		0.865
		Number/%									
		Yes	9	6.9%	8	5.6%	7	5.5%	M vs. L	0.80 (0.30,2.13)	0.838
		No	122	93.1%	136	94.4%	121	94.5%	H vs. L	0.78 (0.28,2.17)	0.834

TABLE 10-14. (continued)

Unadjusted Exposure Index for Malignancy Variables by Occupation

Variable	Occupation	Statistic	Exposure Index: Low		Exposure Index: Medium		Exposure Index: High		Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
Malignant Systemic Neoplasms (Verified*)	Officer	n	130		124		125		Overall		0.464
		Number/%									
		Yes	2	1.5%	3	2.4%	5	4.0%	M vs. L	1.59 (0.26,9.66)	0.956
		No	128	98.5%	121	97.6%	120	96.0%	H vs. L	2.67 (0.51,14.01)	0.414
	Enlisted Flyer	n	55		63		53		Overall		0.393
		Number/%									
		Yes	2	3.6%	2	3.2%	0	0.0%	M vs. L	0.87 (0.12,6.38)	0.999
		No	53	96.4%	61	96.8%	53	100.0%	H vs. L	--[b]	0.514
	Enlisted Groundcrew	n	147		158		140		Overall		0.135
		Number/%									
		Yes	1	0.7%	5	3.2%	1	0.7%	M vs. L	4.77 (0.55,41.33)	0.250
		No	146	99.3%	153	96.8%	139	99.3%	H vs. L	1.05 (0.07,16.96)	0.999

[a]Nonblacks only.

*No suspected malignant neoplasms; therefore, verified and suspected same as verified.

--[b]Estimated relative risk and confidence interval not given due to cell with zero frequency.

TABLE 10-15.

Adjusted Exposure Index for Malignancy Variables by Occupation

Variable	Occupation	Statistic	Exposure Index			Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value
			Low	Medium	High			
Basal Cell Carcinoma (Verified)[a]	Officer	n	128	118	119	Overall		0.753
						M vs. L	1.37 (0.57,3.28)	0.480
						H vs. L	1.30 (0.54,3.10)	0.561
	Enlisted Flyer	n	49	56	49	Overall		0.058**
						M vs. L	0.21 (0.05,1.01)**	0.051**
						H vs. L	0.26 (0.06,1.18)**	0.080**
	Enlisted Groundcrew	n	126	140	127	Overall		0.673
						M vs. L	0.64 (0.21,1.90)	0.420
						H vs. L	0.69 (0.24,1.96)	0.485
Basal Cell Carcinoma (Verified and Suspected)[a]	Officer	n	128	118	119	Overall		0.753
						M vs. L	1.37 (0.57,3.28)	0.480
						H vs. L	1.30 (0.54,3.10)	0.561
	Enlisted Flyer	n	49	56	49	Overall		0.023**
						M vs. L	0.18 (0.04,0.83)**	0.028**
						H vs. L	0.21 (0.05,0.95)**	0.042**
	Enlisted Groundcrew	n	126	140	127	Overall		0.673
						M vs. L	0.64 (0.21,1.90)	0.420
						H vs. L	0.69 (0.24,1.96)	0.485

TABLE 10-15. (continued)

Adjusted Exposure Index for Malignancy Variables by Occupation

Variable	Occupation	Statistic	Exposure Index			Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value
			Low	Medium	High			
Sun Exposure-Related Malignant Skin Neoplasms (Verified)[a]	Officer	n	128	118	119	Overall		0.762
						M vs. L	1.29 (0.58,2.89)	0.537
						H vs. L	0.98 (0.43,2.26)	0.966
	Enlisted Flyer	n	49	56	49	Overall		0.046**
						M vs. L	0.27 (0.06,1.11)**	0.070**
						H vs. L	0.20 (0.04,0.92)**	0.039**
	Enlisted Groundcrew	n	126	140	127	Overall		0.805
						M vs. L	0.90 (0.33,2.47)	0.834
						H vs. L	0.71 (0.25,2.01)	0.519
Sun Exposure-Related Malignant Skin Neoplasms (Verified and Suspected)[a]	Officer	n	128	118	119	Overall		0.762
						M vs. L	1.29 (0.58,2.89)	0.537
						H vs. L	0.98 (0.43,3.26)	0.966
	Enlisted Flyer	n	49	56	49	Overall		0.017**
						M vs. L	0.22 (0.05,0.92)**	0.038**
						H vs. L	0.16 (0.04,0.75)**	0.020**
	Enlisted Groundcrew	n	126	140	127	Overall		0.805
						M vs. L	0.90 (0.33,2.47)	0.834
						H vs. L	0.71 (0.25,2.01)	0.519

TABLE 10-15. (continued)

Adjusted Exposure Index for Malignancy Variables by Occupation

Variable	Occupation	Statistic	Exposure Index			Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value
			Low	Medium	High			
Systemic Malignant Neoplasms (Verified*)	Officer	n	129	122	125	Overall		0.536
						M vs. L	1.42 (0.22,9.01)	0.708
						H vs. L	2.43 (0.45,13.00)	0.300
	Enlisted Flyer	n	54	62	53	Overall		0.225
						M vs. L	1.99 (0.17,23.56)	0.587
						H vs. L	--[b]	--[b]
	Enlisted Groundcrew	n	144	158	138	Overall		0.024**
						M vs. L	8.97 (0.79,101.9)**	0.077**
						H vs. L	0.42 (0.01,13.01)**	0.621**

[a]Nonblacks only.

**Exposure index-by-covariate interaction ($0.01 < p \leq 0.05$)--relative risk and p-value purposes and derived from a model fitted after deletion of this interaction.

*No suspected malignant neoplasms; therefore, verified and suspected same as verified.

--[b]Relative risk/confidence interval/p-value not given due to cells with zero frequency.

basal cell carcinomas. However, Table 10-16 summarizes significant exposure index-by-age interactions for the Ranch Hand enlisted flyers. There were significant exposure index-by-age interactions for the set of verified basal cell carcinomas (p=0.027) and verified and suspected basal cell carcinomas (p=0.043). Appendix Table G-3 summarizes the results of stratifying the enlisted flyers by age. (Because there were only two Ranch Hands born before 1922 for this occupational cohort, age was dichotomized into born before 1942 and born in or after 1942.) For both sets of basal cell carcinoma analyses, Ranch Hand enlisted flyers born before 1942 had significantly different relative frequencies of the skin neoplasms by exposure category (p=0.014 for verified basal carcinoma; p=0.006 for verified and suspected basal cell carcinoma). However the relative frequencies were inversely related to the exposure index (i.e., the low exposure category had the highest relative frequency). Pairwise contrasts of the medium or high exposure levels with the low exposure level were also significant or borderline significant, although the differences were not consistent with a relationship of increasing exposure. For the enlisted flyer analyses that had significant exposure index-by-age interactions, a second adjusted analysis was performed without this interaction. Table 10-15 presents the results of these secondary analyses. For verified basal cell carcinoma, the group difference for the enlisted flyers was marginally significant (p=0.058), and for the verified and suspected set of basal cell carcinoma, the group difference for the enlisted flyers was significant (p=0.023). Estimated relative risks for the medium versus low, and the high versus low, contrasts were significant or borderline significant; however, these relative risks were less than 1 and not supportive of a dose-response effect.

TABLE 10-16.

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

Variable	Occupation	Covariate	p-Value
Basal Cell Carcinoma (Verified)	Enlisted Flyer	Age	0.027
Basal Cell Carcinoma (Verified and Suspected)	Enlisted Flyer	Age	0.043
Sun Exposure-Related Malignant Skin Neoplasms (Verified)	Enlisted Flyer	Age	0.020
Sun Exposure-Related Malignant Skin Neoplasms (Verified and Suspected)	Enlisted Flyer	Age	0.037
Malignant Systemic Neoplasms (Verified)	Enlisted Groundcrew	Race	0.045

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

Sun Exposure-Related Malignant Skin Neoplasms

The unadjusted analyses for the sun exposure-related malignant skin neoplasms, presented in Table 10-14, displayed similar patterns to basal cell carcinoma of borderline or significant differences among the enlisted flyer group. However, the differences were again due to higher frequencies found in the low exposure category. This observation parallels that seen for basal cell carcinoma since participants with basal cell tumors comprise 90 percent of the participants with sun exposure-related malignancies. For the verified set of sun exposure-related malignant skin neoplasms, there was a borderline significant difference in the Ranch Hand enlisted flyer frequencies ($p=0.059$) across exposure categories. The contrast for high versus low exposure was also borderline significant ($p=0.098$). No significant differences were found for the officers or enlisted groundcrew. For the verified and suspected set, the frequencies for the enlisted flyers differed significantly ($p=0.028$) across the exposure categories. However, the low exposure group again had the highest frequency. The borderline significant contrast of medium versus low exposure ($p=0.062$) had an estimated relative risk of 0.28 (95% C.I.: [0.09,0.96]). The contrast of high versus low exposure also had a borderline significant difference ($p=0.060$) with an estimated relative risk of 0.25 (95% C.I.: [0.07,0.96]).

For the adjusted exposure index analyses, Table 10-15 shows that for the Ranch Hand officers and enlisted groundcrew, there were no significant differences among the exposure levels for either the verified or the verified and suspected set of sun exposure-related malignant skin neoplasms. Table 10-16 summarizes significant exposure index-by-age interactions for the Ranch Hand enlisted flyers. There were significant exposure index-by-age interactions for the set of verified sun exposure-related malignant skin neoplasms ($p=0.020$), and verified and suspected sun exposure-related malignant skin neoplasms ($p=0.037$). Similar to the adjusted analyses for basal cell carcinoma, Appendix Table G-3 summarizes the results of stratifying the enlisted flyers by age for the set of sun exposure-related malignant skin neoplasms. For the verified, and verified and suspected, sun exposure-related malignant skin neoplasms, Ranch Hand enlisted flyers born prior to 1942 had significantly different relative frequencies of the skin neoplasms by exposure index ($p=0.013$ for verified sun exposure-related malignant skin neoplasms; $p=0.005$ for verified and suspected sun exposure-related malignant skin neoplasms). However, similar to basal cell carcinoma, the relative frequencies were inversely related to exposure index (i.e., the low exposure category had the highest relative frequency). Pairwise contrasts of the medium or high exposure levels with the low exposure level were also significant or borderline significant, although the differences were not consistent with a relationship of increasing exposure. For the enlisted flyer analyses having significant exposure index-by-age interactions, a second adjusted analysis was performed without this interaction. Table 10-15 presents the results of these secondary analyses. For verified sun exposure-related malignant skin neoplasms, the enlisted flyer group difference was significant ($p=0.046$). For verified and suspected sun exposure-related malignant skin neoplasms, the enlisted flyer group difference was also significant ($p=0.017$). Again, relative risks were not supportive of an increasing rate of sun exposure-related malignant skin neoplasms with increasing exposure.

Malignant Systemic Neoplasms

For each Ranch Hand occupational group, Table 10-14 summarizes the unadjusted analyses comparing the relative frequencies of verified malignant systemic neoplasms by exposure index. There were no significant differences across the exposure levels (officers: p=0.464; enlisted flyers: p=0.393; enlisted groundcrew: p=0.135). Table 10-14 presents comparisons only for verified malignant systemic neoplasms because there were no suspected malignant systemic neoplasms.

For malignant systemic neoplasms, Table 10-15 summarizes by occupation the adjusted exposure index analyses for the Ranch Hands. As noted above for the unadjusted analyses, there were no suspected malignant systemic neoplasms; therefore, adjusted analysis results were presented only for verified malignant systemic neoplasms.

Table 10-15 shows that for the Ranch Hand officers and enlisted flyers, there were no significant differences among the exposure levels for verified malignant systemic neoplasms (p=0.536 and p=0.225, respectively). However, for the enlisted groundcrew, there was a significant exposure index-by-race interaction (p=0.045), as presented in Table 10-16. For this interaction, the enlisted groundcrew results were stratified by race. The stratified results are presented in Appendix Table G-3. The overall comparison of the relative frequencies of verified malignant systemic neoplasms across exposure index levels was significant for the nonblack Ranch Hand enlisted groundcrew (p=0.046). Relative risks and confidence intervals for contrasts of the exposure index categories were not given due to sparse occurrence of malignant systemic neoplasms. For the enlisted groundcrew, a second adjusted analysis, presented in Table 10-15, was performed without this interaction. For this secondary analysis, the exposure index contrast was significant (p=0.024), but still not supportive of a dose-response relationship across the three exposure categories with higher rates in the medium exposure category.

Mortality and Malignant Neoplasm History

This section summarizes the survival status and malignant neoplasm history of the fully compliant Baseline participants through the 1987 followup examination. Survival status was determined through the end of 1987.

Of the 1,045 Ranch Hands and 1,224 Comparisons who were fully compliant at Baseline, 944 Ranch Hands (90.3%) and 1,113 Comparisons (90.9%) returned for the 1987 followup examination. Table 10-17 presents numbers of fully compliant Baseline Ranch Hands and Comparisons by participation/nonparticipation in the 1987 followup examination and by survival status at the end of 1987.

For the 101 Ranch Hands and 111 Comparisons who did not return for the 1987 followup examination, Table 10-18 shows that in 5 of the 20 deaths among Ranch Hands, malignant neoplasm was the primary cause of death. Of the five dead Ranch Hands, three died with lung cancer, one died with a malignant neoplasm of the pancreas, and one died with a histiocytoma of the lower limb.

TABLE 10-17.

Number of Fully Compliant Baseline Participants by Participation at 1987 Followup Examination, Survival Status, and Group

Participated in 1987 Followup Examination	Survival Status	Group		Total
		Ranch Hand	Comparison	
Yes	Dead[a]	2	2	4[b]
	Alive	942	1,111	2,053
No	Dead	20	29	49
	Alive	81	82	163
Total		1,045	1,224	2,269

[a]Died in 1987, but subsequent to participation in the 1987 followup examination.

[b]One Comparison died of malignant neoplasm of the lung; the other three deaths (two Ranch Hands, one Comparison) were not cancer-related.

Similarly, 11 of the 29 deaths among Comparisons had malignant neoplasm listed as the primary cause of death. Of the 11 dead Comparisons, 4 died with lung cancer, 4 with cancer of the colon, 1 had cancer of the stomach, 1 died with cancer of the mouth, and 1 died with cancer of the neck. One Ranch Hand died with a malignant neoplasm (basal cell carcinoma of the right temple) that was not the primary cause of death. The primary cause of death for the Ranch Hand was listed as "complications from thromboembolism following heart surgery."

Among the 81 surviving Ranch Hands who did not return for the 1987 followup, 5 Ranch Hands had verified malignant neoplasms at Baseline. Two of the five Ranch Hands had malignant neoplasms at multiple sites. One Ranch Hand was diagnosed as having basal cell carcinoma of the skin of the external ear, skin of the cheek, and skin of the nose; the other Ranch Hand had basal cell carcinoma of the skin of the forehead and skin of the external ear. For the other three Ranch Hands, the malignant neoplasms were an adenocarcinoma of the kidney, basal cell carcinoma of the skin of the forearm, and squamous cell carcinoma of the lower lip. In contrast, 4 of the 82 nonreturning but surviving Comparisons had a verified malignant neoplasm. Among the four Comparisons, one participant had basal cell carcinoma of the skin of the shoulder, skin of the neck, and skin of the back. One Comparison had a basal cell carcinoma of the skin of the external ear, and the other two Comparisons each had basal cell carcinoma of the skin of the nose.

TABLE 10-18.

Fully Compliant Baseline Participants
Who Did Not Participate in the 1987 Followup Examination
by Survival Status and Group

Survival Status	Group		Total
	Ranch Hand	Comparison	
Dead: Primary Cause of Death			
Malignant Neoplasm	5[a]	11[b]	16
Other Causes	15[c]	18	33
Alive			
Verified Malignant Neoplasm at Baseline	5[d]	4[•]	9
No Verified Malignant Neoplasm at Baseline	76	78	154

[a]Three Ranch Hands with lung cancer, one with malignant neoplasm of the pancreas, and one with histiocytoma of lower limb.

[b]Four Comparisons with lung cancer, four with cancer of the colon, one with cancer of the stomach, one with cancer of the mouth, and one with cancer of the neck.

[c]One Ranch Hand had a basal cell carcinoma of the right temple, which was not the primary cause of death. The primary cause of death was listed as "complications from thromboembolism following heart surgery."

[d]One Ranch Hand with basal cell carcinoma of the skin of the external ear, skin of the cheek, and skin of the nose; one with basal cell carcinoma of the skin of the forehead and skin of the external ear; one with adenocarcinoma of the kidney; one with basal cell carcinoma of the skin of the forearm; one with squamous cell carcinoma of the lower lip.

[•]One Comparison with basal cell carcinoma of the skin of the shoulder, skin of the neck, and skin of the back; two with basal cell carcinoma of the skin of the nose; and one with basal cell carcinoma of the skin of the external ear.

In summary, 11 of the 101 Ranch Hands (10.9%) not returning for the 1987 followup examination had incident or fatal neoplasms, compared to 15 of the 111 Comparisons (13.5%). This group difference was not significant (p=0.712).

For fully compliant Baseline participants who also attended the 1985 and the 1987 followup studies, Table 10-19 presents numbers and percentages of Ranch Hands and Comparisons having verified malignant skin neoplasms first diagnosed at the specified Baseline and/or 1985 followup, 1987 and/or followup examinations. Table 10-20 is a similar summary for the verified malignant systemic neoplasms.

TABLE 10-19.

Frequencies of Verified Malignant Skin Neoplasms[a] for Participants at the Baseline, 1985, and 1987 Followup Examinations by Group

Presence of Neoplasm at Examination			Ranch Hand		Comparison	
Baseline	1985	1987	Number	Percent	Number	Percent
Yes	Yes	Yes	1	(0.1%)	1	(0.1%)
Yes	Yes	No	6	(0.7%)	7	(0.7%)
Yes	No	Yes	3	(0.3%)	7	(0.7%)
Yes	No	No	28	(3.2%)	30	(2.9%)
No	Yes	Yes	4	(0.5%)	0	(0.0%)
No	Yes	No	17	(2.0%)	24	(2.3%)
No	No	Yes	17	(2.0%)	18	(1.8%)
No	No	No	794	(91.3%)	941	(91.5%)
			870		1,028	

[a]Blacks excluded.

TABLE 10-20.

Frequencies of Verified Malignant Systemic Neoplasms for Participants at the Baseline, 1985, and 1987 Followup Examinations by Group

Presence of Neoplasm at Examination			Ranch Hand		Comparison	
Baseline	1985	1987	Number	Percent	Number	Percent
Yes	Yes	Yes	0	(0.0%)	0	(0.0%)
Yes	Yes	No	0	(0.0%)	1	(0.1%)
Yes	No	Yes	0	(0.0%)	1	(0.1%)
Yes	No	No	10	(1.1%)	8	(0.7%)
No	Yes	Yes	0	(0.0%)	0	(0.0%)
No	Yes	No	2	(0.2%)	8	(0.7%)
No	No	Yes	8	(0.9%)	3	(0.3%)
No	No	No	904	(97.8%)	1,075	(98.1%)
			924		1,096	

DISCUSSION

In ambulatory medicine, the recommendation that asymptomatic individuals undergo periodic physical examinations is based largely on the assumption that such screening will reveal occult malignancy. Although the guidelines for the frequency and content of such examinations are subject to debate, there is no doubt that early detection affords the best and, in most forms of cancer, the only chance for cure. In this regard, while no one screening test is absolutely reliable, the scope and depth of the protocol employed in this longitudinal study far exceed what would be considered routine in clinical practice.

As the anatomic point of contact with industrial toxins and as the only organ system with a clearly defined clinical endpoint (chloracne) for TCDD exposure, the skin deserves the special emphasis it has received in this and in previous examination cycles. Though to date there is no epidemiologic evidence that TCDD exposure causes or that chloracne is associated with the development of basal cell carcinoma, an increased incidence of these skin cancers in the Ranch Hand cohort was found in the Baseline, and in the 1985 followup and 1987 followup examinations. Subsequent to the Baseline,

heightened efforts were made to clarify the contribution of such well-known risk factors as hair and eye color, complexion, ethnic background, and lifetime sun exposure.

While most of the systemic neoplasms subjected to analysis can be detected based on the history, physical examination, and laboratory data collected, several would require diagnostic studies beyond the scope of the current study. Reliably found on physical exam are tumors of the face, head and neck, oral cavity and pharynx (but not the hypopharynx or larynx), thyroid, prostate, and genitalia. The chest x ray can be relied upon to screen for tumors of the thymus, mediastinum, and lung, while the routine urinalysis, in disclosing hematuria, can signal the presence of kidney and bladder cancer. Recognizing the silent nature of digestive tract cancers, particularly those of colorectal origin, participants were encouraged to complete Hemoccult panels and, in positive cases, were offered sigmoidoscopy during their examinations.

Most of the significant dependent variable-covariate associations defined in these analyses would be expected based on patterns established in clinical practice. For basal cell skin cancers, positive associations were found with the classical risk factors of age, fair complexion, and average residential latitude.

Given the current knowledge of exposure levels in the Ranch Hand cohort, the higher frequency of basal cell carcinomas in the officers relative to the enlisted groundcrew (8.7% vs. 5.3%) does not provide evidence for the role of herbicides in the etiology of these cutaneous cancers. Of interest was the reduced frequency of basal cell cancer in those participants with the greatest skin sensitivity to sunlight, a finding that is consistent with behavior modification and exposure precaution in those most at risk.

In practice, dermatologists will vary in what they consider to be indications for the biopsy of suspicious lesions as called for in the study protocol. Acting independently and strictly blinded to the participants' exposure status, three dermatologists performed a total of 39 biopsies. As noted in Chapter 14, the close to equal number of biopsies in the Ranch Hands (19) and Comparisons (20) provides reassurance against the possibility of any significant selection bias in those lesions verified histologically.

With reference to the analysis of systemic neoplasms, the expected age-related increase in the incidence of cancer was documented in the total study population. The well-established clinical correlation of alcohol consumption with the development of systemic cancer was also observed ($p=0.041$). The Ranch Hand and the Comparison groups did not differ with respect to the frequency of systemic neoplasms. As in the Baseline and 1985 followup examinations, the relative frequency of verified cases of malignant systemic neoplasms did not differ significantly by group (2.1% in Ranch Hands, 1.6% in Comparisons). The number of cancers in specific categories was small and therefore statistical power to detect relative risks for specific cancers was low.

For the 1985 followup, one Ranch Hand and one Comparison had verified STS (fibrous histiocytoma and fibrosarcoma, respectively). The Ranch Hand was not part of the 1987 followup because he died; the Comparison with the fibro-

sarcoma was part of the 1987 followup. At the 1985 followup, one Ranch Hand was classified as a suspected leukemia, Hodgkin's Disease, or NHL. He was diagnosed as a verified leukemia by the time of the 1987 followup. At the 1987 followup, there was one verified case of NHL in a Ranch Hand.

In summary, the incidence of systemic cancer in all participants enrolled in this longitudinal study remains similar to the general population. As in the 1985 examination cycle, basal cell skin cancer appears to occur more frequently in the Ranch Hand cohort. With respect to systemic cancers, the Ranch Hand and Comparison group frequencies did not differ significantly. As in the past, no significant difference in cancer-related mortality was found between the study groups. To date, there has been one death in the Ranch Hand group related to soft tissue malignancy. One individual in the Comparison group has this diagnosis, but is still alive.

SUMMARY

For the 1987 followup analyses of skin neoplasms, a number of unadjusted analyses were performed to compare the Ranch Hand and Comparison groups on specified sets of verified skin malignancies and specified sets of verified and suspected skin malignancies. Selected adjusted analyses, which accounted for effects of specified covariates, were also undertaken. Table 10-21 summarizes the outcomes of the various unadjusted and adjusted analyses that were performed for the skin neoplasm assessment.

The unadjusted analyses of verified malignant skin neoplasms indicated a significant difference between the Ranch Hand and Comparison relative frequencies ($p=0.047$). For the verified and suspected malignant skin neoplasms, the relative frequencies for the Ranch Hands and Comparisons did not differ significantly ($p=0.101$). Unadjusted analyses of both the benign skin neoplasms and skin neoplasms of uncertain behavior or unspecified nature did not display significant group differences. Analyzing all skin neoplasms, (i.e., including the benign skin neoplasms and skin neoplasms of uncertain behavior or unspecified nature), unadjusted analyses indicated significant group differences at the 1987 followup ($p=0.012$ for the verified set; $p=0.029$ for the verified and suspected set).

For the 1987 followup, unadjusted analyses were performed comparing the Ranch Hands and Comparisons on their relative frequencies of basal cell carcinoma, squamous cell carcinoma, melanoma, and sun exposure-related malignant skin neoplasms. For basal cell carcinoma, there was a borderline significant unadjusted group difference for the verified set ($p=0.076$), and there was no significant difference for the verified and suspected set. Following adjustment by covariates, the group contrast for the verified set of basal cell carcinoma was significant ($p=0.030$). The adjusted group contrast for the verified and suspected set of basal cell carcinoma was borderline significant ($p=0.053$). At Baseline, a significantly higher rate of verified basal cell carcinoma was found for Ranch Hands in the unadjusted analysis. For the 1985 followup, the adjusted analysis of verified basal cell carcinoma displayed a significant group difference and the unadjusted analysis did not exhibit a significant group difference.

TABLE 10-21.

Overall Summary Results of Unadjusted and Adjusted Group Contrast Analyses of Malignancy Variables

Variable	Verification Status	Unadjusted	Adjusted	Direction of Results
Skin Neoplasms				
Behavior				
Malignant	V	0.047	--	RH>C[d]
	VS	NS	--	
Benign	V[a]	NS	--	
Uncertain Behavior or Unspecified Nature	V	NS	--	
	VS	NS	--	
All	V	0.012	--	RH>C[d]
	VS	0.029	--	RH>C[d]
Cell Type				
Basal Cell Carcinoma	V	NS*	0.030	RH>C[d]
	VS	NS	NS*	RH>C[d]
Squamous Cell Carcinoma	V[a]	NS	--	
Melanoma	V[a]	NS	--	
Sun Exposure-Related Malignant Skin Neoplasm	V	0.042	0.019	RH>C[d]
	VS	NS*	0.044	RH>C[d]
Basal Cell Carcinoma by Location/Site				
Ear, Face, Head, and Neck	V	NS	--	
	VS	NS	--	
Trunk	V	NS	--	
	VS	NS	--	
Upper Extremities	V[a]	NS	--	
Lower Extremities	V[a]	--[b]	--	
Other Sites and Sites NOS	V	NS	--	
	VS	NS	--	

TABLE 10-21. (continued)

Overall Summary Results of Unadjusted and Adjusted Group Contrast Analyses of Malignancy Variables

Variable	Verification Status	Unadjusted	Adjusted	Direction of Results
Melanoma by Location/Site				
Ear, Face, Head, and Neck	V[a]	NS	--	
Trunk	V[a]	NS	--	
Upper Extremities	V[a]	--[b]	--	
Lower Extremities	V[a]	--[b]	--	
Other Sites and Sites NOS	V[a]	--[b]	--	
Sun Exposure-Related Malignant Skin Neoplasms by Location/Site				
Ear, Face, Head, and Neck	V	NS	--	
	VS	NS	--	
Trunk	V	NS	--	
	VS	NS	--	
Upper Extremities	V[a]	0.044	--	RH>C[d]
Lower Extremities	V	--[b]	--	
Other Sites and Sites NOS	V	NS	--	
	VS	NS	--	
Basal Cell Carcinoma of the Ear, Face, Head and Neck by Occupation				
Officer	V	NS	--	
	VS	NS	--	
Enlisted Flyer	V	NS	--	
	VS	NS	--	
Enlisted Groundcrew	V	NS	--	
	VS	NS	--	

TABLE 10-21. (continued)

Overall Summary Results of Unadjusted and Adjusted Group Contrast Analyses of Malignancy Variables

Variable	Verification Status	Unadjusted	Adjusted	Direction of Results
Sun Exposure-Related Malignant Skin Neoplasms of the Ear, Face, Head, and Neck by Occupation				
Officer	V	NS*	--	RH>C[d]
	VS	NS	--	
Enlisted Flyer	V	NS	--	
	VS	NS	--	
Enlisted Groundcrew	V	NS	--	
	VS	NS	--	
Conditional Analyses				
Skin Neoplasm Conditioned on Neoplasm	V	NS*	--	RH>C[d]
	VS	NS*	--	RH>C[d]
Malignant Skin Conditioned on Skin Neoplasm	V	NS	--	
	VS	NS	--	
Basal Cell Carcinoma Conditioned on Malignant Skin Neoplasm	V	NS	--	
	VS	NS	--	
Basal Cell Carcinoma of Ear, Face, Head, and Neck Conditioned on Basal Cell Carcinoma	V	NS	--	
	VS	NS	--	
Sun Exposure-Related Malignant Skin Neoplasm of Ear, Face, Head, and Neck Conditioned on Sun Exposure-Related Malignant Skin Neoplasm	V	NS	--	
	VS	NS	--	
Multiple Basal Cell Carcinoma				
Zero, One, or Multiple	V	0.050	--	RH>C[d]
	VS	NS	--	
One vs. Zero	V	NS	--	
	VS	NS	--	
Multiple vs. Zero	V	0.032	--	RH>C[d]
	VS	NS*	--	RH>C[d]

TABLE 10-21. (continued)

Overall Summary Results of Unadjusted and Adjusted Group Contrast Analyses of Malignancy Variables

Variable	Verification Status	Unadjusted	Adjusted	Direction of Results
Systemic Neoplasms				
Behavior				
Malignant	V	NS	NS	
	VS	NS	NS	
Benign	V	NS	--	
	VS	NS	--	
Uncertain Behavior or Unspecified Nature	V	NS	--	
	VS	NS	--	
All	V	NS	--	
	VS	NS	--	
Malignant Systemic Neoplasms by Location/Site				
Oral Cavity, Pharynx, and Larynx	V[a]	NS	--	
Thyroid	V[a]	NS	--	
Bronchus and Lung	V	NS	--	
	VS	NS	--	
Colon and Rectum	V[a]	NS	--	
Kidney and Bladder	V[a]	NS	--	
Prostate	V[a]	NS	--	
Testicles	V[a]	NS	--	
Hodgkin's Disease	V[a]	NS	--	
Ill-Defined Sites	VS[c]	NS	--	
Thymus and Mediastinum	V[a]	NS	--	
Head, Face, and Neck	V[a]	NS	--	

TABLE 10-21. (continued)

Overall Summary Results of Unadjusted and Adjusted Group Contrast Analyses of Malignancy Variables

Variable	Verification Status	Unadjusted	Adjusted	Direction of Results
Malignant Systemic Neoplasms by Location/Site (continued)				
Brain	V[a]	NS	--	
Other Malignant Neoplasms of Lymphoid and Histiocytic Tissue	V[a]	NS	--	
Leukemia	V[a]	NS	--	
Carcinoma In Situ of Penis	V[a]	NS	--	
Carcinoma In Situ of Other Specified Sites	V[a]	NS	--	
Conditional Analyses				
Malignant Systemic Neoplasm	V	NS	--	
Conditioned on All Systemic	VS	NS	--	
Skin and Systemic				
All Skin and Systemic Neoplasms Combined	V	0.032	--	RH>C[d]
	VS	NS*	--	RH>C[d]
Nonverifiable Neoplasm	--	NS	--	

V: Verified neoplasms.
--Analysis not performed or not applicable.
RH>C: Larger incidence in Ranch Hands.
VS: Verified and suspected neoplasms.
NS: Not significant ($p>0.10$).
[a]No suspected neoplasms.
NS*: Borderline significant ($0.05<p\leq0.10$).
[b]No neoplasms for either Ranch Hands or Comparisons.
[c]No verified neoplasms.
[d]These group contrasts are related. For example, basal cell carcinoma is part of the sun exposure-related malignant skin neoplasms, and the sun exposure-related malignant skin neoplasms are part of the malignant skin neoplasms, which are part of all skin neoplasms.

The group contrast for the unadjusted analyses of sun exposure-related malignant skin neoplasms was significant for the verified set ($p=0.042$) and borderline significant for the verified and suspected set ($p=0.081$). Covariate adjustment analyses produced significant group contrasts ($p=0.019$ and $p=0.044$, respectively).

The unadjusted group contrast analyses for squamous cell carcinoma and melanoma were not significant.

Unadjusted analyses comparing the Ranch Hand and Comparison groups on relative frequency of basal cell carcinoma, melanoma, and sun exposure-related malignant skin neoplasms by anatomical location/site were also performed. For sun exposure-related malignant skin neoplasms, Ranch Hands and Comparisons differed for malignancies of the upper extremities ($p=0.044$ for the verified set; there were no suspected malignant neoplasms at this site). No other significant differences were found at the sites of interest for the sun exposure-related malignant skin neoplasms, or for any of these sites for basal cell carcinoma or melanoma.

Unadjusted group comparisons were performed comparing the frequencies of basal cell carcinoma and sun exposure-related malignant skin neoplasms occurring on the ear, face, head, and neck by occupation. For basal cell carcinoma (both the verified set and the verified and suspected set), there were no significant group differences for any occupation. For sun exposure-related malignant skin neoplasms, the officers exhibited a borderline significant group difference ($p=0.078$) for the verified set. For these unadjusted analyses, there were no other significant differences for sun exposure-related malignant skin neoplasms.

The following conditional unadjusted analyses of relative frequencies were performed for the Ranch Hand and Comparison groups: skin neoplasm conditioned on the presence of any neoplasm; malignant skin neoplasm conditioned on the presence of any skin neoplasm; basal cell carcinoma conditioned on the presence of a malignant skin neoplasm; basal cell carcinomas of the ear, face, head, neck, or upper extremities conditioned on the presence of basal cell carcinoma; and sun exposure-related malignant skin neoplasms of the ear, face, head, neck, or upper extremities conditioned on the presence of sun exposure-related malignant skin neoplasms. Conditioned on the presence of a neoplasm, the Ranch Hand and Comparison percentages of skin neoplasms were marginally significantly different ($p=0.095$ for the verified set of neoplasms; $p=0.100$ for the verified and suspected set of neoplasms). None of the other conditional analyses exhibited significant group differences.

The Ranch Hand and Comparison groups were also compared on the distributions of participants with zero, one, or multiple basal cell carcinomas. For the verified set, there was a significant group difference ($p=0.050$). For the verified and suspected set of basal cell carcinoma, the Ranch Hand and Comparison groups did not differ significantly on the frequency of participants with zero, one, or multiple basal cell carcinoma. Contrasting 1987 followup participants with zero basal cell carcinomas versus multiple basal cell carcinomas, the groups differed on their relative frequencies ($p=0.032$) for the verified set. For the verified and suspected set, the groups were borderline significantly different ($p=0.069$). For the 1985

followup, the group contrasts for none versus multiple basal cell carcinomas were not significant.

Table 10-21 also summarizes the results of the unadjusted and adjusted analyses performed for the systemic neoplasm assessment. Unadjusted analyses comparing the Ranch Hands and Comparisons on their relative frequencies of systemic neoplasms by behavior (malignant, benign, and uncertain behavior or unspecified nature) and all systemic neoplasms were not significant. Analyses of malignant systemic neoplasms adjusting for covariate information also indicated no significant differences between the Ranch Hands and Comparisons.

For specified locations/sites, Ranch Hands and Comparisons did not differ with respect to their relative frequencies of malignant systemic neoplasms. Ranch Hands and Comparisons also did not differ on their relative frequencies of malignant systemic neoplasms conditioned on the occurrence of a systemic neoplasm.

Table 10-21 also presents the results of unadjusted analyses for the combined set of all skin and systemic neoplasms. For the combined set of verified skin and verified systemic neoplasms, the Ranch Hand and Comparison 1987 followup groups differed significantly ($p=0.032$). For the verified and suspected combined set of skin and systemic neoplasms, the Ranch Hand and Comparison 1987 followup groups were borderline significant ($p=0.079$). This difference is due to the previously described group difference in skin malignancy. Table 10-21 also presents the results of unadjusted analyses comparing Ranch Hands and Comparisons on the frequency of nonverifiable skin and systemic neoplasms. No significant group difference was found.

The statistical power for detecting group differences on the frequency of systemic neoplasms at specified sites is low. The statistical power of the systemic neoplasm analyses improved somewhat when malignancies were aggregated across sites. Statistical power was strongest for the aggregated skin neoplasm analyses.

The frequency of basal cell carcinomas and sun exposure-related malignant skin neoplasms in the Ranch Hand group was compared across exposure index categories within each occupation strata. For the unadjusted analyses of basal cell carcinomas, there was a borderline significant difference among enlisted flyers for the verified set ($p=0.067$) and a significant difference among enlisted flyers for the verified and suspected ($p=0.031$) basal cell carcinomas. For adjusted analyses, significant exposure index-by-age interactions were present among the enlisted flyers for both sets of basal cell carcinomas. Analysis of the exposure index data within age strata did not support a dose-response relationship. For the unadjusted analyses of sun exposure-related malignant skin neoplasms, there was a borderline significant difference among enlisted flyers for the verified set ($p=0.059$) and a significant difference among enlisted flyers for the verified and suspected set ($p=0.028$). Again adjusting for covariate information resulted in significant exposure index-by-age interactions for both sets of sun exposure-related malignant skin neoplasms for the enlisted flyers. Results of stratified analyses did not support a dose-response relationship. No other significant differences were found for the exposure index analyses of these skin neoplasms.

The frequency of verified systemic malignant neoplasms in the Ranch Hand group was compared across exposure index categories within each occupation strata. For the unadjusted exposure index analyses, there were no significant differences by occupation. For the officers and enlisted flyers, the adjusted analyses were nonsignificant. However, there was a significant exposure index-by-race interaction for the enlisted groundcrew. Comparing the relative frequencies of systemic neoplasms across exposure levels within each race category for the enlisted groundcrew produced a significant difference for the nonblack Ranch Hands ($p=0.046$). However, the results from analyses stratified by race did not support a dose-response relationship (the midrange exposure group had more malignancies than either the low or high strata).

Table 10-22 displays the unadjusted relative risks for verified basal cell carcinoma at the Baseline, 1985 followup, and 1987 followup examinations. Ranch Hands showed a higher frequency of basal cell carcinoma than the Comparisons, a finding also noted at Baseline and the 1985 followup.

In addition to the higher frequency of basal cell carcinoma, Ranch Hands had a greater relative frequency of multiple basal cell carcinomas than the Comparisons at the 1987 followup. Sun exposure-related malignant skin neoplasms also exhibited an increased frequency for the Ranch Hands relative to the Comparisons. The increase was not surprising because the majority of the sun exposure-related malignancies were basal cell carcinomas. Ranch Hands and Comparisons did not differ significantly for systemic neoplasms. There has been one case of soft tissue sarcoma in both the Ranch Hand and the Comparison groups (both described in the report of the 1985 physical examination) and one case of Hodgkin's lymphoma in a Ranch Hand. The results of the exposure index analyses were not supportive of a dose-response relationship.

TABLE 10-22.

Unadjusted Analyses of Verified Basal Cell Carcinoma at Baseline, 1985 Followup, and 1987 Followup Examinations

Number of Participants[d] With Neoplasms/Percent	Baseline[a]	1985 Followup[b]	1987 Followup[c]
Ranch Hand	31 3.0%	53 5.5%	78 8.3%
Comparison	21 1.7%	50 4.1%	76 6.2%
Est. Relative Risk	1.71	1.36	1.36
p-Value	0.047*	0.128*,f	0.076*,f

[a]Baseline participants: 1,045 Ranch Hands, 1,224 Comparisons.

[b]1985 followup participants: 1,016 Ranch Hands, 1,293 Comparisons.

[c]1987 followup participants: 995 Ranch Hands, 1,299 Comparisons.

[d]Nonblacks only for the 1985 followup (956 Ranch Hands, 1,210 Comparisons); nonblacks only for the 1987 followup (938 Ranch Hands, 1,219 Comparisons); both nonblacks and Blacks for the Baseline.

*Baseline p-value based on chi-square test; 1985 and 1987 followup p-values based on Fisher's exact test.

[f]Adjusted analyses performed for the 1985 and 1987 followups produced the following estimated relative risks and associated p-values: 1.56 (p=0.035) and 1.46 (p=0.030), respectively.

CHAPTER 10

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