

**Appendix N**

**Endocrine Assessment**

**TABLE N-1.**  
**Summary of Dioxin-by-Covariate Interactions for Endocrine Variables**

Ranch Hands and Comparisons by Current Dioxin Category									
Variable/ (Table Ref.)	Interaction	Stratum	Current Dioxin Category	n	Adj. Mean	Contrast	Difference of Adj. Means (95% C.I.) <sup>a</sup>	p-Value	
T <sub>3</sub> % Uptake <sup>b</sup> (15-7 [j])	Categorized Current Dioxin-by- Age	Born ≥1942	Background	319	30.59	A11		0.030	
			Unknown	116	30.83	U vs. B	0.24 --	0.357	
			Low	80	31.12	L vs. B	0.53 --	0.081	
			High	114	30.13	H vs. B	-0.46 --	0.083	
	Born <1942		Background	453	30.69	A11		<0.001	
			Unknown	222	30.57	U vs. B	-0.12 --	0.543	
			Low	114	29.82	L vs. B	-0.87 --	<0.001	
			High	67	29.87	H vs. B	-0.82 --	0.009	
Ranch Hands and Comparisons by Current Dioxin Category									
Variable/ (Table Ref.)	Interaction	Stratum	Current Dioxin Category	n	Percent Abnormal High	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	
T <sub>3</sub> % Uptake (15-8 [j])	Categorized Current Dioxin-by- Age	Born ≥1942	Background	319	2.5	A11		0.289	
			Unknown	116	4.3	U vs. B	1.75 (0.56,5.47)	0.335	
			Low	80	6.3	L vs. B	2.59 (0.82,8.15)	0.103	
			High	114	1.8	H vs. B	0.69 (0.15,3.32)	0.647	
	Born <1942		Background	453	4.9	A11		0.319	
			Unknown	222	4.5	U vs. B	0.92 (0.43,1.99)	0.840	
			Low	114	1.8	L vs. B	0.35 (0.08,1.51)	0.159	
			High	67	1.5	H vs. B	0.30 (0.04,2.24)	0.239	
Ranch Hands - Log <sub>2</sub> (Current Dioxin) and Time									
Variable/ (Assumption-- Table Ref.)	Interaction	Stratum	Time (Yrs.)	Percent Abnormal High/(n)			Adj. Relative Risk (95% C.I.) <sup>c</sup>	p-Value	
				Current	Dioxin				
TSH (Maximal-- 15-10 [h])	Current-by- Time-by- Personality	Type A	≤18.6	2.0 (50)	0.0 (85)	6.3 (32)	1.70 (0.68,4.26)	0.026 <sup>d</sup>	
				12.1 (33)	2.5 (80)	0.0 (44)		0.256 <sup>e</sup>	
		Type B	>18.6	2.0 (49)	1.0 (97)	2.2 (46)	0.40 (0.14,1.15)	0.089 <sup>e</sup>	
				0.0 (42)	2.2 (92)	5.6 (54)		0.382 <sup>d</sup>	
	Type		>18.6	0.0 (42)	2.2 (92)	5.6 (54)	1.50 (0.89,2.53)	0.904 <sup>e</sup>	
				2.0 (49)	1.0 (97)	2.2 (46)		0.132 <sup>e</sup>	

**TABLE N-1. (Continued)**  
**Summary of Dioxin-by-Covariate Interactions for Endocrine Variables**

**Ranch Hands - Log<sub>2</sub> (Initial Dioxin)**

Variable/ (Assumption-- Table Ref.)	Interaction	Stratum	Initial Dioxin	n	Adj. Mean	Adj. Slope (Std. Error)	p-Value
Testosterone <sup>f</sup> (Minimal-- 15-13 [c])	Initial-by- Personality Type	Type A	Low	59	538.3	-0.4928 (0.1801)	0.006
			Medium	107	514.8		
	Type B		High	53	472.1		
			Low	65	516.3	0.1281 (0.1468)	0.383
Testosterone <sup>f</sup> (Maximal-- 15-13 [d])	Initial-by- Personality Type	Type A	Medium	143	522.2	-0.3794 (0.1318)	0.004
			High	74	530.1		
	Type B		Low	83	524.6	0.1494 (0.1142)	0.191
			Medium	200	544.8		
			High	101	548.5		

**Ranch Hands and Comparisons by Current Dioxin Category**

Variable/ (Table Ref.)	Interaction	Stratum	Current Dioxin Category	n	Percent Abnormal Low	Contrast	Adj. Relative Risk (95% C.I.)	p-Value
Testosterone (15-14 [j])	Categorized Current Dioxin-by- Personality Type	Type A	Background	316	0.6	All		0.096
			Unknown	158	1.3	U vs. B	3.11 (0.42,23.27)	0.268
			Low	80	0.0	L vs. B	--	--
			High	78	3.8	H vs. B	6.72 (1.06,42.73)	0.044
	Type B		Background	434	2.5	All		0.350
			Unknown	168	0.6	U vs. B	0.30 (0.04,2.39)	0.256
			Low	109	2.8	L vs. B	1.07 (0.29,4.04)	0.916
			High	103	1.0	H vs. B	0.32 (0.04,2.79)	0.303

**TABLE N-1. (Continued)**  
**Summary of Dioxin-by-Covariate Interactions for Endocrine Variables**

**Ranch Hands - Log<sub>2</sub> (Current Dioxin) and Time**

Variable/ (Assumption-- Table Ref.)	Interaction	Stratum	Time (Yrs.)	Adj. Mean/(n) <u>Current Dioxin</u>			Adj. Slope (Std. Error)	p-Value
				Low	Medium	High		
Fasting Glucose <sup>b</sup> (Maximal-- 15-15 [h])	Current-by- Time-by-Age	Born ≥1942	≤18.6	95.9 (46)	94.7 (81)	96.7 (55)	0.0017 (0.0095)	0.031 <sup>b</sup>
			>18.6	94.3 (13)	95.3 (53)	100.1 (59)		0.854 <sup>c</sup>
		Born <1942	≤18.6	103.4 (58)	109.1 (107)	122.8 (25)	0.0319 (0.0104)	0.002 <sup>c</sup>
	Categorized Current Dioxin-by- Age	Born ≥1942	≤18.6	105.1 (65)	109.0 (123)	114.8 (43)	0.0370 (0.0124)	0.451 <sup>b</sup>
			>18.6	105.1 (65)	109.0 (123)	114.8 (43)		0.003 <sup>c</sup>
							0.0254 (0.0093)	0.006 <sup>c</sup>

**Ranch Hands and Comparisons by Current Dioxin Category**

Variable/ (Table Ref.)	Interaction	Stratum	Current Dioxin Category	n	Adj. Mean	Difference of Adj. Means (95% C.I.) <sup>a</sup>		p-Value
						Contrast		
Fasting Glucose <sup>b</sup> (15-15 [j])	Categorized Current Dioxin-by- Age	Born ≥1942	Background	321	96.1	A vs. B		0.017
			Unknown	115	95.5	U vs. B	-0.6 --	0.601
		Born <1942	Low	79	96.5	L vs. B	0.4 --	0.830
			High	114	100.0	H vs. B	3.9 --	0.004
	Categorized Current Dioxin-by- Lifetime Alcohol History	Born <1942	Background	35	101.4	A vs. B		0.567
			Unknown	15	101.6	U vs. B	0.2 --	0.957
		>0-40	Low	10	102.2	L vs. B	0.8 --	0.883
			High	15	108.5	H vs. B	7.1 --	0.172
	>40	Born <1942	Background	285	102.5	A vs. B		0.003
			Unknown	160	100.7	U vs. B	-1.8 --	0.285
		>0-40	Low	74	106.1	L vs. B	3.6 --	0.091
			High	29	112.2	H vs. B	9.7 --	0.004
		>40	Background	136	107.2	A vs. B		<0.001
			Unknown	48	105.4	U vs. B	-1.8 --	0.543
			Low	28	105.8	L vs. B	-1.4 --	0.692
			High	24	127.4	H vs. B	20.2 --	<0.001

**TABLE N-1. (Continued)**  
**Summary of Dioxin-by-Covariate Interactions for Endocrine Variables**

**Ranch Hands - Log<sub>2</sub> (Current Dioxin) and Time**

Variable/ (Assumption-- Table Ref.)	Interaction	Stratum	Time (Yrs.)	Percent Abnormal High/(n)			Adj. Relative Risk (95% C.I.) <sup>c</sup>	p-Value
				<u>Current Dioxin</u>				
Fasting Glucose (Maximal-- 15-16 [h])	Current-by- Time-by-Race	Black	≤18.6	0.0 (4)	0.0 (10)	50.0 (2)	--	--
			>18.6	100.0 (1)	25.0 (12)	33.3 (6)	0.65 (0.17,2.50)	0.533 <sup>j</sup>
		Non-Black	≤18.6	6.0 (100)	13.5 (178)	16.7 (78)	1.39 (1.07,1.82)	0.015 <sup>j</sup>
	Initial-by- Percent Body Fat	Normal	≤18.6	10.4 (77)	14.0 (164)	21.9 (96)	1.57 (1.27,1.94)	0.001 <sup>j</sup>
			>18.6	107.7 (182)	110.5 (81)	109.6	0.0169 (0.0126)	0.181
			Obese	123.8 (23)	121.6 (49)	129.2 (38)	0.0287 (0.0199)	0.150

**Ranch Hands - Log<sub>2</sub> (Initial Dioxin)**

Variable/ (Assumption-- Table Ref.)	Interaction	Stratum	Initial Dioxin	n	Adj.	Adj. Slope (Std. Error)	p-Value
					Mean		
2-Hour Post- Prandial Glucose <sup>b</sup> (Minimal-- 15-17 [c])	Initial-by- Percent Body Fat	Normal	Low	94	107.7	0.0169 (0.0126)	0.181
			Medium	182	110.5		
		High	81		109.6		
	Initial-by- Type	Obese	Low	23	123.8	0.0287 (0.0199)	0.150
			Medium	49	121.6		
			High	38	129.2		

**Ranch Hands - Log<sub>2</sub> (Current Dioxin) and Time**

Variable/ (Assumption-- Table Ref.)	Interaction	Stratum	Time (Yrs.)	Adj. Mean/(n)			Adj. Slope (Std. Error)	p-Value
				<u>Current Dioxin</u>				
2-Hour Post- Prandial Glucose <sup>b</sup> (Minimal-- 15-17 [g])	Current-by- Time-by- Personality	Type A	≤18.6	110.7 (33)	107.6 (45)	106.4 (19)	-0.0175 (0.0280)	0.534 <sup>h</sup>
			>18.6	120.7 (21)	109.3 (51)	120.1 (30)	0.0250 (0.0216)	0.248 <sup>h</sup>
		Type B	≤18.6	104.6 (27)	114.7 (69)	115.8 (29)	0.0358 (0.0220)	0.104 <sup>h</sup>
	Current-by- Type	Type B	>18.6	127.6 (30)	110.8 (62)	116.4 (37)	-0.0155 (0.0189)	0.411 <sup>h</sup>
			≤18.6					0.074 <sup>g</sup>
			>18.6					0.411 <sup>h</sup>

**TABLE N-1. (Continued)**  
**Summary of Dioxin-by-Covariate Interactions for Endocrine Variables**

Ranch Hands and Comparisons by Current Dioxin Category								
Variable/ (Table Ref.)	Interaction	Stratum	Current Dioxin Category	n	Percent Diabetic	Contrast	Adj. Relative Risk (95% C.I.)	p-Value
Composite Diabetes Indicator (15-18 [j])	Categorized Current Dioxin-by-Age	Born ≥1942	Background	321	5.3	All		0.595
			Unknown	118	3.4	U vs. B	0.95 (0.31,2.93)	0.924
			Low	80	2.5	L vs. B	0.50 (0.11,2.28)	0.374
			High	117	9.4	H vs. B	1.49 (0.65,3.41)	0.341
	Born <1942		Background	461	10.2	All		0.002
			Unknown	226	6.6	U vs. B	0.78 (0.42,1.44)	0.420
			Low	113	12.4	L vs. B	1.15 (0.60,2.22)	0.668
			High	70	28.6	H vs. B	3.09 (1.64,5.82)	<0.001

<sup>a</sup>Difference of means after transformation to original scale; confidence interval on difference of means not given because analysis was performed on natural logarithm scale; p-value based on difference of means on natural logarithm scale.

<sup>b</sup>Adjusted means transformed from natural logarithm scale; adjusted slope and standard error based on natural logarithm of the dependent variable versus  $\log_2$  dioxin.

<sup>c</sup>Relative risk for a twofold increase in dioxin.

<sup>d</sup>Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).

<sup>e</sup>Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).

<sup>f</sup>Adjusted means transformed from square root scale; adjusted slope and standard error based on square root of the dependent variable versus  $\log_2$  dioxin.

<sup>g</sup>Test of significance for homogeneity of slopes (current dioxin continuous, time categorized).

<sup>h</sup>Test of significance for slope equal to 0 (current dioxin continuous, time categorized).

--: Analysis not performed due to category with no abnormalities; confidence interval on difference of means not given because analysis was performed on natural logarithm scale.

Notes: Initial Dioxin: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.

Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

Current Dioxin: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.

Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

All: All categories.

Background (B) (Comparisons): Current Dioxin ≤10 ppt.

Unknown (U) (Ranch Hands): Current Dioxin ≤10 ppt.

Low (L) (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.

High (H) (Ranch Hands): Current Dioxin >33.3 ppt.

**TABLE N-2.**  
**Summary of Models Without Adjustment for Percent  
Body Fat for Endocrine Variables**

<b>Ranch Hands - Log<sub>2</sub> (Initial Dioxin)</b>						
<b>Variable/ (Table Ref.)</b>	<b>Assumption</b>	<b>Adj. Relative Risk (95% C.I.)<sup>a</sup></b>		<b>p-Value</b>	<b>Covariate Remarks</b>	
Testes (15-6 [c])	Minimal (n=516)	1.53 (1.07,2.18)		0.027	AGE (p<0.001)	
Testes (15-6 [d])	Maximal (n=736)	1.52 (1.13,2.02)		0.007	AGE (p<0.001)	
<b>Ranch Hands - Log<sub>2</sub> (Current Dioxin) and Time</b>						
<b>Variable/ (Table Ref.)</b>	<b>Assumption</b>	<b>Time (Yrs.)</b>	<b>Adj. Relative Risk (95% C.I.)<sup>a</sup></b>	<b>p-Value</b>	<b>Covariate Remarks</b>	
Testes (15-6 [g])	Minimal (n=516)	≤18.6 >18.6	2.29 (1.21,4.32) 1.32 (0.82,2.14)	0.164 <sup>b</sup> 0.011 <sup>c</sup> 0.253 <sup>c</sup>	AGE (p<0.001)	
Testes (15-6 [h])	Maximal (n=736)	≤18.6 >18.6	1.87 (1.14,3.06) 1.39 (0.94,2.05)	0.345 <sup>b</sup> 0.007 <sup>c</sup> 0.099 <sup>c</sup>	AGE (p<0.001)	
<b>Ranch Hands and Comparisons by Current Dioxin Category</b>						
<b>Variable/ (Table Ref.)</b>	<b>Current Dioxin Category</b>	<b>n</b>	<b>Contrast</b>	<b>Adj. Relative Risk (95% C.I.)</b>	<b>p-Value</b>	<b>Covariate Remarks</b>
Testes (15-6 [j])	Background	785	All Categories		0.022	AGE (p<0.001) RACE (p=0.069)
	Unknown	343	Unknown vs. Background	0.87 (0.39,1.93)	0.732	
	Low	193	Low vs. Background	0.73 (0.24,2.18)	0.575	
	High	187	High vs. Background	3.43 (1.52,7.75)	0.003	
	Total	1,508				

**TABLE N-2. (Continued)**  
**Summary of Models Without Adjustment for Percent  
Body Fat for Endocrine Variables**

**Ranch Hands - Log<sub>2</sub> (Initial Dioxin)**

Variable/ (Table Ref.) Assumption	Initial Dioxin	n	Adj. Mean	Adj. Slope (Std. Error)	p-Value	Covariate Remarks
Testosterone <sup>d</sup> Minimal (15-13 [c]) (n=501)	Low Medium High	124 250 127	527.9** 525.6** 489.7**	-0.2828 (0.1235)**	0.023**	INIT*PERS (p=0.008) AGE (p<0.001)
Testosterone <sup>d</sup> Maximal (15-13 [d]) (n=711)	Low Medium High	175 356 180	559.9** 544.3** 508.5**	-0.3055 (0.0905)**	<0.001**	INIT*PERS (p=0.001) AGE (p<0.001) RACE (p=0.084)

**Ranch Hands - Log<sub>2</sub> (Current Dioxin) and Time**

Variable/ (Table Ref.) Assumption	Time (Yrs.)	Adj. Mean/(n)			Adj. Slope (Std. Error)	p-Value	Covariate Remarks
		Current Dioxin	Low	Medium	High		
Testosterone <sup>d</sup> Minimal (15-13 [g]) (n=516)	≤18.6	533.2 (71)	512.7 (127)	482.0 (54)	-0.3674 (0.2015)	0.456 <sup>e</sup> 0.069 <sup>f</sup>	AGE (p<0.001)
	>18.6	525.8 (57)	536.9 (130)	495.1 (77)	-0.1784 (0.1646)	0.279 <sup>f</sup>	
Testosterone <sup>d</sup> Maximal (15-13 [h]) (n=736)	≤18.6	573.0 (105)	515.1 (189)	538.2 (83)	-0.3531 (0.1407)	0.494 <sup>e</sup> 0.012 <sup>f</sup>	AGE (p<0.001) RACE (p=0.150)
	>18.6	547.0 (79)	550.9 (176)	507.2 (104)	-0.2270 (0.1246)	0.069 <sup>f</sup>	

**Ranch Hands and Comparisons by Current Dioxin Category**

Variable/ (Table Ref.)	Current Dioxin Category	n	Adj. Mean	Contrast	Difference of Adj. Means (95% C.I.) <sup>g</sup>	p-Value <sup>h</sup>	Covariate Remarks
Testosterone <sup>d</sup> Background (15-13 [j])	Background	785	514.0	All Categories		<0.001	AGE*RACE (p=0.019)
	Unknown	343	545.9	Unknown vs. Background	31.9 ..	0.001	
	Low	193	513.3	Low vs. Background	- 0.7 ..	0.953	
	High	187	482.9	High vs. Background	-31.1 ..	0.010	
	Total	1,508					

**TABLE N-2. (Continued)**  
**Summary of Models Without Adjustment for Percent**  
**Body Fat for Endocrine Variables**

**Ranch Hands - Log<sub>2</sub> (Initial Dioxin)**

Variable/ (Table Ref.)	Assumption	Adj. Relative Risk (95% C.I.) <sup>a</sup>	p-Value	Covariate Remarks
Testosterone (15-14 [c])	Minimal (n=516)	0.98 (0.60,1.60)	0.923	AGE (p=0.051)
Testosterone (15-14 [d])	Maximal (n=736)	1.21 (0.85,1.73)	0.309	AGE (p=0.010)

**Ranch Hands - Log<sub>2</sub> (Current Dioxin) and Time**

Variable/ (Table Ref.)	Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.) <sup>a</sup>	p-Value	Covariate Remarks
Testosterone (15-14 [g])	Minimal (n=516)	≤18.6	0.75 (0.26,2.18)	0.983 <sup>b</sup>	--
		>18.6	0.74 (0.40,1.38)	0.600 <sup>c</sup> 0.347 <sup>c</sup>	
Testosterone (15-14 [h])	Maximal (n=736)	≤18.6	1.40 (0.65,3.00)	0.413 <sup>b</sup>	AGE (p=0.033)
		>18.6	0.96 (0.62,1.51)	0.387 <sup>c</sup> 0.873 <sup>c</sup>	

**Ranch Hands and Comparisons by Current Dioxin Category**

Variable/ (Table Ref.)	Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Testosterone	Background	750	All Categories		0.516**	DXCAT*PERS (p=0.045) AGE (p=0.021)
(15-14 [j])	Unknown	326	Unknown vs. Background	0.54 (0.15,1.91)**	0.339**	RACE (p=0.107)
	Low	189	Low vs. Background	0.95 (0.27,3.37)**	0.931**	
	High	181	High vs. Background	1.71 (0.54,5.45)**	0.361**	
	Total	1,446				

**TABLE N-2. (Continued)**  
**Summary of Models Without Adjustment for Percent**  
**Body Fat for Endocrine Variables**

**Ranch Hands - Log<sub>2</sub> (Initial Dioxin)**

Variable/ (Table Ref.) Assumption	Initial Dioxin	n	Adj. Mean	Adj. Slope (Std. Error)	p-Value	Covariate Remarks	
2-Hour Post- Prandial Glucose <sup>i</sup> (15-15 [c])	Minimal (n=467)	Low Medium High	117 231 119	110.7 112.8 115.6	0.0254 (0.0109)	0.020	AGE (p<0.001)
2-Hour Post- Prandial Glucose <sup>i</sup> (15-15 [d])	Maximal (n=654)	Low Medium High	168 328 158	108.0 111.6 115.8	0.0235 (0.0080)	0.003	AGE (p<0.001) PERS (p=0.133)

**Ranch Hands - Log<sub>2</sub> (Current Dioxin) and Time**

Variable/ (Table Ref.) Assumption	Time (Yrs.)	Adj. Mean/(n) <u>Current Dioxin</u>			Adj. Slope (Std. Error)	p-Value	Covariate Remarks	
		Low	Medium	High				
2-Hour Post- Prandial Glucose <sup>i</sup> (15-15 [g])	Minimal (n=453)	≤18.6 (60)	106.3** (114)	111.1** (48)	113.7** (51)	0.0292 (0.0173)** 0.0133 (0.0148)**	0.471*** 0.092** f	CURR*TIME*PERS (p=0.010) AGE (p=0.002)
2-Hour Post- Prandial Glucose <sup>i</sup> (15-15 [h])	Maximal (n=654)	>18.6 (98)	123.5** (113)	109.7** (168)	120.1** (70)	0.0170 (0.0122) 0.0286 (0.0110)	0.469 <sup>e</sup> 0.164 <sup>f</sup> 0.009 <sup>f</sup>	AGE (p<0.001) PERS (p=0.124)

**TABLE N-2. (Continued)**  
**Summary of Models Without Adjustment for Percent**  
**Body Fat for Endocrine Variables**

**Ranch Hands and Comparisons by Current Dioxin Category**

Variable/ (Table Ref.)	Current Dioxin Category	n	Adj. Mean	Contrast	Difference of Adj. Means (95% C.I.) <sup>j</sup>	p-Value <sup>k</sup>	Covariate Remarks
2-Hour Post- Prandial Glucose <sup>i</sup> (15-15 [j])	Background	705	111.1	All Categories		0.010	AGE (p<0.001) PERS (p=0.081)
	Unknown	314	107.0	Unknown vs. Background	-4.1 --	0.035	
	Low	175	110.1	Low vs. Background	-1.0 --	0.676	
	High	160	116.5	High vs. Background	5.4 --	0.041	
	Total	1,354					

**Ranch Hands - Initial Dioxin (Categorized)**

Variable/ (Table Ref.)	Assumption	Initial Dioxin Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
2-Hour Post- Prandial Glucose (15-16 [c])	Minimal (n=467)	Overall <sup>†</sup> M vs. L <sup>l</sup> H vs. L <sup>l</sup> M vs. L <sup>m</sup> H vs. L <sup>m</sup>	1.19 (0.67,2.14) 1.05 (0.51,2.16) 2.97 (0.41,21.43) 7.99 (1.10,57.96)	0.147 0.554 0.894 0.279 0.040	AGE (p<0.001)
2-Hour Post- Prandial Glucose (15-16 [d])	Maximal (n=678)	Overall <sup>†</sup> M vs. L <sup>l</sup> H vs. L <sup>l</sup> M vs. L <sup>m</sup> H vs. L <sup>m</sup>	1.45 (0.92,2.29) 1.31 (0.70,2.43) 1.40 (0.47,4.20) 3.85 (1.28,11.57)	0.091 0.107 0.396 0.543 0.016	AGE (p<0.001)

**TABLE N-2. (Continued)**  
**Summary of Models Without Adjustment for Percent**  
**Body Fat for Endocrine Variables**

**Ranch Hands - Current Dioxin (Categorized) and Time**

Variable/ (Table Ref.)	Assumption	Time (Yrs.)	Current Dioxin Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
2-Hour Post- Prandial (n=467)	Minimal Glucose (15-16 [g])	$\leq 18.6$	C-by-T*		0.421	AGE (p=0.003)
			Overall†		0.177	RACE (p=0.399)
			M vs. L <sup>l</sup>	1.52 (0.60,3.86)	0.381 <sup>n</sup>	
			H vs. L <sup>l</sup>	1.31 (0.39,4.38)	0.661 <sup>n</sup>	
			M vs. L <sup>m</sup>	1.23 (0.15,10.36)	0.847 <sup>n</sup>	
		>18.6	H vs. L <sup>m</sup>	7.13 (0.95,53.61)	0.056 <sup>n</sup>	
			Overall†		0.140	
			M vs. L <sup>l</sup>	0.49 (0.23,1.03)	0.060 <sup>n</sup>	
			H vs. L <sup>l</sup>	0.62 (0.26,1.46)	0.272 <sup>n</sup>	
			M vs. L <sup>m</sup>	0.66 (0.08,5.59)	0.705 <sup>n</sup>	
2-Hour Post- Prandial (n=678)	Maximal Glucose (15-16 [h])	$\leq 18.6$	H vs. L <sup>m</sup>	2.84 (0.39,20.47)	0.299 <sup>n</sup>	
			C-by-T*		0.741	AGE (p<0.001)
			Overall†		0.102	RACE (p=0.141)
			M vs. L <sup>l</sup>	1.28 (0.65,2.50)	0.480 <sup>n</sup>	
			H vs. L <sup>l</sup>	1.12 (0.41,3.08)	0.830 <sup>n</sup>	
		>18.6	M vs. L <sup>m</sup>	1.28 (0.24,6.90)	0.772 <sup>n</sup>	
			H vs. L <sup>m</sup>	7.71 (1.70,35.04)	0.008 <sup>n</sup>	
			Overall†		0.518	
			M vs. L <sup>l</sup>	1.02 (0.54,1.90)	0.963 <sup>n</sup>	
			H vs. L <sup>l</sup>	1.31 (0.61,2.77)	0.487 <sup>n</sup>	
			M vs. L <sup>m</sup>	0.52 (0.11,2.50)	0.413 <sup>n</sup>	
			H vs. L <sup>m</sup>	2.32 (0.61,8.91)	0.219 <sup>n</sup>	

**TABLE N-2. (Continued)**  
**Summary of Models Without Adjustment for Percent**  
**Body Fat for Endocrine Variables**

**Ranch Hands and Comparisons by Current Dioxin Category**

Variable/ (Table Ref.)	Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
2-Hour Post- Prandial Glucose (15-16 [j])	Background	705	All Categories		0.092	AGE (p<0.001) RACE (p=0.250)
	Unknown	314	Unknown vs. Background <sup>l</sup>	0.96 (0.66,1.40)	0.835	PERS (p=0.085)
	Low	175	Low vs. Background <sup>l</sup>	1.09 (0.69,1.72)	0.702	
	High	160	High vs. Background <sup>l</sup>	1.45 (0.90,2.35)	0.126	
			Unknown vs. Background <sup>m</sup>	0.66 (0.27,1.59)	0.357	
Total		1,354	Low vs. Background <sup>m</sup>	0.51 (0.15,1.81)	0.299	
			High vs. Background <sup>m</sup>	2.60 (1.17,5.81)	0.019	

**Ranch Hands - Log<sub>2</sub> (Initial Dioxin)**

Variable/ (Table Ref.)	Assumption	Adj. Relative Risk (95% C.I.) <sup>a</sup>	p-Value	Covariate Remarks
Composite Diabetes Indicator (15-17 [c])	Minimal (n=517)	1.51 (1.21,1.87)	<0.001	AGE (p<0.001)
Composite Diabetes Indicator (15-17 [d])	Maximal (n=738)	1.55 (1.30,1.85)	<0.001	AGE (p<0.001) RACE (p=0.082)

**Ranch Hands - Log<sub>2</sub> (Current Dioxin) and Time**

Variable/ (Table Ref.)	Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.) <sup>a</sup>	p-Value	Covariate Remarks
Composite Diabetes Indicator (15-17 [g])	Minimal (n=517)	$\leq 18.6$	1.52 (1.04,2.21)	0.783 <sup>b</sup>	AGE (p<0.001)
		>18.6	1.62 (1.22,2.14)	0.029 <sup>c</sup> 0.001 <sup>c</sup>	
Composite Diabetes Indicator (15-17 [h])	Maximal (n=738)	$\leq 18.6$	1.72 (1.29,2.30)	0.431 <sup>b</sup>	AGE (p<0.001)
		>18.6	1.49 (1.19,1.87)	<0.001 <sup>c</sup> 0.001 <sup>c</sup>	RACE (p=0.075)

**TABLE N-2. (Continued)**  
**Summary of Models Without Adjustment for Percent**  
**Body Fat for Endocrine Variables**

Ranch Hands and Comparisons by Current Dioxin Category						
Variable/ (Table Ref.)	Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Composite Diabetes Indicator (15-17 [j])	Background	782	All Categories		<0.001**	DXCAT*AGE (p=0.024)
	Unknown	344	Unknown vs. Background	0.63 (0.37,1.08)**	0.095**	
	Low	193	Low vs. Background	1.04 (0.58,1.85)**	0.906**	
	High	187	High vs. Background	2.95 (1.82,4.79)**	<0.001**	
Total		1,506				

<sup>a</sup>Relative risk for a twofold increase in dioxin.

<sup>b</sup>Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).

<sup>c</sup>Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).

<sup>d</sup>Means transformed from square root scale; slope and standard error based on square root of testosterone versus  $\log_2$  dioxin.

<sup>e</sup>Test of significance for homogeneity of slopes (current dioxin continuous, time categorized).

<sup>f</sup>Test of significance for slope equal to 0 (current dioxin continuous, time categorized).

<sup>g</sup>Difference of means after transformation to original scale; confidence interval on difference of means not given because analysis was performed on square root scale.

<sup>h</sup>P-value based on difference of means on square root scale.

<sup>i</sup>Means transformed from natural logarithm scale; slope and standard error based on natural logarithm of 2-hour postprandial glucose versus  $\log_2$  dioxin.

<sup>j</sup>Difference of means after transformation to original scale; confidence interval on difference of means not given because analysis was performed on natural logarithm scale.

<sup>k</sup>P-value based on difference of means on natural logarithm scale.

<sup>l</sup>Impaired contrasted with normal.

<sup>m</sup>Diabetic contrasted with normal.

<sup>n</sup>Test of significance for relative risk equal to 1 (current dioxin and time categorized).

\*\*Dioxin-by-covariate interaction ( $p \leq 0.05$ ); adjusted mean/slope/relative risk, standard error/confidence interval, and p-value derived from a model fitted after deletion of this interaction.

<sup>t</sup>Overall test of independence of current dioxin and 2-hour postprandial glucose within time stratum.

Note: Initial Dioxin: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.  
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.  
Low: 25-93 ppt; Medium: >93-292 ppt; High: >292 ppt (for 2-hour postprandial glucose).

Current Dioxin: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.  
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.  
Low: >5-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt (for 2-hour postprandial glucose).

Background (Comparisons): Current Dioxin  $\leq$  10 ppt.

Unknown (Ranch Hands): Current Dioxin  $\leq$  10 ppt.

Low (Ranch Hands): 15 ppt < Current Dioxin  $\leq$  33.3 ppt.

High (Ranch Hands): Current Dioxin >33.3 ppt.

M vs. L: Medium dioxin category versus low dioxin category.

H vs. L: High dioxin category versus low dioxin category.

**TABLE N-3.**  
**Summary of Dioxin-by-Covariate Interactions Without Adjustment**  
**for Percent Body Fat for Endocrine Variables**

**Ranch Hands - Log<sub>2</sub> (Initial Dioxin)**

Variable/ (Assumption-- Table Ref.)	Interaction	Stratum	Initial Dioxin	n	Adj. Mean	Adj. Slope (Std. Error)	p-Value
Testosterone <sup>a</sup> (Minimal-- 15-13 [c])	Initial-by- Personality Type	Type A	Low	59	542.8	-0.6872 (0.1944)	<0.001
			Medium	107	521.4		
		Type B	High	53	451.0		
	Initial-by- Personality Type	Type B	Low	65	523.0	-0.0315 (0.1586)	0.843
			Medium	143	526.6		
			High	74	518.7		
Testosterone <sup>a</sup> (Maximal-- 15-13 [d])	Initial-by- Personality Type	Type A	Low	92	581.4	-0.6267 (0.1389)	<0.001
			Medium	156	552.3		
		Type B	High	79	487.8		
	Initial-by- Personality Type	Type B	Low	83	538.9	-0.0243 (0.1210)	0.841
			Medium	200	544.7		
			High	101	533.6		

**Ranch Hands and Comparisons by Current Dioxin Category**

Variable/ (Table Ref.)	Interaction	Stratum	Current Dioxin Category	n	Percent Abnormal Low	Contrast	Adj. Relative Risk (95% C.I.)	p-Value
Testosterone (15-14 [j])	Categorized Current Dioxin-by- Personality Type	Type A	Background	316	0.6	All		0.085
			Unknown	158	1.3	U vs. B	2.05 (0.28,14.75)	0.477
			Low	80	0.0	L vs. B	--	--
			High	78	3.8	H vs. B	8.11 (1.31,50.37)	0.025
	Type B	Type B	Background	434	2.5	All		0.346
			Unknown	168	0.6	U vs. B	0.24 (0.03,1.85)	0.169
			Low	109	2.8	L vs. B	1.10 (0.30,4.05)	0.884
			High	103	1.0	H vs. B	0.50 (0.06,3.98)	0.511

**TABLE N-3. (Continued)**  
**Summary of Dioxin-by-Covariate Interactions Without Adjustment**  
**for Percent Body Fat for Endocrine Variables**

<b>Ranch Hands - Log<sub>2</sub> (Current Dioxin) and Time</b>								
Variable/ (Assumption-- Table Ref.)	Interaction	Stratum	Time (Yrs.)	Adj. Mean/(n) <u>Current Dioxin</u>			Adj. Slope (Std. Error)	p-Value
				Low	Medium	High		
2-Hour Post-Prandial Glucose <sup>b</sup> (Minimal--15-15 [g])	Current-by-Time-by-Personality	Type A	≤18.6	111.0 (33)	107.0 (45)	106.6 (19)	-0.0173 (0.0289)	0.551 <sup>d</sup>
			>18.6	119.0 (21)	108.6 (51)	125.0 (30)	0.0392 (0.0221)	0.076 <sup>d</sup>
			≤18.6	103.1 (27)	114.3 (69)	119.5 (29)	0.0525 (0.0225)	0.020 <sup>d</sup>
	Type	Type B	>18.6	127.0 (30)	109.8 (62)	116.2 (37)	-0.0114 (0.0195)	0.558 <sup>d</sup>
			≤18.6	103.1 (27)	114.3 (69)	119.5 (29)	0.0525 (0.0225)	0.020 <sup>d</sup>
			>18.6	127.0 (30)	109.8 (62)	116.2 (37)	-0.0114 (0.0195)	0.558 <sup>d</sup>
<b>Ranch Hands and Comparisons by Current Dioxin Category</b>								
Variable/ (Table Ref.)	Interaction	Stratum	Current Dioxin Category	n	Percent Diabetic	Contrast	Adj. Relative Risk (95% C.I.)	p-Value
Composite Diabetes Indicator (15-17 [j])	Categorized Current Dioxin-by-Age	Born ≥1942	Background	321	5.3	All		0.125
			Unknown	118	3.4	U vs. B	0.63 (0.21,1.90)	0.411
			Low	80	2.5	L vs. B	0.46 (0.10,2.03)	0.304
			High	117	9.4	H vs. B	1.86 (0.84,4.09)	0.125
	Born <1942	Background	Background	461	10.2	All		<0.001
			Unknown	226	6.6	U vs. B	0.63 (0.34,1.15)	0.129
			Low	113	12.4	L vs. B	1.25 (0.66,2.35)	0.498
			High	70	28.6	H vs. B	3.52 (1.93,6.42)	<0.001

<sup>a</sup>Adjusted means transformed from square root scale; adjusted slope and standard error based on square root of testosterone versus log<sub>2</sub> dioxin.

<sup>b</sup>Adjusted means transformed from natural logarithm scale; adjusted slope and standard error based on natural logarithm of 2-hour postprandial glucose versus log<sub>2</sub> dioxin.

<sup>c</sup>Test of significance for homogeneity of slopes (current dioxin continuous, time categorized).

<sup>d</sup>Test of significance for slope equal to 0 (current dioxin continuous, time categorized).

--: Analysis not performed due to category with no abnormalities.

Note: Initial Dioxin: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.

Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

Current Dioxin: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.

Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

All: All categories.

Background (B) (Comparisons): Current Dioxin ≤10 ppt.

Unknown (U) (Ranch Hands): Current Dioxin ≤10 ppt.

Low (L) (Ranch Hands): 15 ppt < Current Dioxin ≤33.3 ppt.

High (H) (Ranch Hands): Current Dioxin >33.3 ppt.

**APPENDIX N-1.**  
**Data Displays for the Endocrine Assessment**

The following figures graphically display relationships between the dependent variables and measures of dioxin for the endocrine assessment. The panels are arranged as follows:

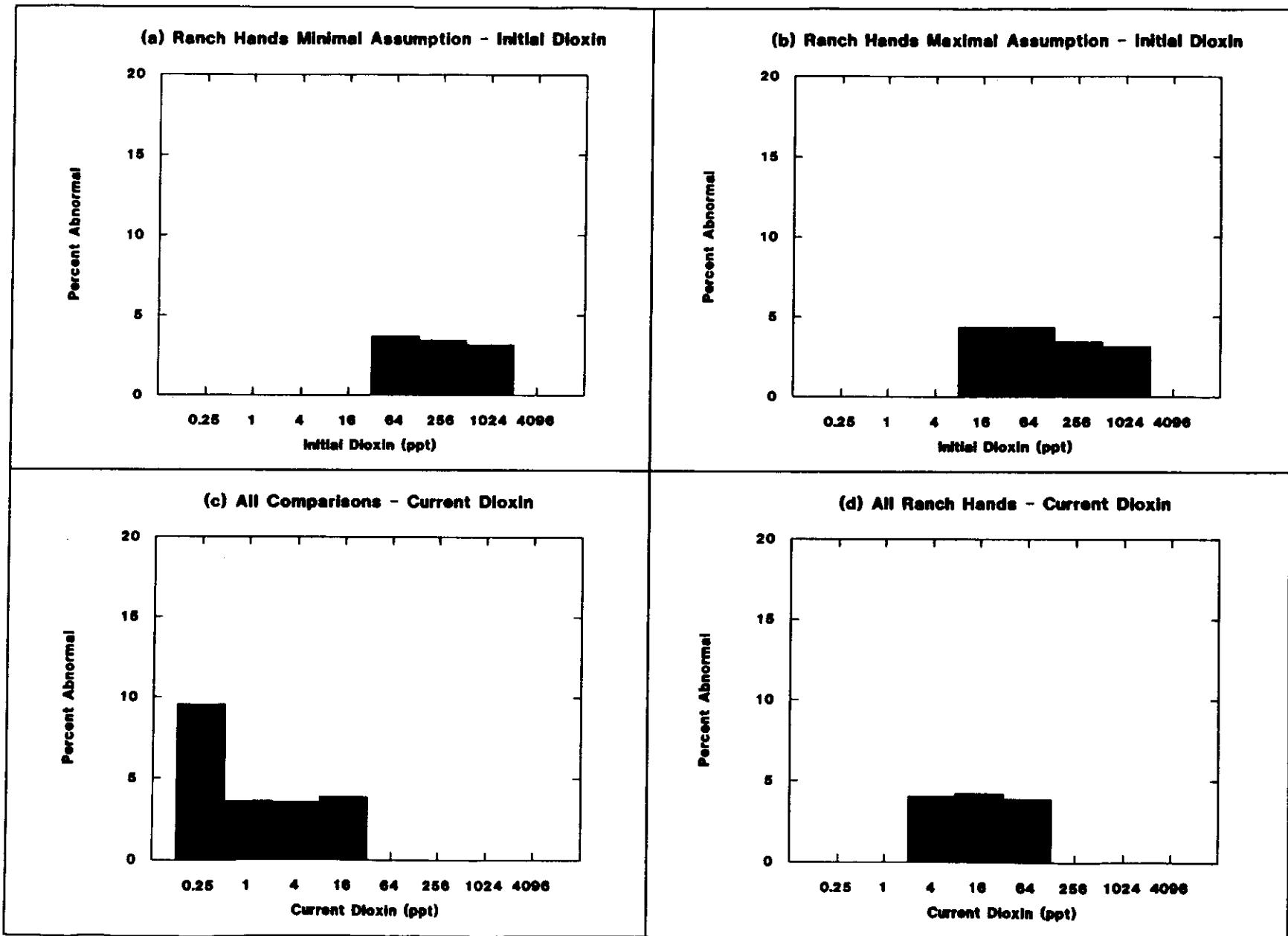
Panel	Group	Assumption	Dioxin Measure
a	Ranch Hand	Minimal	Initial
b	Ranch Hand	Maximal	Initial
c	Comparison	--	Current
d	Ranch Hand	--	Current

Dioxin measures are presented in original units, but spacing of intervals is based on the logarithm (base 2) scale, similar to the statistical analysis. The dependent variable is also presented in original units, but spacing is based on the scale used for analysis, as described in the chapter. For continuous variables, current dioxin values of 0.0 ppt are displayed as 0.3 ppt. For these variables, the reference line indicates the general relationship, unadjusted for any covariates, between the (transform of the) dependent variable and log<sub>2</sub> dioxin. For discrete variables, the percent of participants that exhibited an abnormal condition is displayed on the vertical axis for given intervals of dioxin. The intervals of dioxin and the sample sizes (assuming no missing data or exclusions) for each of these intervals are given below. A list of figures found in this appendix follows the table.

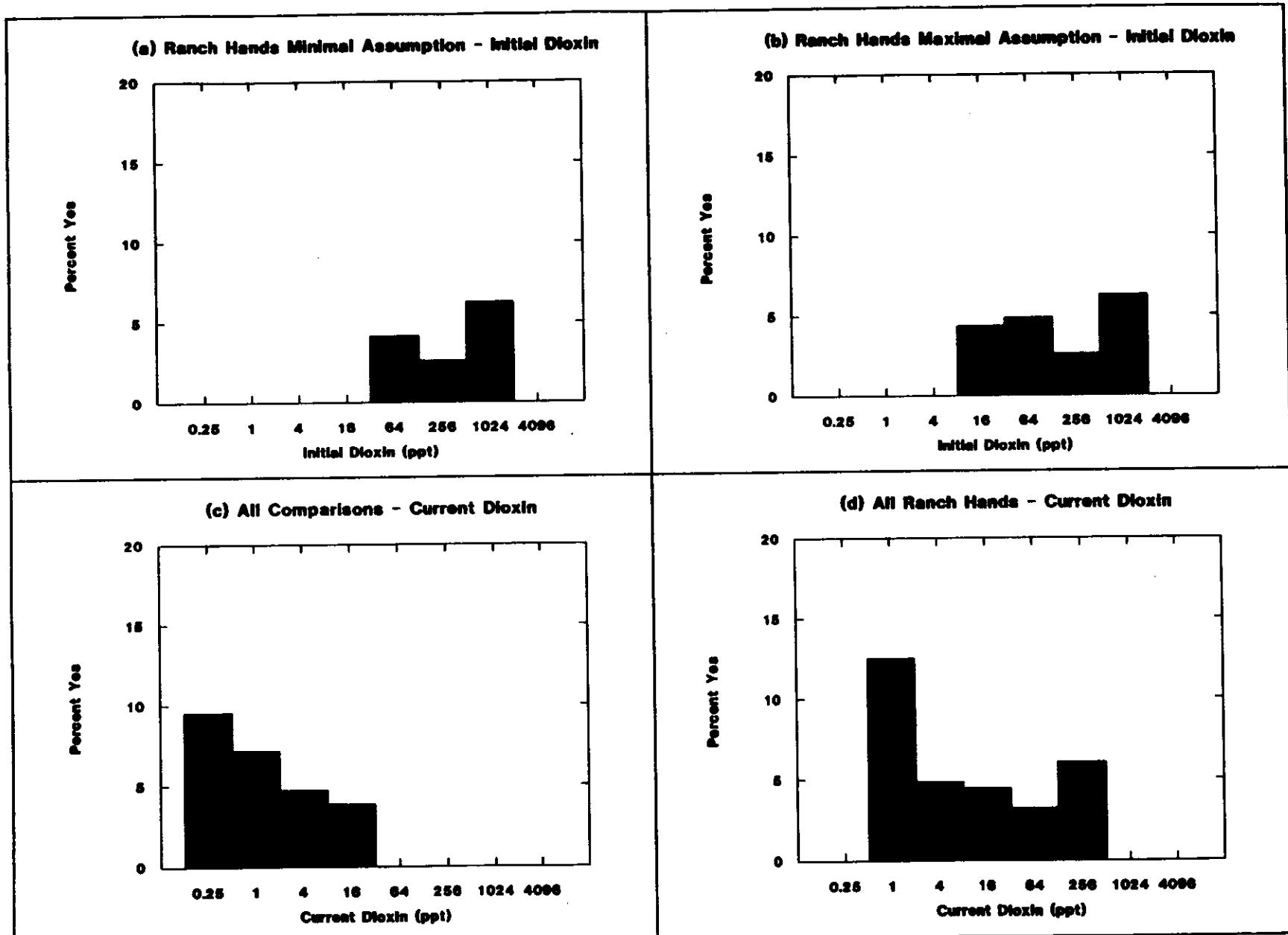
Dioxin Interval	Dioxin Scale Midpoint	Panel			
		a	b	c	d
0.0-0.5	0.25	0	0	42	8
>0.5-2.0	1	0	0	28	8
>2.0-8.0	4	0	0	681	249
>8.0-32.0	16	0	23	52	408
>32.0-128.0	64	219	417	1	158
>128.0-512.0	256	234	234	0	33
>512.0-2,048.0	1024	65	65	0	2
>2,048.0	4096	3	3	0	0

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**FIGURE N-1-1. Current Thyroid Function versus Dioxin**



**FIGURE N-1-2. History of Thyroid Disease versus Dioxin**

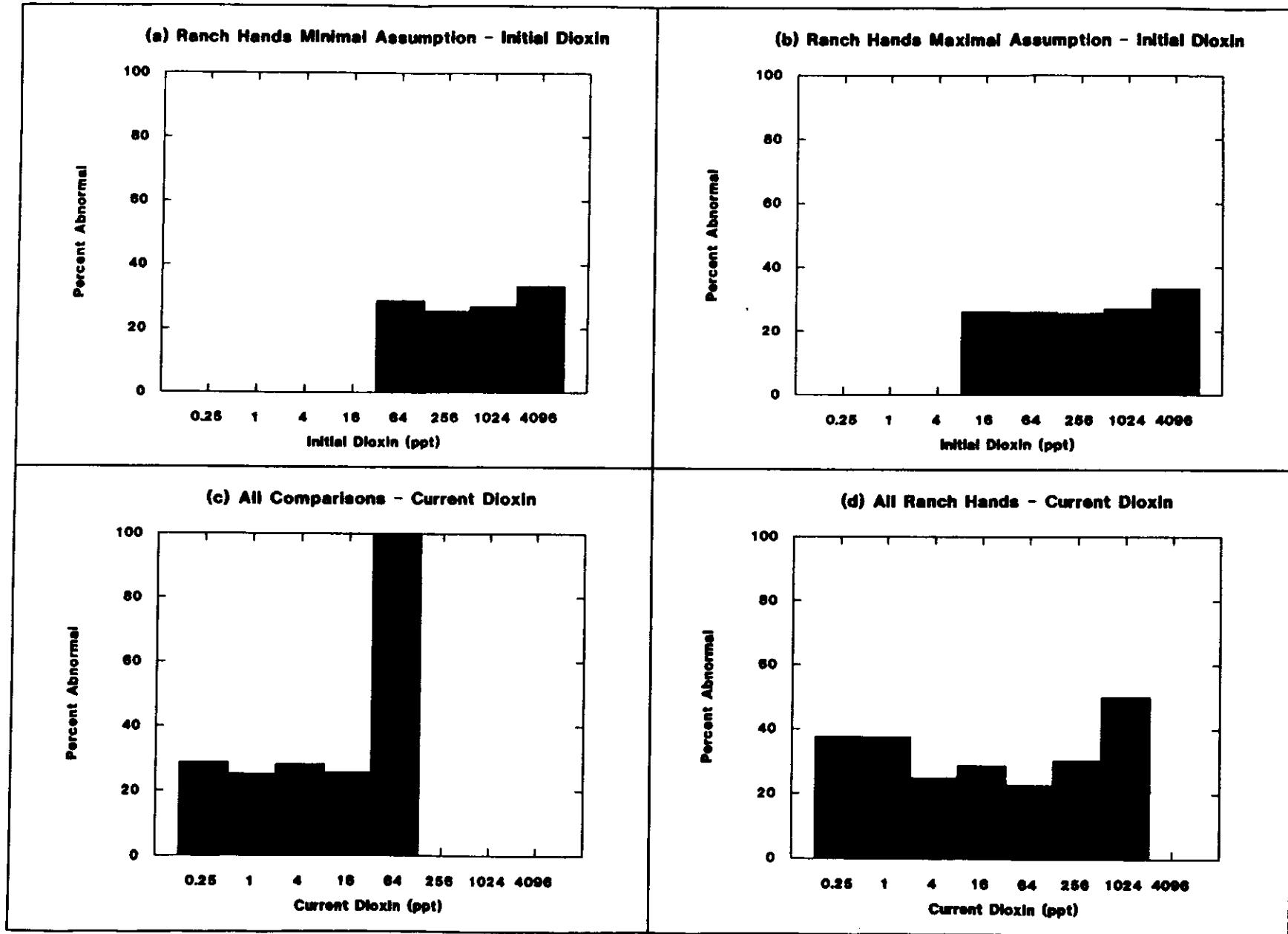


FIGURE N-1-3. Thyroid Gland versus Dioxin

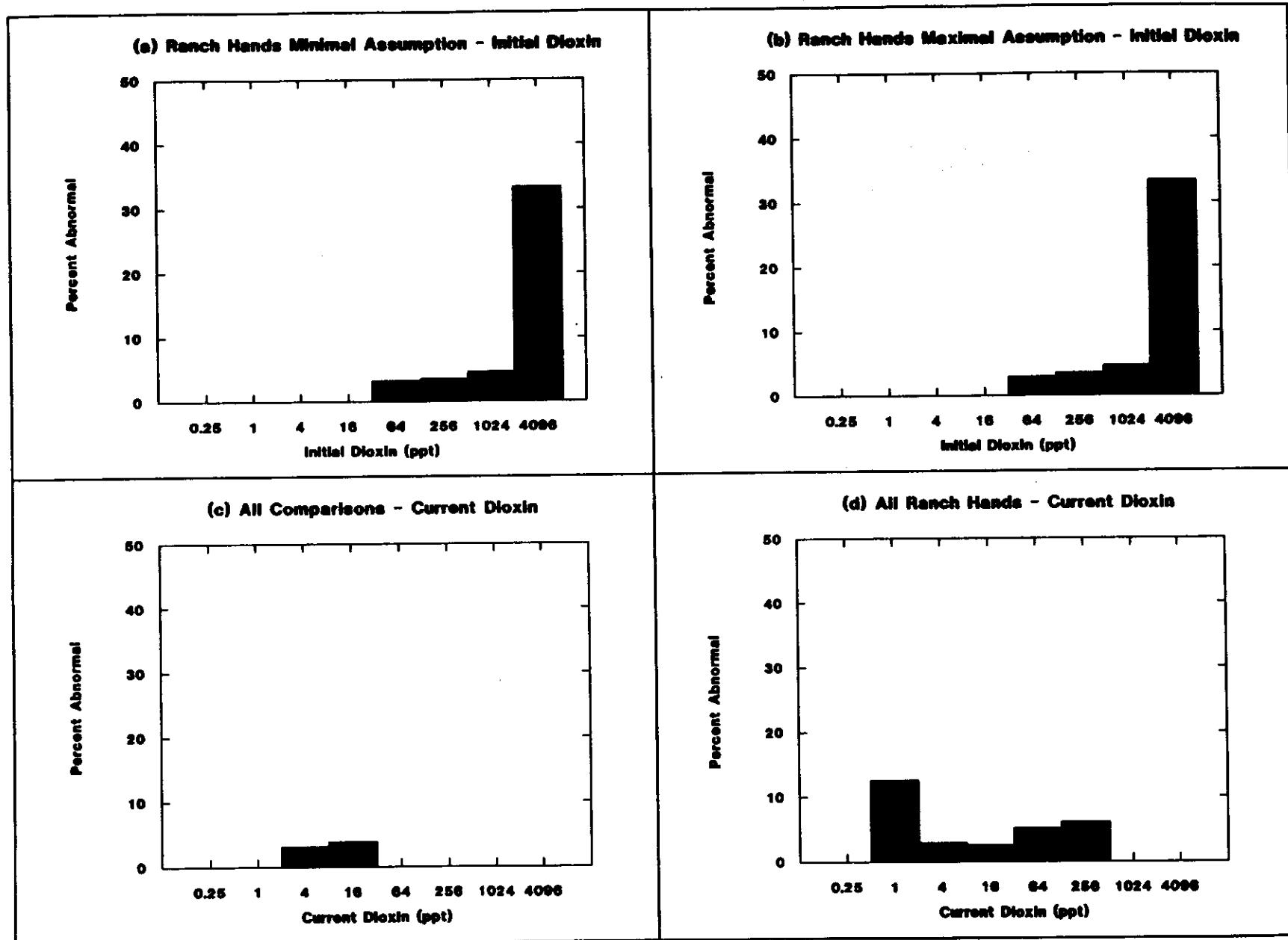
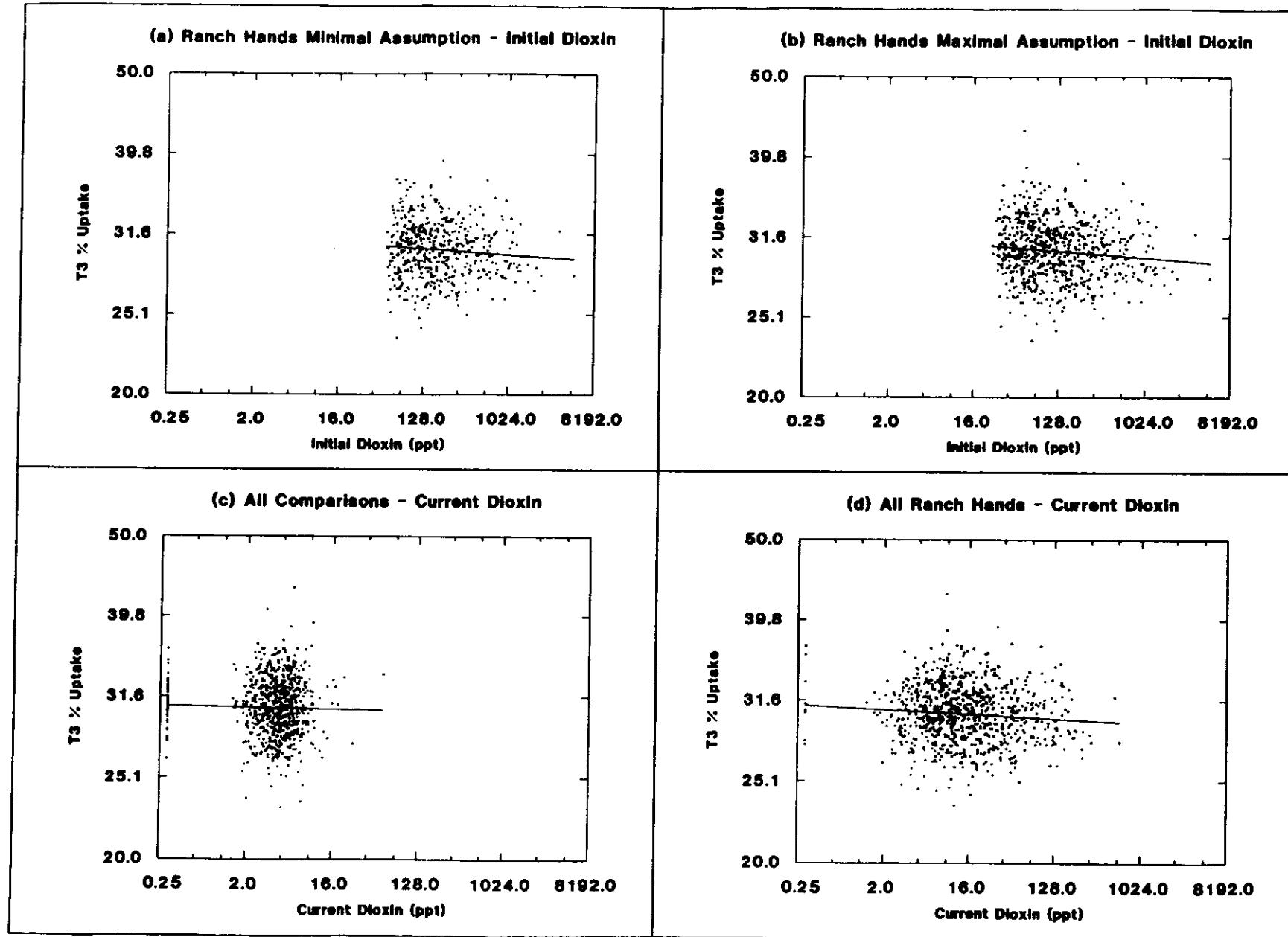
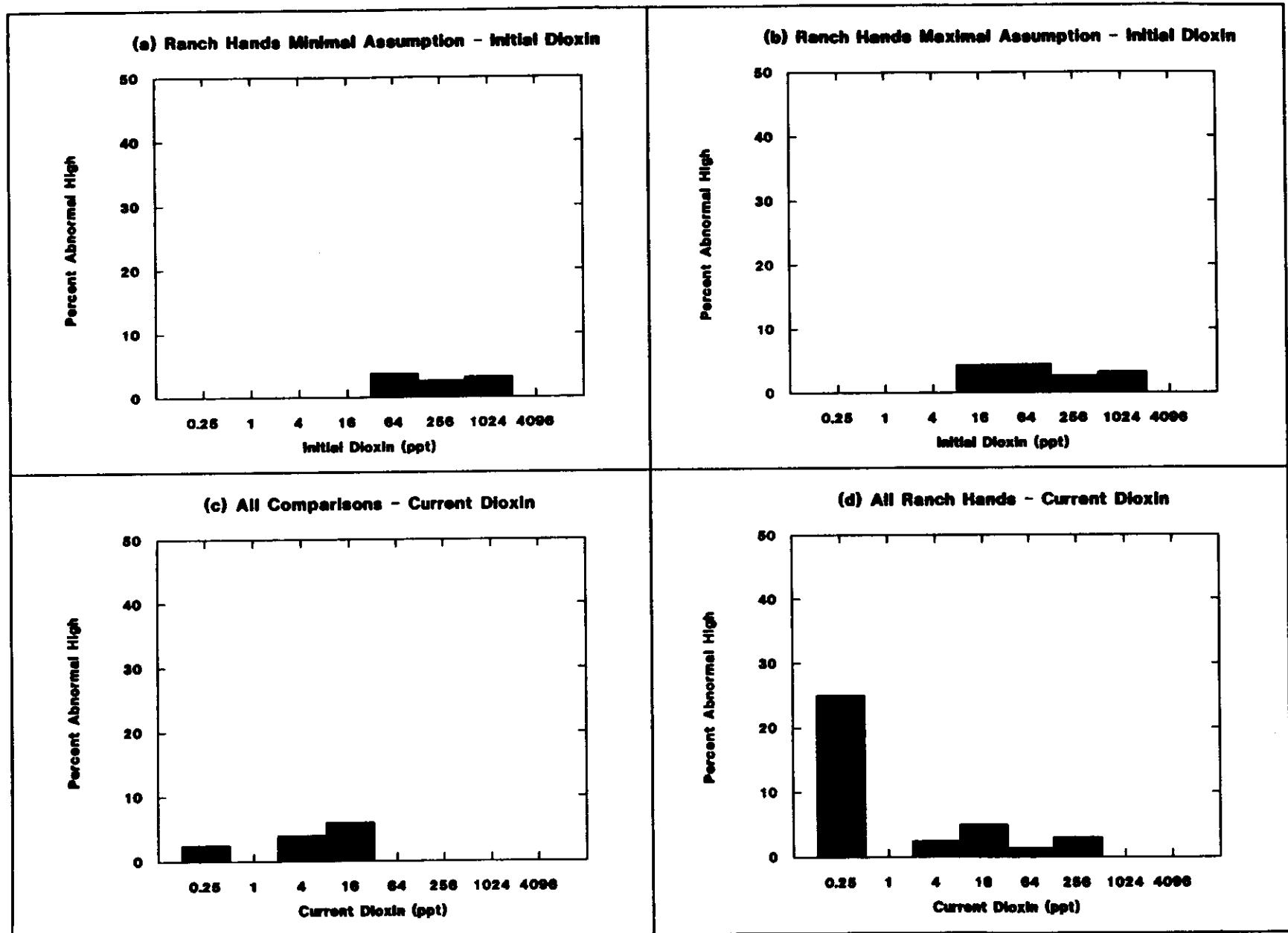


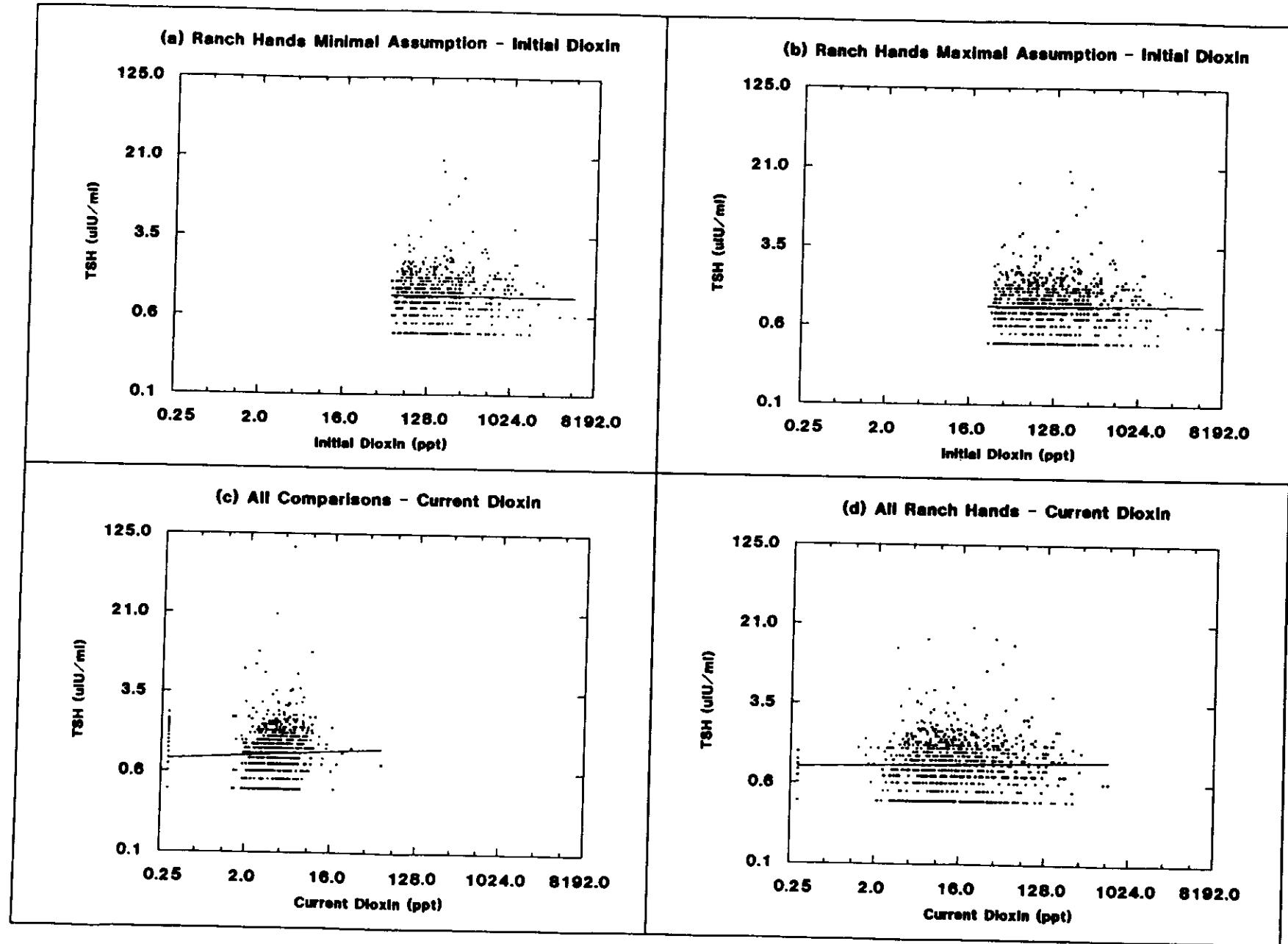
FIGURE N-1-4. Testes Gland versus Dioxin



**FIGURE N-1-5. T3 % Uptake (Continuous) versus Dioxin**

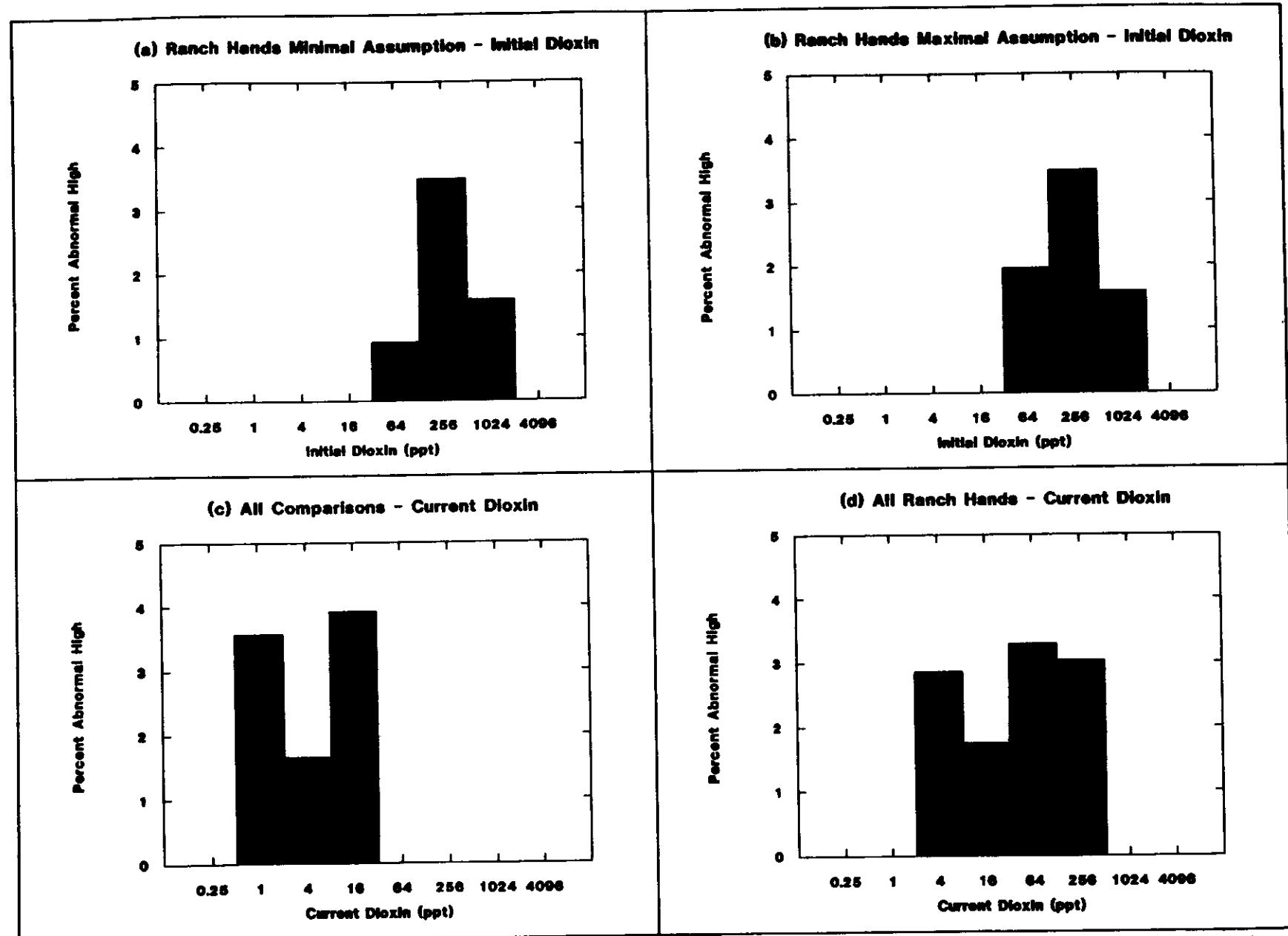


**FIGURE N-1-6. T<sub>3</sub> % Uptake (Discrete) versus Dioxin**



**FIGURE N-1-7. TSH (Continuous) versus Dioxin**

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**FIGURE N-1-8. TSH (Discrete) versus Dioxin**

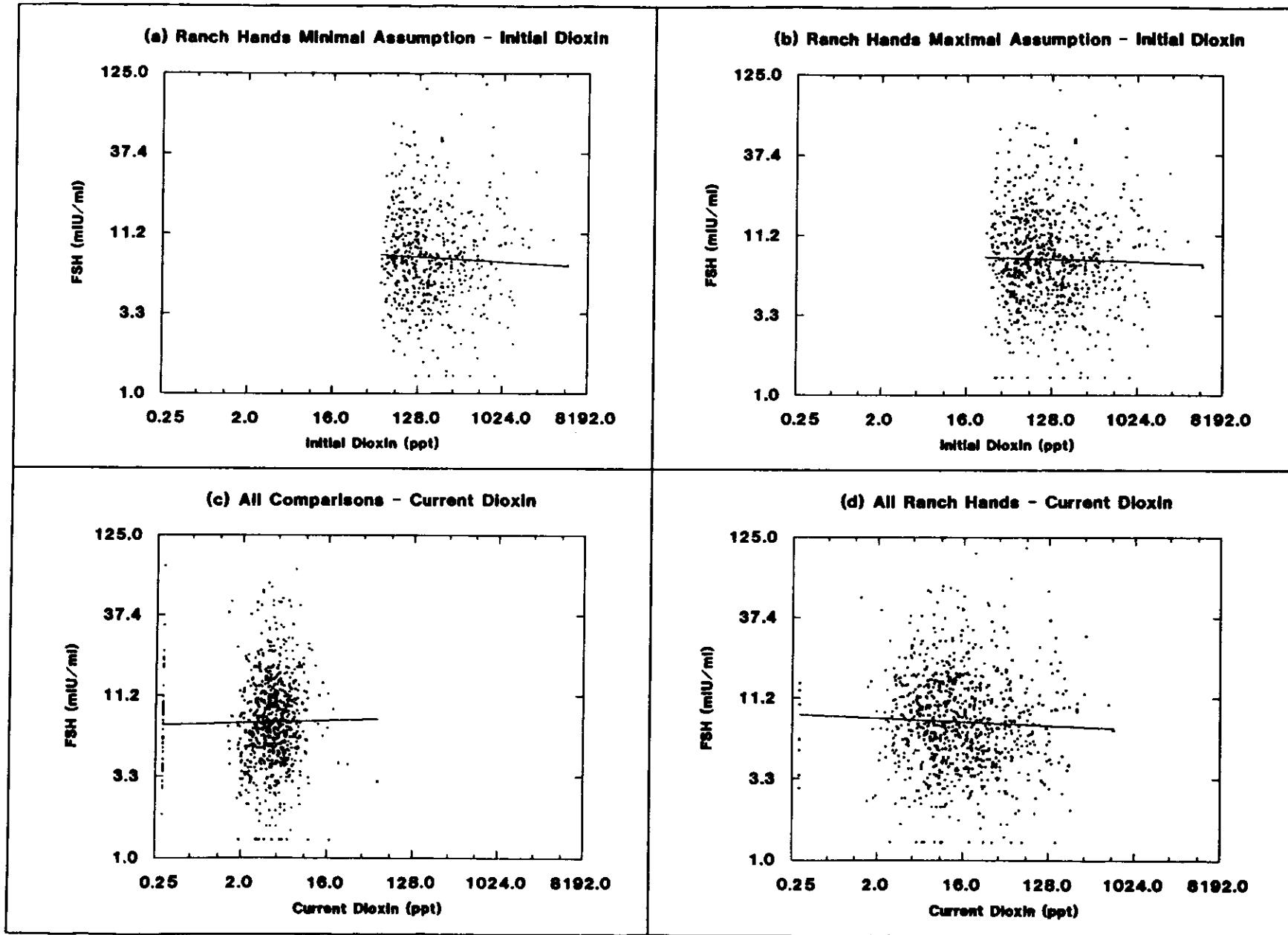


FIGURE N-1-9. FSH (Continuous) versus Dioxin

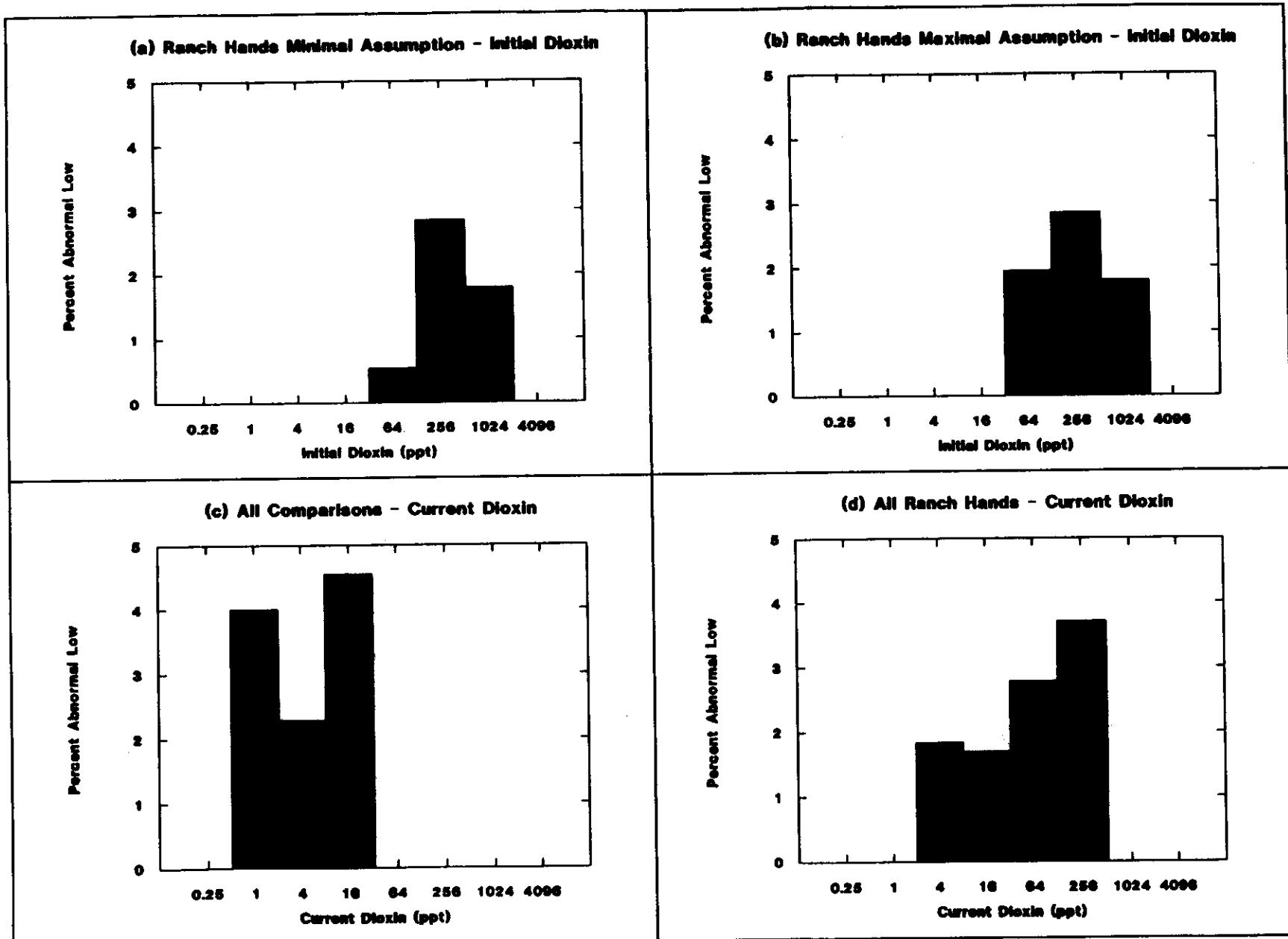


FIGURE N-1-10. FSH (Abnormal Low) versus Dioxin

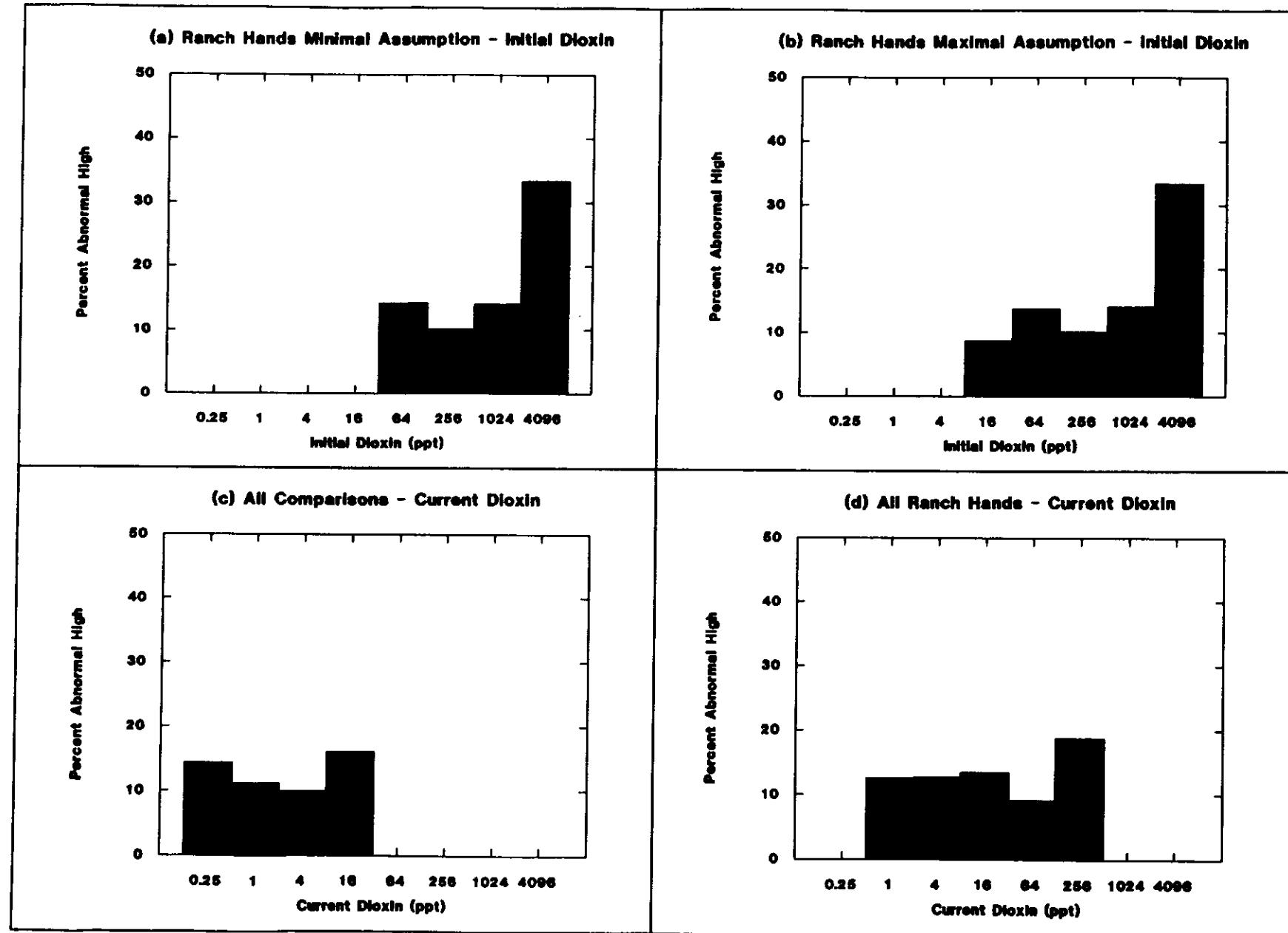
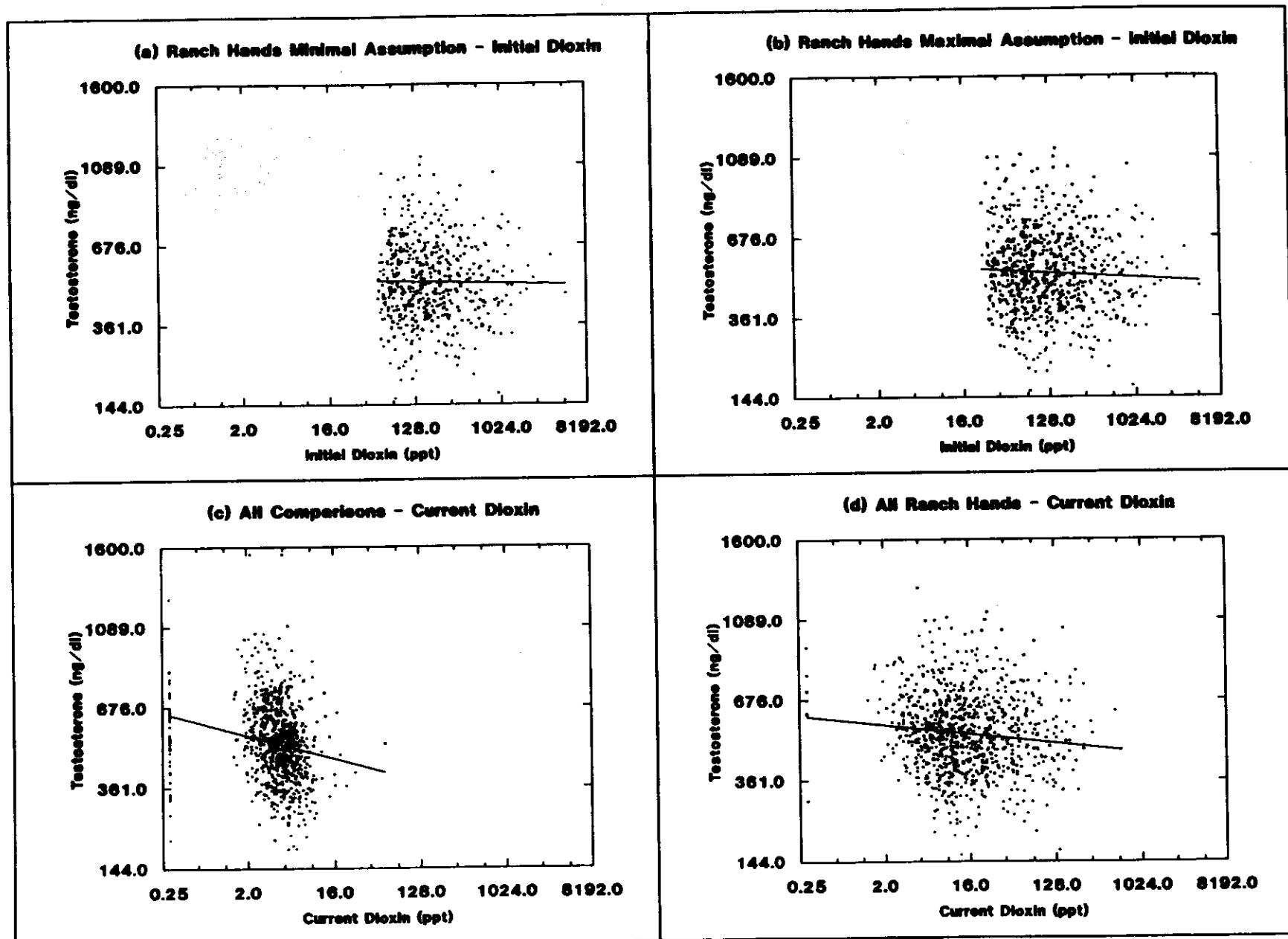
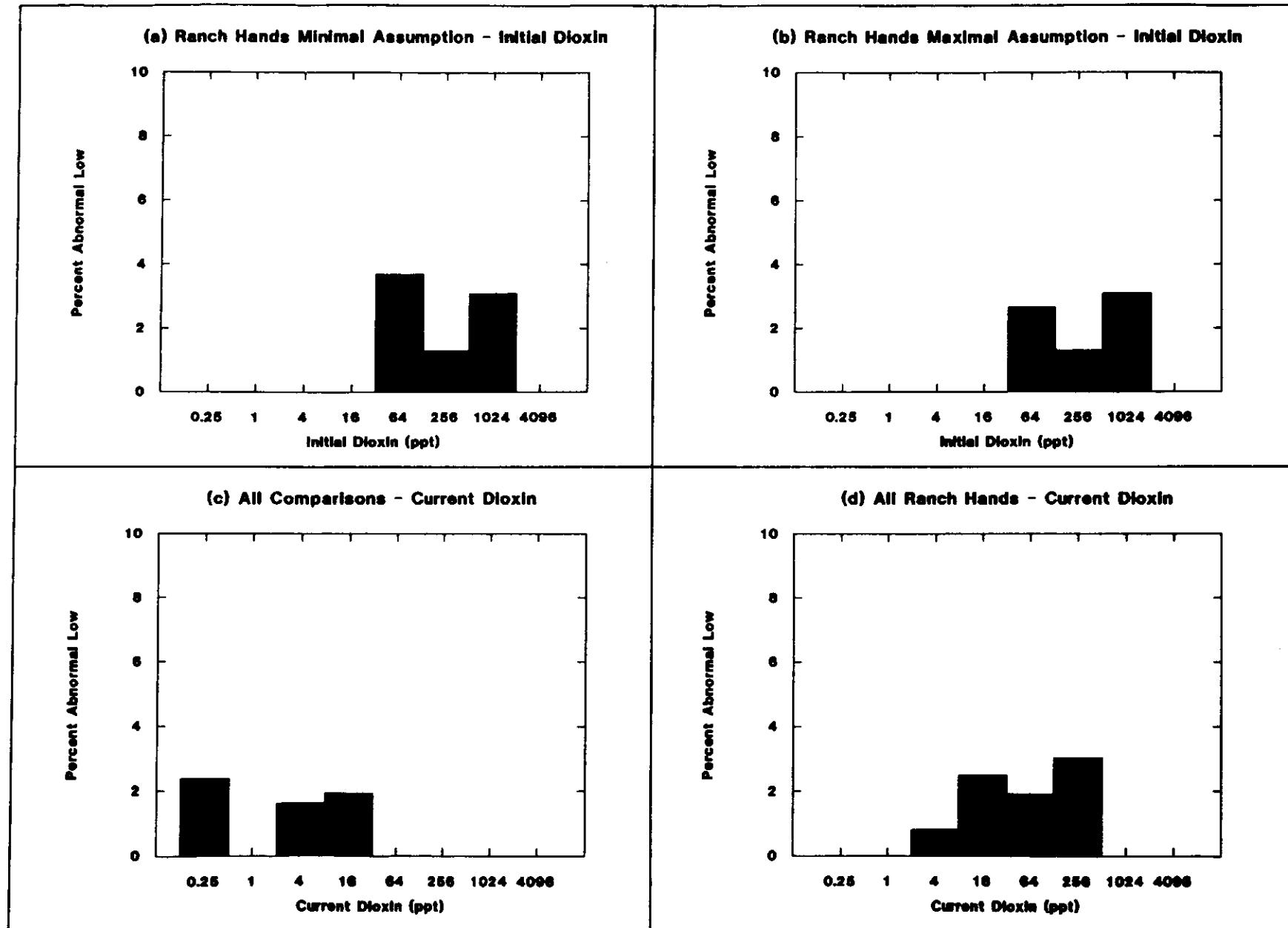


FIGURE N-1-11. FSH (Abnormal High) versus Dioxin



**FIGURE N-1-12. Testosterone (Continuous) versus Dioxin**



**FIGURE N-1-13. Testosterone (Discrete) versus Dioxin**

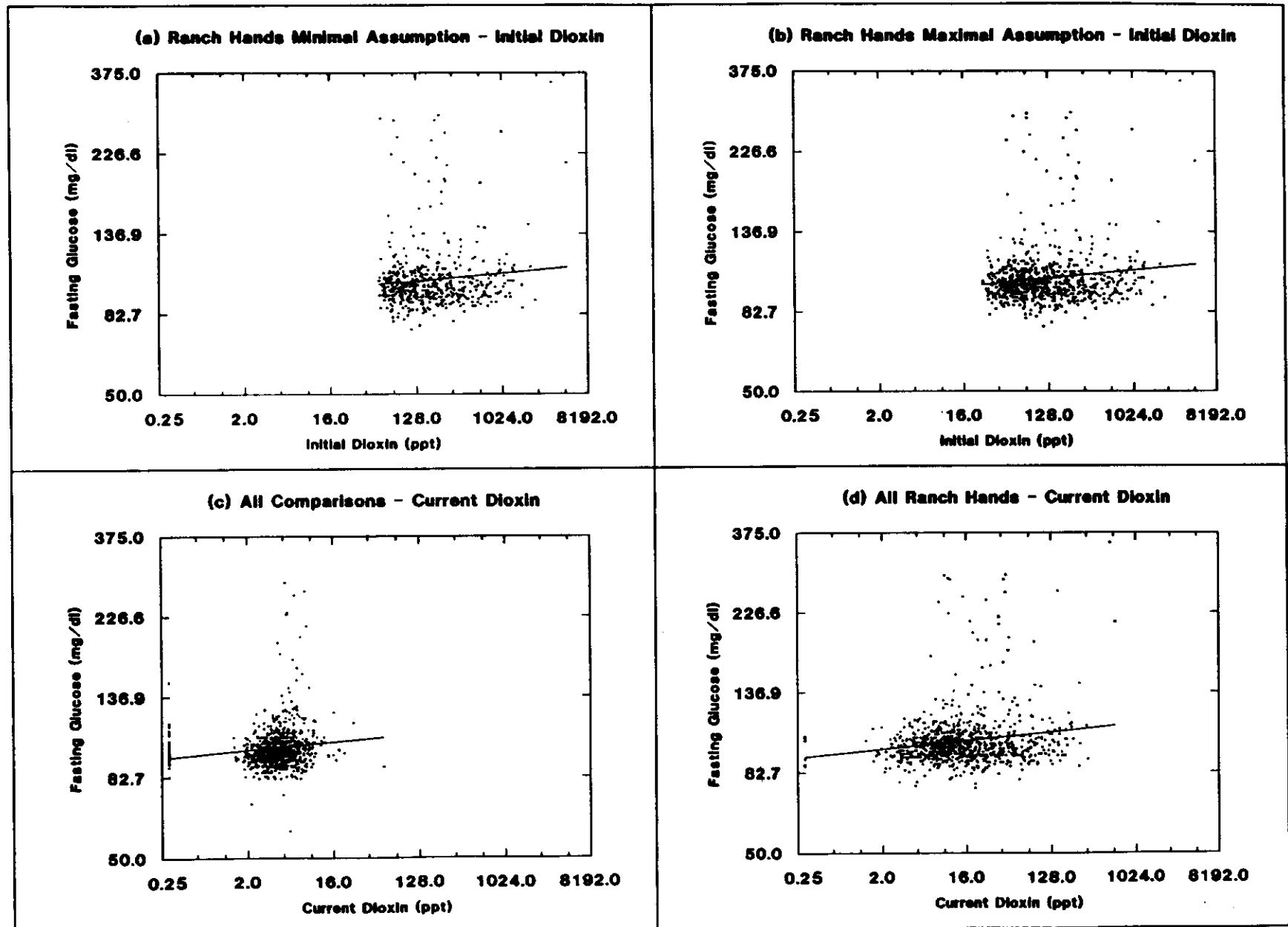
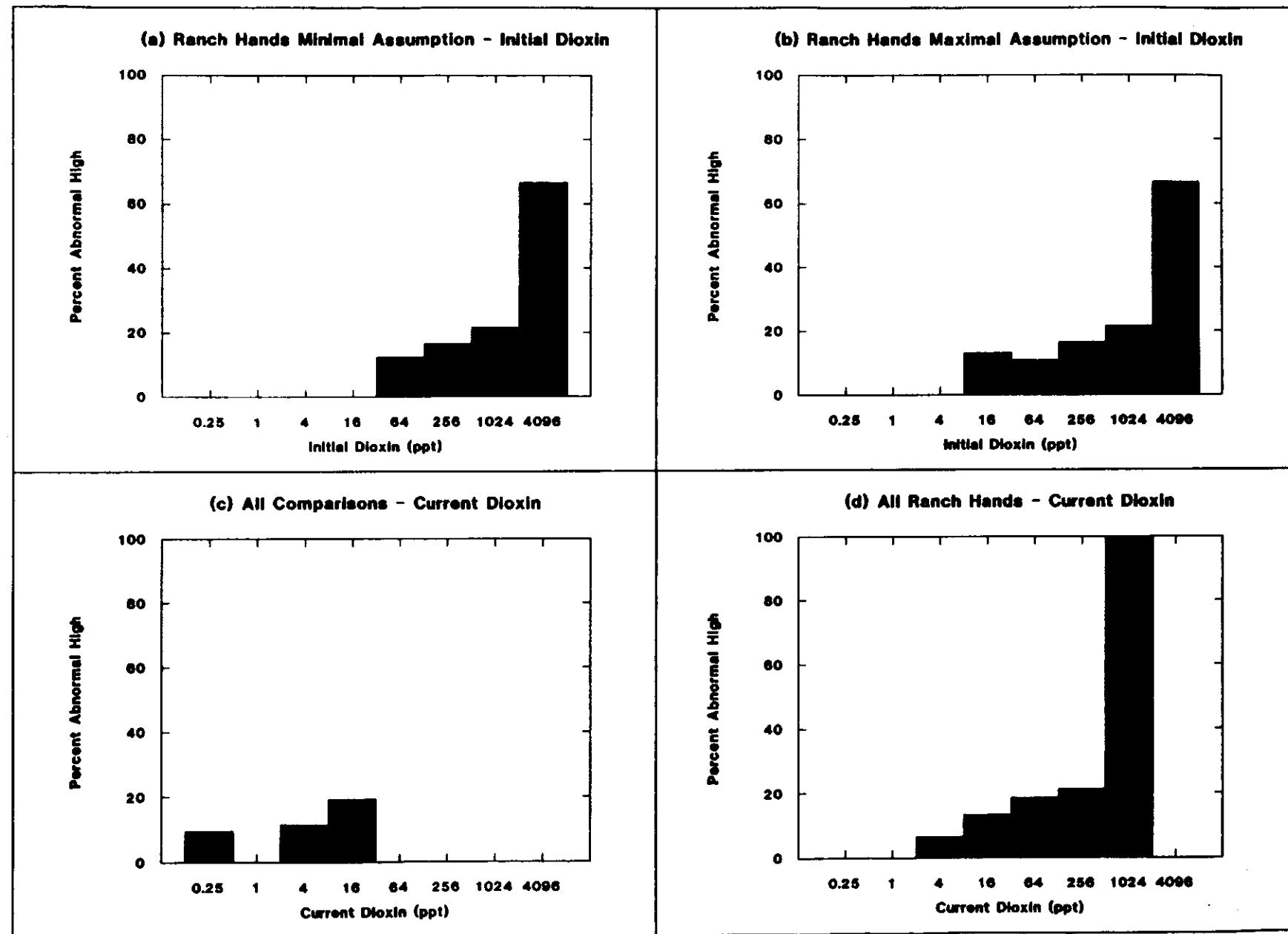
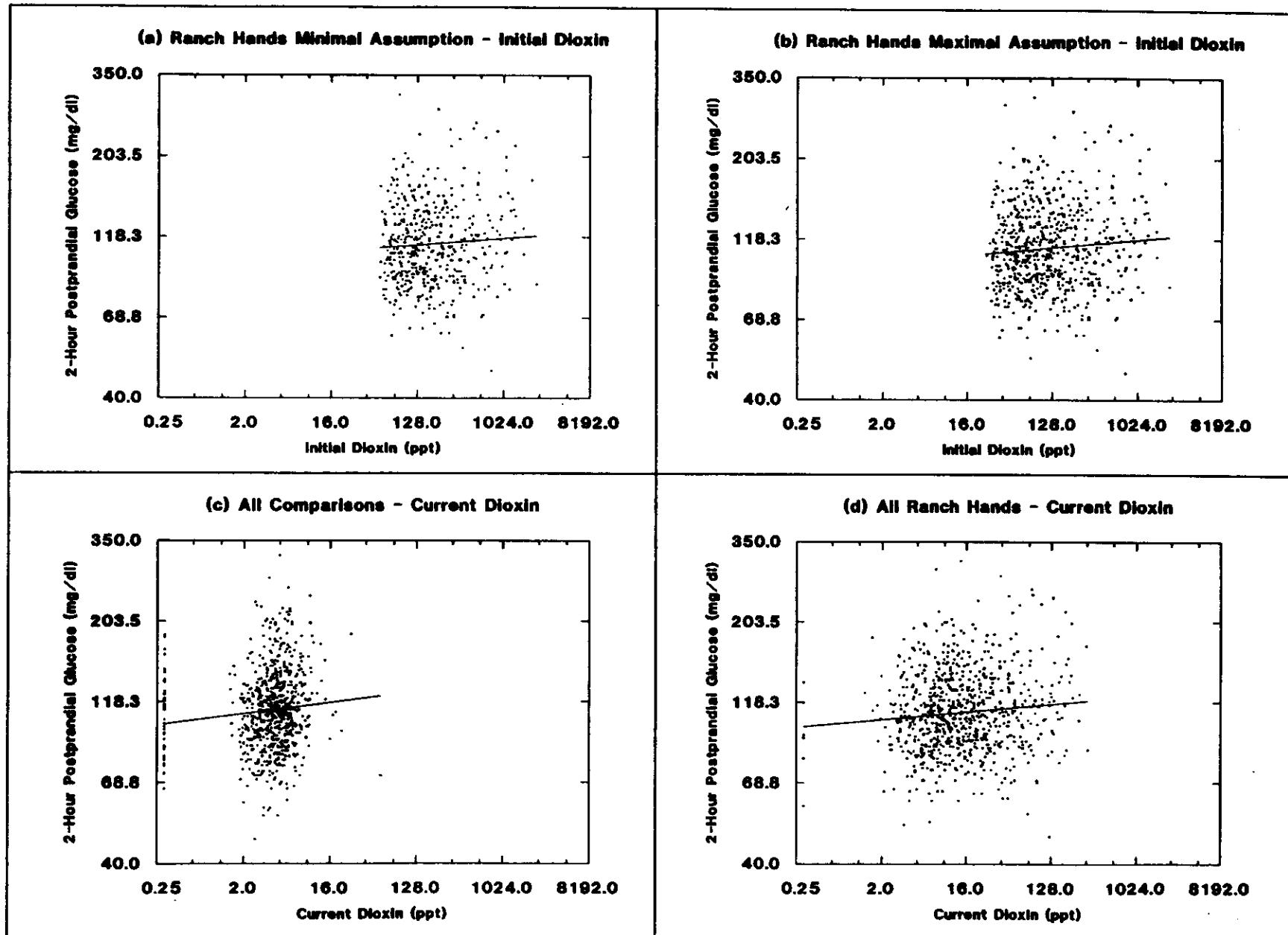


FIGURE N-1-14. Fasting Glucose (Continuous) versus Dioxin



**FIGURE N-1-15. Fasting Glucose (Discrete) versus Dioxin**



**FIGURE N-1-16. 2-Hour Postprandial Glucose (Continuous) versus Dioxin**

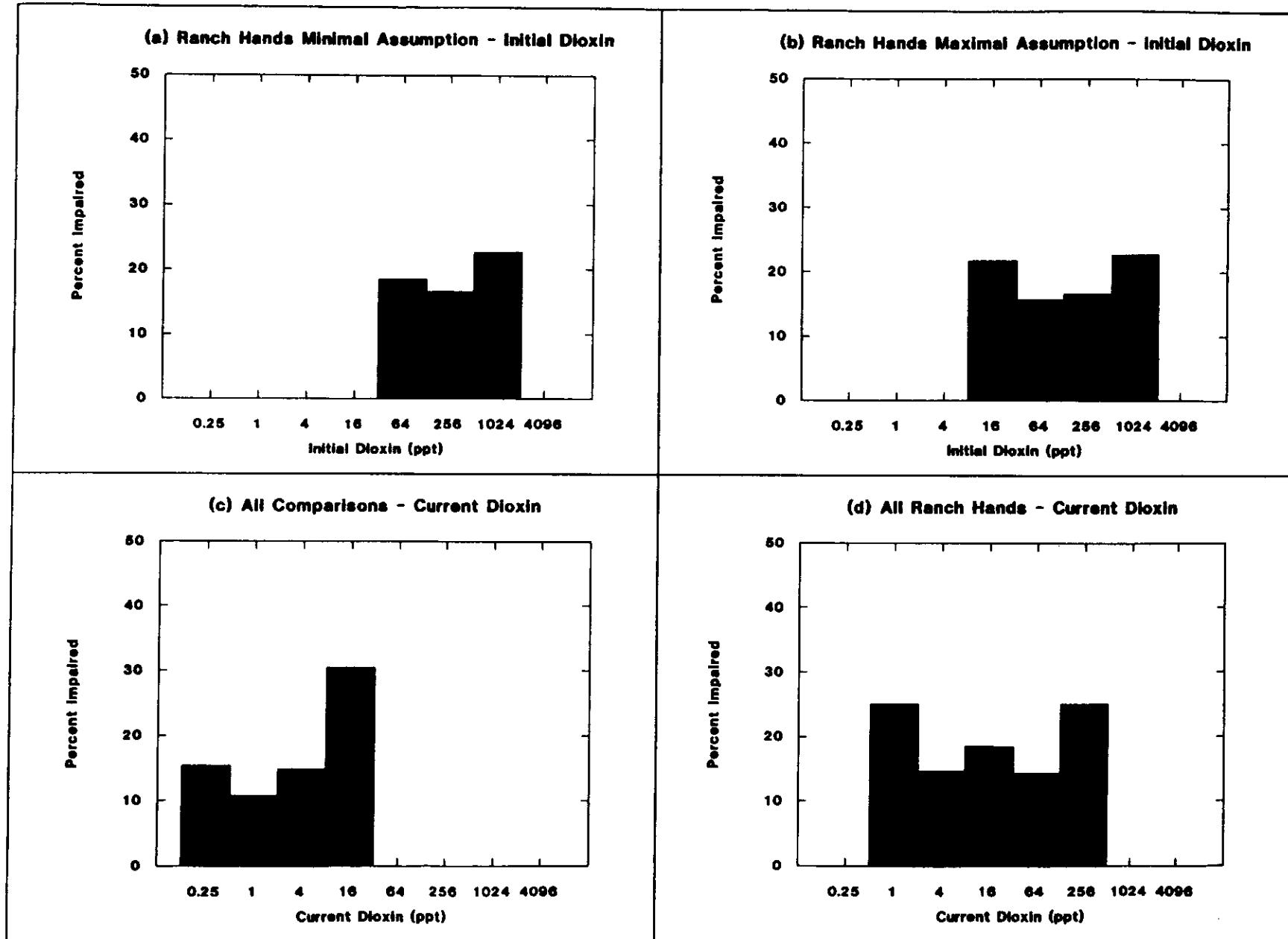


FIGURE N-1-17. 2-Hour Postprandial Glucose (Impaired) versus Dioxin

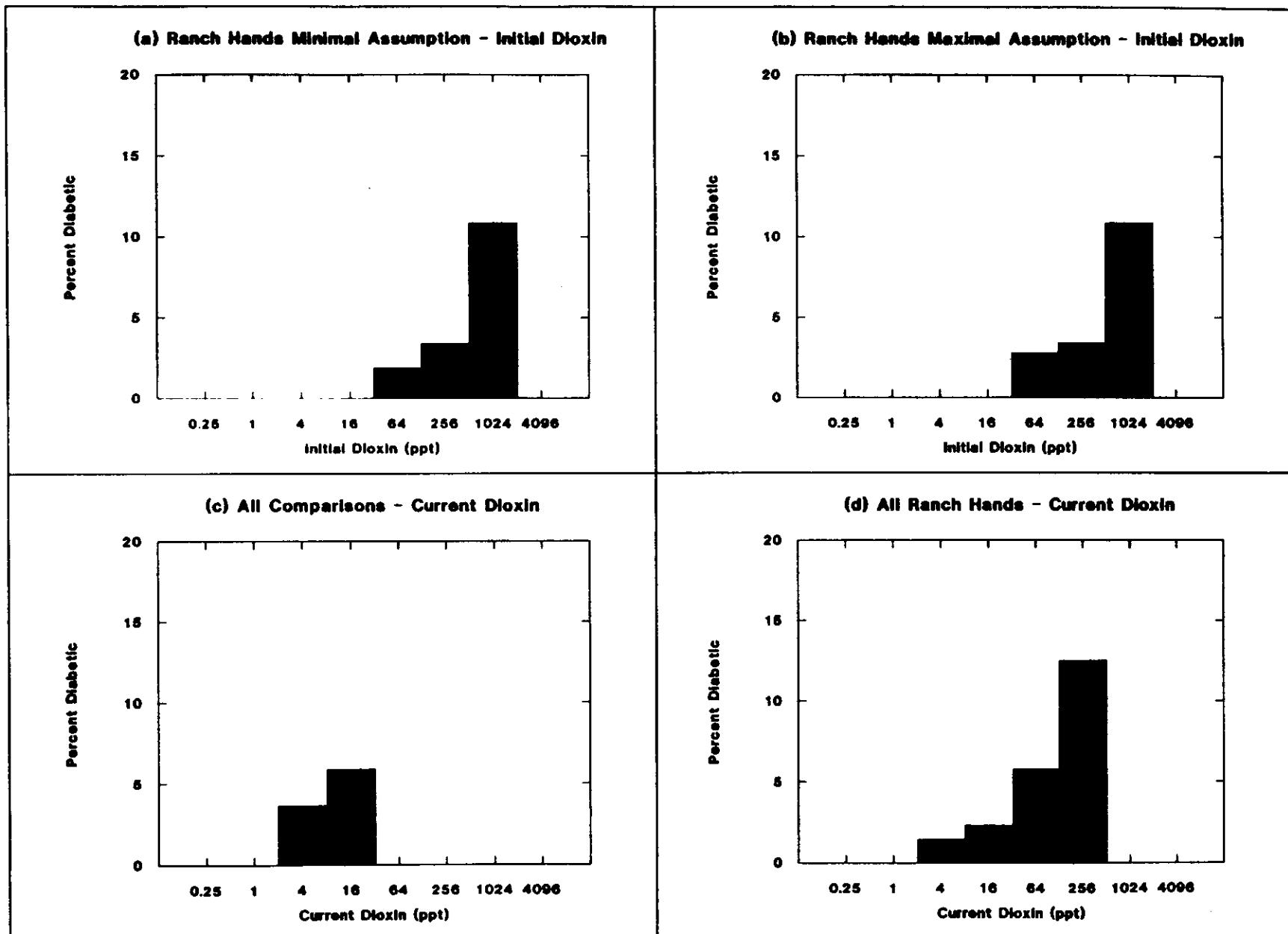


FIGURE N-1-18. 2-Hour Postprandial Glucose (Diabetic) versus Dioxin

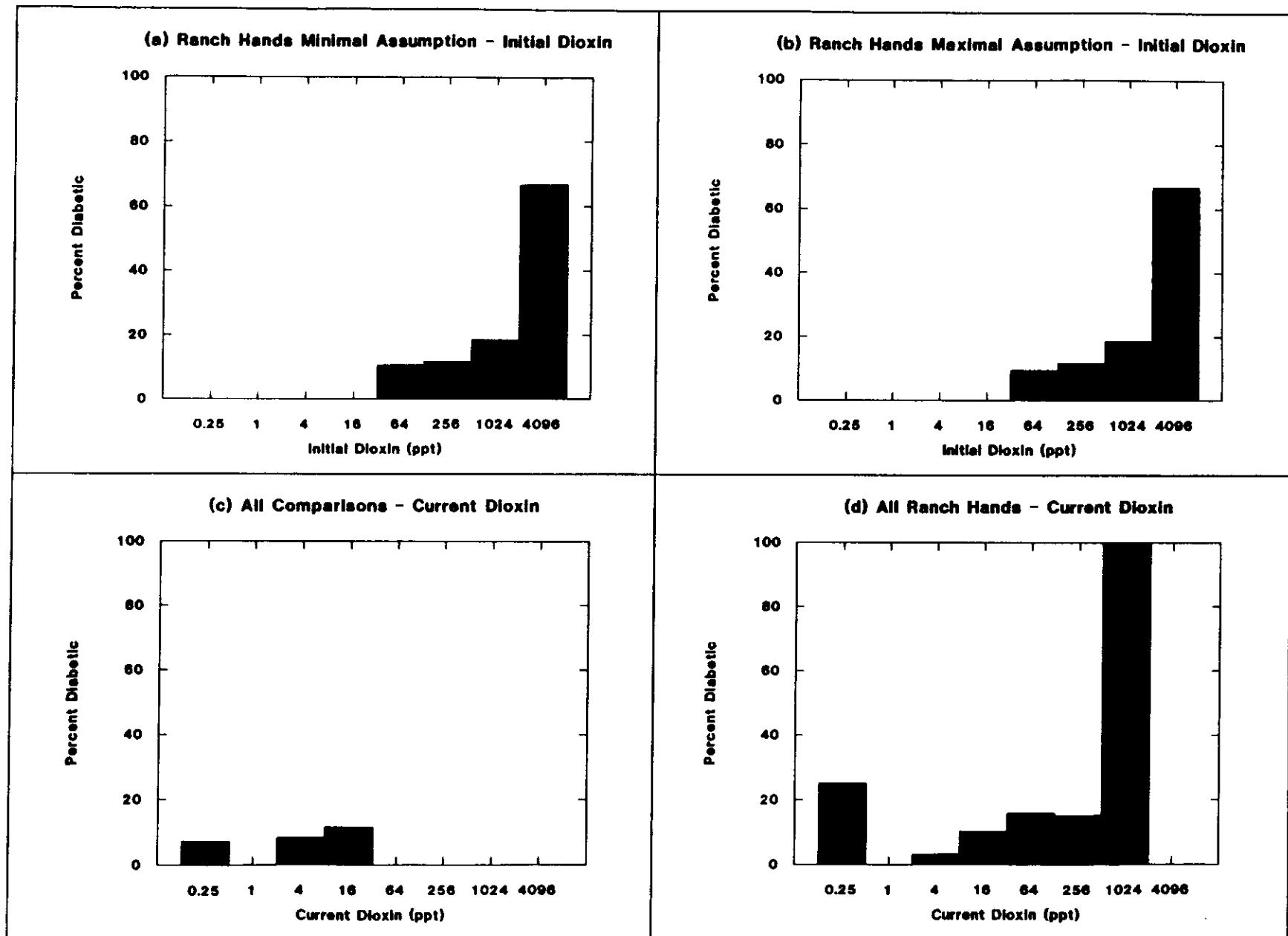


FIGURE N-1-19. Composite Diabetes Indicator versus Dioxin

## APPENDIX N-2.

### Interaction Displays for the Endocrine Assessment

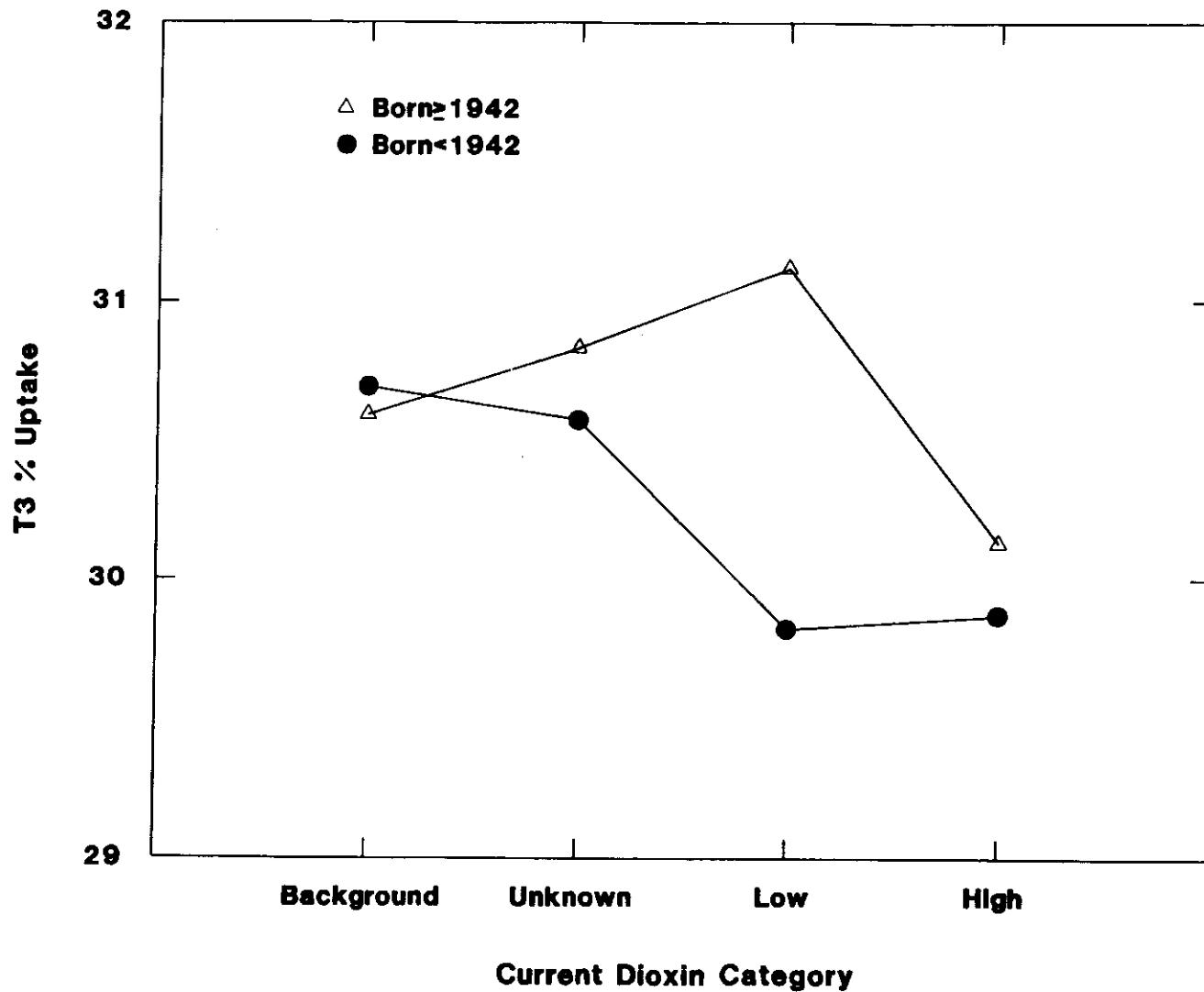
The following figures graphically display dioxin-by-covariate interactions found in the statistical analyses of the dependent variables in the endocrine assessment. For interactions with initial dioxin in the Ranch Hands involving continuous dependent variables, bivariate plots are presented with observations in each stratum represented by different symbols. Initial dioxin is shown in original units (ppt) but spacing of intervals is based on the logarithm (base 2) scale. The dependent variable is also displayed in original units but spacing is based on the scale used for analysis, as described in the chapter. The reference lines indicate the general relationship, unadjusted for any covariates, between the (transform of the) dependent variable and log<sub>2</sub> (initial dioxin). For each stratum, the lines span the range of initial dioxin.

In the Ranch Hands, for current dioxin-by-time-by-covariate interactions with continuous dependent variables, separate bivariate plots (dependent variable versus current dioxin) are presented for each stratum of the covariate. Different symbols represent late tours (time since tour≤18.6 years) and early tours (time since tour>18.6 years) within each plot. The spacing for current dioxin and the dependent variable follows the same conventions as described above, as do the reference lines. For current dioxin-by-time-by-covariate interactions in the Ranch Hands with discrete dependent variables, a stratum-specific percentage of participants that exhibited an abnormal condition is displayed for low, medium, and high current dioxin. Different designs represent separate time since tour categories, and covariate strata are given on separate panels. Appendix Table N-1 provides the sample sizes for each bar on the graph.

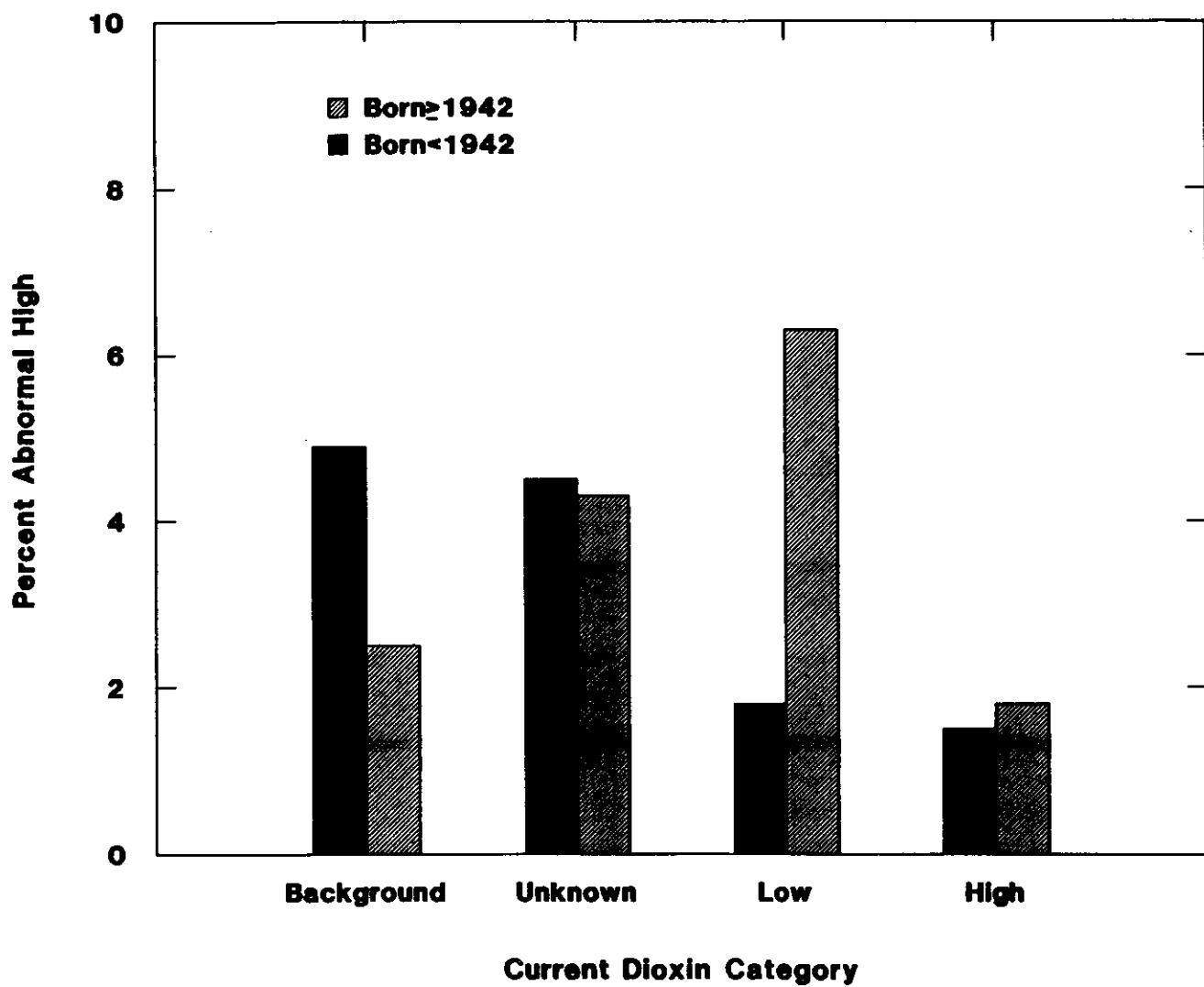
For covariate interactions with current dioxin categorized within the Ranch Hand and Comparison groups involving continuous dependent variables, adjusted means for the background category in the Comparisons, and the unknown, low, and high categories in the Ranch Hands, are shown. Appendix Table N-1 presents the definition of these categories and the sample sizes for each mean. Different symbols distinguish the covariate categories and solid line segments connect the means to display a profile of the adjusted means. For covariate interactions with current dioxin categorized within the Ranch Hand and Comparison groups involving discrete dependent variables, bars representing the percentage of participants that exhibited an abnormal condition are displayed for each of the four current dioxin categories. Different designs represent covariate categories.

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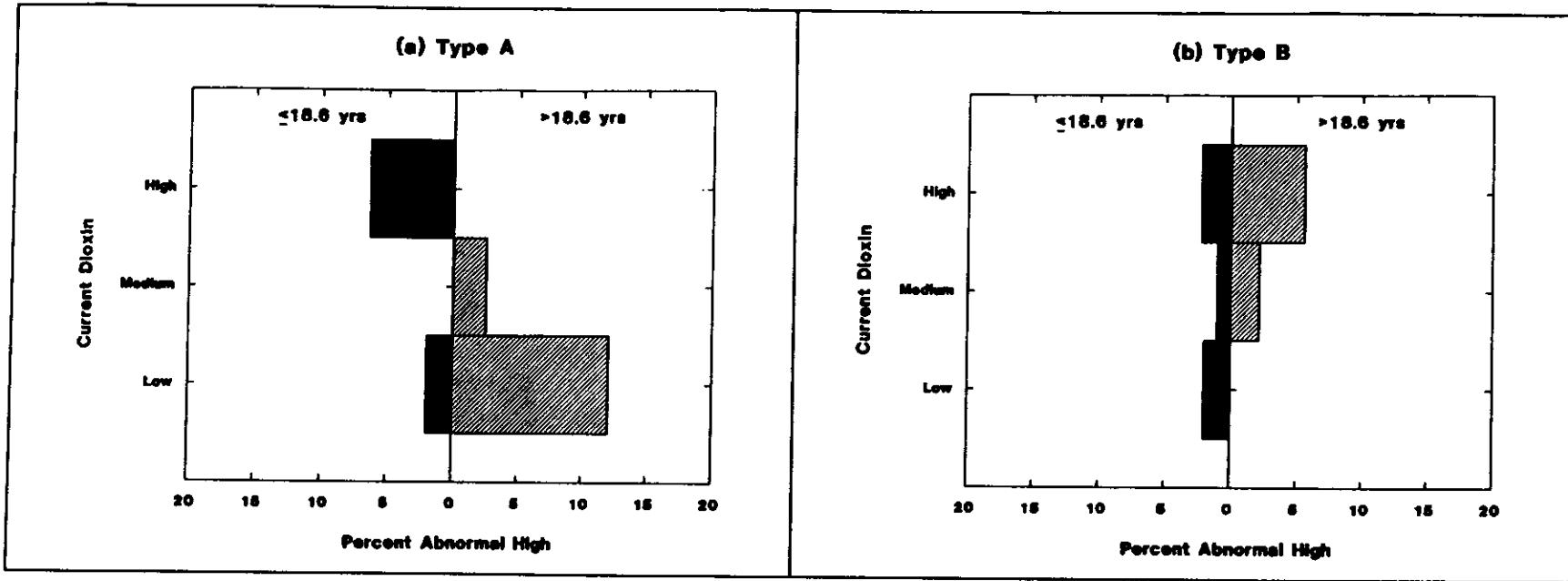
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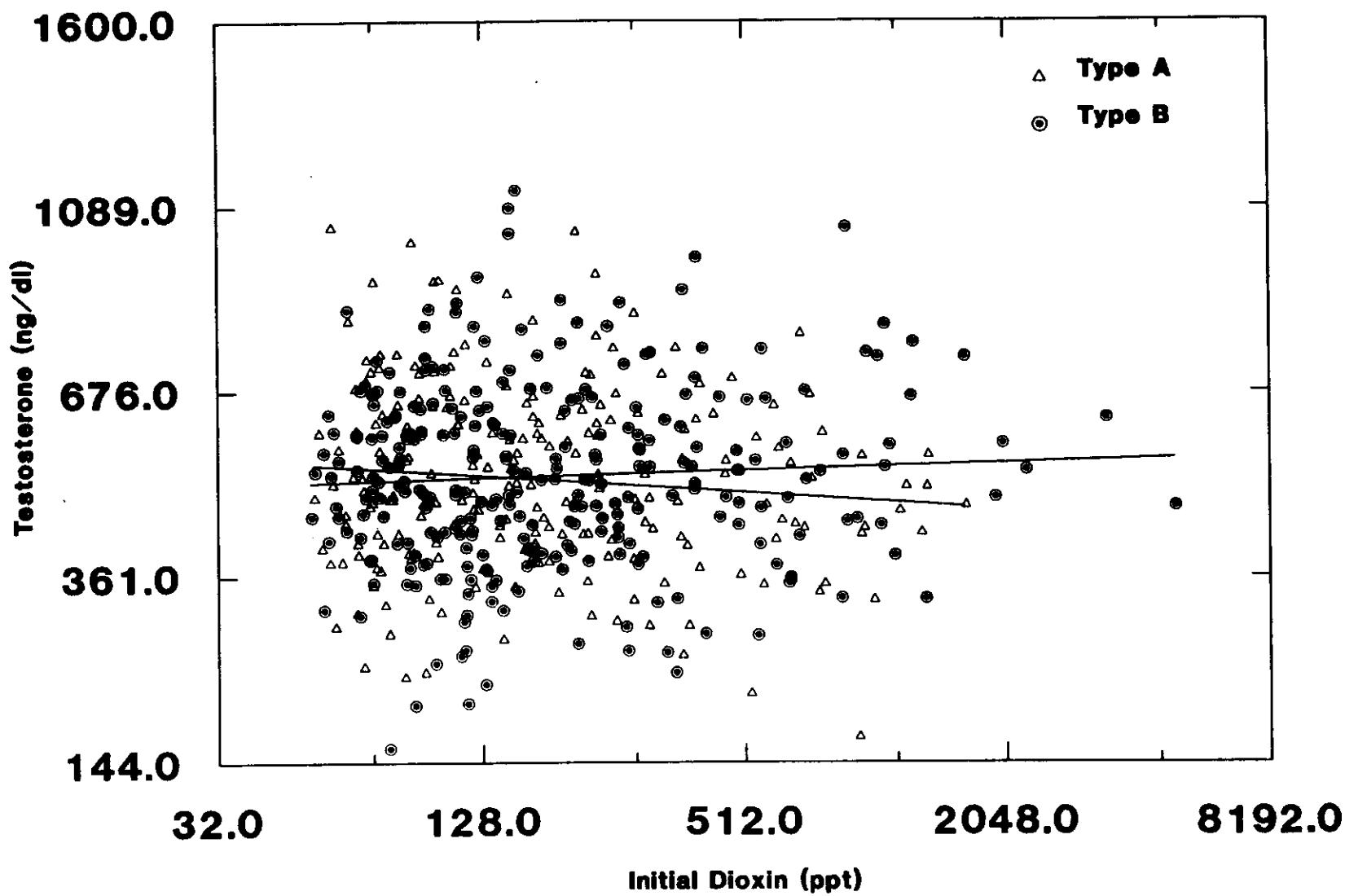
**FIGURE N-2-1. Interaction of Categorized Current Dioxin and Age for T3 % Uptake (Continuous)**



**FIGURE N-2-2. Interaction of Categorized Current Dioxin and Age for T3 % Uptake (Discrete)**

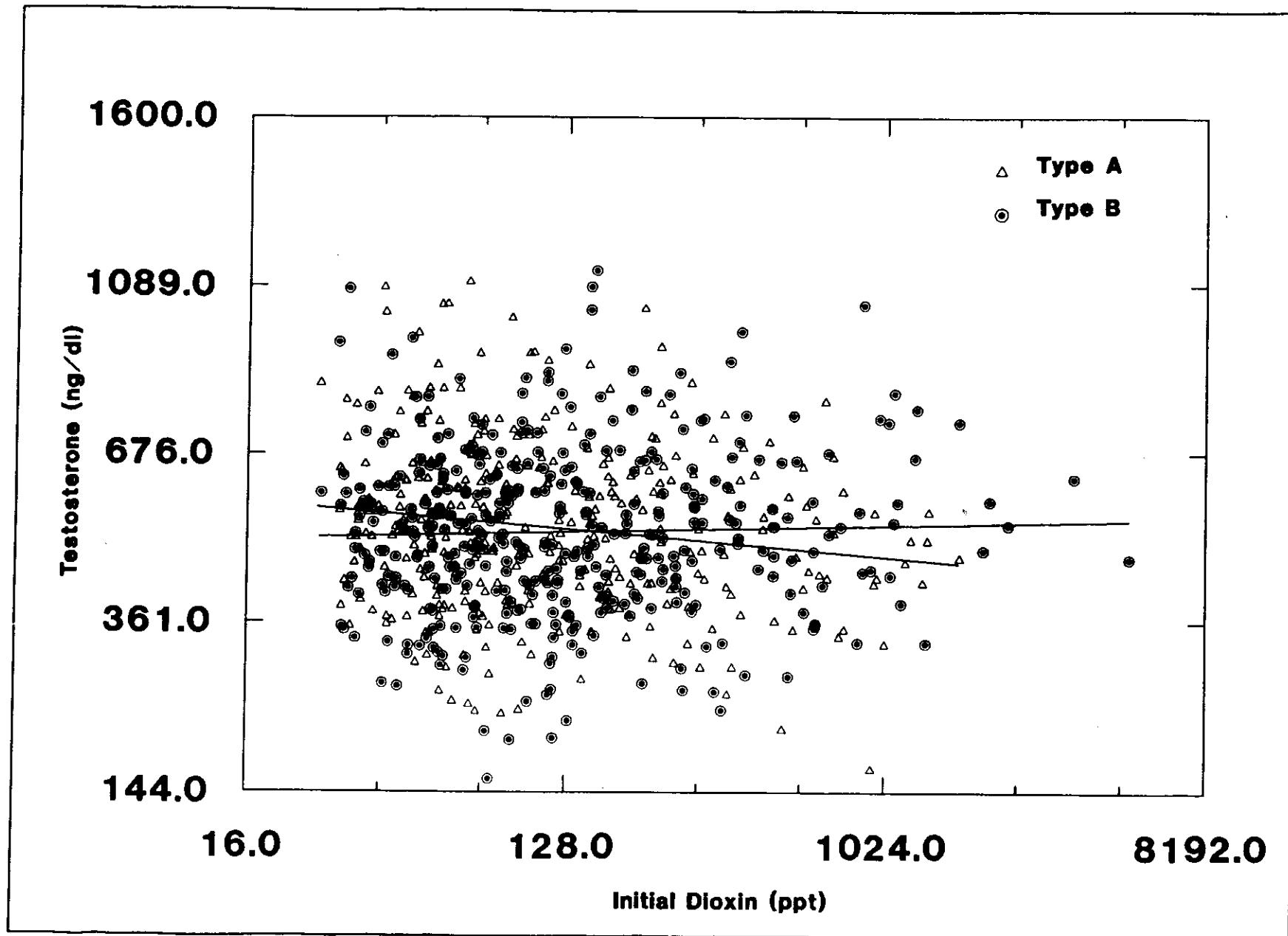


**FIGURE N-2-3. Interaction of Current Dioxin, Time, and Personality Type  
for TSH (Discrete - Ranch Hands, Maximal Assumption)**

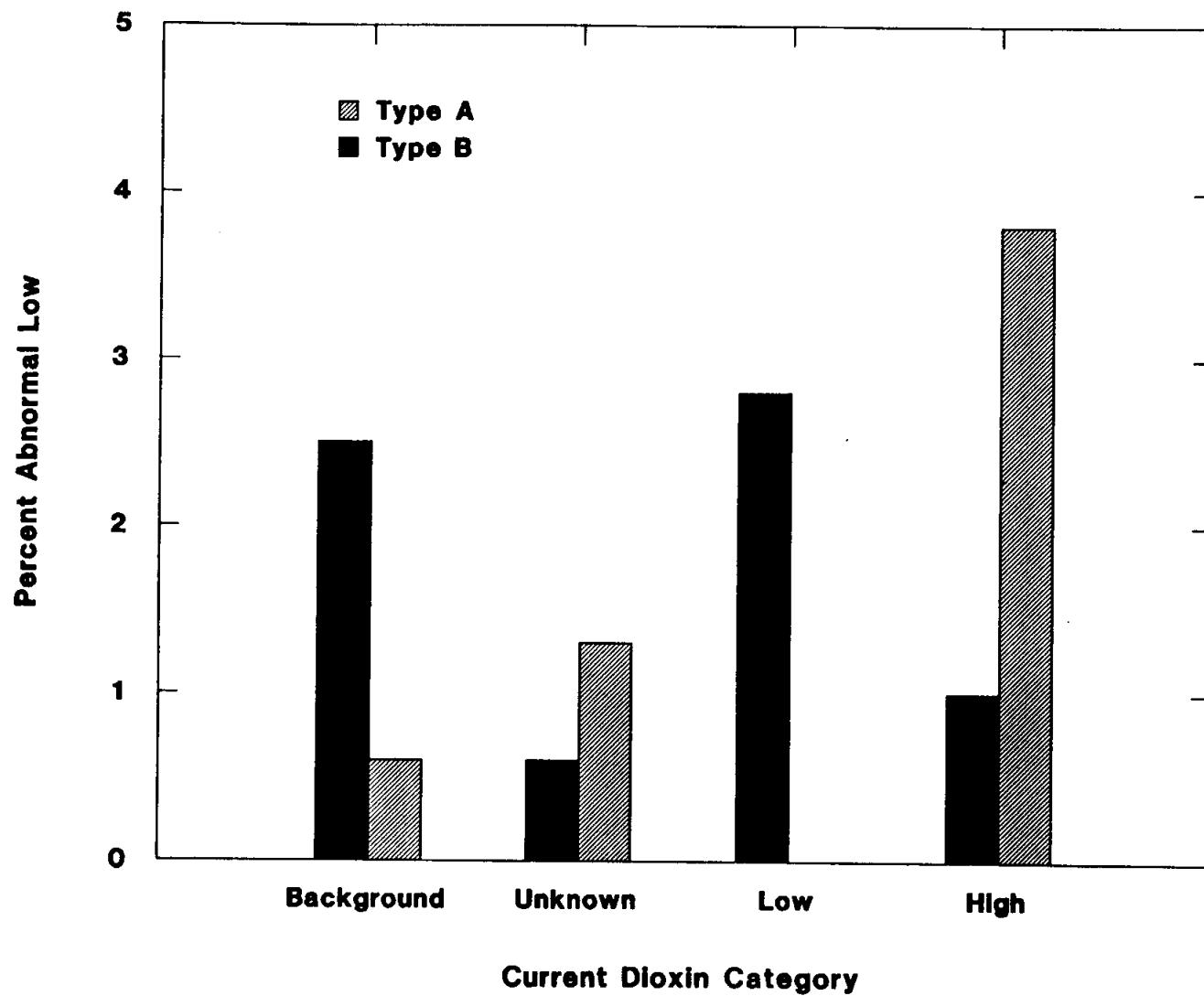


**FIGURE N-2-4. Interaction of Initial Dioxin and Personality Type for Testosterone  
(Continuous - Ranch Hands, Minimal Assumption)**

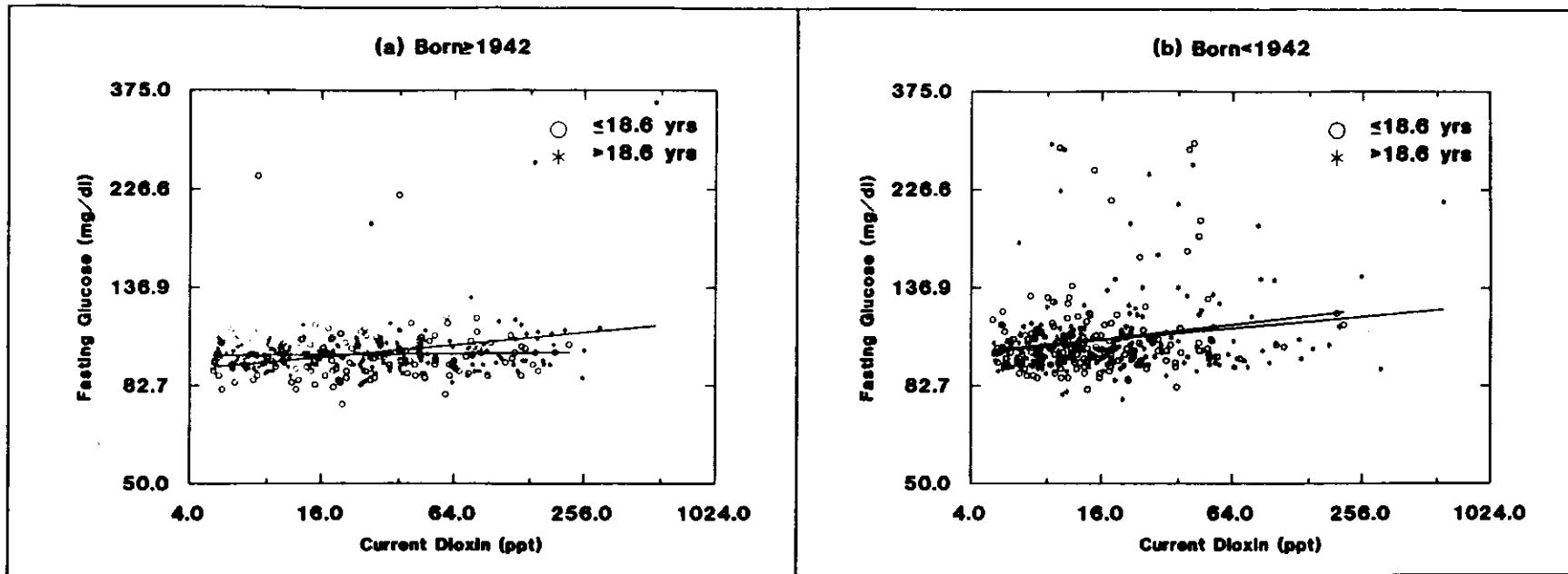
N-2-7



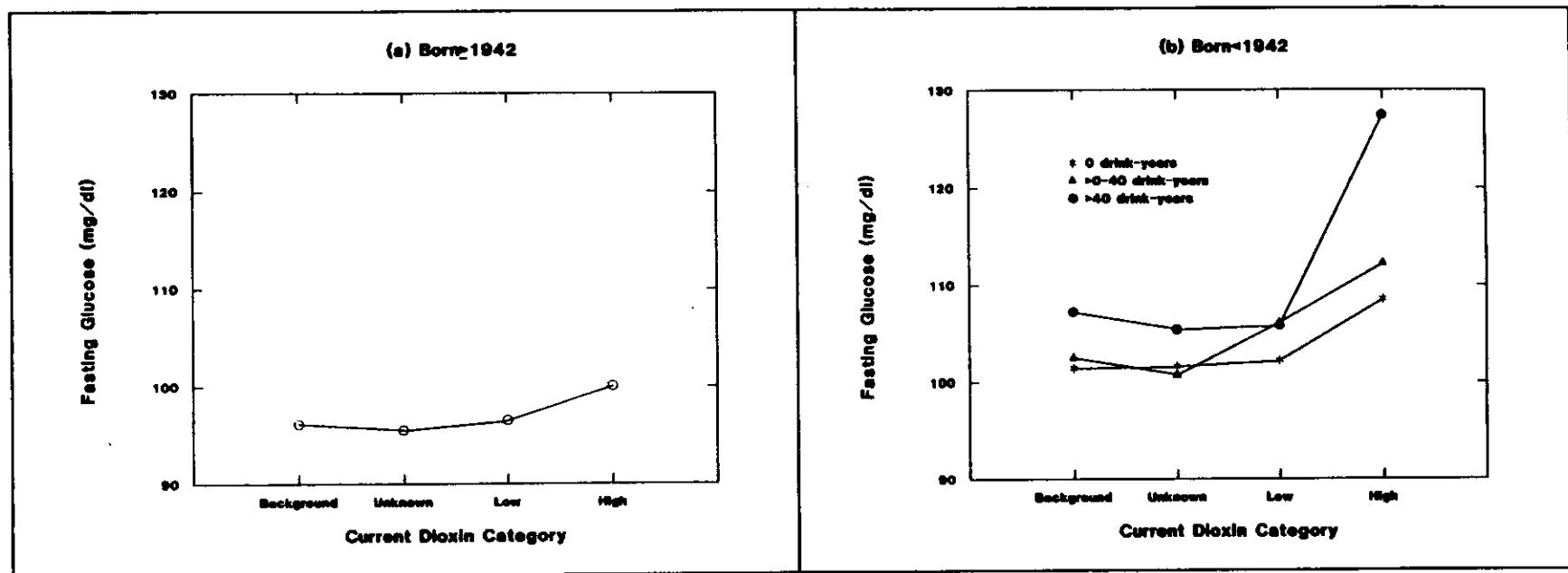
**FIGURE N-2-5. Interaction of Initial Dioxin and Personality Type for Testosterone  
(Continuous - Ranch Hands, Maximal Assumption)**



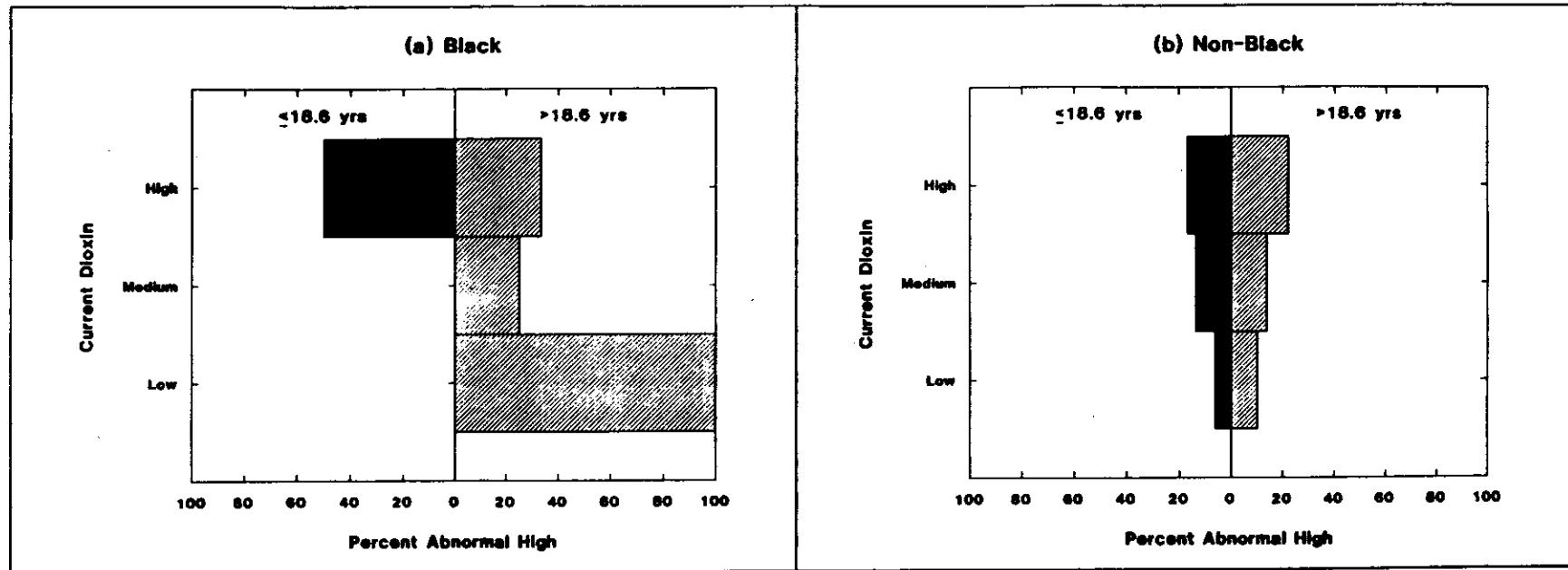
**FIGURE N-2-6. Interaction of Categorized Current Dioxin and Personality Type for Testosterone (Discrete)**



**FIGURE N-2-7. Interaction of Current Dioxin, Time, and Age for Fasting Glucose  
(Continuous - Ranch Hands, Maximal Assumption)**

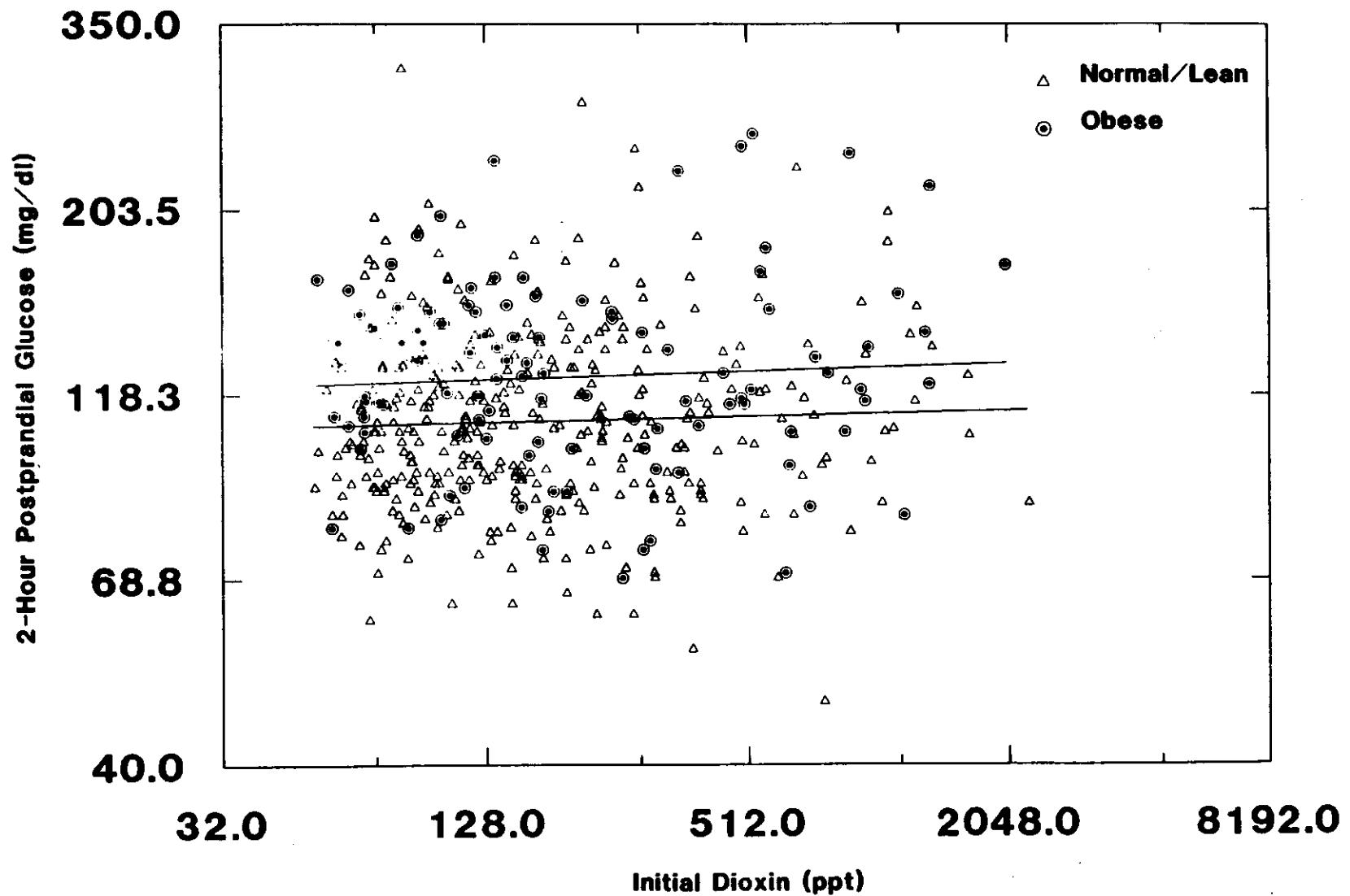


**FIGURE N-2-8. Interaction of Categorized Current Dioxin, Age, and Lifetime Alcohol History for Fasting Glucose (Continuous)**

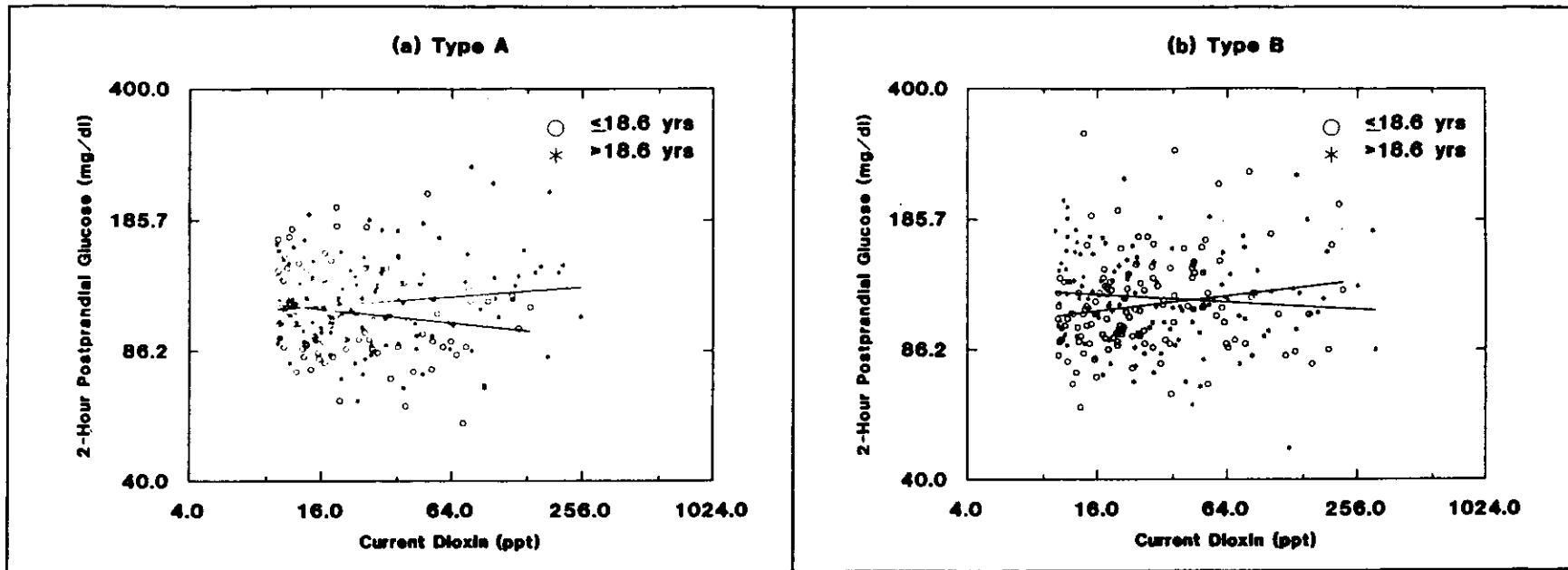


**FIGURE N-2-9. Interaction of Current Dioxin, Time, and Race for Fasting Glucose (Discrete - Ranch Hands, Maximal Assumption)**

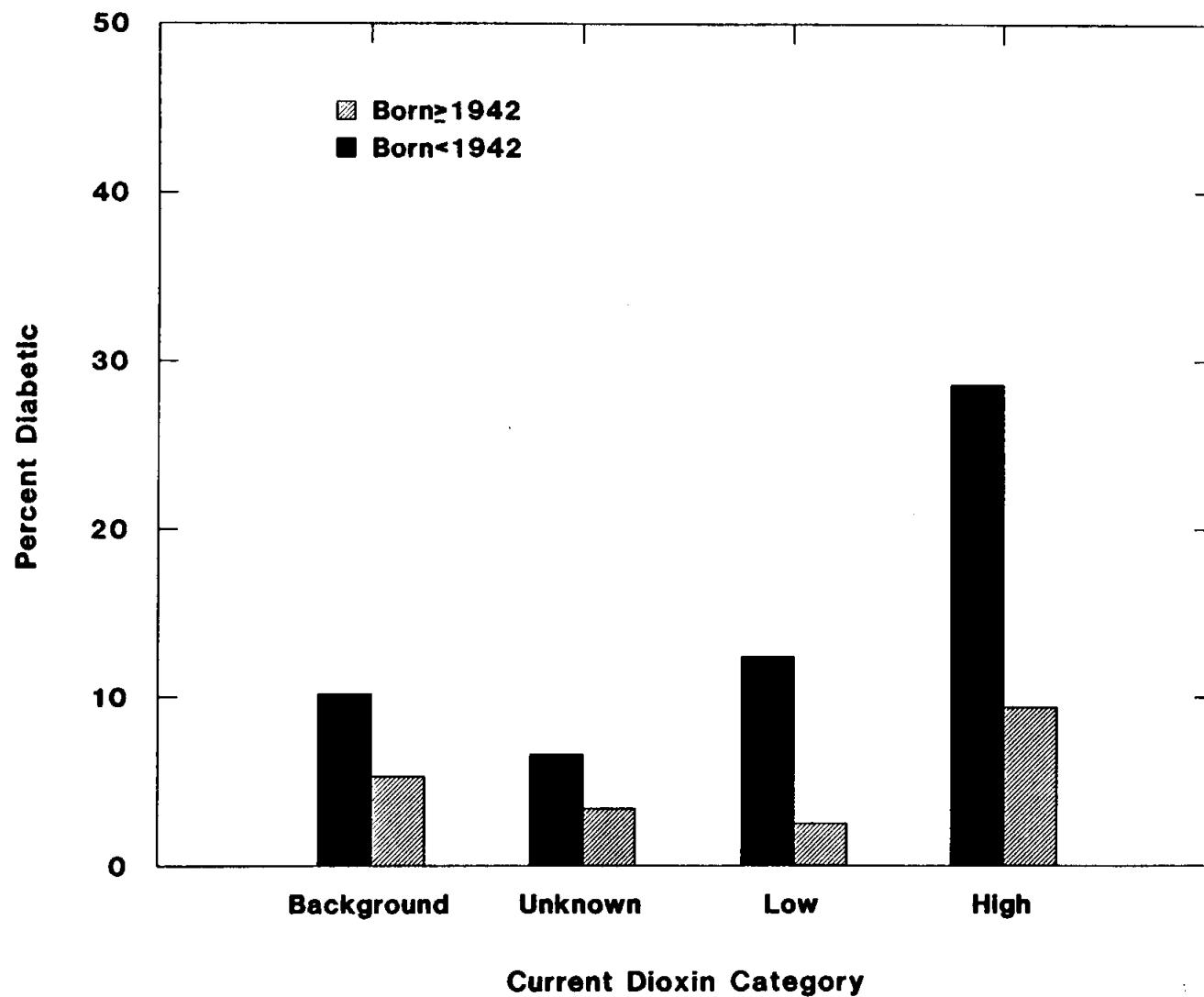
N-2-12



**FIGURE N-2-10. Interaction of Initial Dioxin and Percent Body Fat for 2-Hour Postprandial Glucose (Continuous - Ranch Hands, Minimal Assumption)**



**FIGURE N-2-11. Interaction of Current Dioxin, Time, and Personality Type for 2-Hour Postprandial Glucose (Continuous - Ranch Hands, Minimal Assumption)**



**FIGURE N-2-12. Interaction of Categorized Current Dioxin and Age for the Composite Diabetes Indicator**