Table 4-18

Post-SEA Birth Weight

Variable: Birth Weight (Grams)
Restrictions: Full Siblings of Ranch Hands and Comparisons Children Conceived during or after the Father's Duty in SEA
Model 3: Categorized Current Dioxin

a) Unadjusted

Exposure Category	n	Mean	Category Contrast	Difference of Means (95% C.I.)	p-Value
Background	803	3407.1	All Exp Categ		0.032
Unknown	216	3293.2	Unk vs Bkgd	-113.9(-200.3,-27.5)	0.008
Low	147	3427.0	Low vs Bkgd	19.9(-81.2,121.0)	0.680
High	194	3335.9	High vs Bkgd	-71.2(-161.4,19.0)	0.113
Total	1360	(R^2=0.006)			

b) Adjusted

Exposure Category	n	Adj. Mean	Category Contrast	Diff. of Adj. Means (95% C.I.)	p-Value	Covariate Remarks
Background	713	3256.8	All Exp Categ		0.001	RACE(p=0.048)
Unknown	197	3194.2	Unk vs Bkgd	-62.6(-149.5,24.3)	0.166	OCC(p=0.001
Low	137	3285.9	Low vs Bkgd	29.1(-71.6,129.8)	0.575	SMOKE(p=0.001)
High	180	3104.0	High vs Bkgd	-152.8(-242.9,-62.7)	0.002	DRINK(p=0.046)
						OCC*DIOXIN
Total	1227	(R^2=0.073)				(p=0.065)

Low Birth Weight (All Children)

Model 1: **Conceptions of Ranch Hands - Log_2(Initial Dioxin)**

Without adjustment for covariates (Table 4-19 [a] and [b]), there is no association between abnormally low birth weight and initial dioxin among children of Ranch Hands having more than 10 ppt (p=0.759) or more than 5 ppt (p=0.625) current dioxin.

After adjustment for covariates (Table 4-19 [c]), there is no significant association between abnormally low birth weight and initial dioxin among children of Ranch Hands with more than 10 ppt (p=0.250).

After adjustment for covariates (Table 4-19 [d]), there is significant variation in the association between the abnormally low birth weight and initial dioxin with the mother's drinking (p=0.014) and the father's race (p=0.040) among children of Ranch Hands with more than 5 ppt. The basis for this association in risk is displayed in Appendix B-1. There is a significant association between low birth weight and initial dioxin in children of non-black fathers whose mothers drank during pregnancy (p=0.017). A borderline significant association was observed in children of Black fathers whose mothers did not drink during pregnancy (p=0.084).

If this variation is ignored (Table 4-19 [d]), there is no significant association between abnormally low birth weight and initial dioxin among children of Ranch Hands having more than 5 ppt current dioxin (p=0.883).

Table 4-19

Post-SEA Low Birth Weight

Variable: Low Birth Weight
Restrictions: All Children of Ranch Hands
Children Conceived during or after the Father's Duty in SEA
Model 1: Log_2(Initial Dioxin)

Ranch Hands - Log_2(Initial Dioxin) - Unadjusted

Exposure Restriction	Initial Dioxin	n	Abnormal Number	Abnormal Rate	Est. Relative Risk (95% C.I.)	p-Value
a) D>10 ppt (n=496)	Low	106	7	66.0	1.05(0.79,1.38)	0.759
	Medium	237	17	71.7		
	High	153	13	85.0		
b) D>5 ppt (n=670)	Low	151	14	92.7	0.95(0.78,1.16)	0.625
	Medium	299	23	76.9		
	High	220	18	81.8		

Table 4-19 (Continued)

Ranch Hands - Log_2(Initial Dioxin) - Adjusted

Exposure Restriction	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
c) D>10 ppt (n=456)	1.21(0.87,1.68)	0.250	RACE(p=0.042) SMOKE(p=0.045) OCC(p=0.001) SMOKE*DIOXIN(p=0.066)
d) D>5 ppt (n=612)	0.98(0.77,1.25)***	0.883***	SMOKE(p=0.036) OCC(P=0.017) RACE*DIOXIN(p=0.040) DRINK*DIOXIN(p=0.014)

Low Birth Weight (All Children)

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

Without adjustment for covariates (Table 4-20 [a] and [b]), there is no significant variation in the association between abnormally low birth weight and current dioxin with time since duty in SEA among children of Ranch Hands having more than 10 ppt (p=0.868) or more than 5 ppt current dioxin (p=0.977). Furthermore, there is no significant association between abnormally low birth weight and current dioxin among Ranch Hands with late or early tours for either exposure restriction.

After adjustment for covariates (Table 4-20 [c]), there is no significant variation in the association between abnormally low birth weight and current dioxin with time since duty in SEA among children of Ranch Hands having more than 10 ppt current dioxin (p=0.918). Furthermore, there is no association between low birth weight and current dioxin among children of Ranch Hands with late (p=0.378) or early (p=0.715) tours.

After adjustment for covariates (Table 4-20 [d]), there is significant variation in the association between abnormally low birth weight and current dioxin with time since duty in SEA and conception time since end of tour among children of Ranch Hands having more than 5 ppt current dioxin (p=0.031). The basis for this variation is displayed in Appendix B-1. There is a borderline significant decrease in abnormally low birth weight with current dioxin in children of fathers with early tours for conceptions within 2 years of duty in SEA (p=0.060) and a significant increase in low birth rate with current dioxin in conceptions more the 6.5 years after SEA (p=0.030) fathered by Ranch Hands with early tours. The other four strata did not show a significant association between abnormally low birth weight and current dioxin.

If this variation is ignored (Table 4-20 [d]), there is no significant variation in the association between the low birth weight and current dioxin with time since duty in SEA among children of Ranch Hands having more than 5 ppt current dioxin (p=0.550). Furthermore, there is no significant association between the low birth weight and current dioxin among children of Ranch Hands with late (p=0.527) or early (p=0.894) tours.

Table 4-20

Post SEA Low Birth Weight

Variable: Low Birth Weight (Discrete)
Restrictions: All Children of Ranch Hands
Children Conceived during or after the Father's Duty in SEA
Model 2: Log_2(Current Dioxin), Time

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

Exposure Restriction	Time Since SEA (years)	Abnormal (No./n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)	p-Value
a) D>10 ppt (n=497)						0.868
	≤18.6	32.3 (2/62)	91.6 (12/131)	70.4 (5/71)	1.01(0.65,1.58)	0.959
	>18.6	100.0 (4/40)	76.9 (8/104)	67.4 (6/89)	1.06(0.72,1.56)	0.756
b) D>5 ppt (n=670)						0.977
	≤18.6	80.5 (7/87)	81.9 (14/171)	73.4 (8/109)	0.93(0.69,1.25)	0.623
	>18.6	133.3 (8/60)	45.5 (6/132)	108.1 (12/111)	0.92(0.70,1.22)	0.568

Table 4-20 (Continued)

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

Exposure Restriction	Time Since SEA (years)	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
c) D>10 ppt (n=457)			0.918	RACE(p=0.039) OCC(P=0.001)
	≤18.6	1.26(0.75,2.12)	0.378	SMOKE(P=0.043)
	>18.6	1.22(0.42,3.55)	0.715	
d) D>5 ppt (n=612)			0.550***	SMOKE(p=0.018) OCC(p=0.022)
	≤18.6	0.89(0.62,1.27)***	0.527***	C-TIME*DIOXIN (p=0.031)
	>18.6	1.02(0.75,1.39)***	0.894***	

Low Birth Weight (All Children)

Model 3: Children of Ranch Hands and Comparisons - Categorized Current Dioxin

Without adjustment for covariates (Table 4-21 [a]), there is a significant overall association between abnormally low birth weight and categorized current dioxin (p=0.002). Furthermore, the rates of low birth weight among children of Ranch Hands in the High (p=0.003) and Unknown (p=0.001) categories are significantly higher than the rate among children of Comparisons in the Background category. The rate of abnormally low birth weight among children of Ranch Hands in the Low category is not significantly different from the rate among children of Comparisons in the Background category (p=0.189).

After adjustment for the covariates (Table 4-21 [b]), there is significant variation in the overall association between abnormally low birth weight and categorized current dioxin with the father's military occupation (p=0.004). The basis for this variation is displayed in Appendix B-1. For the enlisted flyers, the rates of abnormally low birth weight among children of Ranch Hands in the High (p=0.003) and Unknown (p=0.003) categories are significantly higher than the rate among children of Comparisons in the Background category. For the enlisted ground personnel, the rates of abnormally low birth weight among children of Ranch Hands in the High (p=0.007) and Unknown (p=0.003) categories are also significantly higher than the rate among children of Comparisons in the Background category.

For the officers, significance testing could be done only between the Unknown and the Background categories because of the small number of children in the other categories. No significant difference exists between the rate of abnormally low birth weight in children of Ranch Hands in the Unknown category and the rate in children of Comparisons in the Background category (p=0.215).

Table 4-21

Post SEA Low Birth Weight

Variable: Low Birth Weight (Discrete)
Restrictions: All Children of Ranch Hands and Comparisons Children Conceived during or after the Father's Duty in SEA
Model 3: Categorized Current Dioxin

a) Unadjusted

Exposure Category	n	Abnormal Number	Abnormal Rate	Category Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	954	40	41.9	All Exp Categ		0.002
Unknown	268	25	93.3	Unk vs Bkgd	2.35(1.40,3.91)	0.001
Low	170	11	64.7	Low vs Bkgd	1.58(0.79,3.14)	0.189
High	220	20	90.9	High vs Bkgd	2.28(1.31,4.00)	0.003
Total	1612					

b) Adjusted

Exposure Category	n	Category Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	837	All Exp Categ	****	****	SMOKE(p=0.001)
Unknown	244	Unk vs Bkgd			OCC*DIOXIN
Low	156	Low vs Bkgd			(p=0.004)
High	201	High vs Bkgd			
Total	1438				

Low Birth Weight (Full Siblings)

Model 1: Conceptions of Ranch Hands - Log_2(Initial Dioxin)

Without adjustment for covariates (Table 4-22 [a] and [b]), there is no association between abnormally low birth weight and initial dioxin among full siblings fathered by Ranch Hands having more than 10 ppt (p=0.743) or more than 5 ppt (p=0.629) current dioxin.

After adjustment for covariates (Table 4-22 [c]), there is significant variation in the association between the abnormally low birth weight and initial dioxin with conception time since the end of the SEA tour (p=0.038) and the mother's smoking (p=0.009) among children of Ranch Hands with more than 10 ppt. The basis for this interaction is displayed in Appendix B-1. In children of mothers who did not smoke during pregnancy and whose conceptions occurred within 2 years after the father's SEA tour there is a borderline significant decrease in the rate of abnormally low birth weight with initial dioxin (p=0.082). None of the remaining five combinations of conception time since SEA and mother's smoking show any significant association between abnormally low birth weight and initial dioxin.

After adjustment for covariates (Table 4-22 [d]), there is significant variation in the association between the abnormally low birth weight and initial dioxin with the mother's smoking (p=0.032) and conception time since the SEA tour (p=0.021) among children of Ranch Hands with more than 5 ppt. The basis for this interaction is displayed in Appendix B-1. In children of mothers who did not smoke during pregnancy and whose conceptions occurred within 2 years after the father's SEA tour there is a significant decrease in the rate of abnormally low birth weight with initial dioxin (p=0.006). None of the remaining five combinations of conception time since SEA duty and the mother's smoking show any significant association between abnormally low birth weight and initial dioxin.

If this interaction is ignored (Table 4-22 [d]), there is no significant association between abnormally low birth weight and initial dioxin among children of Ranch Hands having more than 5 ppt current dioxin (p=0.984).

Table 4-22

Post SEA Low Birth Weight

Variable: Low Birth Weight (Discrete)
Restrictions: Full Siblings of Ranch Hands
Children Conceived during or after the Father's Duty in SEA
Model 1: Log_2(Initial Dioxin)

Ranch Hands - Log_2(Initial Dioxin) - Unadjusted

Exposure Restriction	Initial Dioxin	n	Abnormal Number	Abnormal Rate	Est. Relative Risk (95% C.I.)	p-Value
a) D>10 ppt (n=418)	Low	78	5	64.1	1.05(0.78,1.42)	0.743
	Medium	205	16	78.0		
	High	135	12	88.9		
b) D>5 ppt (n=552)	Low	113	11	97.3	0.95(0.77,1.17)	0.629
	Medium	242	20	82.6		
	High	197	17	86.3		

Ranch Hands - Log_2(Initial Dioxin) - Adjusted

Exposure Restriction	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
c) D>10 ppt (n=390)	****	****	RACE(p=0.028) OCC(p=0.001) SMOKE*DIOXIN(p=0.009) C-TIME*DIOXIN (p=0.038)
d) D>5 ppt (n=511)	1.01(0.93,1.09)***	0.984***	RACE(p=0.065) OCC(p=0.011) SMOKE*DIOXIN(p=0.032) C-TIME*DIOXIN (p=0.021)

Low Birth Weight (Full Siblings)

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

Without adjustment for covariates (Table 4-23 [a] and [b]), there is no significant variation in the association between abnormally low birth weight and current dioxin with time since duty in SEA among full siblings fathered by Ranch Hands having more than 10 ppt (p=0.921) or more than 5 ppt current dioxin (p=0.863). Furthermore, there is no significant association between abnormally low birth weight and current dioxin among children of Ranch Hands with late or early tours for either exposure restriction.

After adjustment for covariates (Table 4-23 [c] and [d]), there is no significant variation in the association between abnormally low birth weight and current dioxin with time since duty in SEA among full siblings fathered by Ranch Hands having more than 10 ppt (p=0.819) or 5 ppt (p=0.655) current dioxin. Furthermore, there is no significant association between abnormally low birth weight and current dioxin among children of Ranch Hands with late or early tours for either exposure restriction.

Table 4-23

Post SEA Low Birth Weight

Variable: Low Birth Weight (Discrete)
Restrictions: Full Siblings of Ranch Hands
Children Conceived during or after the Father's Duty in SEA
Model 2: Log_2(Current Dioxin), Time

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

Exposure Restriction	Time Since SEA (years)	Abnormal (No./n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)	p-Value
a) D>10 ppt (n=419)						0.921
	≤18.6	21.3 (1/47)	105.3 (12/114)	78.1 (5/64)	1.04(0.66,1.64)	0.856
	>18.6	107.1 (3/28)	76.1 (7/92)	67.6 (5/74)	1.08(0.70,1.64)	0.734
b) D>5 ppt (n=552)						0.863
	≤18.6	86.2 (5/58)	90.9 (13/143)	81.6 (8/98)	0.95(0.69,1.31)	0.763
	>18.6	134.6 (7/52)	38.1 (4/105)	114.6 (11/96)	0.92(0.49,1.70)	0.782

Table 4-23 (Continued)

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

Exposure Restriction	Time Since SEA (years)	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
c) D>10 ppt (n=391)			0.819	RACE(p=0.025) SMOKE(p=0.109) OCC(p=0.003)
	≤18.6	1.31(0.77,2.23)	0.318	
	>18.6	1.21(0.75,1.97)	0.438	
d) D>5 ppt (n=511)			0.665	RACE(p=0.076) OCC(p=0.024)
	≤18.6	0.91(0.62,1.35)	0.640	
	>18.6	1.01(0.72,1.41)	0.944	

Low Birth Weight (Full Siblings)

Model 3: Conceptions of Ranch Hands and Comparisons - Categorized Current Dioxin

Without adjustment for covariates (Table 4-24 [a]), there is a significant overall association between abnormally low birth weight and categorized current dioxin among full siblings (p=0.004). Furthermore, the rates of low birth weight among children of Ranch Hands in the High (p=0.004) and Unknown (p=0.001) categories are significantly higher than the rate among children of Comparisons in the Background category. The rate of abnormally low birth weight among children of Ranch Hands in the Low category is not significantly different from the rate among children of Comparisons in the Background category (p=0.228).

After adjustment for covariates (Table 4-24 [b]), there is significant variation in the overall association between abnormally low birth weight and categorized current dioxin with the father's military occupation (p=0.004) and race (p=0.021) among full siblings. The basis for this variation is displayed in Appendix B-1. In children of nonblack enlisted flyers, the rates of abnormally low birth weight among children of fathers in the High (p=0.012) and Low (p=0.011) categories are significantly higher than the rate among children of fathers in the Background category. In children of nonblack enlisted ground personnel, the rates of abnormally low birth weight among children of fathers in the High (p=0.039) and Unknown (p=0.038) categories are significantly higher than the rate among children of fathers in the Background category.

In children of Black fathers, significance testing could be done only in children of officers in the Unknown and the Background categories because of sparse data. No significant difference exists between rate of abnormally low birth weight in children of fathers in the Unknown category and the rate in children of fathers in the Background category (p=0.180).

Table 4-24

Post SEA Low Birth Weight

Variable: Low Birth Weight (Discrete)
Restrictions: Full Siblings of Ranch Hands and Comparisons
Children Conceived during or after the
Father's Duty in SEA
Model 3: Categorized Current Dioxin

a) **Unadjusted**

Exposure Category	n	Abnormal Number	Abnormal Rate	Category Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	803	36	44.8	All Exp Categ		0.004
Unknown	216	22	101.9	Unk vs Bkgd	2.42(1.39,4.20)	0.001
Low	147	10	68.0	Low vs Bkgd	1.56(0.75,3.21)	0.228
High	194	19	97.9	High vs Bkgd	2.31(1.30,4.13)	0.004
Total	1360					

b) **Adjusted**

Exposure Category	n	Category Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	713	All Exp Categ	****	****	SMOKE(p=0.001)
Unknown	197	Unk vs Bkgd			RACE*DIOXIN(p=0.021)
Low	137	Low vs Bkgd			OCC*DIOXIN(p=0.004)
High	180	High vs Bkgd			
Total	1227				

4.4 Conclusion

Throughout this section, nonsignificant results are indicated by NS, borderline significant results are indicated by NS* and the presence of interactions with the p-value greater than or equal to 0.01 and less than 0.05 are indicated with a preceding asterisk (**). Four asterisks (****) represent the presence of an interaction between a covariate and dioxin with a p-value less than 0.01.

Assessments of the association between paternal dioxin and birth weight and abnormally low birth weight were carried out based on pre-SEA and post-SEA children using Models 1, 2 and 3. Each analysis was carried out without adjustment for covariates. All analyses were first based on all children and again on full sibling children. The results are summarized in Tables 4-25 through 4-27.

Table 4-25

P-Value Summary of Initial Dioxin (Model 1) Analyses
of Pre-Post Birth Weight
(Children of Ranch Hands)

a) All Children

Variable	Unadjusted D>10 ppt	Unadjusted D>5 ppt
Birth Weight	NS*	0.003
Low Birth Weight	NS	NS

b) Full Siblings

Variable	Unadjusted D>10 ppt	Unadjusted D>5 ppt
Birth Weight	0.039	0.004
Low Birth Weight	NS	NS

Table 4-26

P-Value Summary of Current Dioxin and Time Analyses (Model 2) of Pre-Post SEA Birth Weight (Children of Ranch Hands)

a) All Children

Variable	Unadjusted D>10 ppt	Unadjusted D>5 ppt
Birth Weight	NS	NS
Low Birth Weight	NS	NS

b) Full Siblings

Variable	Unadjusted D>10 ppt	Unadjusted D>5 ppt
Birth Weight	NS	NS
Low Birth Weight	NS	NS

Table 4-27

P-Value Summary of Pre-Post SEA Categorized Current Dioxin (Model 3) Analyses of Birth Weight (Children of Ranch Hands and Comparisons)

a) All Children

Variable	All	Unadjusted Contrasts with Background: Unknown	Low	High
Birth Weight	0.018	NS	0.044	NS
Low Birth Weight	0.011	0.001	NS*	NS

b) Full Siblings

Variable	All	Unadjusted Contrasts with Background: Unknown	Low	High
Birth Weight	0.045	NS*	NS	NS
Low Birth Weight	0.014	0.002	NS*	NS

Assessments of the association between paternal dioxin and birth weight and abnormally low birth weight were carried out based on post-SEA children using Models 1, 2 and 3. Each analysis was carried out without and then with adjustment for covariates. All analyses were first based on all post-SEA children and again on post-SEA full sibling children. The results are summarized in Tables 4-28 through 4-30.

Table 4-28

P-Value Summary of Initial Dioxin (Model 1) Analyses of Post-SEA Birth Weight (Children of Ranch Hands)

a) All Children

Variable	Unadjusted D>10 ppt	Unadjusted D>5 ppt	Adjusted D>10 ppt	Adjusted D>5 ppt
Birth Weight	NS	NS	**NS	****
Low Birth Weight	NS	NS	NS	**NS

b) Full Siblings

Variable	Unadjusted D>10 ppt	Unadjusted D>5 ppt	Adjusted D>10 ppt	Adjusted D>5 ppt
Birth Weight	NS	NS*	**NS	NS
Low Birth Weight	NS	NS	****	**NS

Table 4-29

P-Value Summary of Current Dioxin and Time Analyses (Model 2) of Post-SEA Birth Weight (Children of Ranch Hands)

a) All Children

	Unadjusted					
	D>10 ppt Dioxin by			D>5 ppt Dioxin by		
Variable	Time	Late	Early	Time	Late	Early
Birth Weight	NS	NS	NS	NS	NS	NS
Low Birth Weight	NS	NS	NS	NS	NS	NS

Table 4-29 (Continued)

Variable	Adjusted D>10 ppt Dioxin by Time	Late	Early	Adjusted D>5 ppt Dioxin by Time	Late	Early
Birth Weight	**NS	**NS*	**NS	**NS	**NS	**NS
Low Birth Weight	NS	NS	NS	**NS	**NS	**NS

b) Full Siblings

Variable	Unadjusted D>10 ppt Dioxin by Time	Late	Early	Unadjusted D>5 ppt Dioxin by Time	Late	Early
Birth Weight	NS	NS	NS	NS	NS	NS
Low Birth Weight	NS	NS	NS	NS	NS	NS

Variable	Adjusted D>10 ppt Dioxin by Time	Late	Early	Adjusted D>5 ppt Dioxin by Time	Late	Early
Birth Weight	NS	NS*	NS	NS	NS	NS
Low Birth Weight	NS	NS	NS	NS	NS	NS

Table 4-30

P-Value Summary of Categorized Current Dioxin Analyses (Model 3) of Post-SEA Birth Weight (Children of Ranch Hands and Comparisons)

a) All Children

Variable	All	Unadjusted Contrasts with Background Unknown	Low	High
Birth Weight	0.017	0.010	NS	NS*
Low Birth Weight	0.002	0.001	NS	0.003

Table 4-30 (Continued)

Variable	All	Adjusted Contrasts with Background Unknown	Low	High
Birth Weight	**0.002	**NS	**NS	**0.001
Low Birth Weight	****	****	****	****

b) **Full Siblings**

Variable	All	Unadjusted Contrasts with Background Unknown	Low	High
Birth Weight	0.032	0.008	NS	NS
Low Birth Weight	0.004	0.001	NS	0.004

Variable	All	Adjusted Contrasts with Background Unknown	Low	High
Birth Weight	0.001	NS	NS	0.002
Low Birth Weight	****	****	****	****

Pre-post SEA analyses of birth weight were generally negative. The few significant findings were not suggestive of a dioxin effect. For example, a Model 1 analysis of birth weight (Table 4-1) found a significant interaction with time since tour caused by decreasing birth weights in pre-SEA children and increasing birth weights in post-SEA children. This change was caused by an increase in mean birth weight from pre- to post-SEA in children of Ranch Hands with the highest dioxin levels. Because low birth weights are considered the adverse direction, this finding was not interpretable as an adverse effect of dioxin. A similar significant change in slope was found after restriction to full sibling children. In a Model 3 analysis of abnormally low birth weight (Table 4-9), a significant interaction was found with time of conception in the contrast of children of Ranch Hands in the Unknown category with children of Comparisons in the Background category. Among pre-SEA children, the rate of abnormally low birth weight in Ranch Hand children (61.2 per 1000) was less than that in children of Comparisons (73.5 per 1000) and in post-SEA children, the rate in Ranch Hand children (93.3 per 1000) was greater than that in children of Comparisons (41.9 per 1000), but this change was due more to the decrease in the Comparison rate than to the increase in the Ranch Hand rate, a pattern that cannot be attributed to dioxin. A similar finding was revealed after restriction to full sibling children (Table 4-12).

Post-SEA analyses of birth weight were also generally negative or were complicated by interactions with covariates that lack coherent explanation. For example, a Model 1 analysis of birth weight found a significant interaction with the father's race and the mother's smoking (Table 4-13 [c]), caused by a significant decrease in birth weight with dioxin in children of Black fathers whose mother did not smoke during pregnancy and a borderline significant weight reduction in children of nonblack fathers whose mother did smoke during pregnancy. After restriction to full sibling children, a significant interaction with only the mother's smoking was found (Table 4-16 [d]). In that analysis, there was a significant reduction in birth weight with dioxin in children of mothers who smoked during pregnancy and no significant reduction in children of mothers who did not smoke during pregnancy. A Model 2 analysis of birth weight found a significant interaction with the father's race (Table 4-14 [c]); birth weight decreased borderline significantly with dioxin in children of Black fathers who had early tours but there were no significant associations in the other 3 strata. A Model 3 analysis of birth weight found significant interaction with the father's race (Table 4-15 [b]); the birth weight of children fathered by Black Ranch Hands in the High category was significantly less than that of children born to Black Comparisons in the Background category and a weaker reduction was found in children of nonblack Ranch Hands in the High category. After restriction to full siblings (Table 4-18 [b]), children of Ranch Hands in the High category were found to have significantly lower birth weight than children of Comparisons in the Background category.

Post-SEA analyses of abnormally low birth weight were generally negative or were complicated by interactions with covariates. For example, a Model 1 analysis (Table 4-19 [d]) found a significant interaction with the father's race and with the mother's drinking during pregnancy. This interaction was caused by a significant increase in the rate of abnormally low birth weight in children of nonblack fathers whose mother drank during pregnancy, however, the number of children (35) and the number with abnormally low birth weight (3) in this stratum were small; no significant associations were found in the other 3 strata. After restriction to full siblings (Table 4-22 [d]), a significant interaction was found with the mother's smoking during pregnancy and with the time of conception. This interaction was caused by a significant reduction in the risk of abnormally low birth weight in children conceived within 2 years of the father's departure from SEA whose mother did not smoke during pregnancy. A Model 2 analysis of abnormally low birth weight (Table 4-20 [d]) found a significant interaction with time of conception. This interaction was caused by a significant increase in risk in children conceived more than 6.5 years after the father's departure from SEA whose father had an early tour. In the same analysis, however, there was a borderline significant decrease in risk in children conceived within 2 years of the father's departure from SEA whose father had an early tour. After restriction to full sibling children (Table 4-23), no significant associations were found between abnormally low birth weight and dioxin and no significant interaction with covariates were found. A Model 3 analysis of abnormally low birth weight (Table 4-21 [b]) found a significant interaction with the father's military occupation in SEA,

caused by a significant increase in risk in children of father's who were enlisted ground personnel. After restriction to full sibling children (Table 4-24 [b]), a significant interaction with the father's race and military occupation in SEA were found, caused by significant increases in risk in children of nonblack Ranch Hands in the High category who were enlisted flyers or who were enlisted ground personnel.

These findings are inconsistent because the nature of an interaction sometimes changes after restriction to full sibling children and because birth weight decreases with dioxin in some strata and increases in others. These findings are also weak because many of the interactions are based on sparse data. Therefore these results appear unrelated to dioxin. We find no evidence in these data that birth weight is adversely associated with the father's dioxin exposure.

5. PRE-POST SEA BIRTH DEFECTS

5.1 Introduction

Four issues are addressed here: (1) Can the baseline analysis be reproduced with the current database? (2) Does the baseline result hold for verified data? (3) If the baseline result holds for verified data, is the effect related to dioxin body burden? and (4) If the baseline result holds for verified data, is the effect more predominant in one or more of the 12 CDC categories of birth defects?

5.2 The Baseline Birth Defect Definition

At baseline, we used ICD-9-CM birth defect categories [14] which included 12 additional categories of anomalies not included in the CDC definition (Table 1-11). These 12 categories are summarized in Table 5-1. Table 5-1 also shows the numbers of children in each category by group and time of conception of the child relative to the father's duty in SEA and the corresponding rate per 1000 live births. The denominators for the rate calculations are shown in each column heading. These denominators are the total number of post-SEA live births of Ranch Hands and Comparisons who are included, according to their dioxin level, in any of the three statistical analyses. These denominators can be referenced to Table 1-6. For example, the 1772 post-SEA live births for all live births in Table 1-6 is the sum of the 791 Ranch Hands and 981 Comparisons in Table 5-1.

Table 5-1

Counts and Rates Of Live Births by Category of Anomaly Included in the Baseline Definition but not Included in the CDC Definition of Birth Defect

Restriction: All Live Births in Models 1, 2 or 3
Categories: Time of Conception the Father's Group Membership

Category	Time of Conception Relative to the Father's Duty in SEA			
	Pre-SEA		Post-SEA	
	RH n=1283	Comparisons n=1459	RH n=791	Comparisons n=981
1. All 12 categories	88(68.6)	95(65.1)	101(127.7)	129(131.5)
2. Benign neoplasm of skin 216	36(28.1)	34(24.7)	35(44.2)	43(43.8)
3. Hemangioma and Lymphangioma any site 228	12(9.4)	16(11.0)	14(17.7)	25(25.5)
4. Neoplasms of unspecified nature of bone,skin etc 239.2	0(0.0)	0(0.0)	0(0.0)	0(0.0)
5. Chorioretinitis 363.2	0(0.0)	0(0.0)	0(0.0)	0(0.0)
6. Wolff-Parkinson-White syndrome 426.7	2(1.6)	1(0.7)	2(2.5)	0(0.0)
7. Major anomalies of jaw size 524.0	1(0.8)	3(2.1)	2(2.5)	2(2.0)
8. Inguinal hernia 550	24(18.7)	30(20.6)	17(21.5)	29(29.6)
9. Umbilical hernia 553.1	14(10.9)	7(4.8)	23(29.1)	21(21.4)
10. Epigastric hernia 553.29	0(0.0)	0(0.0)	0(0.0)	0(0.0)
11. Amniotic bands 658.8	0(0.0)	0(0.0)	0(0.0)	0(0.0)
12. Pilonidal sinus or dimple 685.1	0(0.0)	1(0.7)	2(2.5)	1(1.0)
13. Hydrocele 778.6	14(10.9)	12(8.2)	22(27.8)	23(23.4)

If a child was verified as having multiple birth defects, the child was counted in each category for which a birth defect was verified (see Section 1.6), but only once within a given category. For example, if a child had a verified nervous system defect and a verified circulatory defect, that child was counted in both categories. However, if a child had two verified nervous system defects, that child was counted only once in the nervous system category.

The corresponding cross classification of children according to the 12 additional baseline birth defect categories without the restriction to children whose fathers dioxin level included him in Model 1, 2 or 3 analyses is shown in Appendix Table C-1. The live births shown in Table C-1 are fathered by participants whose dioxin assay result was quantitable, not quantitable or missing.

5.3 The Baseline Analysis using Mother's Report, the Baseline Birth Defect Definition and Current Data

The current database is improved relative to the baseline database. At baseline, none of the information regarding children was verified. Therefore, the file contained errors in childrens birth dates, parentage, and birth defect status. Additionally, some children were not accounted for at all. In the interim, all of these errors have been corrected. Using the current database, all live births occurring at or before the participants baseline examination were considered and only the spouses reported assessment was used to categorize children. These inclusion criteria are identical to those used in the initial baseline birth defect analysis. The results were cross classified by reported defect (yes,no), group (Ranch Hand, Comparison) and time of conception relative to the father's duty in SEA. The results are shown in Table 5-2.

Table 5-2

Reported Birth Defects in Children Born At or Prior to Baseline by Time of Conception Relative to the Father's Duty in SEA Using Current Data and the Baseline Definition of Birth Defect

Time of Conception	Group	Any Reported Birth Defect Yes (Rate)	No	Total	Odds Ratio	p-Value
Pre-SEA	Ranch Hand	93(58.8)	1489	1582	0.752	0.001
	Comparison	136(76.7)	1637	1773		
Post-SEA	Ranch Hand	105(128.0)	715	820	1.558	
	Comparison	89(86.2)	944	1033		

An analysis of Table 5-2 reveals that the change in the odds ratio from 0.752 to 1.558 is statistically significant (p=0.001).

These data were further analyzed to determine whether the significant effect is explained by group differences in the mother's age at the time of conception. An analysis adjusted for the mother's age found that the change in the odds ratio for reported defect with time of conception relative to father's service in SEA was not significantly influenced by the mother's age (p=0.835).

5.4 The Baseline Analysis using Mother's Report, the Baseline Birth Defect Definition, Restricted to Children Born During or Prior to the Father's Baseline Physical Examination, Adjusted for Dioxin Level

These data were further analyzed to assess the relationship between the change in relative risk (Table 5-3) and levels of dioxin body burden of the father. The change in the odds ratios is significantly associated with categorized dioxin (p=0.038). The association between reported birth defect and time of conception among children of Ranch Hands in the High category (OR=2.82) is significantly greater than that in children of Comparisons in the Background category (OR=1.14), p=0.040. The corresponding odds ratio in children of Ranch Hands in the Low category is also significantly increased relative to that in children of Comparisons in the Background category (p=0.024). The odds ratio in children of Ranch Hands in the Unknown category is not significantly different from that in the Background category (p=0.163). Thus, the baseline finding appears to be dose-related.

Table 5-3

Odds Ratios for Mothers Reported Birth Defect by the Father's Categorized Current Dioxin by Time of Conception Relative to the Father's Duty in SEA Tour Among Children Born At or Prior to the Baseline Physical Examination

Categorized Dioxin	Time of Conception	Reported Birth Defect Yes (Rate)	Total	Odds Ratio	p-value for Comparison with Background OR
Background	Pre-SEA	109 (79.3)	1374		
	Post-SEA	72 (89.2)	807	1.14	0.038
Unknown	Pre-SEA	36 (61.9)	582		
	Post-SEA	25 (104.2)	240	1.76	0.163
Low	Pre-SEA	20 (70.9)	282		
	Post-SEA	26 (160.5)	162	2.50	0.024
High	Pre-SEA	8 (48.8)	164		
	Post-SEA	25 (126.3)	198	2.82	0.040

5.5 The Baseline Analysis using Mother's Report and Subsequently Verified using the Baseline Birth Defect Definition, Restricted to Children Born During or Prior to the Father's Baseline Physical Examination

These data were reanalyzed by restricting birth defects to only those that were both reported by the mother and subsequently verified by review of medical records of the child. These data are summarized in Table 5-4 by the fathers group (Ranch Hand, Comparison) and time of conception (pre-SEA, post-SEA).

The change in the odds ratio with time of conception relative to fathers duty in SEA (Table 5-4) is significant for birth defects reported by the mother and subsequently verified ($p=0.032$). Analyses with adjustment for mothers age did not alter this finding.

Table 5-4

Reported and Subsequently Verified Birth Defects in Children Born at or Prior to Baseline by Time of Conception Relative to the Father's Duty in SEA

Time of Conception	Group	Reported and Verified Birth Defect Yes	(Rate)	No	Total	Odds Ratio	p-Value
Pre-SEA	Ranch Hand	58	(36.7)	1524	1582	0.850	0.032
	Comparison	76	(42.9)	1697	1773		
Post-SEA	Ranch Hand	75	(91.5)	745	820	1.451	
	Comparison	67	(64.9)	966	1033		

5.6 The Baseline Analysis using Mother's Report and Subsequently Verified using the Baseline Definition of Birth Defect, Restricted to Children Born During or Prior to the Father's Baseline Physical Examination, Adjusted for Dioxin Level

Reanalysis of the data in Table 5-5 to assess the significance of variation in the association between reported birth defects and time of conception with categorized dioxin were carried out. The results are shown in Table 5-5.

There is no variation in the overall association between reported and subsequently verified birth defects and categorized dioxin with time of birth relative to the fathers SEA duty (p=0.549). The association between reported and subsequently verified birth defect and time of birth in children of Ranch Hands in the High (p=0.528), Low (p=0.382) and Unknown (p=0.196) categories does not differ significantly from that in children of Comparisons in the Background category.

Table 5-5

Odds Ratios for Mothers Reported Birth Defect and Subsequently Verified, By Father's Categorized Current Dioxin by Time of Birth Relative to Father's Duty in SEA Tour Among Children Born At or Prior to Baseline Physical Examination

Categorized Dioxin	Time of Birth	Reported & Verified Birth Defect yes (Rate)	Total	Odds Ratio	p-Value for Comparison with Background OR
Background	Pre-SEA	59 (42.9)	1374		0.549
	Post-SEA	56 (69.4)	807	1.66	
Unknown	Pre-SEA	20 (34.4)	582		
	Post-SEA	21 (87.5)	240	2.69	0.196
Low	Pre-SEA	14 (49.6)	282		
	Post-SEA	18 (111.1)	162	2.39	0.382
High	Pre-SEA	6 (36.6)	164		
	Post-SEA	16 (80.8)	198	2.32	0.528

5.7 The Baseline Analysis using Verified Data, the CDC Definition of Birth Defect, Restricted to Children Born During or Prior to the Father's Baseline Physical Examination

Live births occurring at or before the participant's baseline examination were categorized by verified birth defect (yes,no), group (Ranch Hand, Comparison) and time of conception relative to father's service in SEA. The results are shown in Table 5-6.

Table 5-6

Verified Birth Defects in Children Born at or Prior to Baseline by Time of Conception Relative to the Father's Duty in SEA Using Current Data and the CDC Definition of Birth Defect

Time of Conception	Group	Verified Birth Defect Yes	(Rate)	No	Total	Odds Ratio	p-Value
Pre-SEA	Ranch Hand	162	(102.4)	1420	1582	0.934	0.164
	Comparison	193	(108.9)	1580	1773		
Post-SEA	Ranch Hand	162	(197.6)	658	820	1.175	
	Comparison	179	(173.3)	854	1033		

The change in the odds ratio (Table 5-6) from 0.934 to 1.175 is not significant (p=0.164).

A cross tabulation of all live births according to the 13 CDC birth defect categories by group and time of conception relative to the father's duty in SEA among all children whose father had a dioxin level that included him in Models 1, 2 or 3 analyses is shown in Table 5-7.

Table 5-7

Counts and Rates Of Live Births by CDC Category of Anomaly

Restriction: All Live Births in Models 1, 2 or 3
Categories: Time of Conception Relative to the Father's Duty in SEA

Category	Time of Conception Relative to the Father's Duty in SEA			
	Pre-SEA		Post-SEA	
	RH n=1283	Comparisons n=1459	RH n=791	Comparisons n=981
1. Total congenital anomalies	140(109.1)	158(108.3)	177(223.8)	204(208.0)
2. Nervous system anomalies	4(3.1)	7(4.8)	5(6.3)	3(3.1)
3. Eye anomalies	6(4.7)	6(4.1)	9(11.4)	7(7.1)
4. Ear,face,neck anomalies	7(5.5)	8(5.5)	13(16.4)	11(11.2)
5. Circulatory system and heart anomalies	15(11.7)	15(10.3)	17(21.5)	16(16.3)
6. Respiratory system anomalies	0(0.0)	1(0.7)	4(5.1)	2(2.0)
7. Digestive system anomalies	18(14.0)	15(10.3)	18(22.8)	24(24.5)
8. Genital anomalies	15(11.7)	15(10.3)	15(19.0)	18(18.3)
9. Urinary system anomalies	18(14.0)	21(14.4)	17(21.5)	12(12.2)
10. Musculoskeletal deformities	68(53.0)	81(55.5)	99(125.2)	132(134.6)
11. Anomalies of the skin	13(10.1)	11(7.5)	15(19.0)	21(21.4)
12. Chromosomal anomalies	2(1.6)	2(1.4)	4(5.1)	3(3.1)
13. Other and Unspecified	6(4.7)	3(2.1)	4(5.1)	2(2.0)

Analyses of the same type used at baseline were carried out for each of the 13 CDC categories of birth defects on children born at or before the father's baseline physical examination using verified birth defect data. Data in only 7 of the 13 categories were analyzable (total congenital, circulatory and heart, digestive system, genital, urinary, musculoskeletal and skin) due to sparse data in the other categories. The results are shown in Table 5-8.

Table 5-8

Verified Birth Defects in Children Born at or Prior to Baseline by Time of Conception Relative to the Father's Duty in SEA Current Data Within each of 7 CDC Birth Defect Categories

Defect Category	Time of Conception	Group	Verified Birth Defect Yes	Total	Rate	Odds Ratio	p-value
Total Congenital	Pre-SEA	RH	162	1582	102.4	0.93	
		C	193	1773	108.9		
	Post-SEA	RH	162	820	197.6	1.17	0.164
		C	179	1033	173.3		
Circulatory and Heart	Pre-SEA	RH	16	1582	10.1	0.90	
		C	20	1773	11.3		
	Post-SEA	RH	13	820	15.9	1.37	0.417
		C	12	1033	11.6		
Digestive System	Pre-SEA	RH	21	1582	13.3		
		C	18	1773	10.2	1.31	
	Post-SEA	RH	16	820	19.5		
		C	18	1033	17.4	1.12	0.742
Genital	Pre-SEA	RH	16	1582	10.1		
		C	20	1773	11.3	0.90	
	Post-SEA	RH	12	820	14.6		
		C	16	1033	15.5	0.94	0.918
Urinary	Pre-SEA	RH	18	1582	11.4		
		C	21	1773	11.8	0.96	
	Post-SEA	RH	15	820	18.3		
		C	8	1033	7.7	2.39	0.092

Table 5-8 (Continued)

Defect Category	Time of Conception	Group	Verified Birth Defect Yes	Total	Rate	Odds Ratio	p-value
Musculo-skeletal	Pre-SEA	RH	82	1582	51.8		
		C	103	1773	58.1	0.89	
	Post-SEA	RH	91	820	111.0		
		C	111	1033	107.5	1.04	0.463
Skin	Pre-SEA	RH	13	1582	8.2		
		C	12	1773	6.8	1.22	
	Post-SEA	RH	18	820	22.0		
		C	21	1033	20.3	1.08	0.821

Without adjustment for covariates (Table 5-8) there is borderline significant variation in the association between urinary anomaly (p=0.092) and the father's group membership with time of conception. This significance is due to a change in the odds ratio from 0.96 to 2.39 from pre-SEA to post-SEA. There is no significant variation in the association between total congenital anomalies (p=0.164), circulatory and heart anomalies (p=0.417), digestive system anomalies (p=0.742), genital anomalies (p=0.918), musculoskeletal deformities (p=0.463) or anomalies of the skin (p=0.821) and fathers group membership with time of conception.

5.8 The Baseline Analysis using Verified Data and the CDC Definition of Birth Defects

These analyses were also carried out without the restriction that the children be born prior to the father's baseline physical examination. In this unrestricted approach, all 13 categories of defects are analyzable. The results are shown in Table 5-9.

Table 5-9

Verified Birth Defects in All Children by Time of Conception Relative to the Father's Duty in SEA Using Current Data Within each of 13 CDC Birth Defect Categories (n=6792)

Defect Category	Time of Conception	Group	Verified Birth Defect Yes	Total	Rate	Odds Ratio	p-value
Total Congenital	Pre-SEA	RH	184	1805	101.9	0.93	
		C	254	2340	108.5		
	Post-SEA	RH	229	1045	219.1	1.28	0.028
		C	289	1602	180.4		
Nervous System	Pre-SEA	RH	4	1805	2.2	0.47	
		C	11	2340	4.7		
	Post-SEA	RH	5	1045	4.8	1.92	0.105
		C	4	1602	2.5		
Eye	Pre-SEA	RH	7	1805	3.9	1.01	
		C	9	2340	3.8		
	Post-SEA	RH	9	1045	8.6	1.26	0.745
		C	11	1602	6.9		
Ear, Face and Neck	Pre-SEA	RH	8	1805	4.4	1.04	
		C	10	2340	4.3		
	Post-SEA	RH	15	1045	14.4	1.78	0.374
		C	13	1602	8.1		
Circulatory and Heart	Pre-SEA	RH	20	1805	11.1	0.93	
		C	28	2340	12.0		
	Post-SEA	RH	19	1045	18.2	1.39	0.344
		C	21	1602	13.1		
Respiratory System	Pre-SEA	RH	0	1805	0.0	----	
		C	4	2340	1.7		
	Post-SEA	RH	5	1045	4.8	2.56	0.028
		C	3	1602	1.9		

Table 5-9 (Continued)

Defect Category	Time of Conception	Group	Verified Birth Defect Yes	Total	Rate	Odds Ratio	p-value
Digestive System	Pre-SEA	RH	22	1805	12.2	1.36	
		C	21	2340	9.0		
	Post-SEA	RH	22	1045	21.1	1.13	0.649
		C	30	1602	18.7		
Genital	Pre-SEA	RH	19	1805	10.5	0.95	
		C	26	2340	11.1		
	Post-SEA	RH	21	1045	20.1	1.04	0.823
		C	31	1602	19.4		
Urinary	Pre-SEA	RH	20	1805	11.1	0.96	
		C	27	2340	11.5		
	Post-SEA	RH	21	1045	20.1	2.51	0.036
		C	13	1602	8.1		
Musculo-skeletal	Pre-SEA	RH	94	1805	52.1	0.92	
		C	132	2340	56.4		
	Post-SEA	RH	132	1045	126.3	1.14	0.239
		C	180	1602	112.4		
Skin	Pre-SEA	RH	16	1805	8.9	0.94	
		C	22	2340	9.4		
	Post-SEA	RH	26	1045	24.9	1.11	0.697
		C	36	1602	22.5		
Chromosomal Abnormality	Pre-SEA	RH	3	1805	1.7	1.30	
		C	3	2340	1.3		
	Post-SEA	RH	6	1045	5.7	1.84	0.729
		C	5	1602	3.1		
Other	Pre-SEA	RH	6	1805	3.3	2.60	
		C	3	2340	1.3		
	Post-SEA	RH	5	1045	4.8	2.56	0.989
		C	3	1602	1.9		

Without adjustment for covariates (Table 5-9), there is significant variation in the association between total congenital (p=0.028), respiratory system (p=0.028), and urinary system (p=0.036) anomalies and the father's group membership with time of conception. There is borderline significant variation in the association between nervous system anomalies (p=0.105) and the father's group membership with time of conception. All of these significant and borderline significant findings are caused by the Ranch Hands rate being less than the Comparison rate in pre-SEA children and greater than the Comparison rate in post-SEA children.

Without adjustment for covariates (Table 5-9), there is no significant variation in the association between eye anomalies (p=0.745), ear, face and neck anomalies (p=0.374), circulatory system and heart anomalies (p=0.344), digestive system anomalies (p=0.649), genital anomalies (p=0.823), musculoskeletal deformities (p=0.239), anomalies of the skin (p=0.697), chromosomal abnormalities (p=0.729) and other anomalies (p=0.989) and the father's group membership with time of conception.

5.9 Pre-Post SEA Exposure Analyses

Further analyses using Models 1, 2 and 3 were carried out to determine whether any of the pre-post SEA changes in verified birth defect odds ratio were related to the father's dioxin body burden. These analyses are not adjusted for covariates.

Total Congenital Anomalies (All Children)

Model 1: Children of Ranch Hands - Log_2(Initial Dioxin)

Without adjustment for covariates (Table 5-10 [a] and [b]), there is no significant variation in the association between total congenital anomalies and initial dioxin with time of conception among children of Ranch Hands having more than 10 ppt (p=0.859) or more than 5 ppt (p=0.875) current dioxin.

Table 5-10

Pre-post SEA Counts and Rates Of Total Congenital Anomalies

Variable: Total Congenital Anomalies
Restrictions: All Children of Ranch Hands
Categories: Time of Conception Relative to the Father's Duty in SEA
Model 1: Log_2(Initial Dioxin)

Ranch Hands - Log_2(Initial Dioxin) - Unadjusted

Exposure Restriction	Initial Dioxin	Time of Conception Relative to the Father's Duty in SEA: Pre-SEA n	Pre-SEA Abn	Pre-SEA Rate	Post-SEA n	Post-SEA Abn	Post-SEA Rate	p-Value
a) D>10 ppt (n=1208)	Low	249	32	128.5	106	20	188.7	0.859
	Medium	338	35	103.6	245	68	277.6	
	High	113	13	115.0	157	31	197.5	
b) D>5 ppt (n=1748)	Low	286	31	108.4	155	35	225.8	0.875
	Medium	616	66	107.1	308	72	233.8	
	High	156	19	121.8	227	49	215.9	

Total Congenital Anomalies (All Children)

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

Without adjustment for covariates (Table 5-11 [a]), there is no significant variation in the association between total congenital anomalies and current dioxin with time since duty in SEA and time of conception among children of Ranch Hands having more than 10 ppt (p=0.162) or more than 5 ppt (p=0.573) current dioxin.

Table 5-11

Pre-post SEA Counts and Rates Of Total Congenital Anomalies

Variable: Total Congenital Anomalies
Restrictions: All Children of Ranch Hands
Categories: Time of Conception Relative to the Father's Duty in SEA
Model 2: Log_2(Current Dioxin), Time

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

Exposure Restriction	Time of Conception	Time Since SEA (years)	Anomaly Rate (No./n) Current Dioxin Low	Medium	High	p-Value
a) D>10 ppt (n=1210)	Pre-SEA	≤18.6	138.7 (19/137)	158.5 (29/183)	135.1 (5/37)	0.162
		>18.6	73.7 (7/95)	70.2 (12/171)	115.4 (9/78)	
	Post-SEA	≤18.6	193.5 (12/62)	253.7 (34/134)	236.1 (17/72)	
		18.6	275.0 (11/40)	250.0 (27/108)	204.3 (19/93)	
b) D>5 ppt (n=1748)	Pre-SEA	≤18.6	95.5 (15/157)	156.5 (49/313)	106.1 (7/66)	0.573
		>18.6	80.0 (12/150)	85.2 (23/270)	98.0 (10/102)	
	Post-SEA	≤18.6	266.7 (24/90)	252.9 (44/174)	209.1 (23/110)	
		>18.6	95.2 (6/63)	279.4 (38/136)	179.5 (21/117)	

Total Congenital Anomalies (All Children)

Model 3: Children of Ranch Hands and Comparisons - Categorized Current Dioxin

Without adjustment for covariates (Table 5-12), there is no significant variation in the overall association between total congenital anomalies and categorized current dioxin with time of conception (p=0.726). Furthermore, the associations between total congenital anomalies and time of conception in children of Ranch Hands in the High (p=0.970), Low (p=0.263) and Unknown (p=0.871) categories do not differ from that in children of Comparisons in the Background category.

Table 5-12

Pre-post SEA Counts and Rates of Total Congenital Anomalies

Variable: Total Congenital Anomalies
Restrictions: All Children of Ranch Hands and Comparisons
Categories: Time of Conception Relative to the Father's Duty in SEA
Model 3: Categorized Current Dioxin

Categorized Current Dioxin - Unadjusted

Time of Conception Relative to the Father's Duty in SEA

Exposure Category	Pre-SEA n	Pre-SEA Abn	Pre-SEA Rate	Post-SEA n	Post-SEA Abn	Post-SEA Rate	Odds Ratio	Category Contrast	p-Value
Background	1459	158	108.3	981	204	208.0	2.16	All Exp Categ	0.726
Unknown	582	59	101.4	282	57	202.1	2.25	Unk vs Bkgd	0.871
Low	290	36	124.1	174	51	293.1	2.93	Low vs Bkgd	0.263
High	168	17	101.2	227	44	193.8	2.14	High vs Bkgd	0.970
Total	2499			1664					

Total Congenital Anomalies (Full Siblings)

Model 1: Children of Ranch Hands - Log_2(Initial Dioxin)

Without adjustment for covariates (Table 5-13 [a] and [b]), there is no significant variation in the association between total congenital anomalies and initial dioxin with time of conception among full sibling children of Ranch Hands having more than 10 ppt (p=0.570) or more than 5 ppt (p=0.772) current dioxin.

Table 5-13

Pre-post SEA Counts and Rates of Total Congenital Anomalies

Variable: Total Congenital Anomalies
Restrictions: Full Siblings of Ranch Hands
Categories: Time of Conception Relative to the Father's Duty in SEA
Model 1: Log_2(Initial Dioxin)

Ranch Hands - Log_2(Initial Dioxin) - Unadjusted

Exposure Restriction	Initial Dioxin	Time of Conception Relative to the Father's Duty in SEA: Pre-SEA n	Pre-SEA Abn	Pre-SEA Rate	Post-SEA n	Post-SEA Abn	Post-SEA Rate	p-Value
a) D>10 ppt (n=1030)	Low	231	30	129.9	78	16	205.1	0.570
	Medium	276	26	94.2	206	57	276.7	
	High	103	13	126.2	136	27	198.5	
b) D>5 ppt (n=1489)	Low	252	29	115.1	114	20	175.4	0.772
	Medium	545	59	108.3	245	58	236.7	
	High	135	16	118.5	198	44	222.2	

Total Congenital Anomalies (Full Siblings)

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

Without adjustment for covariates (Table 5-14 [a]), there is no significant change in the association between total congenital anomalies and current dioxin with time since duty in SEA and time of conception among full sibling children of Ranch Hands having more than 10 ppt current dioxin (p=0.116).

Without adjustment for covariates (Table 5-14 [b]), there is no significant variation in the association between total congenital anomalies and current dioxin with time since duty in SEA and the time of conception among full sibling children of Ranch Hands having more than 5 ppt current dioxin (p=0.932).

Table 5-14

Pre-post SEA Counts and Rates of Total Congenital Anomalies

Variable: Total Congenital Anomalies
Restrictions: Full Siblings of Ranch Hands
Categories: Time of Conception Relative to the Father's Duty in SEA
Model 2: Log_2(Current Dioxin), Time

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

Exposure Restriction	Time of Conception	Time Since SEA (years)	Anomaly Rate (No./n) Current Dioxin Low	Medium	High	p-Value
a) D>10 ppt (n=1032)	Pre-SEA	≤18.6	145.2 (18/124)	141.9 (22/155)	142.9 (5/35)	0.116
		>18.6	82.4 (7/85)	62.9 (9/143)	130.4 (9/69)	
	Post-SEA	≤18.6	234.0 (11/47)	234.8 (27/115)	265.6 (17/64)	
		>18.6	285.7 (8/28)	260.9 (24/92)	186.7 (14/75)	
b) D>5 ppt (n=1489)	Pre-SEA	≤18.6	111.1 (14/126)	152.2 (42/276)	100.0 (6/60)	0.932
		>18.6	82.8 (12/145)	84.4 (20/237)	113.6 (10/88)	
	Post-SEA	≤18.6	203.4 (12/59)	263.9 (38/144)	214.3 (21/98)	
		>18.6	75.5 (4/53)	292.5 (31/106)	164.9 (16/97)	

Total Congenital Anomalies (Full Siblings)

Model 3: Children of Ranch Hands and Comparisons - Categorized Current Dioxin

Without adjustment for covariates (Table 5-15), there is no significant variation in the overall association between total congenital anomalies and categorized current dioxin with time of conception (p=0.336) among full siblings. The association between total congenital anomalies and time of conception among children of Ranch Hands in the Low current dioxin category is borderline significantly increased relative to that among children of Comparisons in the Background category (p=0.089). The association between total congenital anomalies and time of conception among children of Ranch Hands in the High (p=0.867) and Unknown (p=0.835) categories are not significantly different from that among children of Comparisons in the Background category.

Table 5-15

Pre-post SEA Counts and Rates of Total Congenital Anomalies

Variable: Total Congenital Anomalies
Restrictions: Full Siblings of Ranch Hands and Comparisons
Categories: Time of Conception Relative to the Father's Duty in SEA
Model 3: Categorized Current Dioxin

Categorized Current Dioxin - Unadjusted

Time of Conception Relative to the Father's Duty in SEA

Exposure Category	Pre-SEA n	Pre-SEA Abn	Pre-SEA Rate	Post-SEA n	Post-SEA Abn	Post-SEA Rate	Odds Ratio	Category Contrast	p-Value
Background	1250	147	117.6	812	174	214.3	2.05	All Exp Categ	0.336
Unknown	514	54	105.1	221	41	185.5	1.94	Unk vs Bkgd	0.835
Low	244	27	110.7	148	44	297.3	3.40	Low vs Bkgd	0.089
High	148	16	108.1	195	37	189.7	1.93	High vs Bkgd	0.867
Total	2156			1376					

Nervous System Anomalies (All Live Births)

Model 1: Children of Ranch Hands - Log_2(Initial Dioxin)

There is insufficient data (Table 5-16) to assess the significance of variation in the association between nervous system anomalies and initial dioxin with time of conception among children of Ranch Hands.

Table 5-16

Pre-post SEA Counts and Rates of Nervous System Anomalies

Variable: Nervous System Anomalies
Restrictions: All Children of Ranch Hands
Categories: Time of Conception Relative to the Father's Duty in SEA
Model 1: Log_2(Initial Dioxin)

Ranch Hands - Log_2(Initial Dioxin) - Unadjusted

Exposure Restriction	Initial Dioxin	Time of Conception Relative to the Father's Duty in SEA: Pre-SEA n	Pre-SEA Abn	Pre-SEA Rate	Post-SEA n	Post-SEA Abn	Post-SEA Rate	p-Value
a) D>10 ppt (n=1208)	Low	249	1	4.0	106	1	9.4	
	Medium	338	0	0.0	245	2	8.2	
	High	113	0	0.0	157	2	12.7	
b) D>5 ppt (n=1748)	Low	286	1	3.5	155	0	0.0	
	Medium	616	2	3.2	308	2	6.5	
	High	156	0	0.0	227	3	13.2	

Nervous System Anomalies (All Children)

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

There is insufficient data (Table 5-17) to assess the significance of variation in the association between nervous system anomalies and current dioxin with time since duty in SEA and time of conception among children of Ranch Hands.

Table 5-17

Pre-post SEA Counts and Rates of Nervous System Anomalies

Variable: Nervous System Anomalies
Restrictions: All Children of Ranch Hands
Categories: Time of Conception Relative to the Father's Duty in SEA
Model 2: Log_2(Current Dioxin), Time

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

Exposure Restriction	Time of Conception	Time Since SEA (years)	Anomaly Rate (No./n) Current Dioxin Low	Medium	High	p-Value
a) D>10 ppt (n=1210)	Pre-SEA	≤18.6	0.0 (0/137)	0.0 (0/183)	0.0 (0/37)	
		>18.6	10.5 (1/95)	0.0 (0/171)	0.0 (0/78)	
	Post-SEA	≤18.6	0.0 (0/62)	7.5 (1/134)	13.9 (1/72)	
		>18.6	25.0 (1/40)	9.3 (1/108)	10.8 (1/93)	
b) D>5 ppt (n=1748)	Pre-SEA	≤18.6	0.0 (0/157)	3.2 (1/313)	0.0 (0/66)	
		>18.6	6.7 (1/150)	3.7 (1/270)	0.0 (0/102)	
	Post-SEA	≤18.6	0.0 (0/90)	0.0 (0/174)	18.2 (2/110)	
		>18.6	0.0 (0/63)	14.7 (2/136)	8.5 (1/117)	

Nervous System Anomalies (All Children)

Model 3: Children of Ranch Hands and Comparisons - Categorized Current Dioxin

There is insufficient data (Table 5-18) to assess the significance of variation in the association between nervous system anomalies and categorized current dioxin with time of conception.

Table 5-18

Pre-post SEA Counts and Rates of Nervous System Anomalies

Variable: Nervous System Anomalies
Restrictions: All Children of Ranch Hands and Comparisons
Categories: Time of Conception Relative to the Father's Duty in SEA
Model 3: Categorized Current Dioxin

Categorized Current Dioxin - Unadjusted

Time of Conception Relative to the Father's Duty in SEA

Exposure Category	Pre-SEA n	Pre-SEA Abn	Pre-SEA Rate	Post-SEA n	Post-SEA Abn	Post-SEA Rate	Odds Ratio	Category Contrast	p-Value
Background	1459	7	4.8	981	3	3.1	0.64	All Exp Categ	
Unknown	582	3	5.2	282	0	0.0	----	Unk vs Bkgd	
Low	290	0	0.0	174	1	5.7	----	Low vs Bkgd	
High	168	0	0.0	227	3	13.2	----	High vs Bkgd	
Total	2499			1664					

Nervous System Anomalies (Full Siblings)

Model 1: Children of Ranch Hands - Log_2(Initial Dioxin)

There is insufficient data (Table 5-19) to assess the significance of variation in the association between nervous system anomalies and initial dioxin with time of conception among full sibling children of Ranch Hands.

Table 5-19

Pre-post SEA Counts and Rates of Nervous System Anomalies

Variable: Nervous System Anomalies
Restrictions: Full Siblings of Ranch Hands
Categories: Time of Conception Relative to the Father's Duty in SEA
Model 1: Log_2(Initial Dioxin)

Ranch Hands - Log_2(Initial Dioxin) - Unadjusted

Exposure Restriction	Initial Dioxin	Time of Conception Relative to the Father's Duty in SEA: Pre-SEA n	Pre-SEA Abn	Pre-SEA Rate	Post-SEA n	Post-SEA Abn	Post-SEA Rate	p-Value
a) D>10 ppt (n=1030)	Low	231	1	4.3	78	0	0.0	
	Medium	276	0	0.0	206	2	9.7	
	High	103	0	0.0	136	2	14.7	
b) D>5 ppt (n=1489)	Low	252	1	4.0	114	0	0.0	
	Medium	545	2	3.7	245	1	4.1	
	High	135	0	0.0	198	3	15.2	

Nervous System Anomalies (Full Siblings)

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

There is insufficient data (Table 5-20) to assess the significance of variation in the association between nervous system anomalies and current dioxin with time since duty in SEA and time of conception among full sibling children of Ranch Hands.

Table 5-20

Pre-post SEA Counts and Rates of Nervous System Anomalies

Variable: Nervous System Anomalies
Restrictions: Full Siblings of Ranch Hands
Categories: Time of Conception Relative to the Father's Duty in SEA
Model 2: Log_2(Current Dioxin), Time

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

Exposure Restriction	Time of Conception	Time Since SEA (years)	Anomaly Rate (No./n) Current Dioxin Low	Medium	High	p-Value
a) D>10 ppt (n=1032)	Pre-SEA	≤18.6	0.0 (0/124)	0.0 (0/155)	0.0 (0/35)	
		>18.6	11.8 (1/85)	0.0 (0/143)	0.0 (0/69)	
	Post-SEA	≤18.6	0.0 (0/47)	8.7 (1/115)	15.6 (1/64)	
		>18.6	0.0 (0/28)	10.9 (1/92)	13.3 (1/75)	
b) D>5 ppt (n=1489)	Pre-SEA	≤18.6	0.0 (0/126)	3.6 (1/276)	0.0 (0/60)	
		>18.6	6.9 (1/145)	4.2 (1/237)	0.0 (0/88)	
	Post-SEA	≤18.6	0.0 (0/59)	0.0 (0/144)	20.4 (2/98)	
		>18.6	0.0 (0/53)	9.4 (1/106)	10.3 (1/97)	

Nervous System Anomalies (Full Siblings)

Model 3: Children of Ranch Hands and Comparisons - Categorized Current Dioxin

There is insufficient data (Table 5-21) to assess variation in the association between nervous system anomalies and categorized current dioxin with time of conception among full siblings.

Table 5-21

Pre-post SEA Counts and Rates of Nervous System Anomalies

Variable: Nervous System Anomalies
Restrictions: Full Siblings of Ranch Hands and Comparisons
Categories: Time of Conception Relative to the Father's Duty in SEA
Model 3: Categorized Current Dioxin

Categorized Current Dioxin - Unadjusted

Time of Conception Relative to the Father's Duty in SEA

Exposure Category	Pre-SEA n	Pre-SEA Abn	Pre-SEA Rate	Post-SEA n	Post-SEA Abn	Post-SEA Rate	Odds Ratio	Category Contrast	p-Value
Background	1250	6	4.8	812	3	3.7	0.77	All Exp Categ	
Unknown	514	3	5.8	221	0	0.0	----	Unk vs Bkgd	
Low	244	0	0.0	148	1	6.8	----	Low vs Bkgd	
High	148	0	0.0	195	3	15.4	----	High vs Bkgd	
Total	2156			1376					

Eye Anomalies (All Children)

Model 1: Children of Ranch Hands - Log_2(Initial Dioxin)

There is insufficient data (Table 5-22) to assess the significance of variation in the association between eye anomalies and initial dioxin with time of conception among children of Ranch Hands.

Table 5-22

Pre-post SEA Counts and Rates of Eye Anomalies

Variable: Eye Anomalies
Restrictions: All Children of Ranch Hands
Categories: Time of Conception Relative to the Father's Duty in SEA
Model 1: Log_2(Initial Dioxin)

Ranch Hands - Log_2(Initial Dioxin) - Unadjusted

Exposure Restriction	Initial Dioxin	Time of Conception Relative to the Father's Duty in SEA: Pre-SEA n	Pre-SEA Abn	Pre-SEA Rate	Post-SEA n	Post-SEA Abn	Post-SEA Rate	p-Value
a) D>10 ppt (n=1208)	Low	249	1	4.0	106	0	0.0	
	Medium	338	1	3.0	245	3	12.2	
	High	113	0	0.0	157	2	12.7	
b) D>5 ppt (n=1748)	Low	286	2	7.0	155	2	12.9	
	Medium	616	2	3.2	308	2	6.5	
	High	156	0	0.0	227	3	13.2	

Eye Anomalies (All Children)

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

There is insufficient data (Table 5-23) to assess the significance of variation in the association between eye anomalies and current dioxin with time since duty in SEA and time of conception.

Table 5-23

Pre-post SEA Counts and Rates of Eye Anomalies

Variable: Eye Anomalies
Restrictions: All Children of Ranch Hands
Categories: Time of Conception Relative to the Father's Duty in SEA
Model 2: Log_2(Current Dioxin), Time

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

Exposure Restriction	Time of Conception	Time Since SEA (years)	Anomaly Rate (No./n) Current Dioxin Low	Medium	High	p-Value
a) D>10 ppt (n=1210)	Pre-SEA	≤18.6	7.3 (1/137)	5.5 (1/183)	0.0 (0/37)	
		>18.6	0.0 (0/95)	0.0 (0/171)	0.0 (0/78)	
	Post-SEA	≤18.6	0.0 (0/62)	14.9 (2/134)	13.9 (1/72)	
		>18.6	25.0 (1/40)	0.0 (0/108)	10.8 (1/93)	
b) D>5 ppt (n=1748)	Pre-SEA	≤18.6	6.4 (1/157)	6.4 (2/313)	0.0 (0/66)	
		>18.6	6.7 (1/150)	0.0 (0/270)	0.0 (0/102)	
	Post-SEA	≤18.6	11.1 (1/90)	11.5 (2/174)	18.2 (2/110)	
		>18.6	0.0 (0/63)	7.4 (1/136)	8.5 (1/117)	

Eye Anomalies (All Children)

Model 3: Children of Ranch Hands and Comparisons - Categorized Current Dioxin

There is insufficient data (Table 5-24) to assess the significance of variation in the association between eye anomalies and categorized current dioxin with time of conception.

Table 5-24

Pre-post SEA Counts and Rates of Eye Anomalies

Variable: Eye Anomalies
Restrictions: All Children of Ranch Hands and Comparisons
Categories: Time of Conception Relative to the Father's Duty in SEA
Model 3: Categorized Current Dioxin

Categorized Current Dioxin - Unadjusted

Time of Conception Relative to the Father's Duty in SEA

Exposure Category	Pre-SEA n	Pre-SEA Abn	Pre-SEA Rate	Post-SEA n	Post-SEA Abn	Post-SEA Rate	Odds Ratio	Category Contrast	p-Value
Background	1459	6	4.1	981	7	7.1		All Exp Categ	
Unknown	582	4	6.9	282	4	14.2		Unk vs Bkgd	
Low	290	1	3.4	174	1	5.7		Low vs Bkgd	
High	168	0	0.0	227	3	13.2		High vs Bkgd	
Total	2499			1664					

Eye Anomalies (Full Siblings)

Model 1: Children of Ranch Hands - Log_2(Initial Dioxin)

There is insufficient data (Table 5-25) to assess the significance of variation in the association between eye anomalies and initial dioxin with time of conception among full sibling children of Ranch Hands.

Table 5-25

Pre-post SEA Counts and Rates of Eye Anomalies

Variable: Eye Anomalies
Restrictions: Full Siblings of Ranch Hands
Categories: Time of Conception Relative to the Father's Duty in SEA
Model 1: Log_2(Initial Dioxin)

Ranch Hands - Log_2(Initial Dioxin) - Unadjusted

Exposure Restriction	Initial Dioxin	Time of Conception Relative to the Father's Duty in SEA: Pre-SEA n	Pre-SEA Abn	Pre-SEA Rate	Post-SEA n	Post-SEA Abn	Post-SEA Rate	p-Value
a) D>10 ppt (n=1030)	Low	231	1	4.3	78	0	0.0	
	Medium	276	0	0.0	206	3	14.6	
	High	103	0	0.0	136	2	14.7	
b) D>5 ppt (n=1489)	Low	252	2	7.9	114	1	8.8	
	Medium	545	1	1.8	245	2	8.2	
	High	135	0	0.0	198	3	15.2	

Eye Anomalies (Full Siblings)

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

There is insufficient data with which to assess the significance of variation in the association between eye anomalies and current dioxin with time since duty in SEA and time of conception among full sibling children of Ranch Hands (Table 5-26 [a] and [b]).

Table 5-26

Pre-post SEA Counts and Rates of Eye Anomalies

Variable: Eye Anomalies
Restrictions: Full Siblings of Ranch Hands
Categories: Time of Conception Relative to the Father's Duty in SEA
Model 2: Log_2(Current Dioxin), Time

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

Exposure Restriction	Time of Conception	Time Since SEA (years)	Anomaly Rate (No./n) Current Dioxin Low	Medium	High	p-Value
a) D>10 ppt (n=1032)	Pre-SEA	≤18.6	8.1 (1/124)	0.0 (0/155)	0.0 (0/35)	
		>18.6	0.0 (0/85)	0.0 (0/143)	0.0 (0/69)	
	Post-SEA	≤18.6	0.0 (0/47)	17.4 (2/115)	15.6 (1/64)	
		>18.6	35.7 (1/28)	0.0 (0/92)	13.3 (1/75)	
b) D>5 ppt (n=1489)	Pre-SEA	≤18.6	7.9 (1/126)	3.6 (1/276)	0.0 (0/60)	
		>18.6	6.9 (1/145)	0.0 (0/237)	0.0 (0/88)	
	Post-SEA	≤18.6	0.0 (0/59)	13.9 (2/144)	20.4 (2/98)	
		>18.6	0.0 (0/53)	9.4 (1/106)	10.3 (1/97)	

Eye Anomalies (Full Siblings)

Model 3: Children of Ranch Hands and Comparisons - Categorized Current Dioxin

There is insufficient data (Table 5-27) to assess the significance of the variation in the association between eye anomalies and categorized current dioxin with time of conception among full siblings.