TABLE 11-3. (Continued)

Analysis of Acne Relative to SEA Tour
(Pre/Post-SEA and Post-SEA versus Pre-SEA and None)

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

Assumption	Time (Yrs.)	Percent Pre/Post-SEA and Post-SEA (n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e1) Minimal						0.062[b]
(n=521)	≤18.6	52.8 (72)	58.6 (128)	63.0 (54)	1.21 (0.95,1.55)	0.116[c]
	>18.6	53.5 (58)	44.7 (132)	44.2 (77)	0.91 (0.75,1.10)	0.318[c]
f1) Maximal						0.001[b]
(n=742)	≤18.6	45.3 (106)	55.0 (191)	62.7 (83)	1.27 (1.07,1.51)	0.005[c]
	>18.6	55.7 (79)	49.2 (179)	41.4 (104)	0.89 (0.77,1.03)	0.108[c]

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

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g1) Minimal			0.062[b]	- -
(n=521)	≤18.6	1.21 (0.95,1.55)	0.116[c]	
	>18.6	0.91 (0.75,1.10)	0.318[c]	
h1) Maximal			0.001[b]	AGE (p=0.030)
(n=742)	≤18.6	1.23 (1.04,1.46)	0.019[c]	
	>18.6	0.86 (0.74,0.99)	0.043[c]	

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

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

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

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

TABLE 11-3. (Continued)

Analysis of Acne Relative to SEA Tour (Post-SEA versus None)

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

Assumption	Time (Yrs.)	Percent Post-SEA/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e2) Minimal (n=468)	≤18.6	50.8 (65)	53.2 (109)	57.5 (47)	1.13 (0.88,1.47)	0.101[b] 0.340[c]
	>18.6	51.9 (54)	41.9 (124)	39.1 (69)	0.86 (0.70,1.06)	0.157[c]
f2) Maximal (n=671)	≤18.6	44.3 (97)	51.2 (166)	56.9 (72)	1.19 (0.99,1.42)	0.006[b] 0.058[c]
	>18.6	54.1 (74)	47.0 (168)	36.2 (94)	0.85 (0.73,1.00)	0.045[c]

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

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g2) Minimal (n=468)			0.101[b]	- -
	≤18.6	1.13 (0.88,1.47)	0.340[c]	
	>18.6	0.86 (0.70,1.06)	0.157[c]	
h2) Maximal (n=671)			0.006[b]	- -
	≤18.6	1.19 (0.99,1.42)	0.058[c]	
	>18.6	0.85 (0.73,1.00)	0.045[c]	

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

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

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

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

TABLE 11-3. (Continued)

Analysis of Acne Relative to SEA Tour (Pre/Post-SEA versus Pre-SEA)

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

Assumption	Time (Yrs.)	Percent Pre/Post-SEA (n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e3) Minimal						0.184[b]
(n=53)	≤18.6	71.4 (7)	89.5 (19)	100.0 (7)	4.81 (0.74,31.46)	0.101[c]
	>18.6	75.0 (4)	87.5 (8)	87.5 (8)	1.30 (0.49,3.40)	0.598[c]
f3) Maximal						0.072[b]
(n=71)	≤18.6	55.6 (9)	80.0 (25)	100.0 (11)	3.56 (1.21,10.43)	0.021[c]
	>18.6	80.0 (5)	81.8 (11)	90.0 (10)	1.15 (0.56,2.37)	0.701[c]

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

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g3) Minimal			0.184[b]	- -
(n=53)	≤18.6	4.81 (0.74,31.46)	0.101[c]	
	>18.6	1.30 (0.49,3.40)	0.598[c]	
h3) Maximal			0.072[b]	- -
(n=71)	≤18.6	3.56 (1.21,10.43)	0.021[c]	
	>18.6	1.15 (0.56,2.37)	0.701[c]	

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

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

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

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

TABLE 11-3. (Continued)

Analysis of Acne Relative to SEA Tour
(Pre/Post-SEA and Post-SEA versus Pre-SEA and None)

i1) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Pre/Post-SEA and Post-SEA	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	786	48.2	All Categories		0.691
Unknown	345	48.4	Unknown vs. Background	1.01 (0.78,1.30)	0.954
Low	196	52.6	Low vs. Background	1.19 (0.87,1.63)	0.278
High	187	50.8	High vs. Background	1.11 (0.81,1.53)	0.525
Total	1,514				

j1) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	786	All Categories		0.732**	DXCAT*RACE (p=0.022)
Unknown	345	Unknown vs. Background	1.05 (0.81,1.35)**	0.725**	AGE*RACE (p=0.006)
Low	196	Low vs. Background	1.18 (0.86,1.63)**	0.295**	
High	187	High vs. Background	0.97 (0.70,1.34)**	0.858**	
Total	1,514				

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

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

TABLE 11-3. (Continued)

Analysis of Acne Relative to SEA Tour
(Post-SEA versus None)

i2) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Post-SEA	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	700	44.1	All Categories		0.771
Unknown	310	45.5	Unknown vs. Background	1.06 (0.81,1.38)	0.693
Low	175	48.6	Low vs. Background	1.20 (0.86,1.67)	0.293
High	166	45.2	High vs. Background	1.04 (0.74,1.47)	0.809
Total	1,351				

j2) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	700	All Categories		0.660	AGE*RACE (p=0.019)
Unknown	310	Unknown vs. Background	1.09 (0.83,1.42)	0.554	
Low	175	Low vs. Background	1.19 (0.85,1.66)	0.300	
High	166	High vs. Background	0.94 (0.66,1.33)	0.727	
Total	1,351				

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

TABLE 11-3. (Continued)

Analysis of Acne Relative to SEA Tour (Pre/Post-SEA versus Pre-SEA)

i3) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Pre/Post-SEA	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	86	81.4	All Categories		0.245
Unknown	35	74.3	Unknown vs. Background	0.66 (0.26,1.68)	0.522
Low	21	85.7	Low vs. Background	1.37 (0.36,5.24)	0.918
High	21	95.2	High vs. Background	4.57 (0.67,31.30)	0.210
Total	163				

j3) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	86	All Categories		0.336	AGE (p=0.119)
Unknown	35	Unknown vs. Background	0.76 (0.29,1.99)	0.582	
Low	21	Low vs. Background	1.32 (0.34,5.06)	0.690	
High	21	High vs. Background	4.13 (0.51,33.66)	0.185	
Total	163				

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

p=0.531). Under the minimal assumption, no covariates were retained in the adjusted analysis. Under the maximal assumption, age was retained but the association between initial dioxin and post-SEA acne remained nonsignificant (p=0.353).

In the subset of Ranch Hands with acne prior to their first SEA tour, there was a significant positive association in the unadjusted analysis between initial dioxin and post-SEA acne under the maximal assumption, but not under the minimal assumption (Table 11-3 [a3] and [b3]: minimal assumption, p=0.111; maximal assumption, Est. RR=1.92, p=0.013). Among Ranch Hands with acne before their first SEA tour, the percentages under the maximal assumption who also had acne after the start of their SEA tour increased over the low, medium, and high initial dioxin categories (70.6%, 81.1%, and 94.1%).

In the minimal and maximal adjusted analyses, there were significant interactions between initial dioxin and age (Table 11-3 [c3] and [d3]: minimal assumption, p=0.003; maximal assumption, p=0.007), and between initial dioxin and race (minimal assumption, p=0.009; maximal assumption, p=0.016). Under the minimal assumption, there were only two Blacks—both in the low initial dioxin category—with acne both before and after their first SEA tour. For the younger non-Blacks, the association between initial dioxin and post-SEA acne was nonsignificant (Appendix Table J-1: p=0.511). For the older non-Blacks, just two Ranch Hands had acne only before their first SEA tour, both of whom were in the low initial dioxin category. Under the maximal assumption, just one Black Ranch Hand had acne only before the start of his SEA tour. For the younger non-Blacks, the association between initial dioxin and post-SEA acne was not significant (p=0.294). For the older non-Blacks, there was a significant positive association between initial dioxin and post-SEA acne (Adj. RR=9.69, p=0.039). Within this stratum, there were only three Ranch Hands in the low initial dioxin category, three in the medium category, and none in the high category who had only pre-SEA acne.

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

When the Ranch Hands with acne before and after the start of their first SEA tour were included with Ranch Hands with acne only after the start of their first SEA tour, the current dioxin-by-time since tour interaction was marginally significant in unadjusted analyses under the minimal assumption (Table 11-3 [e1]: p=0.062) and significant for the maximal unadjusted analysis (Table 11-3 [f1]: p=0.001). Under the minimal assumption, the association between current dioxin and post-SEA acne was nonsignificant within both time strata (Table 11-3 [e1]: p=0.116 for time≤18.6 years; p=0.318 for time>18.6 years). Under the maximal assumption, there was a significant positive association in the later tour stratum (Table 11-3 [f1]: Est. RR=1.27, p=0.005), but the association was negative but nonsignificant in the earlier tour stratum (p=0.108). The percentages of Ranch Hands in the later tour stratum who had either post-SEA acne or pre/post-SEA acne were 45.3, 55.0, and 62.7 percent for low, medium, and high current dioxin.

In the adjusted analysis, no covariates were retained in the minimal model, so the results were the same as in the unadjusted analysis. Under the maximal assumption, after age was included in the model, the current dioxin-by-time interaction (Table 11-3 [h1]: p=0.001) and the positive association between current dioxin and post-SEA acne within the later tour stratum (Adj. RR=1.23, p=0.019) remained significant. Within the earlier tour stratum, the negative association between current dioxin and post-SEA acne became

significant as well (Adj. RR=0.86, p=0.043). The percentages of post-SEA or pre/post-SEA acne occurrences in this stratum were 55.7, 49.2, and 41.4 percent for low, medium, and high current dioxin.

In the unadjusted analysis of the Ranch Hands without acne prior to the start of their first SEA tour, the interaction between current dioxin and time since tour was nonsignificant under the minimal assumption (Table 11-3 [e2]: p=0.101), but was significant under the maximal assumption (Table 11-3 [f2]: p=0.006). Under the maximal assumption, there was a marginally significant positive association between current dioxin and post-SEA acne when time was 18.6 years or less (Est. RR=1.19, p=0.058) and a significant negative association when time was greater than 18.6 years (Est. RR=0.85, p=0.045). Among the Ranch Hands without pre-SEA acne, the percentages with post-SEA acne were 44.3, 51.2, and 56.9 percent for low, medium, and high current dioxin in the later tour stratum. In the earlier tour stratum, the corresponding percentages were 54.1, 47.0, and 36.2 percent. No covariates were retained in the adjusted analyses under either assumption, so the results remained the same as in the unadjusted analyses.

In the unadjusted analysis of the Ranch Hands with acne prior to the start of their first SEA tour, the current dioxin-by-time since tour interaction was nonsignificant under the minimal analysis (Table 11-3 [e3]: p=0.184), but was marginally significant under the maximal assumption (Table 11-3 [f3]: p=0.072). Under the maximal assumption, the association between current dioxin and post-SEA acne was significant when time was 18.6 years or less (Est. RR=3.56, p=0.021), but was nonsignificant when time was greater than 18.6 years (p=0.701). Within the later tour stratum, the percentages of Ranch Hands with post-SEA acne as well as pre-SEA acne were 55.6, 80.0, and 100.0 percent for low, medium, and high current dioxin. In the adjusted analyses, no covariates were retained in the model under either assumption, so the results were the same as in the unadjusted analyses.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In the unadjusted analysis of participants with post-SEA acne only or with acne both before and after the start of their SEA tour versus participants without acne after the start of their SEA tour, there was no significant difference among the four current dioxin categories (Table 11-3 [i1]: p=0.691). In the adjusted analysis, there was a significant interaction between categorized current dioxin and race (Table 11-3 [j1]: p=0.022). In the Black stratum, the percentages of participants with either post-SEA acne or pre/post-SEA acne differed significantly among the current dioxin categories (Appendix Table J-1: p=0.037). The percentages in the background, unknown, low, and high categories were 52.1, 75.0, 25.0, and 37.5 percent. The percentage in the unknown category was marginally higher than the percentage in the background category (Adj. RR=3.62, 95% C.I.: [0.83,15.82], p=0.088); the percentage in the low category was marginally lower than the percentage in the background category (Adj. RR=0.29, 95% C.I.: [0.07,1.24], p=0.095). There was no significant difference between the high and background categories (p=0.420). In the non-Black stratum, the percentages of participants with either post-SEA acne or pre/post-SEA acne did not differ significantly among the current dioxin categories (Appendix Table J-1: p=0.482). Without the categorized current dioxin-by-race interaction in the model, the overall contrast of the four current dioxin categories was nonsignificant (Table 11-3 [j1]: p=0.732).

In the analysis of participants with post-SEA acne versus participants with no occurrences of acne, the overall contrast of the four current dioxin categories was nonsignificant in the unadjusted and adjusted models (Table 11-3 [i2] and [j2]: unadjusted, p=0.771; adjusted, p=0.660).

In the unadjusted analysis of the participants with pre-SEA acne, the percentages of participants who also had post-SEA acne did not differ significantly among the current dioxin categories (Table 11-3 [i3]: p=0.245). In the adjusted analysis, the overall contrast remained nonsignificant (Table 11-3 [j3]: p=0.336).

Location of Acne

The location of acne was analyzed for the participants in the post-SEA acne category and those in the post-SEA and pre/post-SEA categories combined. Tables 11-4 and 11-5 present the spatial distributions of acne with primary emphasis on the temples, around the eyes, or on the ears. The distributions provided in Table 11-4 are limited to the participants in the post-SEA only category. Table 11-5 shows the distributions of acne by location for the participants in the post-SEA and the pre/post-SEA categories combined.

Due to the sparse numbers at individual sites, the analyses presented below were performed on the contrast of participants with acne on the temples, eyes, ears, or any combination of these sites, versus the participants with acne on other sites.

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

In the post-SEA acne category, there was no significant association between location of acne and initial dioxin in the unadjusted analysis (Table 11-6 [a1] and [b1]: minimal assumption, p=0.611; maximal assumption, p=0.554). Under the minimal assumption, a significant interaction between initial dioxin and age was present in the adjusted analysis (Table 11-6 [c1]: p=0.016). After dividing the Ranch Hands into two age strata (born≥1942 and born<1942), the association between initial dioxin and location of acne was positive for the younger Ranch Hands and negative for the older Ranch Hands, but neither association was significant (Appendix Table J-1: born≥1942: p=0.118; born<1942: p=0.206). Without this interaction in the model, the association between initial dioxin and the location of acne was nonsignificant (Table 11-6 [c1]: p=0.581). Under the maximal assumption, no covariates were retained in the adjusted model so the results remained the same as in the unadjusted analysis.

When the post-SEA acne category was combined with the pre/post-SEA acne category, the association between initial dioxin and location of acne was nonsignificant under both assumptions (Table 11-6 [a2] and [b2]: minimal assumption, p=0.289; maximal assumption, p=0.808). In the adjusted minimal analysis, the association remained nonsignificant (Table 11-6 [c2]: p=0.207). No covariates were retained in the adjusted maximal analysis so the results remained unchanged.

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

In the unadjusted minimal analysis of the post-SEA acne category there was a significant interaction between current dioxin and time since tour (Table 11-6 [e1]: p=0.021). In the later tour stratum, the association between current dioxin and location of acne was

TABLE 11-4.

Location of Post-SEA Acne*

Location	Minimal Assumption			Maximal Assumption		
		Time (yrs.)			Time (yrs.)	
	Total	≤18.6	>18.6	Total	≤18.6	>18.6
Temples Only	28	15	13	44	21	23
Eyes Only	0	0	0	1	0	1
Ears Only	3	1	2	7	4	3
Temples and Eyes	2	2	0	4	3	1
Temples and Ears	5	1	4	6	2	4
Eyes and Ears	0	0	0	1	1	0
Temples, Eyes, and Ears	3	1	2	3	1	2
Other Sites	184	98	86	256	137	119

Location	Current Dioxin Category			
	Background	Unknown	Low	High
Temples Only	29	25	12	6
Eyes Only	5	1	0	0
Ears Only	7	5	1	0
Temples and Eyes	2	3	1	1
Temples and Ears	4	2	3	2
Eyes and Ears	1	1	0	0
Temples, Eyes, and Ears	0	0	0	3
Other Sites	261	104	68	63

*Total indicates sample size used in the $\log_2$ (initial dioxin) analysis; total sample size is broken down by time since tour to indicate sample sizes used in the $\log_2$ (current dioxin) and time analysis; sample size given for each category used in categorized current dioxin analysis.

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

TABLE 11-5.

Location of Post-SEA and Pre/Post-SEA Acne*

Location	Minimal Assumption			Maximal Assumption		
		Time (yrs.)			Time (yrs.)	
	Total	≤18.6	>18.6	Total	≤18.6	>18.6
Temples Only	39	21	18	62	30	32
Eyes Only	1	0	1	2	0	2
Ears Only	3	1	2	7	4	3
Temples and Eyes	2	2	0	4	3	1
Temples and Ears	7	2	5	8	3	5
Eyes and Ears	0	0	0	1	1	0
Temples, Eyes, and Ears	5	2	3	5	2	3
Other Sites	214	119	95	291	162	129

Location	Current Dioxin Category			
	Background	Unknown	Low	High
Temples Only	45	34	17	11
Eyes Only	6	1	0	1
Ears Only	11	5	1	0
Temples and Eyes	2	3	1	1
Temples and Ears	9	3	3	3
Eyes and Ears	2	1	0	0
Temples, Eyes, and Ears	4	1	1	4
Other Sites	300	119	80	75

*Total indicates sample size used in the $\log_2$ (initial dioxin) analysis; total sample size is broken down by time since tour to indicate sample sizes used in the $\log_2$ (current dioxin) and time analysis; sample size given for each category used in categorized current dioxin analysis.

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

TABLE 11-6.

Analysis of Location of Acne (Post-SEA)

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Temples/ Eyes/Ears	Est. Relative Risk (95% C.I.)[a]	p-Value
a1) Minimal (n=225)	Low	59	17.0	1.08 (0.81,1.42)	0.611
	Medium	111	18.9		
	High	55	18.2		
b1) Maximal (n=322)	Low	83	26.5	0.94 (0.76,1.16)	0.554
	Medium	166	19.9		
	High	73	15.1		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c1) Minimal (n=225)	1.09 (0.81,1.46)**	0.581**	INIT*AGE (p=0.016) RACE (p=0.081)
d1) Maximal (n=322)	0.94 (0.76,1.16)	0.554	- -

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

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

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

TABLE 11-6. (Continued)

Analysis of Location of Acne (Pre/Post-SEA and Post-SEA)

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Temples/ Eyes/Ears	Est. Relative Risk (95% C.I.)[a]	p-Value
a2) Minimal (n=271)	Low	67	17.9	1.14 (0.90,1.44)	0.289
	Medium	134	20.9		
	High	70	24.3		
b2) Maximal (n=380)	Low	95	29.5	0.98 (0.82,1.17)	0.808
	Medium	196	21.9		
	High	89	20.2		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c2) Minimal (n=271)	1.17 (0.92,1.48)	0.207	RACE (p=0.142)
d2) Maximal (n=380)	0.98 (0.82,1.17)	0.808	- -

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

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

TABLE 11-6. (Continued)

Analysis of Location of Acne
(Post-SEA)

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

Assumption	Time (Yrs.)	Percent Temples, Eyes, Ears/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e1) Minimal (n=225)	≤18.6	24.2 (33)	17.2 (58)	7.4 (27)	0.71 (0.43,1.17)	0.021[b] 0.177[c]
	>18.6	14.3 (28)	17.3 (52)	29.6 (27)	1.42 (1.00,2.03)	0.051[c]
f1) Maximal (n=322)	≤18.6	23.3 (43)	21.2 (85)	9.8 (41)	0.76 (0.54,1.07)	0.083[b] 0.113[c]
	>18.6	27.5 (40)	19.0 (79)	23.5 (34)	1.11 (0.85,1.44)	0.458[c]

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

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g1) Minimal (n=225)			0.021[b]	- -
	≤18.6	0.71 (0.43,1.17)	0.177[c]	
	>18.6	1.42 (1.00,2.03)	0.051[c]	
h1) Maximal (n=322)			0.083[b]	- -
	≤18.6	0.76 (0.54,1.07)	0.113[c]	
	>18.6	1.11 (0.85,1.44)	0.458[c]	

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

TABLE 11-6. (Continued)

Analysis of Location of Acne (Pre/Post-SEA and Post-SEA)

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

Assumption	Time (Yrs.)	Percent Temples, Eyes, Ears/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e2) Minimal						0.037[b]
(n=271)	≤18.6	26.3 (38)	18.7 (75)	11.8 (34)	0.84 (0.57,1.24)	0.386[c]
	>18.6	12.9 (31)	22.0 (59)	35.3 (34)	1.42 (1.03,1.94)	0.030[c]
f2) Maximal						0.141[b]
(n=380)	≤18.6	25.0 (48)	22.9 (105)	13.5 (52)	0.84 (0.63,1.11)	0.213[c]
	>18.6	31.8 (44)	21.6 (88)	30.2 (43)	1.10 (0.87,1.38)	0.433[c]

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

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g2) Minimal			0.037[b]	- -
(n=271)	≤18.6	0.84 (0.57,1.24)	0.386[c]	
	>18.6	1.42 (1.03,1.94)	0.030[c]	
h2) Maximal			0.141[b]	- -
(n=370)	≤18.6	0.84 (0.63,1.11)	0.213[c]	
	>18.6	1.10 (0.87,1.38)	0.433[c]	

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

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

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

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

TABLE 11-6. (Continued)

Analysis of Location of Acne
(Post-SEA)

i1) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Temples/ Eyes/Ears	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	309	15.5	All Categories		0.060
Unknown	141	26.2	Unknown vs. Background	1.93 (1.19,3.14)	0.008
Low	85	20.0	Low vs. Background	1.36 (0.74,2.51)	0.327
High	75	16.0	High vs. Background	1.04 (0.52,2.06)	0.921
Total	610				

j1) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	309	All Categories		0.060	--
Unknown	141	Unknown vs. Background	1.93 (1.19,3.14)	0.008	
Low	85	Low vs. Background	1.36 (0.74,2.51)	0.327	
High	75	High vs. Background	1.04 (0.52,2.06)	0.921	
Total	610				

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

TABLE 11-6. (Continued)

Analysis of Location of Acne (Pre/Post-SEA and Post-SEA)

i2) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Temples/ Eyes/Ears	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	379	20.8	All Categories		0.241
Unknown	167	28.7	Unknown vs. Background	1.53 (1.01,2.32)	0.045
Low	103	22.3	Low vs. Background	1.09 (0.65,1.85)	0.743
High	95	21.1	High vs. Background	1.01 (0.58,1.76)	0.964
Total	744				

j2) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	379	All Categories		0.193	AGE (p=0.118)
Unknown	167	Unknown vs. Background	1.55 (1.02,2.36)	0.039	
Low	103	Low vs. Background	1.09 (0.64,1.84)	0.757	
High	95	High vs. Background	0.94 (0.54,1.65)	0.840	
Total	744				

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

negative but nonsignificant (p=0.177). In the earlier tour stratum, there was a marginally significant positive association between current dioxin and time (Est. RR=1.42, p=0.051). Among Ranch Hands with early tours and acne only after the start of their SEA tour, the percentages with acne on the temples, eyes, ears, or a combination of these sites were 14.3, 17.3, and 29.6 percent for low, medium, and high current dioxin. Under the maximal assumption, the current dioxin-by-time interaction was marginally significant (Table 11-6 [f1]: p=0.083). However, the association between current dioxin and location of acne was nonsignificant in both time strata (time≤18.6: p=0.113; time>18.6: p=0.458). In the adjusted analyses, no covariates were retained in the model.

When the Ranch Hands with acne both before and after the start of their first SEA tour were included in the analysis, the current dioxin-by-time since tour interaction was significant under the minimal assumption (Table 11-6 [e2]: p=0.037). The association between current dioxin and location of acne was negative but nonsignificant in the later tour stratum (p=0.386) and significantly positive in the earlier tour stratum (Est. RR=1.42, p=0.030). Within the earlier tour stratum, the percentage of Ranch Hands used in this analysis with acne on the temples, eyes, ears, or a combination of these sites increased with current dioxin (12.9%, 22.0%, and 35.3% for low, medium, and high current dioxin). Under the maximal assumption, the current dioxin-by-time interaction was not significant (Table 11-6 [f2]: p=0.141). There were no covariates retained in the adjusted model under either assumption, so the results were the same as the unadjusted results.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

When the unadjusted analysis of the location of acne was restricted to the post-SEA acne category, the overall contrast of the four current dioxin categories was marginally significant (Table 11-6 [i1]: p=0.060). Of the participants with post-SEA acne only, the percentages with acne on the temples, eyes, ears, or a combination of these sites were 15.5, 26.2, 20.0, and 16.0 percent in the background, unknown, low, and high categories. The percentage in the unknown category was significantly greater than the percentage in the background category (Est. RR=1.93, 95% C.I.: [1.19,3.14], p=0.008), but the low and high categories were not significantly different from the background category (low versus background: p=0.327; high versus background: p=0.921). The adjusted analysis did not retain any covariates, so the results remained unchanged.

When the participants in the pre/post-SEA acne category were included in the unadjusted analysis, the overall contrast became nonsignificant (Table 11-6 [i2]: p=0.241). However, the percentage of participants used in this analysis with acne on the temples, eyes, ears, or a combination of these sites in the unknown current dioxin category (28.7%) was significantly greater than the percentage in the background category (20.8%) (Est. RR=1.53, 95% C.I.: [1.01,2.32], p=0.045). After the model was adjusted for age, the overall contrast remained nonsignificant (Table 11-6 [j2]: p=0.193) and the contrast between the unknown and background categories remained significant (Adj. RR=1.55, 95% C.I.: [1.02,2.36], p=0.039). The low and high versus background category contrasts were also nonsignificant.

Physical Examination Variables

Comedones

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

The association between initial dioxin and comedones was not significant in the unadjusted minimal or the unadjusted maximal analysis (Table 11-7 [a] and [b]: p=0.335 and p=0.398).

Under the minimal assumption, the association between initial dioxin and comedones became marginally significant after adjustment for age and race (Table 11-7 [c]: Adj. RR=1.18, p=0.076). The percentages of Ranch Hands with comedones for the low, medium, and high initial dioxin categories were 16.9, 22.7, and 19.1 percent. Under the maximal assumption, the association with comedones remained nonsignificant in the adjusted model (Table 11-7 [d]: p=0.157).

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

In the unadjusted analysis of comedones, the current dioxin-by-time since tour interaction was nonsignificant under the minimal and maximal assumptions (Table 11-7 [e] and [f]: p=0.708 and p=0.939).

Under the minimal assumption, after adjustment for age and race, the interaction between current dioxin and time remained nonsignificant (Table 11-7 [g]: p=0.862). However, for Ranch Hands in the earlier tour stratum the relative risk of comedones became marginally significant (Adj. RR=1.24, p=0.074). In this stratum, the percentages of Ranch Hands with comedones were 19.0, 18.2, and 23.4 percent for low, medium, and high current dioxin. Under the maximal assumption, the current dioxin-by-time interaction remained nonsignificant in the adjusted analysis (Table 11-7 [h]: p=0.909).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In the unadjusted analysis of comedones, no significant difference was exhibited among the four current dioxin categories (Table 11-7 [i]: p=0.779). After adjusting the model for covariate information, the difference remained nonsignificant (Table 11-7 [j]: p=0.898).

Acneiform Lesions

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

The association between acneiform lesions and initial dioxin was not significant under the minimal assumption in the unadjusted analysis (Table 11-8 [a]: p=0.763). Under the maximal assumption, however, the relative risk was marginally significant (Table 11-8 [b]: Est. RR=1.17, p=0.080). In the low, medium, and high initial dioxin categories the percentages of Ranch Hands who had acneiform lesions were 4.9, 10.8, and 9.1 percent.

In the adjusted analysis, the association between acneiform lesions and initial dioxin remained nonsignificant under the minimal assumption (Table 11-8 [c]: p=0.243). After age

TABLE 11-7.

Analysis of Comedones

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=521)	Low	130	16.9	1.09 (0.92,1.30)	0.335
	Medium	260	22.7		
	High	131	19.1		
b) Maximal (n=742)	Low	185	19.5	1.06 (0.93,1.20)	0.398
	Medium	371	21.6		
	High	186	18.8		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=521)	1.18 (0.98,1.41)	0.076	AGE (p=0.002) RACE (p=0.141)
d) Maximal (n=742)	1.10 (0.96,1.26)	0.157	AGE (p=0.003)

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

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

TABLE 11-7. (Continued)

Analysis of Comedones

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

Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal (n=521)	≤18.6	12.5 (72)	28.9 (128)	13.0 (54)	1.04 (0.79,1.39)	0.708[b] 0.761[c]
	>18.6	19.0 (58)	18.2 (132)	23.4 (77)	1.12 (0.89,1.41)	0.335[c]
f) Maximal (n=742)	≤18.6	19.8 (106)	22.5 (191)	16.9 (83)	1.06 (0.86,1.29)	0.939[b] 0.595[c]
	>18.6	22.8 (79)	17.9 (179)	22.1 (104)	1.04 (0.87,1.25)	0.632[c]

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

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal (n=521)			0.862[b]	AGE (p=0.001)
	≤18.6	1.20 (0.90,1.61)	0.221[c]	RACE (p=0.121)
	>18.6	1.24 (0.98,1.57)	0.074[c]	
h) Maximal (n=742)			0.909[b]	AGE (p=0.002)
	≤18.6	1.13 (0.92,1.38)	0.256[c]	
	>18.6	1.11 (0.93,1.33)	0.263[c]	

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

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

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

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

TABLE 11-7. (Continued)

Analysis of Comedones

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

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	786	22.8	All Categories		0.779
Unknown	345	21.5	Unknown vs. Background	0.93 (0.68,1.26)	0.623
Low	196	23.5	Low vs. Background	1.04 (0.72,1.51)	0.836
High	187	19.8	High vs. Background	0.84 (0.56,1.24)	0.377
Total	1,514				

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

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	786	All Categories		0.898	SEAACNE (p=0.059) AGE*RACE (p=0.023)
Unknown	345	Unknown vs. Background	0.92 (0.67,1.25)	0.575	
Low	196	Low vs. Background	1.05 (0.72,1.52)	0.807	
High	187	High vs. Background	0.92 (0.61,1.38)	0.685	
Total	1,514				

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

TABLE 11-8.

Analysis of Acneiform Lesions

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=521)	Low	130	10.0	0.97 (0.77,1.22)	0.763
	Medium	260	11.5		
	High	131	10.7		
b) Maximal (n=742)	Low	185	4.9	1.17 (0.98,1.39)	0.080
	Medium	371	10.8		
	High	186	9.1		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=521)	0.86 (0.67,1.11)	0.243	AGE (p=0.004) RACE*SEAACNE (p=0.039)
d) Maximal (n=742)	1.11 (0.93,1.32)	0.270	AGE (p=0.009) RACE*SEAACNE (p=0.042)

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

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

TABLE 11-8. (Continued)

Analysis of Acneiform Lesions

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

Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal (n=521)	≤18.6	9.7 (72)	13.3 (128)	11.1 (54)	1.06 (0.74,1.51)	0.507[b] 0.752[c]
	>18.6	12.1 (58)	9.9 (132)	9.1 (77)	0.90 (0.65,1.25)	0.527[c]
f) Maximal (n=742)	≤18.6	1.9 (106)	12.0 (191)	9.6 (83)	1.39 (1.06,1.81)	0.110[b] 0.016[c]
	>18.6	6.3 (79)	10.1 (179)	9.6 (104)	1.03 (0.81,1.32)	0.792[c]

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

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal (n=521)	≤18.6	0.89 (0.61,1.29)	0.621[b] 0.530[c]	AGE (p=0.003)
	>18.6	0.78 (0.55,1.12)	0.179[c]	RACE*SEAACNE (p=0.045)
h) Maximal (n=742)	≤18.6	1.26 (0.96,1.66)	0.124[b] 0.091[c]	AGE (p=0.009)
	>18.6	0.95 (0.74,1.23)	0.709[c]	RACE*SEAACNE (p=0.044)

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

TABLE 11-8. (Continued)

Analysis of Acneiform Lesions

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

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	786	11.3	All Categories		0.111
Unknown	345	7.0	Unknown vs. Background	0.59 (0.37,0.94)	0.026
Low	196	11.7	Low vs. Background	1.04 (0.64,1.70)	0.871
High	187	9.6	High vs. Background	0.83 (0.49,1.42)	0.505
Total	1,514				

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

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	786	All Categories		0.137	SEAACNE (p<0.001) AGE*RACE (p=0.043)
Unknown	345	Unknown vs. Background	0.63 (0.39,1.01)	0.055	
Low	196	Low vs. Background	1.03 (0.63,1.70)	0.893	
High	187	High vs. Background	0.68 (0.39,1.18)	0.170	
Total	1,514				

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

and the interaction between race and the presence of pre-SEA acne were included in the model for the maximal analysis, the association became nonsignificant (Table 11-8 [d]: p=0.270).

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

The association between acneiform lesions and current dioxin did not differ significantly between the time since tour strata in the unadjusted analyses under either the minimal or the maximal assumption (Table 11-8 [e] and [f]: p=0.507 and p=0.110). However, under the maximal assumption, there was a significant association between acneiform lesions and current dioxin when time was 18.6 years or less (Table 11-8 [f]: Est. RR=1.39, p=0.016). Within this stratum, 1.9, 12.0, and 9.6 percent of the Ranch Hands with low, medium, and high current dioxin had acneiform lesions.

After the models had been adjusted for significant covariate information, the current dioxin-by-time interactions remained nonsignificant (Table 11-8 [g] and [h]: minimal assumption, p=0.621; maximal assumption, p=0.124). Under the maximal assumption, the association between acneiform lesions and current dioxin for Ranch Hands with a later tour (time≤18.6 years) became marginally significant after age and the race-by-presence of pre-SEA acne interaction were included in the model (Table 11-8 [h]: p=0.091).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In the unadjusted analysis of acneiform lesions, the overall contrast of the four current dioxin categories was nonsignificant (Table 11-8 [i]: p=0.111). However, there was a significant difference between the unknown and background categories (Est. RR=0.59, 95% C.I.: [0.37,0.94], p=0.026). The percentages of acneiform lesion occurrences for the background, unknown, low, and high current dioxin categories were 11.3, 7.0, 11.7, and 9.6 percent.

Following the adjustment for significant covariates (the presence of pre-SEA acne and the age-by-race interaction), the overall contrast remained nonsignificant (Table 11-8 [j]: p=0.137). However, the relative risk under the unknown versus background contrast became only marginally significant (Adj. RR=0.63, 95% C.I.: [0.39,1.01], p=0.055).

Acneiform Scars

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

No significant association was shown to exist between acneiform scars and current dioxin under the minimal assumption based on the unadjusted analysis (Table 11-9 [a]: p=0.105). Under the maximal assumption, however, this association was marginally significant with a relative risk greater than 1 (Table 11-9 [b]: Est. RR=1.17, p=0.058). The percentages of Ranch Hands in the low, medium, and high initial dioxin categories who had acneiform scars were 9.7, 11.3, and 12.4 percent.

In the adjusted minimal analysis, the association between acneiform scars and initial dioxin remained nonsignificant (Table 11-9 [c]: p=0.273). After the model in the maximal

TABLE 11-9.

Analysis of Acneiform Scars

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=521)	Low	130	7.7	1.19 (0.97,1.47)	0.105
	Medium	260	13.1		
	High	131	13.7		
b) Maximal (n=742)	Low	185	9.7	1.17 (1.00,1.37)	0.058
	Medium	371	11.3		
	High	186	12.4		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=521)	1.14 (0.91,1.43)	0.273	AGE*SEAACNE (p=0.032)
d) Maximal (n=742)	1.12 (0.94,1.33)	0.200	AGE*SEAACNE (p=0.049)

[a]Relative risk for a twofold increase in dioxin.
Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 11-9. (Continued)

Analysis of Acneiform Scars

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

Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal (n=521)	≤18.6	2.8 (72)	18.0 (128)	14.8 (54)	1.54 (1.12,2.12)	0.100[b] 0.009[c]
	>18.6	6.9 (58)	12.9 (132)	10.4 (77)	1.07 (0.79,1.44)	0.666[c]
f) Maximal (n=742)	≤18.6	5.7 (106)	12.0 (191)	16.9 (83)	1.46 (1.15,1.85)	0.030[b] 0.002[c]
	>18.6	12.7 (79)	9.5 (179)	12.5 (104)	1.02 (0.81,1.28)	0.888[c]

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

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal (n=521)	≤18.6	1.43 (1.01,2.03)	0.097[b] 0.047[c]	AGE*SEAACNE (p=0.034)
	>18.6	0.97 (0.69,1.34)	0.833[c]	
h) Maximal (n=742)	≤18.6	1.38 (1.06,1.78)	0.032[b] 0.016[c]	AGE*SEAACNE (p=0.047)
	>18.6	0.94 (0.74,1.21)	0.644[c]	

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

TABLE 11-9. (Continued)

Analysis of Acneiform Scars

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

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	786	9.5	All Categories		0.151
Unknown	345	11.0	Unknown vs. Background	1.17 (0.78,1.77)	0.447
Low	196	13.8	Low vs. Background	1.51 (0.95,2.43)	0.084
High	187	14.4	High vs. Background	1.60 (1.00,2.57)	0.051
Total	1,514				

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

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	786	All Categories		0.182	AGE (p=0.028) SEAACNE (p<0.001)
Unknown	345	Unknown vs. Background	1.27 (0.82,1.95)	0.284	
Low	196	Low vs. Background	1.58 (0.96,2.60)	0.070	
High	187	High vs. Background	1.53 (0.92,2.52)	0.098	
Total	1,514				

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

analysis had been adjusted for significant covariate information (specifically the age-by-presence of pre-SEA acne interaction), the association between acneiform scars and initial dioxin became nonsignificant (Table 11-9 [d]: p=0.200).

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

In the unadjusted minimal analysis, there was a marginally significant difference in the association between acneiform scars and current dioxin between the time since tour strata (Table 11-9 [e]: p=0.100). When time did not exceed 18.6 years, the association was significant (Est. RR=1.54, p=0.009). For low, medium, and high levels of current dioxin the percentages of men with acneiform scars were 2.8, 18.0, and 14.8 percent. When time was greater than 18.6 years, the association between acneiform scars and current dioxin was not significant (p=0.666). Under the maximal assumption, the association between acneiform scars and current dioxin was significantly different between the time strata (Table 11-9 [f]: p=0.030). The association was significant when time was 18.6 years or less (Est. RR=1.46, p=0.002) and nonsignificant when time was greater than 18.6 years (p=0.888). In the later tour stratum (time≤18.6 years), the percentages of Ranch Hands with low, medium, and high current dioxin who had acneiform scars were 5.7, 12.0, and 16.9 percent.

After adjusting the models for significant covariate information, the current dioxin-by-time interaction remained marginally significant under the minimal assumption (Table 11-9 [g]: p=0.097) and significant under the maximal assumption (Table 11-9 [h]: p=0.032). The association between acneiform scars and current dioxin when time was 18.6 years or less remained significant under both assumptions (Table 11-9 [g] and [h]: minimal assumption: Adj. RR=1.43, p=0.047; maximal assumption: Adj. RR=1.38, p=0.016). When time was greater than 18.6 years, the association remained nonsignificant under both assumptions (minimal assumption, p=0.833; maximal assumption, p=0.644).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In the unadjusted analysis of acneiform scars, the overall contrast of the four current dioxin categories was nonsignificant (Table 11-9 [i]: p=0.151). However, there were marginally significant differences between the low and background categories (Est. RR=1.51, 95% C.I.: [0.95,2.43], p=0.084) and between the high and background categories (Est. RR=1.60, 95% C.I.: [1.00,2.57], p=0.051). In both cases, the percentage of men with acneiform scars in the Ranch Hand category exceeded the percentage in the background category. The percentages for the background, unknown, low, and high categories were 9.5, 11.0, 13.8, and 14.4 percent.

After adjusting for significant covariates, the overall contrast remained nonsignificant (Table 11-9 [j]: p=0.182). The contrasts between the low and background categories (Adj. RR=1.58, 95% C.I.: [0.96,2.60], p=0.070) and between the high and background categories (Adj. RR=1.53, 95% C.I.: [0.92,2.52], p=0.098) remained marginally significant.

Depigmentation

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

The association between depigmentation and initial dioxin was not significant in the unadjusted minimal analysis and in the unadjusted maximal analysis (Table 11-10 [a] and

TABLE 11-10.

Analysis of Depigmentation

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=521)	Low	130	8.5	0.91 (0.68,1.21)	0.498
	Medium	260	6.5		
	High	131	7.6		
b) Maximal (n=742)	Low	185	3.2	1.06 (0.86,1.30)	0.599
	Medium	371	7.6		
	High	186	7.5		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=521)	0.93 (0.69,1.24)	0.606	RACE (p=0.109)
d) Maximal (n=742)	1.06 (0.86,1.31)	0.581	RACE (p=0.123)

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

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

TABLE 11-10. (Continued)

Analysis of Depigmentation

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

Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal (n=521)	≤18.6	11.1 (72)	3.9 (128)	11.1 (54)	1.05 (0.68,1.62)	0.381[b] 0.813[c]
	>18.6	8.6 (58)	7.6 (132)	5.2 (77)	0.81 (0.53,1.22)	0.308[c]
f) Maximal (n=742)	≤18.6	1.9 (106)	6.8 (191)	8.4 (83)	1.30 (0.94,1.79)	0.087[b] 0.110[c]
	>18.6	6.3 (79)	7.8 (179)	6.7 (104)	0.89 (0.66,1.19)	0.433[c]

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

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal (n=521)	≤18.6	1.09 (0.70,1.69)	0.346[b] 0.695[c]	RACE (p=0.100)
	>18.6	0.82 (0.54,1.24)	0.344[c]	
h) Maximal (n=742)	≤18.6	1.32 (0.95,1.82)	0.076[b] 0.094[c]	RACE (p=0.110)
	>18.6	0.88 (0.65,1.19)	0.414[c]	

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

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

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

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

TABLE 11-10. (Continued)
Analysis of Depigmentation

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

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	786	5.7	All Categories		0.702
Unknown	345	4.9	Unknown vs. Background	0.85 (0.48,1.51)	0.588
Low	196	5.6	Low vs. Background	0.98 (0.50,1.93)	0.951
High	187	7.5	High vs. Background	1.33 (0.72,2.48)	0.366
Total	1,514				

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

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	786	All Categories		0.536	AGE (p=0.057) RACE (p=0.100)
Unknown	345	Unknown vs. Background	0.86 (0.48,1.53)	0.610	
Low	196	Low vs. Background	0.98 (0.50,1.94)	0.965	
High	187	High vs. Background	1.50 (0.80,2.83)	0.209	
Total	1,514				

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

[b]: p=0.498 and p=0.599). In the adjusted analyses, this association was also nonsignificant (Table 11-10 [c] and [d]: minimal assumption, p=0.606; maximal assumption, p=0.581).

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

In the unadjusted minimal analysis of depigmentation, the interaction between current dioxin and time since tour was not significant (Table 11-10 [e]: p=0.381). Under the maximal assumption, however, the current dioxin-by-time interaction was marginally significant (Table 11-10 [f]: p=0.087). The relative risk was greater than 1 when time was no more than 18.6 years and was less than 1 when time was more than 18.6 years, although both risks were nonsignificant (time≤18.6: p=0.110; time>18.6: p=0.433).

Under the minimal assumption, the current dioxin-by-time interaction remained nonsignificant in the adjusted analysis of depigmentation (Table 11-10 [g]: p=0.346). When race was included in the maximal analysis, the current dioxin-by-time interaction remained marginally significant (Table 11-10 [h]: p=0.076). However, the risk of depigmentation became marginally significant within the later tour stratum (Adj. RR=1.32, p=0.094). In the earlier tour stratum the risk remained less than 1 but nonsignificant (p=0.414).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In the unadjusted model, no significant difference in the percentages of depigmentation was detected among the four current dioxin categories (Table 11-10 [i]: p=0.702). Even after adjusting for covariate information, the difference remained nonsignificant (Table 11-10 [j]: p=0.536).

Inclusion Cysts

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

The association between initial dioxin and inclusion cysts was not significant in the unadjusted analysis under the minimal assumption (Table 11-11 [a]: p=0.615). Under the maximal assumption, however, the association was marginally significant, with a relative risk less than 1 (Table 11-11 [b]: Est. RR=0.86, p=0.098). The percentages of Ranch Hands in the low, medium, and high initial dioxin categories who had inclusion cysts decreased as initial dioxin increased (13.5%, 12.7%, and 5.9%, respectively).

In the adjusted minimal analysis, the association between initial dioxin and inclusion cysts remained nonsignificant (Table 11-11 [c]: p=0.557). The relative risk remained marginally less than 1 under the maximal assumption after adjusting the model for significant covariates (Table 11-11 [d]: Adj. RR=0.85, p=0.075).

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

In the unadjusted analysis, the association between current dioxin and inclusion cysts did not differ significantly between the two time since tour strata under either assumption (Table 11-11 [e] and [f]: minimal assumption, p=0.305; maximal assumption, p=0.923). After adjusting the models under both assumptions for significant covariates, the interaction

TABLE 11-11.

Analysis of Inclusion Cysts

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=521)	Low	130	5.4	0.94 (0.73,1.20)	0.615
	Medium	260	13.9		
	High	131	5.3		
b) Maximal (n=742)	Low	185	13.5	0.86 (0.72,1.03)	0.098
	Medium	371	12.7		
	High	186	5.9		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=521)	0.93 (0.72,1.19)	0.557	SEAACNE (p=0.009)
d) Maximal (n=742)	0.85 (0.71,1.02)	0.075	SEAACNE (p=0.003)

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

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

TABLE 11-11. (Continued)

Analysis of Inclusion Cysts

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

Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal (n=521)	≤18.6	6.9 (72)	14.8 (128)	0.0 (54)	0.78 (0.50,1.21)	0.305[b] 0.270[c]
	>18.6	5.2 (58)	12.1 (132)	9.1 (77)	1.03 (0.75,1.42)	0.840[c]
f) Maximal (n=742)	≤18.6	12.3 (106)	12.0 (191)	4.8 (83)	0.82 (0.61,1.10)	0.923[b] 0.179[c]
	>18.6	20.3 (79)	10.6 (179)	7.7 (104)	0.84 (0.65,1.07)	0.147[c]

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

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal (n=521)	≤18.6	0.76 (0.49,1.18)	0.297[b] 0.223[c]	SEAACNE (p=0.003)
	>18.6	1.01 (0.73,1.39)	0.943[c]	
h) Maximal (n=742)	≤18.6	0.80 (0.59,1.06)	0.870[b] 0.124[c]	SEAACNE (p=0.003)
	>18.6	0.82 (0.64,1.05)	0.111[c]	

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

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

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

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

TABLE 11-11. (Continued)

Analysis of Inclusion Cysts

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

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	786	10.4	All Categories		0.041
Unknown	345	12.5	Unknown vs. Background	1.22 (0.83,1.81)	0.316
Low	196	14.8	Low vs. Background	1.49 (0.95,2.35)	0.086
High	187	6.4	High vs. Background	0.59 (0.31,1.10)	0.098
Total	1,514				

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

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	786	All Categories		0.070	AGE (p=0.062) RACE (p=0.072)
Unknown	345	Unknown vs. Background	1.19 (0.80,1.77)	0.384	SEAACNE (p=0.066)
Low	196	Low vs. Background	1.51 (0.95,2.38)	0.080	
High	187	High vs. Background	0.63 (0.33,1.18)	0.148	
Total	1,514				

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

between current dioxin and time remained nonsignificant (Table 11-11 [g] and [h]: minimal assumption, p=0.297; maximal assumption, p=0.870).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In the unadjusted analysis of inclusion cysts, the overall contrast showed a significant difference among the four current dioxin categories (Table 11-11 [i]: p=0.041). The percentages of participants in the background, unknown, low, and high categories who had inclusion cysts were 10.4, 12.5, 14.8, and 6.4 percent. The risk of inclusion cysts was marginally greater than 1 when contrasting the low and background categories (Est. RR=1.49, 95% C.I.: [0.95,2.35], p=0.086) and was marginally less than 1 when contrasting the high and background categories (Est. RR=0.59, 95% C.I.: [0.31,1.10], p=0.098).

The overall contrast in the adjusted analysis of inclusion cysts became marginally significant after age, race, and the presence of pre-SEA acne were accounted for in the model (Table 11-11 [j]: p=0.070). The relative risk remained marginally significant under the low versus background contrast (Adj. RR=1.51, 95% C.I.: [0.95,2.38], p=0.080), but became nonsignificant but still less than 1 under the high versus background contrast (p=0.148).

Hyperpigmentation

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

Under the unadjusted analysis for the minimal assumption, no significant association was exhibited between initial dioxin and hyperpigmentation (Table 11-12 [a]: p=0.319). Under the maximal assumption, however, the risk of hyperpigmentation was significantly greater than 1 (Table 11-12 [b]: Est. RR=1.22, p=0.008). The percentages of hyperpigmentation in the low, medium, and high initial dioxin categories were 8.7, 14.8, and 18.3 percent.

The association between initial dioxin and hyperpigmentation remained nonsignificant in the adjusted minimal analysis (Table 11-12 [c]: p=0.159). In the adjusted maximal analysis, significant interactions between initial dioxin and age (Table 11-12 [d]: p=0.029) and between initial dioxin and the presence of pre-SEA acne (p=0.048) were present. Age was then divided into two strata—born in or after 1942 and born before 1942—to explore these interactions. Within the younger-age stratum, the interaction between initial dioxin and the presence of pre-SEA acne remained significant; consequently, the presence of pre-SEA acne was dichotomized as yes or no and analyzed further. For those who had pre-SEA acne, there were only two Ranch Hands who also had hyperpigmentation, both of whom were in the high initial dioxin category. For those who did not have pre-SEA acne, the association between initial dioxin and hyperpigmentation was not significant (Appendix Table J-1: p=0.883). Within the older-age stratum, the initial dioxin-by-presence of pre-SEA acne interaction was not significant, and no further stratification was pursued. Within this stratum, the risk of hyperpigmentation was significantly greater than 1 (Adj. RR=1.47, p<0.001), with the percentages in the low, medium, and high initial dioxin categories equal to 4.4, 15.9, and 21.7 percent. Without these two interactions in the adjusted maximal analysis, the risk of hyperpigmentation was significantly greater than 1 (Table 11-12 [d]: Adj. RR=1.25, p=0.005).

TABLE 11-12.

Analysis of Hyperpigmentation

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=521)	Low	130	13.9	1.10 (0.91,1.33)	0.319
	Medium	260	16.9		
	High	131	17.6		
b) Maximal (n=742)	Low	185	8.7	1.22 (1.06,1.40)	0.008
	Medium	371	14.8		
	High	186	18.3		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=521)	1.15 (0.95,1.40)	0.159	RACE (p<0.001) SEAACNE (p=0.012)
d) Maximal (n=742)	1.25 (1.07,1.45)**	0.005**	INIT*AGE (p=0.029) INIT*SEAACNE (p=0.048) RACE (p<0.001)

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

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

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

TABLE 11-12. (Continued)

Analysis of Hyperpigmentation

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

Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal (n=521)	≤18.6	13.9 (72)	20.3 (128)	16.7 (54)	1.14 (0.85,1.53)	0.961[b] 0.390[c]
	>18.6	10.3 (58)	14.4 (132)	19.5 (77)	1.15 (0.89,1.48)	0.286[c]
f) Maximal (n=742)	≤18.6	5.7 (106)	15.7 (191)	21.7 (83)	1.35 (1.09,1.68)	0.305[b] 0.007[c]
	>18.6	12.7 (79)	12.3 (179)	18.3 (104)	1.16 (0.95,1.41)	0.145[c]

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

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal (n=521)			0.808[b]	AGE (p=0.097)
	≤18.6	1.32 (0.96,1.82)	0.084[c]	RACE (p<0.001)
	>18.6	1.26 (0.96,1.64)	0.090[c]	SEAACNE (p=0.014)
h) Maximal (n=742)			0.216[b]	RACE (p<0.001)
	≤18.6	1.42 (1.13,1.79)	0.003[c]	SEAACNE
	>18.6	1.17 (0.96,1.44)	0.123[c]	(p=0.002)

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

TABLE 11-12. (Continued)

Analysis of Hyperpigmentation

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

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	786	16.0	All Categories		0.037
Unknown	345	11.0	Unknown vs. Background	0.65 (0.44,0.95)	0.028
Low	196	14.3	Low vs. Background	0.87 (0.56,1.36)	0.548
High	187	19.8	High vs. Background	1.29 (0.86,1.94)	0.217
Total	1,514				

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

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	786	All Categories		0.049	RACE (p<0.001)
Unknown	345	Unknown vs. Background	0.68 (0.46,1.00)	0.052	
Low	196	Low vs. Background	0.87 (0.56,1.36)	0.541	
High	187	High vs. Background	1.35 (0.89,2.03)	0.157	
Total	1,514				

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

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

In the unadjusted analysis of hyperpigmentation, the interaction between current dioxin and time since tour was nonsignificant under the minimal and maximal assumptions (Table 11-12 [e] and [f]: p=0.961 and p=0.305). However, under the maximal assumption, the risk of hyperpigmentation was significantly greater than 1 when time since tour was no more than 18.6 years (Table 11-12 [f]: Est. RR=1.35, p=0.007). Within this time stratum, the percentages of hyperpigmentation were 5.7, 15.7, and 21.7 percent for low, medium, and high current dioxin.

The current dioxin-by-time interaction remained nonsignificant in the adjusted analyses of hyperpigmentation (Table 11-12 [g] and [h]: minimal assumption, p=0.808; maximal assumption, p=0.216). In the minimal analysis, however, the risk of hyperpigmentation became marginally significant in both time strata after the model was adjusted for age, race, and the presence of pre-SEA acne (time≤18.6 years: Adj. RR=1.32, p=0.084; time>18.6 years: Adj. RR=1.26, p=0.090). Within the later tour stratum, the percentages of Ranch Hands with hyperpigmentation for low, medium, and high current dioxin were 13.9, 20.3, and 16.7 percent. The corresponding percentages in the earlier tour stratum were 10.3, 14.4, and 19.5 percent, respectively. Under the maximal assumption, the risk in the later tour stratum remained significantly greater than 1 after adjusting for significant covariates (Table 11-12 [h]: Adj. RR=1.42, p=0.003).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The percentages of hyperpigmentation differed significantly among the four current dioxin categories in the unadjusted analysis (Table 11-12 [i]: p=0.037). The percentages in the background, unknown, low, and high current dioxin categories were 16.0, 11.0, 14.3, and 19.8 percent. Under the unknown versus background contrast, the risk of hyperpigmentation was significantly less than 1 (Adj. RR=0.65, 95% C.I.: [0.44,0.95], p=0.028). The risk, however, was nonsignificant under the low versus background contrast (p=0.548) and the high versus background contrast (p=0.217).

After the model was adjusted for race, the overall contrast of the four current dioxin categories remained significant (Table 11-12 [j]: p=0.049). However, the risk of hyperpigmentation under the unknown versus background contrast became only marginally significant in the adjusted analysis (Adj. RR=0.68, 95% C.I.: [0.46,1.00], p=0.052). The risks under the other two contrasts remained nonsignificant (low versus background: p=0.541; high versus background: p=0.157).

Other Abnormalities

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

In the unadjusted minimal analysis, no significant association was detected between initial dioxin and the composite variable containing all other dermatologic abnormalities (Table 11-13 [a]: p=0.226). However, under the maximal assumption, the association was marginally significant with a relative risk less than 1 (Table 11-13 [b]: Est. RR=0.89, p=0.057). The percentages of Ranch Hands with at least one abnormality in the category of other dermatologic disorders were 76.2, 76.8, and 71.0 percent for low, medium, and high initial dioxin.

TABLE 11-13.

Analysis of Other Abnormalities

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=521)	Low	130	76.2	0.91 (0.77,1.06)	0.226
	Medium	260	73.1		
	High	131	71.0		
b) Maximal (n=742)	Low	185	76.2	0.89 (0.79,1.00)	0.057
	Medium	371	76.8		
	High	186	71.0		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=521)	0.96 (0.81,1.13)	0.616	AGE (p<0.001) RACE (p=0.020)
d) Maximal (n=742)	0.94 (0.83,1.06)	0.308	AGE (p<0.001) RACE (p=0.007)

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

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

TABLE 11-13. (Continued)

Analysis of Other Abnormalities

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

Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal (n=521)						0.928[b]
	≤18.6	75.0 (72)	71.9 (128)	68.5 (54)	0.88 (0.69,1.14)	0.338[c]
	>18.6	84.5 (58)	72.0 (132)	71.4 (77)	0.87 (0.70,1.08)	0.199[c]
f) Maximal (n=742)						0.821[b]
	≤18.6	77.4 (106)	73.8 (191)	68.7 (83)	0.87 (0.73,1.05)	0.141[c]
	>18.6	81.0 (79)	77.1 (179)	73.1 (104)	0.85 (0.72,1.00)	0.052[c]

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

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal (n=521)			0.872[b]	AGE (p<0.001)
	≤18.6	0.96 (0.74,1.26)	0.791[c]	RACE (p=0.019)
	>18.6	0.94 (0.75,1.17)	0.574[c]	
h) Maximal (n=742)			0.864[b]	AGE (p<0.001)
	≤18.6	0.93 (0.77,1.13)	0.470[c]	RACE (p=0.006)
	>18.6	0.91 (0.77,1.09)	0.304[c]	

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

TABLE 11-13. (Continued)

Analysis of Other Abnormalities

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

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	786	74.6	All Categories		0.154
Unknown	345	78.8	Unknown vs. Background	1.27 (0.94,1.72)	0.121
Low	196	71.9	Low vs. Background	0.87 (0.62,1.24)	0.455
High	187	71.1	High vs. Background	0.84 (0.59,1.20)	0.337
Total	1,514				

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

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	786	All Categories		0.583	AGE (p<0.001) RACE (p<0.001)
Unknown	345	Unknown vs. Background	1.17 (0.86,1.60)	0.324	
Low	196	Low vs. Background	0.88 (0.61,1.26)	0.477	
High	187	High vs. Background	1.02 (0.71,1.47)	0.922	
Total	1,514				

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

In the adjusted minimal analysis, the association between initial dioxin and other abnormalities remained nonsignificant (Table 11-13 [c]: p=0.616). After adjusting the model in the maximal analysis for age and race, the association between initial dioxin and other abnormalities became nonsignificant (Table 11-13 [d]: p=0.308).

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

The association between current dioxin and other abnormalities was not significantly different between the time since tour strata under either the minimal or the maximal assumption (Table 11-13 [e] and [f]: p=0.928 and p=0.821). Under the maximal assumption, however, there was a marginally significant negative association between current dioxin and other abnormalities within the earlier tour stratum (Table 11-13 [f]: Est. RR=0.85, p=0.052). Within this stratum, the percentages of Ranch Hands with low, medium, and high current dioxin with at least one of the other abnormalities were 81.0, 77.1, and 73.1 percent.

After adjusting for significant covariates, the current dioxin-by-time interaction remained nonsignificant under both assumptions (Table 11-13 [g] and [h]: minimal assumption, p=0.872; maximal assumption, p=0.864). The association in the earlier tour stratum, under the maximal assumption, became nonsignificant after the model was adjusted for age and race (Table 11-13 [h]: p=0.304).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In the unadjusted analysis of other abnormalities, the overall contrast of the four current dioxin categories showed no significant difference in the percentages of participants who had at least one of the other dermatologic abnormalities (Table 11-13 [i]: p=0.154). After the model was adjusted for significant covariates, the overall contrast remained nonsignificant (Table 11-13 [j]: p=0.583).

Dermatology Index

The dermatology index was formed by counting the number of abnormalities present for the following conditions: comedones, acneiform lesions, acneiform scars, and inclusion cysts. Table 11-14 shows the frequencies of the number of abnormalities. For the analyses presented below, the dermatology index was dichotomized as normal (no abnormalities) and abnormal (at least one abnormality).

Model 1: Ranch Hands - Log_2 (Initial Dioxin)

In the unadjusted analysis of the dermatology index, classified as either no abnormalities or more than one abnormality, there was no significant association with initial dioxin under the minimal and maximal assumptions (Table 11-15 [a] and [b]: p=0.410 and p=0.246). When the analysis was adjusted for significant covariate information, the association remained nonsignificant under both assumptions (Table 11-15 [c] and [d]: minimal assumption, p=0.471; maximal assumption, p=0.324).

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

In the unadjusted minimal analysis of the dermatology index, the current dioxin-by-time since tour interaction was not significant (Table 11-15 [e]: p=0.431). Under the maximal assumption, however, the association between current dioxin and the dermatology index

TABLE 11-14.

Dermatology Index Frequencies*

Dermatology Index	Minimal Assumption			Maximal Assumption		
		Time (yrs.)			Time (yrs.)	
	Total	≤18.6	>18.6	Total	≤18.6	>18.6
0	323	153	170	464	239	225
1	139	72	67	198	102	96
2	45	23	22	59	29	30
3	10	2	8	17	6	11
4	4	4	0	4	4	0

Dermatology Index	Current Dioxin Category			
	Background	Unknown	Low	High
0	487	213	110	117
1	204	97	57	50
2	67	25	22	16
3	25	8	4	4
4	3	2	3	0

*Total indicates sample size used in the $\log_2$ (initial dioxin) analysis; total sample size is broken down by time since tour to indicate sample sizes used in the $\log_2$ (current dioxin) and time analysis; sample size given for each category used in categorized current dioxin analysis.

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

TABLE 11-15.
Analysis of Dermatology Index

Ranch Hands - Log_2 (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value
a) Minimal (n=521)	Low	130	31.5	1.06 (0.92,1.23)	0.410
	Medium	260	42.3		
	High	131	35.9		
b) Maximal (n=742)	Low	185	35.7	1.07 (0.96,1.19)	0.246
	Medium	371	39.9		
	High	186	34.4		

Ranch Hands - Log_2 (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
c) Minimal (n=521)	1.06 (0.91,1.23)	0.471	SEAACNE (p<0.001)
d) Maximal (n=742)	1.06 (0.95,1.19)	0.324	SEAACNE (p<0.001) AGE*RACE (p=0.041)

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

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

TABLE 11-15. (Continued)

Analysis of Dermatology Index

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

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)[a]	p-Value
e) Minimal						0.431[b]
(n=521)	≤18.6	26.4 (72)	50.8 (128)	31.5 (54)	1.17 (0.92,1.48)	0.202[c]
	>18.6	34.5 (58)	37.1 (132)	36.4 (77)	1.03 (0.85,1.25)	0.763[c]
f) Maximal						0.048[b]
(n=742)	≤18.6	30.2 (106)	40.3 (191)	38.6 (83)	1.20 (1.02,1.42)	0.031[c]
	>18.6	46.8 (79)	34.6 (179)	36.5 (104)	0.96 (0.83,1.11)	0.590[c]

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

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
g) Minimal			0.440[b]	SEAACNE
(n=521)	≤18.6	1.15 (0.90,1.46)	0.265[c]	(p<0.001)
	>18.6	1.01 (0.83,1.24)	0.892[c]	
h) Maximal			0.061[b]	SEAACNE
(n=742)	≤18.6	1.19 (0.99,1.42)	0.059[c]	(p<0.001)
	>18.6	0.95 (0.81,1.11)	0.540[c]	AGE*RACE (p=0.044)

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

TABLE 11-15. (Continued)

Analysis of Dermatology Index

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

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	786	38.0	All Categories		0.479
Unknown	345	38.3	Unknown vs. Background	1.01 (0.78,1.31)	0.944
Low	196	43.9	Low vs. Background	1.27 (0.93,1.75)	0.135
High	187	37.4	High vs. Background	0.97 (0.70,1.35)	0.878
Total	1,514				

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

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	786	All Categories		0.459	SEAACNE (p<0.001)
Unknown	345	Unknown vs. Background	1.02 (0.78,1.33)	0.900	AGE*RACE (p=0.010)
Low	196	Low vs. Background	1.29 (0.93,1.78)	0.122	
High	187	High vs. Background	0.98 (0.70,1.37)	0.896	
Total	1,514				

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