

7.3 Pre-post SEA Exposure Analyses - Full Siblings

Birth Defect Severity (2 Categories; Full Siblings)

Model 1: Children of Ranch Hands - Log₂(Initial Dioxin)

Without adjustment for covariates (Table 7-4 [a] and [b]), there is no significant variation in the association between birth defect severity (not major, major) and initial dioxin with time of conception among full sibling children of Ranch Hands with more than 10 ppt (p=0.481) or more than 5 ppt (p=0.593) current dioxin.

Table 7-4

Pre-Post SEA Counts and Rates of Birth Defect Severity (Not Major, Major)

Variable: Birth Defect Severity (Not Major, Major)
Restrictions: Full Siblings of Ranch Hands
Model 1: Log₂(Initial Dioxin)

Ranch Hands - Log ₂ (Initial Dioxin) - Unadjusted								
Exposure Restriction		Initial Dioxin	Time of Conception Relative to the Father's Duty in SEA					
			n	Pre-SEA Maj	Rate	n	Post-SEA Maj	Rate
a) D>10 ppt (n=1030)	Low		231	8	34.6	78	3	38.5
	Medium		276	11	39.9	206	19	92.2
	High		103	5	48.5	136	7	51.5
b) D>5 ppt (n=1489)	Low		252	9	35.7	114	7	61.4
	Medium		545	18	33.0	245	18	73.5
	High		135	8	59.3	198	12	60.6

Birth Defect Severity (2 Categories; Full Siblings)

Model 2: Children of Ranch Hands - Log₂(Current Dioxin) and Time

Without adjustment for covariates (Table 7-5 [a] and [b]), there is no significant variation in the association between birth defect severity (not major, major) and current dioxin with time since duty in SEA and time of conception among full sibling children of Ranch Hands with more than 10 ppt (p=0.423) or more than 5 ppt (p=0.985) current dioxin.

Table 7-5

**Pre-Post SEA Counts and Rates of
Birth Defect Severity (Not Major, Major)**

Variable: Birth Defect Severity (Not Major, Major)
Restrictions: Full Siblings of Ranch Hands
Model 2: \log_2 (Current Dioxin), Time

Ranch Hands - \log_2 (Current Dioxin), Time - Unadjusted						
Exposure Restriction	Time of Conception	Time Since SEA (years)	Severity Rate (No./n) Current Dioxin			p-Value
			Low	Medium	High	
a) D>10 ppt (n=1032)	Pre-SEA	≤18.6	40.3 (5/124)	45.2 (7/155)	85.7 (3/35)	0.423
		>18.6	23.5 (2/85)	28.0 (4/143)	43.5 (3/69)	
	Post-SEA	≤18.6	42.6 (2/47)	95.7 (11/115)	46.9 (3/64)	
		>18.6	35.7 (1/28)	97.8 (9/92)	53.3 (4/75)	
b) D>5 ppt (n=1489)	Pre-SEA	≤18.6	31.7 (4/126)	47.1 (13/276)	50.0 (3/60)	0.985
		>18.6	27.6 (4/145)	29.5 (7/237)	45.5 (4/88)	
	Post-SEA	≤18.6	67.8 (4/59)	83.3 (12/144)	51.0 (5/98)	
		>18.6	18.9 (1/53)	103.8 (11/106)	41.2 (4/97)	

Birth Defect Severity (2 Categories; Full Siblings)

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

Without adjustment for covariates (Table 7-6), there is no significant variation in the overall association between birth defect severity (not major, major) and categorized current dioxin with time of conception ($p=0.106$) among full siblings. However, the association between birth defect severity and time of conception among children of Ranch Hands in the Low category is significantly different from the association among children of Comparisons in the Background category ($p=0.030$). This finding is caused by a high rate of major severity (121.6 per 1000) among post-SEA children of Ranch Hands in the Low category relative to that of children of Comparisons in the Background category (56.7 per 1000). The associations between birth defect severity and time of conception among children of Ranch Hands in the High ($p=0.600$) and Unknown ($p=0.332$) categories are not significantly different from the association among children of Comparisons in the Background category.

Table 7-6

Pre-Post SEA Counts and Rates of Birth Defect Severity (Not Major, Major)

Variable: Birth Defect Severity (Not Major, Major)
Restrictions: Full Siblings of Ranch Hands and Comparisons
Model 3: Categorized Current Dioxin

Time of Conception Relative to the Father's Duty in SEA									
Exposure Category	n	Pre-SEA		Post-SEA		Odds		Category	p-Value
		Maj	Rate	n	Maj	Rate	Ratio	Contrast	
Background	1250	55	44.0	812	46	56.7	1.30	All Exp Categ	0.106
Unknown	514	20	38.9	221	16	72.4	1.93	Unk vs Bkgd	0.332
Low	244	9	36.9	148	18	121.6	3.62	Low vs Bkgd	0.030
High	148	7	47.3	195	9	46.2	0.97	High vs Bkgd	0.600
Total	2156			1376					

7.4 Post-SEA Exposure Analyses - All Children

Birth Defect Severity (3 Categories; All Children)

Model 1: Children of Ranch Hands - $\text{Log}_2(\text{Initial Dioxin})$

Without adjustment for covariates (Table 7-7 [a] and [b]), there is no association between birth defect severity (none, minor, major) and initial dioxin among children of Ranch Hands having more than 10 ppt ($p=0.252$) or more than 5 ppt ($p=0.828$) current dioxin.

Table 7-7

Post-SEA Counts and Rates of Birth Defect Severity (None, Minor, Major)

Variable: Birth Defect Severity (None, Minor, Major)
Restrictions: All Children of Ranch Hands
Children Conceived during or after the
Father's Duty in SEA
Model 1: $\text{Log}_2(\text{Initial Dioxin})$

Ranch Hands - $\text{Log}_2(\text{Initial Dioxin})$ - Unadjusted						
Exposure Restriction	Initial Dioxin	n	Rate (count)			p-Value
			Severity Index Level None	Minor	Major	
a) D>10 ppt	Low	106	811.3 (86)	132.1 (14)	56.6 (6)	0.252
	Medium	245	722.4 (177)	175.5 (43)	102.0 (25)	
	High	157	802.5 (126)	133.8 (21)	63.7 (10)	
b) D>5 ppt	Low	155	774.2 (120)	167.7 (26)	58.1 (9)	0.828
	Medium	308	766.2 (236)	149.4 (46)	84.4 (26)	
	High	227	784.1 (178)	149.8 (34)	66.1 (15)	

Birth Defect Severity (2 Categories; All Children)

Model 1: Children of Ranch Hands - $\text{Log}_2(\text{Initial Dioxin})$

Without adjustment for covariates (Table 7-8 [a] and [b]), there is no association between birth defect severity (not major, major) and initial dioxin among children of Ranch Hands with more than 10 ppt ($p=0.585$) or more than 5 ppt ($p=0.568$) current dioxin.

After adjustment for covariates (Table 7-8 [c] and [d]), there is no association between birth defect severity and initial dioxin among children of Ranch Hands having more than 10 ppt ($p=0.868$) or more than 5 ppt ($p=0.418$) current dioxin.

Table 7-8

Post-SEA Counts and Rates of Birth Defect Severity (Not Major, Major)

Variable: Birth Defect Severity (Not Major, Major)
Restrictions: All Children of Ranch Hands
Children Conceived during or after the
Father's Duty in SEA
Model 1: $\text{Log}_2(\text{Initial Dioxin})$

Ranch Hands - $\text{Log}_2(\text{Initial Dioxin})$ - Unadjusted					
Exposure Restriction	Initial Dioxin	n	Major Rate (n)	Est. Relative Risk (95% C.I.)	p-Value
a) D>10 ppt (n=508)	Low	106	56.6(6)	0.93(0.70,1.22)	0.585
	Medium	245	102.0(25)		
	High	157	63.7(10)		
b) D>5 ppt (n=690)	Low	155	58.1(9)	1.06(0.87,1.30)	0.568
	Medium	308	84.4(26)		
	High	227	66.1(15)		

Table 7-8 (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=458)	1.02(0.77,1.37)	0.868	SMOKE(p=0.024)
d) D>5 ppt (n=616)	1.09(0.88,1.35)	0.418	RACE(p=0.097) SMOKE(p=0.048) OCC(p=0.074)

Birth Defect Severity (3 Categories; All Children)

Model 2: Children of Ranch Hands - \log_2 (Current Dioxin) and Time

Without adjustment for covariates (Table 7-9 [a]), there is no significant variation in the association between birth defect severity (none, minor, major) and current dioxin with time since duty in SEA among children of Ranch Hands with more than 10 ppt current dioxin (p=0.616). Furthermore, there is no significant association between birth defect severity and current dioxin among children of Ranch Hands with late (p=0.290) or early (p=0.798) tours.

Without adjustment for covariates (Table 7-9 [b]), there is no significant variation in the association between birth defect severity and current dioxin with time since duty in SEA among children of Ranch Hands with more than 5 ppt current dioxin (p=0.204). There is no significant association between birth defect severity and current dioxin among children of Ranch Hands with late tours (p=0.535). However, there is a significant association between birth defect severity and current dioxin among children of Ranch Hands with early tours (p=0.032). The rate of minor birth defects among children of Ranch Hands in the medium dioxin category (169.1 per 1000) is greater than that of children of Ranch Hands in the low (79.4 per 1000) or high (119.7 per 1000) dioxin categories.

Table 7-9

**Post-SEA Counts and Rates of
Birth Defect Severity (None, Minor, Major)**

Variable: Birth Defect Severity (None, Minor, Major)
 Restrictions: All Children of Ranch Hands
 Children Conceived during or after the
 Father's Duty in SEA
 Model 2: $\text{Log}_2(\text{Current Dioxin})$, Time

Ranch Hands - $\text{Log}_2(\text{Current Dioxin})$, Time - Unadjusted							
Exposure Restriction	Time Since SEA (years)	Exposure Category	n	Rate (Count) Severity Index Level			p-Value
				None	Minor	Major	
a) D>10 ppt (n=509)							0.616
	≤18.6	Low	62	806.5 (50)	145.2 (9)	48.4 (3)	0.290
		Medium	134	746.3 (100)	141.8 (19)	111.9 (15)	
		High	72	763.9 (55)	194.4 (14)	41.7 (3)	
	>18.6	Low	40	725.0 (29)	200.0 (8)	75.0 (3)	0.798
		Medium	108	750.0 (81)	148.1 (16)	101.9 (11)	
		High	93	795.7 (74)	129.0 (12)	75.3 (7)	

Table 7-9 (Continued)

Exposure Restriction	Time Since SEA (years)	Exposure Category	n	Rate (count) Severity Index Level			p-Value
				None	Minor	Major	
b) D>5 ppt (n=690)							0.204
	≤18.6	Low	90	733.3 (66)	211.1 (19)	55.6 (5)	0.535
		Medium	174	747.1 (130)	160.9 (28)	92.0 (16)	
		High	110	790.9 (87)	154.5 (17)	54.5 (6)	
	>18.6	Low	63	904.8 (57)	79.4 (5)	15.9 (1)	0.032
		Medium	136	720.6 (98)	169.1 (23)	110.3 (15)	
		High	117	820.5 (96)	119.7 (14)	59.8 (7)	

Birth Defect Severity (2 Categories; All Children)

Model 2: Children of Ranch Hands - $\text{Log}_2(\text{Current Dioxin})$ and Time

Without adjustment for covariates (Table 7-10 [a]), there is no significant variation in the association between birth defect severity (not major, major) and current dioxin with time since duty in SEA among children of Ranch Hands having more than 10 ppt current dioxin ($p=0.703$). Furthermore, there is no significant association between birth defect severity and current dioxin among children of Ranch Hands with late ($p=0.789$) or early ($p=0.784$) tours.

Without adjustment for covariates (Table 7-10 [b]), there is no significant variation in the association between birth defect severity (not major, major) and current dioxin with time since duty in SEA among children of Ranch Hands having more than 5 ppt current dioxin ($p=0.976$). Furthermore, there is no significant association between birth defect severity and current dioxin among children of Ranch Hands late ($p=0.621$) or early ($p=0.576$) tours.

After adjustment for covariates (Table 7-10 [c]), there is significant variation in the association between birth defect severity (not major, major) and current dioxin with time since duty in SEA and the father's military occupation among children of Ranch Hands having more than 10 ppt current dioxin ($p=0.050$). The basis for this significance is displayed in Appendix Table E-1. After stratification, there is no significant change in the association between birth defect severity and current dioxin with time since duty in SEA for any of the three military occupations. Additionally, for no occupational stratum is there a significant association between birth defect severity and current dioxin among children of Ranch Hands with late or early tours.

If the above interaction is ignored, there is no significant change in association between birth defects severity and current dioxin with time since duty in SEA ($p=0.682$). Furthermore, there is no significant association between birth defect severity and current dioxin among children of Ranch Hands late ($p=0.933$) or early ($p=0.576$) tours.

After adjustment for covariates (Table 7-10 [d]), there is no significant variation in the association between birth defect severity (not major, major), current dioxin level and time since duty in SEA among children of Ranch Hands having more than 10 ppt current dioxin ($p=0.807$). Furthermore, there is no significant association between birth defect severity and current dioxin among children of Ranch Hands with late ($p=0.748$) or early ($p=0.457$) tours.

Table 7-10

Post-SEA Counts and Rates of
Birth Defect Severity (Not Major, Major)

Variable: Birth Defect Severity (Not Major, Major)
 Restrictions: All Children of Ranch Hands
 Children Conceived during or after the
 Father's Duty in SEA
 Model 2: $\text{Log}_2(\text{Current Dioxin}), \text{Time}$

Ranch Hands - $\text{Log}_2(\text{Current Dioxin}), \text{Time}$ - Unadjusted						
Exposure Restriction	Time Since SEA (years)	Major Rate (No./n)			Est. Relative Risk (95% C.I.)	p-Value
		Low	Medium	High		
a) D>10 ppt (n=509)						0.703
	≤18.6	48.4 (3/62)	111.9 (15/134)	41.7 (3/72)	0.94(0.61,1.45)	0.789
	>18.6	75.0 (3/40)	101.9 (11/108)	75.3 (7/93)	1.05(0.72,1.54)	0.784
b) D>5 ppt (n=690)						0.976
	≤18.6	55.6 (5/90)	92.0 (16/174)	54.5 (6/110)	1.08(0.80,1.46)	0.621
	>18.6	15.9 (1/63)	110.3 (15/136)	59.8 (7/117)	1.08(0.81,1.44)	0.576

Table 7-10 (Continued)

Ranch Hands - Log₂(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=459)			0.682***	OCC*TIME*DIOXIN (p=0.050)
	≤18.6	1.02(0.63,1.66)***	0.933***	SMOKE(p=0.025)
	>18.6	0.90(0.62,1.31)***	0.576***	
d) D>5 ppt (n=616)			0.807	RACE(p=0.098)
	≤18.6	1.06(0.76,1.47)	0.748	SMOKE(p=0.048)
	>18.6	1.12(0.84,1.49)	0.457	OCC(p=0.070)

Birth Defect Severity (3 Categories; All Children)

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

Without adjustment for covariates (Table 7-11 [a]), there is a significant overall association between birth defect severity (none, minor, major) and categorized current dioxin (p=0.033). The distribution of severity among children of Ranch Hands in the Low category is significantly different from that of children of Comparisons in the Background category (p=0.002). This finding is caused by a high rate of major severity in children of Ranch Hands in the Low dioxin category (126.4 per 1000) relative to that of Comparisons in the Background category (57.1 per 1000). However, the distributions of birth defect severity among children of Ranch Hands in the High (p=0.860) and Unknown (p=0.919) categories are not significantly different from that of children of Comparisons in the Background category.

Table 7-11

**Post-SEA Counts and Rates of
Birth Defect Severity (None, Minor, Major)**

Variable: Birth Defect Severity (None, Minor, Major)
 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	Rate (n) Severity Index Level			Category Contrast	p-Value
		None	Minor	Major		
Background	981	792.0 (777)	150.9 (148)	57.1 (56)	All Exp Categ	0.033
Unknown	282	797.9 (225)	141.8 (40)	60.3 (17)	Unk vs Bkgd	0.919
Low	174	706.9 (123)	166.7 (29)	126.4 (22)	Low vs Bkgd	0.002
High	227	806.2 (183)	136.6 (31)	57.3 (13)	High vs Bkgd	0.860

Birth Defect Severity (2 Categories; All Children)**Model 3: Children of Ranch Hands and Comparisons - Categorized Current Dioxin**

Without adjustment for covariates (Table 7-12 [a]), there is a significant overall association between birth defect severity (not major, major) and categorized current dioxin ($p=0.018$). The rate of major birth defects among children of Ranch Hands in the Low current dioxin category (126.4 per 1000) is significantly greater than the rate among children of Comparisons in the Background category, 57.1 per 1000 ($p=0.001$). The rates of major birth defects among children of Ranch Hands in the High ($p=0.991$) and Unknown ($p=0.839$) categories are not significantly different from that in children of Comparisons in the Background category.

After adjustment for covariates (Table 7-12 [b]), there is significant variation in the overall association between birth defect severity (not major, major) and categorized current dioxin with the mother's smoking ($p=0.008$) and also with the father's military occupation ($p=0.027$). The basis for this significance is displayed in Appendix Table E-1. There is a significant increase ($p=0.005$) in the rate of major birth defects among children of Ranch Hands in the Low category (233.3 per 1000) relative to the rate among children of Comparisons in the Background category whose mother who smoked during pregnancy and whose father was in the enlisted ground occupational category (48.5 per 1000). Among children whose mother did not smoke and whose father was an enlisted flyer, the rate of major birth defects among children of Ranch Hands in the Unknown category (266.7 per 1000) was significantly greater ($p=0.023$) than the rate in children of Comparisons in the Background category (52.6 per 1000). For many other strata there was insufficient data to assess the significance of these associations.

Table 7-12

Post-SEA Counts and Rates of
Birth Defect Severity (Not Major, Major)

Variable: Birth Defect Severity (Not Major, Major)
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	Major Count Rate	Category Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	981	56 57.1	All Exp Categ		0.018
Unknown	282	17 60.3	Unk vs Bkgd	1.06(0.60,1.86)	0.839
Low	174	22 126.4	Low vs Bkgd	2.39(1.42(4.03)	0.001
High	227	13 57.3	High vs Bkgd	1.00(0.54,1.87)	0.991
Total	1664				

Table 7-12 (Continued)

b) Adjusted

Exposure Category	n	Category Contrast	Est. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	843	All Exp Categ		****	DRINK(p=0.035)
Unknown	246	Unk vs Bkgd	****	****	F-AGE(p=0.021)
Low	156	Low vs Bkgd	****	****	SMOKE*DIOXIN
High	203	High vs Bkgd	****	****	(p=0.008)
					OCC*DIOXIN
Total	1448				(p=0.027)

7.5 Post-SEA Exposure Analyses - Full Siblings

Birth Defect Severity (3 Categories; Full Siblings)

Model 1: Children of Ranch Hands - \log_2 (Initial Dioxin)

Without adjustment for covariates (Table 7-13 [a] and [b]), there is no association between birth defect severity (none, minor, major) and initial dioxin among full sibling children of Ranch Hands with more than 10 ppt (p=0.315) or more than 5 ppt (p=0.717) current dioxin.

Table 7-13

**Post-SEA Counts and Rates of
Birth Defect Severity (None, Minor, Major)**

Variable: Birth Defect Severity (None, Minor, Major)
 Restrictions: Full Siblings of Ranch Hands
 Children Conceived during or after the
 Father's Duty in SEA
 Model 1: $\text{Log}_2(\text{Initial Dioxin})$

Ranch Hands - $\text{Log}_2(\text{Initial Dioxin})$ - Unadjusted						
Exposure Restriction	Initial Dioxin	n	Rate (count) Severity Index Level			p-Value
			None	Minor	Major	
a) D>10 ppt	Low	78	794.9 (62)	166.7 (13)	38.5 (3)	0.315
	Medium	206	723.3 (149)	184.5 (38)	92.2 (19)	
	High	136	801.5 (109)	147.1 (20)	51.5 (7)	
b) D>5 ppt	Low	114	824.6 (94)	114.0 (13)	61.4 (7)	0.717
	Medium	245	763.3 (187)	163.3 (40)	73.5 (18)	
	High	198	777.8 (154)	161.6 (32)	60.6 (12)	

Birth Defect Severity (2 Categories; Full Siblings)

Model 1: Children of Ranch Hands - $\text{Log}_2(\text{Initial Dioxin})$

Without adjustment for covariates (Table 7-14 [a] and [b]), there is no significant association between birth defect severity (not major, major) and initial dioxin among full sibling children of Ranch Hands with more than 10 ppt ($p=0.770$) or more than 5 ppt ($p=0.941$) current dioxin.

After adjustment for covariates (Table 7-14 [c]), there is no significant association between birth defect severity and initial dioxin among full sibling children of Ranch Hands with more than 10 ppt current dioxin ($p=0.919$).

After adjustment for covariates (Table 7-14 [d]), there is no significant association between birth defect severity and initial dioxin among full sibling children of Ranch Hands with more than 5 ppt current dioxin ($p=0.970$).

Table 7-14

Post-SEA Counts and Rates of
Birth Defect Severity (Not Major, Major)

Variable: Birth Defect Severity (Not Major, Major)
Restrictions: Full Siblings of Ranch Hands
Children Conceived during or after the
Father's Duty in SEA
Model 1: $\log_2(\text{Initial Dioxin})$

Ranch Hands - $\log_2(\text{Initial Dioxin})$ - Unadjusted						
Exposure Restriction	Initial Dioxin	n	Major Count Rate		Est. Relative Risk (95% C.I.)	p-Value
a) D>10 ppt (n=420)	Low	78	3	38.5	0.95(0.69,1.32)	0.770
	Medium	206	19	92.2		
	High	136	7	51.5		
b) D>5 ppt (n=557)	Low	114	7	61.4	1.01(0.80,1.28)	0.941
	Medium	245	18	73.5		
	High	198	12	60.6		

Ranch Hands - $\log_2(\text{Initial Dioxin})$ - Adjusted

Exposure Restriction	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
c) D>10 ppt (n=390)	1.02(0.73,1.42)	0.919	DRINK($p=0.085$) SMOKE($p=0.012$)
d) D>5 ppt (n=513)	1.01(0.79,1.28)	0.970	SMOKE($p=0.055$)

Birth Defect Severity (3 Categories; Full Siblings)

Model 2: Children of Ranch Hands - \log_2 (Current Dioxin) and Time

Without adjustment for covariates (Table 7-15 [a]), there is no significant variation in the association between birth defect severity (none, minor, major) and current dioxin with time since duty in SEA among full sibling children of Ranch Hands with more than 10 ppt current dioxin ($p=0.679$). Furthermore, there is no significant association between birth defect severity and current dioxin among children of Ranch Hands with late ($p=0.442$) or early ($p=0.430$) tours.

Without adjustment for covariates (Table 7-15 [b]), there is no significant variation in the association between birth defect severity and current dioxin with time since duty in SEA among full sibling children of Ranch Hands with more than 5 ppt current dioxin ($p=0.415$). There is no significant association between birth defect severity and current dioxin among children of Ranch Hands with late tours ($p=0.794$). However, there is a significant association between birth defect severity and current dioxin among children of Ranch Hands with early tours ($p=0.016$). This finding is caused by the high rate of major defects in children of Ranch Hands with medium current dioxin levels (103.8 per 1000) and the low rates in children of Ranch Hands with low current dioxin levels (18.9 per 1000).

Table 7-15

Post-SEA Counts and Rates of
Birth Defect Severity (None, Minor, Major)

Variable: Birth Defect Severity (None, Minor, Major)
 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)	Current Dioxin	n	Rate (count) Severity Index Level			p-Value
				None	Minor	Major	
a) D>10 ppt (n=421)							0.679
	≤18.6	Low	47	766.0 (36)	191.5 (9)	42.6 (2)	0.442
		Medium	115	765.2 (88)	139.1 (16)	95.7 (11)	
		High	64	734.4 (47)	218.8 (14)	46.9 (3)	
	>18.6	Low	28	714.3 (20)	250.0 (7)	35.7 (1)	0.430
		Medium	92	739.1 (68)	163.0 (15)	97.8 (9)	
		High	75	813.3 (61)	133.3 (10)	53.3 (4)	

Table 7-15 (Continued)

Ranch Hands - \log_2 (Current Dioxin), Time - Unadjusted

Exposure Restriction	Time Since SEA (years)	Current Dioxin	n	Rate (count) Severity Index Level			p-Value
				None	Minor	Major	
b) D>5 ppt (n=557)							0.415
	≤18.6	Low	59	796.6 (47)	135.6 (8)	67.8 (4)	0.794
		Medium	144	736.1 (106)	180.6 (26)	83.3 (12)	
		High	98	785.7 (77)	163.3 (16)	51.0 (5)	
	>18.6	Low	53	924.5 (49)	56.6 (3)	18.9 (1)	0.016
		Medium	106	707.5 (75)	188.7 (20)	103.8 (11)	
		High	97	835.1 (81)	123.7 (12)	41.2 (4)	

Birth Defect Severity (2 Categories; Full Siblings)

Model 2: Children of Ranch Hands - \log_2 (Current Dioxin) and Time

Without adjustment for covariates (Table 7-16 [a]), there is no significant variation in the association between birth defect severity (not major, major) and current dioxin with time since duty in SEA among full sibling children of Ranch Hands having more than 10 ppt current dioxin ($p=0.688$). Furthermore, there is no significant association between birth defect severity and current dioxin among children of Ranch Hands with late ($p=0.860$) or early ($p=0.446$) tours.

Without adjustment for covariates (Table 7-16 [b]), there is no significant variation in the association between birth defect severity (not major, major) and current dioxin with time since duty in SEA among full sibling children of Ranch Hands having more than 5 ppt current dioxin ($p=0.899$). Furthermore, there is no significant association between birth defect severity and current dioxin among children of Ranch Hands with late ($p=0.948$) or early ($p=0.804$) tours.

After adjustment for covariates (Table 7-16 [c]), there is no significant variation in the association between birth defect severity (not major, major) and current dioxin with time since duty in SEA among full sibling children of Ranch Hands having more than 10 ppt current dioxin ($p=0.755$). Furthermore, there is no significant association between birth defect severity and current dioxin among children of Ranch Hands with late ($p=0.992$) or early ($p=0.651$) tours.

After adjustment for covariates (Table 7-16 [d]), there is no significant variation in the association between birth defect severity (not major, major) and current dioxin with time since duty in SEA among full sibling children of Ranch Hands having more than 5 ppt current dioxin ($p=0.853$). Furthermore, there is no significant association between birth defect severity and current dioxin among children of Ranch Hands with late ($p=0.971$) or early ($p=0.818$) tours.

Table 7-16

Post-SEA Counts and Rates of
Birth Defect Severity (Not Major, Major)

Variable: Birth Defect Severity (Not Major, Major)
Restrictions: Full Siblings of Ranch Hands
Children Conceived during or after the
Father's Duty in SEA
Model 2: $\text{Log}_2(\text{Current Dioxin})$, Time

Ranch Hands - $\text{Log}_2(\text{Current Dioxin})$, Time - Unadjusted						
Exposure Restriction	Time Since SEA (years)	Major Rate (No./n)			Est. Relative Risk (95% C.I.)	p-Value
		Low	Medium	High		
a) D>10 ppt (n=421)						0.688
	≤18.6	42.6 (2/47)	95.7 (11/115)	46.9 (3/64)	0.96(0.59,1.56)	0.860
	>18.6	35.7 (1/28)	97.8 (9/92)	53.3 (4/75)	0.83(0.52,1.33)	0.446
b) D>5 ppt (n=557)						0.899
	≤18.6	67.8 (4/59)	83.3 (12/144)	51.0 (5/98)	1.01(0.72,1.43)	0.948
	>18.6	18.9 (1/53)	103.8 (11/106)	41.2 (4/97)	1.04(0.74,1.46)	0.804

Table 7-16 (Continued)

Ranch Hands - Log₂(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)			0.755	SMOKE(p=0.020)
	≤18.6	1.00(0.60,1.67)	0.992	
	>18.6	0.90(0.57,1.42)	0.651	
d) D>5 ppt (n=513)			0.853	SMOKE(p=0.052)
	≤18.6	0.99(0.70,1.42)	0.971	
	>18.6	1.04(0.74,1.45)	0.818	

Birth Defect Severity (3 Categories, Full Siblings)

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

Without adjustment for covariates (Table 7-17 [a]), there is a significant overall association between birth defect severity (none, minor, major) and categorized current dioxin (p=0.028) among full siblings. There is a significant difference between the rates of birth defect severity among children of Ranch Hands in the Low category (p=0.010) and no significant differences between the rates among children of Ranch Hands in the Unknown (p=0.200) and High (p=0.727) categories with the rate in children of Comparisons in the Background category. Among children of Ranch Hands in the Low category, the rate of major defects (121.6 per 1000) is greater than that in Comparison children (56.7 per 1000) and the rates of minor birth defects are nearly equal in the two groups (175.7 versus 157.6 per 1000).

Table 7-17

**Post-SEA Counts and Rates of
Birth Defect Severity (None, Minor, Major)**

Variable: Birth Defect Severity (None, Minor, Major)
 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

Dioxin Category	n	Rate (count) Severity Index Level			Category Contrast	p-Value
		None	Minor	Major		
Background	812	785.7 (638)	157.6 (128)	56.7 (46)	All Exp Categ	0.028
Unknown	221	814.5 (180)	113.1 (25)	72.4 (16)	Unk vs Bkgd	0.200
Low	148	702.7 (104)	175.7 (26)	121.6 (18)	Low vs Bkgd	0.010
High	195	810.3 (158)	143.6 (28)	46.2 (9)	High vs Bkgd	0.727

Birth Defect Severity (2 Categories; Full Siblings)**Model 3: Children of Ranch Hands and Comparisons - Categorized Current Dioxin**

Without adjustment for covariates (Table 7-18 [a]), there is a significant overall association between birth defect severity (not major, major) and categorized current dioxin ($p=0.033$) among full siblings. The rate of major birth defects among children of Ranch Hands in Low category (121.6 per 1000) is significantly greater ($p=0.005$) than that in children of Comparisons in the Background category (56.7 per 1000). The rates in major birth defects among children of Ranch Hands in the High ($p=0.563$) and Unknown ($p=0.383$) categories are not significantly different from that of children of Comparisons in the Background category.

After adjustment for covariates (Table 7-18 [b]), there is significant variation in the overall association between birth defect severity (not major, major) and categorized current dioxin with the mother's smoking during pregnancy ($p=0.016$) among full siblings. The basis for this variation is shown in Appendix Table E-1. There is a significant overall association between birth defect severity (not major, major) and categorized current dioxin in children whose mother smoked during pregnancy ($p=0.014$), while there was no significant association in children whose mother did not smoke during pregnancy ($p=0.229$). Furthermore, among children whose mother smoked, the rate of major birth defects in children of Ranch Hands in the Low category (235.3 per 1000) is significantly greater than that in children of Comparisons in the Background category (39.7 per 1000), $p=0.004$. The rates in the High ($p=0.308$) and the Unknown ($p=0.513$) categories are not significantly different from that in the Background category.

Table 7-18

Post-SEA Counts and Rates of
Birth Defect Severity (Not Major, Major)

Variable: Birth Defect Severity (Not Major, Major)
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					
Dioxin Category	n	Major Rate (No.)	Category Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	812	56.7(46)	All Exp Categ		0.033
Unknown	221	72.4(16)	Unk vs Bkgd	1.30(0.72,2.34)	0.383
Low	148	121.6(18)	Low vs Bkgd	2.31(1.30,4.10)	0.005
High	195	46.2(9)	High vs Bkgd	0.81(0.39,1.68)	0.563
Total	1376				

Table 7-18 (Continued)

b) Adjusted

Dioxin Category	n	Category Contrast	Est. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	715	All Exp Categ		0.059***	RACE(p=0.069)
Unknown	199	Unk vs Bkgd	1.31(0.72,2.37)***	0.381***	DRINK(p=0.009)
Low	137	Low vs Bkgd	2.11(1.16,3.82)***	0.014***	M-AGE(p=0.053)
High	180	High vs Bkgd	0.75(0.36,1.58)***	0.452***	F-AGE(p=0.060)
					C-TIME(p=0.079)
Total	1231				SMOKE*DIOXIN (p=0.016)

7.6 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 double asterisk (**). Four asterisks (****) represent the presence of an interaction between a covariate and dioxin with a p-value less than 0.01. The p-value is replaced by a double hyphen (--) when the analysis was not carried out due to sparse data.

All live births were assigned to one of three birth defect severity categories (none, minor, major) according to standardized definitions and medical record review. The significance of the association between birth defect severity and the father's dioxin level was assessed with Models 1, 2 and 3 under various combinations of constraints on severity, sibship and statistical adjustment.

Pre-post SEA analyses were carried out with severity reduced to two categories (major, not major) and unadjusted for covariates, first based on all children and then based on full siblings, using each of the 3 models. The results are summarized in Tables 7-19 through 7-21.

Table 7-19

P-Value Summary of Unadjusted Pre-post Initial Dioxin (Model 1)
 Analysis of Two-Category Severity
 (Major, Not Major)

Sibship	p-Value	
	D>10 ppt	D>5 ppt
All Children	NS	NS
Full Siblings	NS	NS

Table 7-20

P-Value Summary of Pre-post Current Dioxin (Model 2)
 and Time Analyses of Two-Category Severity
 (Major, Not Major)

Sibship	p-Value	
	D>10 ppt	D>5 ppt
All Children	NS	NS
Full Siblings	NS	NS

Table 7-21

P-Value Summary of Pre-post Categorized Current Dioxin (Model 3)
 Analyses of Two-Category Severity
 (Major, Not Major)

Sibship	All	Unadjusted Contrasts with Background		
		Unknown	Low	High
All Children	NS	NS	0.038	NS
Full Siblings	NS	NS	0.030	NS

Pre-post SEA analyses of birth defect severity in two categories (major, not major) found significant associations in Model 3 but not in Model 1 or Model 2 analyses. The Model 3 findings are caused by the rate of major post-SEA defects being elevated in Ranch Hands in the Low current dioxin category relative to Comparisons in the Background category. In the analysis of all children, the Low and Background post-SEA rates were 126.4 per 1000 and 57.1 per 1000; in full sibling children the rates were 121.6 per 1000 and 56.7 per 1000. However, the rate of major defects was not significantly elevated in children of Ranch Hands in the High dioxin category. The post-SEA rate in all children of Ranch Hands in the High category was 57.3 per 1000 and the rate in full sibling children of Ranch Hands in this category was 46.2 per 1000. We conclude that there is no consistent evidence that post-SEA birth defect severity is associated with dioxin after adjustment for pre-SEA severity.

Assessments of the association between the father's dioxin level and post-SEA birth defect severity in 3 categories (major, minor, none) were carried out using Models 1, 2 and 3 without adjustment for covariates. Each series of analyses was applied first to all children and then to full siblings. Assessments of the association between the father's dioxin level and post-SEA birth defect severity in 2 categories (major, not major) were carried out using Models 1, 2 and 3 without and then with adjustment for covariates. Each series of analyses was applied first to all children and then to full siblings. The results are summarized in Tables 7-22 through 7-24.

Table 7-22

P-Value Summary of Initial Dioxin Analyses of (Model 3)
Post-SEA Birth Defect Severity

a) All Children

Variable	Unadjusted		Adjusted	
	D>10 ppt	D>5 ppt	D>10 ppt	D>5 ppt
Severity (3 category)	NS	NS	--	--
Severity (2 category)	NS	NS	NS	NS

Table 7-22 (Continued)

b) Full Siblings

Variable	Unadjusted		Adjusted	
	D>10 ppt	D>5 ppt	D>10 ppt	D>5 ppt
Severity (3 category)	NS	NS	--	--
Severity (2 category)	NS	NS	NS	NS

Table 7-23

P-Value Summary of Current Dioxin and Time Analyses (Model 2) of
Post-SEA Birth Defect Severity

a) All Children

Variable	Unadjusted					
	D>10 ppt			D>5 ppt		
	Time Since			Time Since		
	Dioxin by Time	SEA (years) ≤18.6	>18.6	Dioxin by Time	SEA (years) ≤18.6	>18.6
Severity (3 category)	NS	NS	NS	NS	NS	0.032
Severity (2 category)	NS	NS	NS	NS	NS	NS

b) All Children

Variable	Adjusted					
	D>10 ppt			D>5 ppt		
	Time Since			Time Since		
	Dioxin by Time	SEA (years) ≤18.6	>18.6	Dioxin by Time	SEA (years) ≤18.6	>18.6
Severity (3 category)	--	--	--	--	--	--
Severity (2 category)	**NS	**NS	**NS	NS	NS	NS

Table 7-23 (Continued)

c) Full Siblings

Variable	Unadjusted					
	D>10 ppt Time Since Dioxin SEA (years) by Time ≤18.6 >18.6			D>5 ppt Time Since Dioxin SEA (years) by Time ≤18.6 >18.6		
Severity (3 category)	NS	NS	NS	NS	NS	0.016
Severity (2 category)	NS	NS	NS	NS	NS	NS

d) Full Siblings

Variable	Adjusted					
	D>10 ppt Time Since Dioxin SEA (years) by Time ≤18.6 >18.6			D>5 ppt Time Since Dioxin SEA (years) by Time ≤18.6 >18.6		
Severity (3 category)	--	--	--	--	--	--
Severity (2 category)	NS	NS	NS	NS	NS	NS

Table 7-24

P-Value Summary of Categorized Current Dioxin Analyses of
Post-SEA Birth Defect Severity (Model 3)

a) All Children

Variable	Unadjusted			
	All	Contrasts with Background		
		Unknown	Low	High
Severity (3 category)	0.033	NS	0.002	NS
Severity (2 category)	0.018	NS	0.001	NS

b) All Children

Variable	Adjusted			
	All	Contrasts with Background		
		Unknown	Low	High
Severity (3 category)	--	--	--	--
Severity (2 category)	****	****	****	****

Table 7-24 (Continued)

c) Full Siblings

Variable	All	Unadjusted		
		Contrasts with Background		
		Unknown	Low	High
Severity (3 category)	0.028	NS	0.010	NS
Severity (2 category)	0.033	NS	0.005	NS

d) Full Siblings

Variable	All	Adjusted		
		Contrasts with Background		
		Unknown	Low	High
Severity (3 category)	--	--	--	--
Severity (2 category)	NS*	NS	0.014	NS

Model 2 analyses of severity in 3 categories found significant associations with dioxin in all children and in full siblings, but Tables 7-9 and 7-15 show that these findings were caused by the highest rate of major defect occurring in children of Ranch Hands having intermediate dioxin levels. Corresponding analyses of severity in 2 categories were negative. These findings are not suggestive of a dioxin effect.

Without and with restriction to full sibling children, unadjusted Model 3 analyses of severity in 3 and in 2 categories found significant differences between children of Ranch Hands in the Low dioxin category and children of Comparisons in the Background dioxin category. Tables 7-11, 7-12, 7-17 and 7-18 show, however, that these findings are caused by a high rate of major defects in children of fathers in the Low dioxin category relative to children of fathers in the Background category, while the rate of major defects in children of fathers in the High dioxin category is not significantly elevated. These patterns are consistent with those of the Model 2 analyses but are not suggestive of a dioxin effect.

An adjusted Model 3 analysis of severity in 2 categories found significant interactions with the mother's smoking and the father's military occupation in SEA. However, within 4 of the 6 smoking by occupation strata the children of fathers in the High dioxin category had the lowest rate of major defects. The two significant findings in these strata were caused by the rate of major defects in children of Ranch Hands in the Low and Unknown dioxin categories being greater than that of children of Comparisons in the Background category.

In summary, analyses of birth defect severity found few significant associations. Those associations that were significant were generally caused by children of Ranch Hands with intermediate dioxin levels having the highest rates of major birth defects. In most of these analyses, children of Ranch Hands with the highest dioxin levels had the lowest rates of major defects. These patterns are inconsistent with the expected dose-response pattern and are not suggestive of a dioxin effect. We conclude that there is no evidence in these data to suggest that dioxin is associated with major birth defects.

8. SELECTED BIRTH DEFECTS AND DEVELOPMENTAL DISABILITIES

8.1 Introduction

Twelve selected birth defects and 4 developmental disabilities, defined by ICD-9-CM code in Table 8-1, have been suggested as possibly dioxin-related [14] or have been the focus of veteran and public interest.

In this section, rates are expressed per 1000 children.

Table 8-1

ICD Definitions of Twelve Selected Birth Defects and Four Developmental Disabilities

a) Birth Defects

Name	ICD Codes
Anencephaly	740.0
Spina bifida	741.0 741.9
Hydrocephalus	742.3
Cleft Palate	749.0
Cleft lip/palate	749.1 749.2
Esophageal atresia	750.3
Anorectal atresia	751.2
Hypospadias	752.6
Congenital hip dislocation	754.3
Polydactyly	755.0
Limb reduction deformities	755.2 755.3 755.4
Down's syndrome	758.0

b) Developmental Disabilities

Name	ICD Codes
Disturbance of emotion specific to childhood and adolescence	313
Hyperkinetic syndrome of childhood	314
Specific Delays in Development	315
Mental Retardation	317 318 319

Counts of these 16 selected anomalies among all pre-SEA (n=4145) and post-SEA (n=2647) Ranch Hand and Comparison children and among all pre-SEA (n=2742) and post-SEA (n=1772) children whose father is a Ranch Hand or Comparison who satisfies the conditions of Models 1, 2 and 3 are shown in Table 8-2.

Table 8-2

Counts of 12 Selected Birth Defects and 4 Developmental Disabilities in Pre-SEA and Post-SEA Ranch Hand and Comparison Children By the Fathers Inclusion in Models 1, 2 or 3

a) Birth Defects

Name	All		Models 1,2,3	
	Pre-SEA	Post-SEA	Pre-SEA	Post-SEA
Anencephaly	1	1	1	1
Spina bifida	3	3	3	3
Hydrocephalus	5	1	5	1
Cleft Palate	6	6	6	4
Cleft lip/palate	7	5	7	4
Esophageal atresia	2	2	0	1
Anorectal atresia	2	1	1	1
Polydactyly	3	1	3	1
Limb reduction deformities	2	4	1	4
Hypospadias	4	15	3	10
Congenital hip dislocation	8	25	8	14
Down's syndrome	4	11	2	7

b) Developmental Disabilities

Name	All		Models 1,2,3	
	Pre-SEA	Post-SEA	Pre-SEA	Post-SEA
Disturbance of emotion specific to childhood and adolescence	11	18	9	10
Hyperkinetic syndrome of childhood	54	77	39	62
Specific Delays in Development	103	179	73	142
Mental Retardation	12	13	10	7

Occurrences of these selected anomalies among pre-SEA and post-SEA Ranch Hand children by exposure restriction ($D > 10$ ppt, $D > 5$ ppt) are shown in Table 8-3 for those children who enter a Model 1 or Model 2 analysis.

Table 8-3

**Occurrences of Selected Anomalies in Ranch Hand
Children Who Enter a Model 1 or Model 2 Analysis**

a) Birth Defects

Counts by Time of Conception
and the Father's Initial Dioxin

Name	Exposure Restriction	n	Pre-SEA			n	Post-SEA		
			Low	Medium	High		Low	Medium	High
Anencephaly/ Ancephalus	D>10 ppt	700	0	0	0	508	0	1	0
	D>5 ppt	1058	1	0	0	690	0	1	0
Spina Bifida	D>10 ppt	700	1	0	0	508	1	1	1
	D>5 ppt	1058	0	1	0	690	0	1	2
Hydrocephalus	D>10 ppt	700	1	0	0	508	0	0	0
	D>5 ppt	1058	0	2	0	690	0	0	0
Cleft Palate	D>10 ppt	700	1	1	1	508	0	0	0
	D>5 ppt	1058	0	2	1	690	0	0	0
Cleft Lip/palate	D>10 ppt	700	1	1	0	508	0	1	0
	D>5 ppt	1058	1	2	0	690	0	1	1
Esophageal atresia	D>10 ppt	700	0	0	0	508	1	0	0
	D>5 ppt	1058	0	0	0	690	0	1	0
Anorectal atresia	D>10 ppt	700	0	0	0	508	0	0	1
	D>5 ppt	1058	0	0	0	690	0	0	1
Polydactyly	D>10 ppt	700	0	0	0	508	0	1	0
	D>5 ppt	1058	1	0	0	690	0	0	1
Limb reduction deformities	D>10 ppt	700	0	1	0	508	1	0	0
	D>5 ppt	1058	0	1	0	690	0	1	0
Hypospadias	D>10 ppt	700	0	0	0	508	0	4	0
	D>5 ppt	1058	1	0	0	690	0	4	0
Congenital Hip Dislocation	D>10 ppt	700	0	2	1	508	0	2	1
	D>5 ppt	1058	0	2	2	690	1	2	1
Down's Syndrome	D>10 ppt	700	0	1	0	508	0	0	1
	D>5 ppt	1058	0	1	0	690	1	0	1

Table 8-3 (Continued)

b) Developmental Disabilities

Counts by Time of Conception and the Father's Initial Dioxin									
Name	Exposure Restriction	n	Pre-SEA			n	Post-SEA		
			Low	Medium	High		Low	Medium	High
Emotional Disturbance	D>10 ppt	700	1	1	1	508	0	3	0
	D>5 ppt	1058	1	2	1	690	1	2	1
Hyperkinetic Syndrome	D>10 ppt	700	5	6	0	508	3	7	6
	D>5 ppt	1058	2	11	0	690	10	8	10
Delays in Development	D>10 ppt	700	4	9	6	508	12	25	10
	D>5 ppt	1058	5	14	6	690	13	29	18
Mental Retardation	D>10 ppt	700	0	1	0	508	0	1	1
	D>5 ppt	1058	0	2	0	690	1	1	1

8.2 Pre-post SEA Exposure Analyses

Only delays in development and hyperkinetic syndrome can be analyzed for an association with dioxin because the counts of abnormalities in the other 14 categories are too small to permit statistical analysis. Analyses using Models 1, 2 and 3 were carried out to determine whether any of the pre-SEA to post-SEA changes in delays in development or hyperkinetics syndrome odds ratios were related to the father's dioxin body burden without adjustment for covariates. The results from all children and full sibling children are shown in tables 8-4 through 8-15.

Specific Delays in Development (All Children)

Model 1: Children of Ranch Hands - $\text{Log}_2(\text{Initial Dioxin})$

Without adjustment for covariates (Table 8-4 [a]), there is significant variation in the association between specific delays in development and initial dioxin with time of conception among children of Ranch Hands having more than 10 ppt current dioxin ($p=0.035$). This significance is due to a reversal in the pattern of the rates of delays in development with time of conception. The delays in development rate increases with initial dioxin in pre-SEA children while the rate decreases with initial dioxin in post-SEA children.

Without adjustment for covariates (Table 8-4 [b]), there is significant variation in the association between specific delays in development and initial dioxin with time of conception among children of Ranch Hands having more than 5 ppt current dioxin ($p=0.044$). This significance is due to a difference in the pattern of rates of delays in development with time of conception. The rate increases with initial dioxin in pre-SEA children while the rate is constant with respect to initial dioxin post-SEA children.

Table 8-4

Pre-Post SEA Counts and Rates of
Specific Delays in Development

Variable: Specific Delays in Development
Restrictions: All Children of Ranch Hands
Category: Time of Conception Relative to the
Father's Duty in SEA
Model 1: $\text{Log}_2(\text{Initial Dioxin})$

Ranch Hands - $\text{Log}_2(\text{Initial Dioxin})$ - Unadjusted								
		Time of Conception Relative to the Father's Duty in SEA						
Exposure Restriction	Initial Dioxin	n	Pre-SEA		Post-SEA			p-Value
			Abn	Rate	n	Abn	Rate	
a) $D > 10$ ppt ($n=1208$)	Low	249	4	16.1	106	12	113.2	0.035
	Medium	338	9	26.6	245	25	102.0	
	High	113	6	53.1	157	10	63.7	
b) $D > 5$ ppt ($n=1748$)	Low	286	5	17.5	155	13	83.9	0.044
	Medium	616	14	22.7	308	29	94.2	
	High	156	6	38.5	227	18	79.3	

Specific Delays of Development (All Children)

Model 2: Children of Ranch Hands - $\text{Log}_2(\text{Current Dioxin})$ and Time

Without adjustment for covariates (Table 8-5 [a]), there is borderline significant variation in the association between specific delays in development and current dioxin with time since duty in SEA and time of conception in children of Ranch Hands having more than 10 ppt current dioxin ($p=0.074$). This significance is due to the inconsistent pattern in the rates of delays in development across levels of current dioxin, time since tour and time of conception. The finding is caused by the changing pre-SEA patterns which, of course, have no relationship with the father's subsequent dioxin exposure.

Without adjustment for covariates (Table 8-5 [b]), there is significant variation in the association between specific delays in development and current dioxin with time since duty in SEA and time of conception among children of Ranch Hands having more than 5 ppt current dioxin ($p=0.032$). This significance is due to the inconsistent pattern of the delays in development rates across levels of dioxin, time since tour and time of conception. Like the corresponding finding in Table 8-5 [a], this finding is caused by the changing pre-SEA patterns which have no relationship with the father's subsequent dioxin exposure.

Table 8-5

**Pre-Post SEA Counts and Rates of
Specific Delays in Development**

Variable: Specific Delays in Development
 Restrictions: All Children of Ranch Hands
 Category: Time of Conception Relative to the
 Father's Duty in SEA
 Model 2: $\text{Log}_2(\text{Current Dioxin})$, Time

Ranch Hands - $\text{Log}_2(\text{Initial Dioxin})$ - Unadjusted						
Exposure Restriction	Time of Conception	Time Since SEA (years)	Rate (No./n) Current Dioxin			p-Value
			Low	Medium	High	
a) D>10 ppt	Pre-SEA	≤18.6	14.6 (2/137)	27.3 (5/183)	108.1 (4/37)	0.074
		>18.6	21.1 (2/95)	23.4 (4/171)	25.6 (2/78)	
	Post-SEA	≤18.6	96.8 (6/62)	104.5 (14/134)	55.6 (4/72)	
		>18.6	100.0 (4/40)	111.1 (12/108)	75.3 (7/93)	
	Pre-SEA	≤18.6	6.4 (1/157)	28.8 (9/313)	60.6 (4/66)	
		>18.6	20.0 (3/150)	22.2 (6/270)	19.6 (2/102)	
b) D>5 ppt	Post-SEA	≤18.6	88.9 (8/90)	103.4 (18/174)	72.7 (8/110)	0.032
		>18.6	47.6 (3/63)	110.3 (15/136)	68.4 (8/117)	

Specific Delays in Development (All Children)

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

Without adjustment for covariates (Table 8-6), there is no significant overall variation in the association between specific delays in development and categorized current dioxin with time of conception ($p=0.664$). Furthermore the association between specific delays in development and time of conception among children of Ranch Hands in the High ($p=0.471$), Low ($p=0.374$) and Unknown ($p=0.937$) categories are not significantly different from the corresponding association among children of Comparisons in the Background category.

Table 8-6

Pre-Post SEA Counts and Rates of Specific Delays in Development

Variable: Specific Delays in Development
 Restrictions: All Children of Ranch Hands and Comparisons
 Category: 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	n	Pre-SEA		Post-SEA			Odds Ratio	Category Contract	p-Value
		Abn	Rate	n	Abn	Rate			
Background	1459	37	25.4	981	71	72.4	3.00	All Exp Categ	0.664
Unknown	582	17	29.2	282	24	85.1	3.09	Unk vs Bkgd	0.937
Low	290	8	27.6	174	20	114.9	4.58	Low vs Bkgd	0.374
High	168	6	35.7	227	16	70.5	2.05	High vs Bkgd	0.471

Specific Delays in Development (Full Siblings)

Model 1: Children of Ranch Hands - $\text{Log}_2(\text{Initial Dioxin})$

Without adjustment for covariates (Table 8-7 [a]), there is significant variation in the association between specific delays in development and initial dioxin with time of conception among children of Ranch Hands having more than 10 ppt current dioxin ($p=0.045$). This significance is due to a reversal in the pattern of rates of delays in development with time of conception. The delays in development rate increases with initial dioxin in pre-SEA children while the rate decreases with initial dioxin in post-SEA children.

Without adjustment for covariates (Table 8-7 [b]), there is significant variation in the association between specific delays in development and initial dioxin with time of conception among children of Ranch Hands having more than 5 ppt current dioxin ($p=0.053$). This significance is due to a difference in the pattern of rates of delays in development with time of conception. The delays in development rates increases with the initial dioxin in pre-SEA children while the rate is constant with initial dioxin in post-SEA children.

Table 8-7

**Pre-Post SEA Counts and Rates of
Specific Delays in Development**

Variable: Specific Delays in Development
 Restrictions: Full Siblings of Ranch Hands
 Category: Time of Conception Relative to the
 Father's Duty in SEA
 Model 1: $\text{Log}_2(\text{Initial Dioxin})$

Ranch Hands - $\text{Log}_2(\text{Initial Dioxin})$ - Unadjusted								
Time of Conception Relative to the Father's Duty in SEA								
Exposure Restriction	Initial Dioxin	n	Pre-SEA Abn	Rate	n	Post-SEA Abn	Rate	p-Value
a) D>10 ppt (n=1030)	Low	231	4	17.3	78	10	128.2	0.045
	Medium	276	9	32.6	206	21	101.9	
	High	103	6	58.3	136	10	73.5	
b) D>5 ppt (n=1489)	Low	252	5	19.8	114	10	87.7	0.053
	Medium	545	14	25.7	245	23	93.9	
	High	135	6	44.4	198	18	90.9	

Specific Delays of Development (Full Siblings)

Model 2: Children of Ranch Hands - $\text{Log}_2(\text{Current Dioxin})$ and Time

Without adjustment for covariates (Table 8-8 [a]), there is borderline significant variation in the association between specific delays in development and current dioxin with time since duty in SEA and time of conception among children of Ranch Hands having more than 10 ppt current dioxin ($p=0.070$). This borderline significance is due to the inconsistent pattern of rates of delays in development across levels of dioxin, time since tour, and time of conception. In pre-SEA children, the highest (16.1 per 1000) and the lowest (114.3 per 1000) rates occur in children of fathers who had late tours, but the rates appear constant with respect to dioxin in children of fathers who had early tours.

Without adjustment for covariates (Table 8-8 [b]), there is significant variation in the association between specific delays in development and current dioxin with time since duty in SEA and time of conception among children of Ranch Hands having more than 5 ppt current dioxin ($p=0.053$). This significance is due to the inconsistent pattern of the delays in development rates in children of fathers who had late tours and in children of fathers who had early tours. In post-SEA children the highest rates occur in children of Ranch Hands with intermediate dioxin levels.

Table 8-8

Pre-Post SEA Counts and Rates of
Specific Delays in Development

Variable: Specific Delays in Development
Restrictions: Full Siblings of Ranch Hands
Category: Time of Conception Relative to the
Father's Duty in SEA
Model 1: \log_2 (Current Dioxin), Time

Ranch Hands - \log_2 (Initial Dioxin) - Unadjusted						
Exposure Restriction	Time of Conception	Time Since SEA (years)	Rate (No./n) Current Dioxin			p-Value
			Low	Medium	High	
a) D>10 ppt	Pre-SEA	≤ 18.6	16.1 (2/124)	32.3 (5/155)	114.3 (4/35)	0.070
		>18.6	23.5 (2/85)	28.0 (4/143)	29.0 (2/69)	
	Post-SEA	≤ 18.6	106.4 (5/47)	113.0 (13/115)	62.5 (4/64)	
		>18.6	107.1 (3/28)	97.8 (9/92)	93.3 (7/75)	

Table 8-8 (Continued)

Exposure Restriction	Time of Conception	Time Since SEA (years)	Rate (No./n) Current Dioxin			p-Value
			Low	Medium	High	
b) D>5 ppt	Pre-SEA	≤18.6	7.9 (1/126)	32.6 (9/276)	66.7 (4/60)	0.053
		>18.6	20.7 (3/145)	25.3 (6/237)	22.7 (2/88)	
	Post-SEA	≤18.6	84.7 (5/59)	111.1 (16/144)	81.6 (8/98)	
		>18.6	56.6 (3/53)	103.8 (11/106)	82.5 (8/97)	

Specific Delays in Development (Full Siblings)

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

Without adjustment for covariates (Table 8-9), there is no significant overall variation in the association between specific delays in development and categorized current dioxin with time of conception in full siblings ($p=0.841$). Furthermore the association between specific delays in development and time of conception among children of Ranch Hands in the High ($p=0.475$), Low ($p=0.670$) and Unknown ($p=0.905$) categories are not significantly different from the corresponding associations among children of Comparisons in the Background category.

Table 8-9

**Pre-Post SEA Counts and Rates of
Specific Delays in Development**

Variable: Specific Delays in Development
 Restrictions: Full Siblings of Ranch Hands and Comparisons
 Category: 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	n	Pre-SEA		Post-SEA		Odds	Category	p-Value
		Abn	Rate	n	Abn	Rate	Ratio	
Background	1250	33	26.4	812	63	77.6	3.10	All Exp Categ
Unknown	514	15	29.2	221	18	81.4	2.95	Unk vs Bkgd
Low	244	8	32.8	148	17	114.9	3.83	Low vs Bkgd
High	148	6	40.5	195	16	82.1	2.12	High vs Bkgd

Hyperkinetic Syndrome of Childhood (All Children)

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

Without adjustment for covariates (Table 8-10 [a] and [b]), there is no significant variation in the association between hyperkinetic syndrome and initial dioxin with time of conception among children of Ranch Hands with more than 10 ppt ($p=0.172$) or with more than 5 ppt ($p=0.830$) current dioxin.

Table 8-10

**Pre-Post SEA Counts and Rates of
Hyperkinetic Syndrome of Childhood**

Variable: Hyperkinetic Syndrome of Childhood
 Restrictions: All Children of Ranch Hands
 Category: Time of Conception Relative to the
 Father's Duty in SEA
 Model 1: $\text{Log}_2(\text{Initial Dioxin})$

Ranch Hands - $\text{Log}_2(\text{Initial Dioxin})$ - Unadjusted

		Time of Conception Relative to the Father's Duty in SEA						
Exposure Restriction	Initial Dioxin	n	Pre-SEA		n	Post-SEA		p-Value
			Abn	Rate		Abn	Rate	
a) D>10 ppt (n=1208)	Low	249	5	20.1	106	3	28.3	0.172
	Medium	338	6	17.8	245	7	28.6	
	High	113	0	0.0	157	6	38.2	
b) D>5 ppt (n=1748)	Low	286	2	7.0	155	10	64.5	0.830
	Medium	616	11	17.9	308	8	26.0	
	High	156	0	0.0	227	10	44.1	

Hyperkinetic Syndrome of Childhood (All Children)

Model 2: Children of Ranch Hands - $\text{Log}_2(\text{Current Dioxin})$, and Time

Without adjustment for covariates (Table 8-11 [a] and [b]), there is no significant variation in the association between hyperkinetic syndrome and current dioxin with time since duty in SEA and time of conception among children of Ranch Hands having more than 10 ppt ($p=0.405$) or more than 5 ppt ($p=0.331$) current dioxin.

Table 8-11

**Pre-Post SEA Counts and Rates of
Hyperkinetic Syndrome of Childhood**

Variable: Hyperkinetic Syndrome of Childhood
 Restrictions: All Children of Ranch Hands
 Category: Time of Conception Relative to the
 Father's Duty in SEA
 Model 1: $\log_2(\text{Current Dioxin})$, Time

Ranch Hands - $\log_2(\text{Initial Dioxin})$ - Unadjusted						
Exposure Restriction	Time of Conception	Time Since SEA (years)	Rate (No./n) Current Dioxin			p-Value
			Low	Medium	High	
a) D>10 ppt	Pre-SEA	≤18.6	21.9 (3/137)	21.9 (4/183)	0.0 (0/37)	0.405
		>18.6	10.5 (1/95)	17.5 (3/171)	0.0 (0/78)	
	Post-SEA	≤18.6	0.0 (0/62)	29.9 (4/134)	55.6 (4/72)	
		>18.6	50.0 (2/40)	37.0 (4/108)	21.5 (2/93)	
b) D>5 ppt	Pre-SEA	≤18.6	12.7 (2/157)	22.4 (7/313)	0.0 (0/66)	0.331
		>18.6	0.0 (0/150)	14.8 (4/270)	0.0 (0/102)	
	Post-SEA	≤18.6	33.3 (3/90)	28.7 (5/174)	54.5 (6/110)	
		>18.6	79.4 (5/63)	36.8 (5/136)	34.2 (4/117)	

Hyperkinetic Syndrome of Childhood (All Children)

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

Without adjustment for covariates (Table 8-12), there is no significant variation in the overall association between hyperkinetic syndrome and categorized current dioxin with time of conception ($p=0.161$). The association between hyperkinetic syndrome and time of conception among children of Ranch Hands in the High current dioxin category is borderline significantly lower than that among children of Comparisons in the Background category ($p=0.089$) due to the lack of hyperkinetic pre-SEA children of fathers in the High dioxin category. The association between hyperkinetic syndrome and time of conception among children of Ranch Hands in the Low ($p=0.238$) and Unknown ($p=0.614$) categories are not significantly different from that among children of Comparisons in the Background category.

Table 8-12

Pre-Post SEA Counts and Rates of Hyperkinetic Syndrome of Childhood

Variable: Hyperkinetic Syndrome of Childhood
Restrictions: All Children of Ranch Hands and Comparisons
Category: 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	n	Pre-SEA		Post-SEA		Odds Ratio	Category Contract	p-Value
		Abn	Rate	n	Abn	Rate		
Background	1459	19	13.0	981	32	32.6	All Exp Categ	0.161
Unknown	582	9	15.5	282	14	49.6	Unk vs Bkgd	0.614
Low	290	6	20.7	174	4	23.0	Low vs Bkgd	0.238
High	168	0	0.0	227	10	44.1	High vs Bkgd	0.089

Hyperkinetic Syndrome of Childhood (Full Siblings)

Model 1: Children of Ranch Hands - Log₂(Initial Dioxin)

Without adjustment for covariates (Table 8-13 [a] and [b]), there is no significant variation in the association between hyperkinetic syndrome and initial dioxin with time of conception among full sibling children of Ranch Hands with more than 10 ppt (p=0.245) or with more than 5 ppt (p=0.540) current dioxin.

Table 8-13

Pre-Post SEA Counts and Rates of Hyperkinetic Syndrome of Childhood

Variable: Hyperkinetic Syndrome of Childhood
Restrictions: Full Siblings of Ranch Hands
Category: Time of Conception Relative to the
Father's Duty in SEA
Model 1: Log₂(Initial Dioxin)

Ranch Hands - Log₂(Initial Dioxin) - Unadjusted

		Time of Conception Relative to the Father's Duty in SEA							
Exposure Restriction		Initial Dioxin	n	Pre-SEA		n	Post-SEA		p-Value
				Abn	Rate		Abn	Rate	
a)	D>10 ppt (n=1030)	Low	231	5	21.6	78	2	25.6	0.245
		Medium	276	5	18.1	206	5	24.3	
		High	103	0	0.0	136	4	29.4	
b)	D>5 ppt (n=1489)	Low	252	2	7.9	114	10	87.7	0.540
		Medium	545	10	18.3	245	5	20.4	
		High	135	0	0.0	198	7	35.4	

Hyperkinetic Syndrome of Childhood (Full Siblings)

Model 2: Children of Ranch Hands - \log_2 (Current Dioxin), and Time

Without adjustment for covariates (Table 8-14 [a] and [b]), there is no significant variation in the association between hyperkinetic syndrome 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 ($p=0.258$) or more than 5 ppt ($p=0.433$) current dioxin.

Table 8-14

Pre-Post SEA Counts and Rates of Hyperkinetic Syndrome of Childhood

Variable: Hyperkinetic Syndrome of Childhood
Restrictions: Full Siblings of Ranch Hands
Category: Time of Conception Relative to the
Father's Duty in SEA
Model 1: \log_2 (Current Dioxin), Time

Ranch Hands - \log_2 (Initial Dioxin) - Unadjusted						
Exposure Restriction	Time of Conception	Time Since SEA (years)	Rate (No./n) Current Dioxin			p-Value
			Low	Medium	High	
a) D>10 ppt	Pre-SEA	≤ 18.6	24.2 (3/124)	19.4 (3/155)	0.0 (0/35)	0.258
		>18.6	11.8 (1/85)	21.0 (3/143)	0.0 (0/69)	
	Post-SEA	≤ 18.6	0.0 (0/47)	17.4 (2/115)	31.3 (2/64)	
		>18.6	71.4 (2/28)	43.5 (4/92)	13.3 (1/75)	

Table 8-14 (Continued)

Exposure Restriction	Time of Conception	Time Since SEA (years)	Rate (No./n) Current Dioxin			p-Value
			Low	Medium	High	
b) D>5 ppt	Pre-SEA	≤18.6	15.9 (2/126)	21.7 (6/276)	0.0 (0/60)	0.433
		>18.6	0.0 (0/145)	16.9 (4/237)	0.0 (0/88)	
	Post-SEA	≤18.6	50.8 (3/59)	27.8 (4/144)	30.6 (3/98)	
		>18.6	94.3 (5/53)	37.7 (4/106)	30.9 (3/97)	

Hyperkinetic Syndrome of Childhood (Full Siblings)

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

Without adjustment for covariates (Table 8-15), there is no significant variation in the overall association between hyperkinetic syndrome and categorized current dioxin with time of conception ($p=0.203$) in full siblings. Furthermore, the associations between hyperkinetic syndrome and time of conception among children of Ranch Hands in the High ($p=0.167$), Low ($p=0.256$) or Unknown ($p=0.358$) current dioxin categories are not significantly different from that among children of Comparisons in the Background category.

Table 8-15

**Pre-Post SEA Counts and Rates of
Hyperkinetic Syndrome of Childhood**

Variable: Hyperkinetic Syndrome of Childhood
 Restrictions: Full Siblings of Ranch Hands and Comparisons
 Category: 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	n	Pre-SEA Abn	Rate	n	Post-SEA Abn	Rate	Odds Ratio	Category Contract	p-Value
Background	1250	19	15.2	812	29	35.7	2.40	All Exp Categ	0.203
Unknown	514	8	15.6	221	13	58.8	3.95	Unk vs Bkgd	0.358
Low	244	5	20.5	148	3	20.3	0.99	Low vs Bkgd	0.256
High	148	0	0.0	195	6	30.8	--	High vs Bkgd	0.167

8.3 Post-SEA Exposure Analyses

Analyses using Models 1, 2 and 3 were carried out in post-SEA children to determine if delays in development or hyperkinetic syndrome were associated with the father's dioxin body burden, with and without adjustment for covariates. The results, without and with restriction to full siblings, are summarized in tables 8-16 through 8-27.

Specific Delays in Development (All Children)

Model 1: Children of Ranch Hands - \log_2 (Initial Dioxin)

Without adjustment for covariates (Table 8-16 [a] and [b]), there is no significant association between specific delays in development and initial dioxin in children of Ranch Hands having more than 10 ppt ($p=0.321$) or more than 5 ppt ($p=0.758$) current dioxin.

After adjustment for covariates (Table 8-16 [c] and [d]), there is no significant association between specific delays in development and initial dioxin in children of Ranch Hands having more than 10 ppt current dioxin ($p=0.318$) or more than 5 ppt ($p=0.900$) current dioxin.