



Research Report 192, Pt 1

# **Multicenter Ozone Study in oldEr Subjects (MOSES): Part 1. Effects of Exposure to Low Concentrations of Ozone on Respiratory and Cardiovascular Outcomes**

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## **Appendix B.2 Analyses of Systemic Inflammation and Vascular Function**

This Appendix was reviewed solely for spelling, grammar, and  
cross-references to the main text. It has not been formatted or fully edited by HEI.

This document was reviewed by the HEI MOSES Review Panel.

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## Primary Endpoints

### 1. Descriptive Statistics

**Table B.2.1a. Descriptive Statistics**

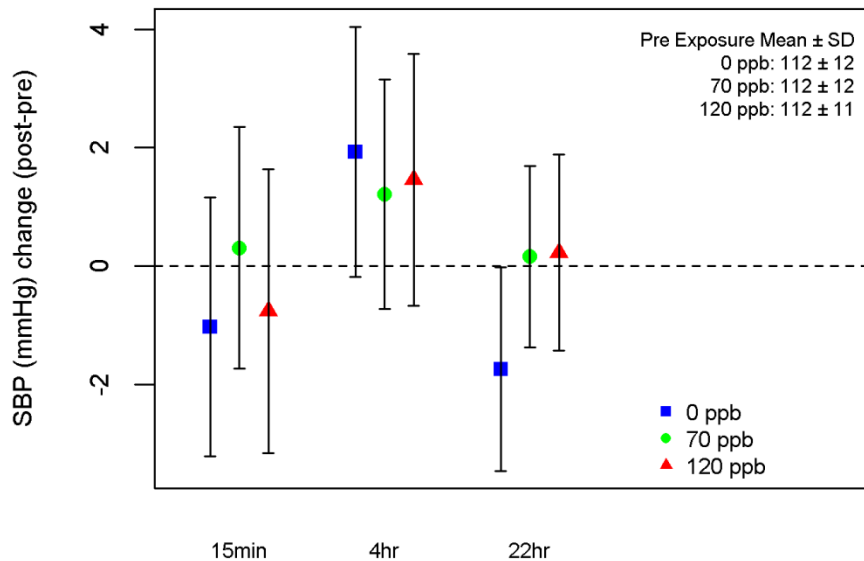
	0 ppb			70 ppb			120 ppb		
	<i>N</i>	Mean	SD	<i>N</i>	Mean	SD	<i>N</i>	Mean	SD
SBP (mmHg)									
Pre-exposure	87	111.9	11.8	87	111.9	11.8	87	112.2	10.5
15-min post-exposure	87	110.5	11.2	87	109.6	9.6	87	110.0	9.9
4-hr post-exposure	87	113.9	11.8	87	113.1	10.6	87	113.7	10.1
22-hr post-exposure	87	110.2	11.8	87	112.1	10.9	87	112.4	10.6
CRP (mg/L)									
Pre-exposure	85	2.7	3.6	85	2.9	3.7	84	3.1	4.0
4-hr post-exposure	85	2.5	3.4	85	2.5	3.4	84	2.7	3.7
22-hr post-exposure	82	2.7	3.7	85	2.8	3.8	82	2.7	3.8
FMD (%)									
Pre-exposure	75	5.1	2.9	74	5.1	2.9	75	5.1	3.0
4-hr post-exposure	75	5.9	2.6	74	5.9	3.3	75	5.7	3.3

**Table B.2.1b. Median and IQR of Skewed Data**

	0 ppb			70 ppb			120 ppb		
	<i>N</i>	Median	IQR	<i>N</i>	Median	IQR	<i>N</i>	Median	IQR
CRP (mg/L)									
Pre-exposure	85	1.51	(0.59, 3.43)	85	1.91	(0.65, 3.75)	84	1.73	(0.65, 3.17)
4-hr post-exposure	85	1.48	(0.65, 2.97)	85	1.44	(0.52, 2.87)	84	1.33	(0.67, 2.88)
22-hr post-exposure	82	1.39	(0.60, 3.60)	85	1.40	(0.63, 3.27)	82	1.45	(0.72, 3.61)

## 2. Systolic Blood Pressure (mmHg)

The following figure shows the change in systolic blood pressure (SBP) from pre- to post-exposure over time. The data come from Table B.2.1a.



**Figure B.2.2. Change in SBP at different post-exposure times and at each ozone exposure.**

### Main Analysis of Ozone Effect

As we can see from the tables below, site and time are statistically significant. This means that:

- there were differences among the 15-minute, 4-hour, and 22-hour post-exposure SBP;
- there were no differences in SBP across the ozone exposures; and
- there were differences in SBP across the 3 sites.

**Table B.2.2a. Type III Sum of Squares for Change in SBP (mmHg)**

<b>Effect</b>	<b>P Value</b>
15-min vs. 4-hr vs. 22-hr change	<0.0001
Ozone exposure	0.9504
Site	<0.0001

**Table B.2.2b. Mixed Model for Change in SBP (mmHg)**

<b>Effect</b>	<b>Estimate</b>	<b>Lower 95% CI</b>	<b>Upper 95% CI</b>	<b>P Value</b>
Intercept	-4.8389	-6.9928	-2.6850	<0.0001
Change between pre- and post-exposure				
22-hr change	1.5172	0.1382	2.8963	0.0313
4-hr change	3.5019	2.1229	4.8810	<0.0001
15-min change	0			
Ozone exposure				
120 ppb	0.2222	-1.1568	1.6013	0.7508
70 ppb	0.09579	-1.2833	1.4748	0.8911
0 ppb	0			
Site				
URMC	2.0946	-0.3704	4.5595	0.0948
UNC	5.9909	3.4694	8.5124	<0.0001
UCSF	0			

## Analyses of Interactions

As we can see from the tables below, the ozone effect did not differ by age.

**Table B.2.2c. Type III Sum of Squares for Change in SBP (mmHg), Including Ozone Exposure, by Age Interaction**

<b>Effect</b>	<b>P Value</b>
Ozone exposure	0.9452
15-min vs. 4-hr vs. 22-hr change	<0.0001
Site	<0.0001
Age	0.1781
Ozone exposure by age	0.5797

**Table B.2.2d. Mixed Model for Change in SBP (mmHg), Including Ozone Exposure, by Age Interaction**

<b>Effect</b>	<b>Estimate</b>	<b>Lower 95% CI</b>	<b>Upper 95% CI</b>	<b>P Value</b>
Intercept	-4.8742	-7.0218	-2.7265	<0.0001
22-hr change	1.5172	0.1373	2.8972	0.0314
4-hr change	3.5019	2.1220	4.8819	<0.0001
15-min change	0			
Ozone exposure				
120 ppb	0.2335	-1.1494	1.6163	0.7394
70 ppb	0.1412	-1.2417	1.5240	0.8405
0 ppb	0			
Site				
URMC	2.2794	-0.1886	4.7474	0.0698
UNC	5.9695	3.4599	8.4790	<0.0001
UCSF	0			
Age	-0.08762	-0.3730	0.1978	0.5431
Ozone exposure by age				
120 ppb by age	-0.03850	-0.3429	0.2659	0.8040
70 ppb by age	-0.1555	-0.4599	0.1489	0.3162
0 ppb by age	0			

As we can see from the tables below, the ozone effect did not differ by sex.

**Table B.2.2e. Type III Sum of Squares for Change in SBP (mmHg), Including Ozone Exposure, by Sex Interaction**

<b>Effect</b>	<b>P Value</b>
	0.9998
15-min vs. 4-hr vs. 22-hr change	<0.0001
Site	0.0001
Sex	0.0612
Ozone exposure by sex	0.3269

**Table B.2.2f. Mixed Model for Change in SBP (mmHg), Including Ozone Exposure, by Sex Interaction**

<b>Effect</b>	<b>Estimate</b>	<b>Lower 95% CI</b>	<b>Upper 95% CI</b>	<b>P Value</b>
Intercept	-5.1457	-7.6733	-2.6181	0.0001
22-hr change	1.5172	0.1384	2.8960	0.0312
4-hr change	3.5019	2.1231	4.8807	<0.0001
15-min change	0			
Ozone exposure				
120 ppb	-1.0476	-3.2216	1.1264	0.3428
70 ppb	-0.4190	-2.5931	1.7550	0.7041
0 ppb	0			
Site				
URMC	1.7752	-0.6759	4.2263	0.1535
UNC	5.5452	3.0179	8.0725	<0.0001
UCSF	0			
Sex				
Female	0.9584	-1.6625	3.5793	0.4691
Male	0			
Ozone exposure by sex				
120 ppb by female	2.1245	-0.6875	4.9366	0.1377
70 ppb by female	0.8614	-1.9507	3.6734	0.5462
0 ppb by female	0			
120 ppb by male	0			
70 ppb by male	0			
0 ppb by male	0			

As we can see from the tables below, the ozone effect did not differ by GSTM1 status.

**Table B.2.2g. Type III Sum of Squares for Change in SBP (mmHg), Including Ozone Exposure, by GSTM1 Status Interaction**

<b>Effect</b>	<b>P Value</b>
	0.9525
15-min vs. 4-hr vs. 22-hr change	<0.0001
Site	<0.0001
GSTM1 status	0.8012
Ozone exposure by GSTM1 status	0.7128

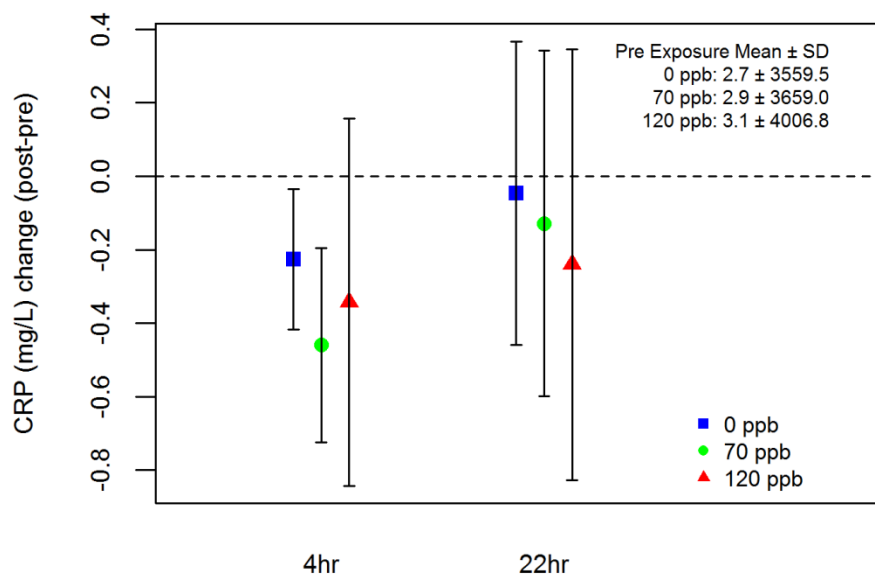
**Table B.2.2h. Mixed Model for Change in SBP (mmHg), Including Ozone Exposure, by GSTM1 Status Interaction**

<b>Effect</b>	<b>Estimate</b>	<b>Lower 95% CI</b>	<b>Upper 95% CI</b>	<b>P Value</b>
Intercept	-4.8229	-7.2022	-2.4437	0.0001
22-hr change	1.5172	0.1369	2.8976	0.0314
4-hr change	3.5019	2.1216	4.8823	<0.0001
15-min change	0			
Ozone exposure				
120 ppb	0.2933	-1.5276	2.1143	0.7509
70 ppb	-0.2933	-2.1143	1.5276	0.7509
0 ppb	0			
Site				
URMC	2.0627	-0.4293	4.5546	0.1035
UNC	5.9643	3.4196	8.5090	<0.0001
UCSF	0			
GSTM1 status				
Sufficient	0.01089	-2.6029	2.6247	0.9934
Null	0			
Ozone exposure by GSTM1 status				
120 ppb by sufficient	-0.1672	-2.9595	2.6251	0.9060
70 ppb by sufficient	0.9150	-1.8774	3.7073	0.5186
0 ppb by sufficient	0			
120 ppb by null	0			
70 ppb by null	0			
0 ppb by null	0			



### 3. C-Reactive Protein (mg/L)

The following figure shows the change in C-reactive protein (CRP) from pre- to post-exposure over time. The data come from Table B.2.1a.



**Figure B.2.3. Change in CRP at different post-exposure times and at each ozone exposure.**

## Main Analysis of Ozone Effect

As we can see from the tables below, there are no statistically significant results for change in CRP. This means that:

- there were no differences between the 4-hour post-exposure and 22-hour post-exposure CRP;
- there were no differences in CRP across the ozone exposures; and
- there were no differences in CRP across the 3 sites.

**Table B.2.3a. Type III Sum of Squares for Change in CRP (mg/L)**

Effect	<i>P</i> Value
4-hr vs. 22-hr change	0.1806
Ozone exposure	0.6551
Site	0.1866

**Table B.2.3b. Mixed Model for Change in CRP (mg/L)**

Effect	Estimate	Lower 95% CI	Upper 95% CI	<i>P</i> Value
Intercept	-0.1550	-0.6724	0.3623	0.5529
Change between pre- and post-exposure				
4-hr change	-0.2137	-0.5285	0.1010	0.1806
22-hr change	0			
Ozone exposure				
120 ppb	-0.1543	-0.5397	0.2311	0.4304
70 ppb	-0.1561	-0.5388	0.2265	0.4217
0 ppb	0			
Site				
URMC	0.4185	-0.1744	1.0113	0.1641
UNC	-0.08495	-0.6962	0.5263	0.7830
UCSF	0			

## Analyses of Interactions

As we can see from the tables below, the ozone effect did not differ by age.

**Table B.2.3c. Type III Sum of Squares for Change in CRP (mg/L), Including Ozone Exposure, by Age Interaction**

Effect	P Value
Ozone exposure	0.6551
4-hr vs. 22-hr change	0.1810
Site	0.1660
Age	0.5199
Ozone exposure by age	0.8129

**Table B.2.3d. Mixed Model for Change in CRP (mg/L), Including Ozone Exposure, by Age Interaction**

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	-0.1565	-0.6758	0.3628	0.5505
4-hr post change	-0.2139	-0.5293	0.1014	0.1810
22-hr change	0			
Ozone exposure				
120 ppb	-0.1584	-0.5448	0.2280	0.4196
70 ppb	-0.1529	-0.5370	0.2312	0.4330
0 ppb	0			
Site				
URMC	0.4398	-0.1591	1.0386	0.1479
UNC	-0.08791	-0.7017	0.5259	0.7764
UCSF	0			
Age	-0.02726	-0.1009	0.04638	0.4636
Ozone exposure by age				
120 ppb by age	0.02544	-0.05913	0.1100	0.5546
70 ppb by age	0.003408	-0.08096	0.08778	0.9367
0 ppb by age	0			

As we can see from the tables below, the ozone effect did not differ by sex.

**Table B.2.3e. Type III Sum of Squares for Change in CRP (mg/L), Including Ozone Exposure, by Sex Interaction**

<b>Effect</b>	<b>P Value</b>
Ozone exposure	0.5228
4-hr vs. 22-hr change	0.1782
Site	0.1998
Sex	0.4172
Ozone exposure by sex	0.1649

**Table B.2.3f. Mixed Model for Change in CRP (mg/L), Including Ozone Exposure, by Sex Interaction**

<b>Effect</b>	<b>Estimate</b>	<b>Lower 95% CI</b>	<b>Upper 95% CI</b>	<b>P Value</b>
Intercept	-0.06239	-0.6868	0.5621	0.8430
4-hr post change	-0.2144	-0.5285	0.09964	0.1782
22-hr change	0			
Ozone exposure				
120 ppb	-0.5789	-1.1697	0.01196	0.0548
70 ppb	-0.2938	-0.8900	0.3024	0.3319
0 ppb	0			
Site				
URMC	0.3839	-0.2164	0.9843	0.2070
UNC	-0.1237	-0.7462	0.4987	0.6935
UCSF	0			
Sex				
Female	-0.1194	-0.7952	0.5564	0.7262
Male	0			
Ozone exposure by sex				
120 ppb by female	0.7375	-0.04079	1.5159	0.0631
70 ppb by female	0.2392	-0.5373	1.0157	0.5439
0 ppb by female	0			
120 ppb by male	0			
70 ppb by male	0			
0 ppb by male	0			

As we can see from the tables below, the ozone effect did not differ by GSTM1 status.

**Table B.2.3g. Type III Sum of Squares for Change in CRP (mg/L), Including Ozone Exposure, by GSTM1 Status Interaction**

Effect	P Value
Ozone exposure	0.7214
4-hr vs. 22-hr change	0.1834
Site	0.1830
GSTM1 status	0.7974
Ozone exposure by GSTM1 status	0.6761

**Table B.2.3h. Mixed Model for Change in CRP (mg/L), Including Ozone Exposure, by GSTM1 Status Interaction**

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	-0.07759	-0.6554	0.5002	0.7901
4-hr post change	-0.2127	-0.5280	0.1026	0.1834
22-hr change	0			
Ozone exposure				
120 ppb	-0.2925	-0.7964	0.2115	0.2535
70 ppb	-0.1850	-0.6874	0.3175	0.4683
0 ppb	0			
Site				
URMC	0.4278	-0.1714	1.0270	0.1593
UNC	-0.08032	-0.6962	0.5355	0.7960
UCSF	0			
GSTM1 status				
Sufficient	-0.2000	-0.8737	0.4738	0.5566
Null	0			
Ozone exposure by GSTM1 status				
120 ppb by sufficient	0.3342	-0.4499	1.1182	0.4012
70 ppb by sufficient	0.07283	-0.7044	0.8501	0.8534
0 ppb by sufficient	0			
120 ppb by null	0			
70 ppb by null	0			
0 ppb by null	0			

## Sensitivity Analysis

As we can see from the tables below, there are no statistically significant results for change from pre- to post-exposure in CRP in subjects with all three pre-exposure values less than the overall median pre-exposure value

- there were no differences between the 4-hour post-exposure and 22-hour post-exposure CRP;
- there were no differences in CRP across the ozone exposures; and
- there were no differences in CRP across the 3 sites.

**Table B.2.3i. Type III Sum of Squares for Change in CRP (mg/L) for Subjects with All Three Pre-Exposure CRP Values Less Than Overall Median of All Pre-exposure Values (1.799 mg/L)\* (N = 29)**

Effect	P Value
4-hr vs. 22-hr change	0.7487
Ozone exposure	0.1942
Site	0.6368

\*The median is the average of two middle observations.

**Table B.2.3j. Mixed Model for Change in CRP (mg/L) for Subjects with All Three Pre-Exposure CRP Values Less Than Overall Median of All Pre-Exposure Values (1.799 mg/L)\* (N = 29)**

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	0.04133	-0.1483	0.2310	0.6578
Change between pre- and post-exposure				
22-hr change	0.01884	-0.1005	0.1381	0.7487
4-hr change	0			
Ozone exposure				
120 ppb	-0.05000	-0.1942	0.09417	0.4900
70 ppb	-0.1305	-0.2747	0.01365	0.0751
0 ppb	0			
Site				
URMC	0.09263	-0.1207	0.3060	0.3803
UNC	0.08072	-0.1291	0.2905	0.4362
UCSF	0			

\*The median is the average of two middle observations.

As we can see from the tables below, there are no statistically significant results for change from pre- to post exposure in CRP in subjects with at least one pre-exposure value greater than the overall median pre-exposure value. This means that:

- there were no differences between the 4-hour post-exposure and 22-hour post-exposure CRP;
- there were no differences in CRP across the ozone exposures; and
- there were no differences in CRP across the 3 sites.

**Table B.2.3k. Type III Sum of Squares for Change in CRP (mg/L) in Subjects with at Least 1 Pre-Exposure CRP Value Greater Than Overall Median of All Pre-exposure Values (1.799 mg/L)\* (N = 57)**

Effect	P Value
4-hr vs. 22-hr change	0.1963
Ozone exposure	0.7216
Site	0.1553

\*The median is the average of two middle observations.

**Table B.2.3l. Mixed Model for Change in CRP (mg/L) in Subjects with at Least 1 Pre-Exposure CRP Value Greater Than Overall Median of All Pre-Exposure Values (1.799 mg/L)\* (N = 57)**

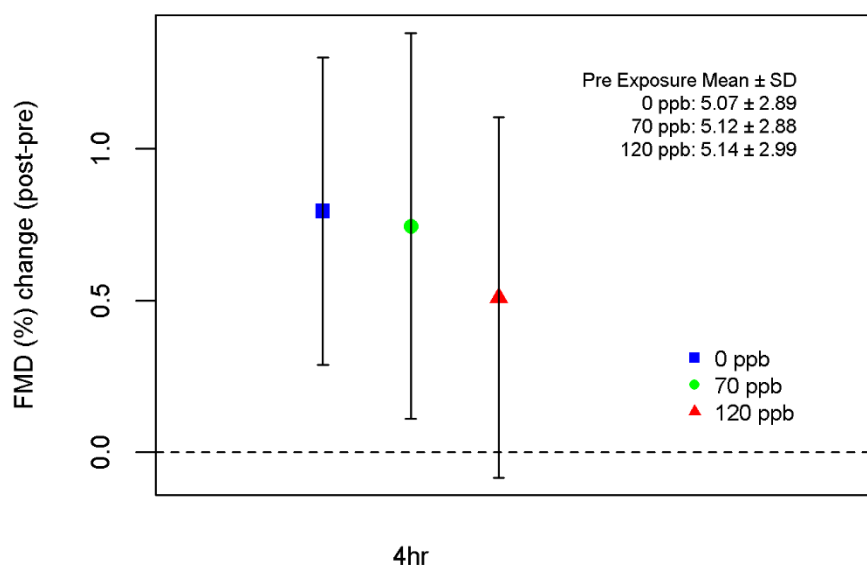
Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	-0.5457	-1.3018	0.2105	0.1538
Change between pre- and post-exposure				
22-hr change	0.3106	-0.1652	0.7864	0.1963
4-hr change	0			
Ozone exposure				
120 ppb	-0.2238	-0.8041	0.3565	0.4463
70 ppb	-0.1758	-0.7496	0.3980	0.5449
0 ppb	0			
Site				
URMC	0.5625	-0.2963	1.4214	0.1947
UNC	-0.2634	-1.1752	0.6483	0.5649
UCSF	0			

\*The median is the average of two middle observations.

## 4. Flow-Mediated Dilation

Image quality was rated by the BAU Core lab at the time of analysis. The data below include all subjects for which images were considered acceptable ( $n = 77$ ). Of these, 75 subjects had pre- and post-exposure data for the 0 ppb exposure; 74 subjects had pre- and post-exposure data for the 70 ppb exposure; and 75 subjects had pre- and post-exposure data for the 120 ppb exposure. A sensitivity analysis (not shown) excluded images that were acceptable but of poorer quality ( $n = 4$  at 0 ppb;  $n = 6$  at 70 ppb; and  $n = 6$  at 120 ppb); excluding these subjects did not alter the findings.

The figure shows the change in flow-mediated dilation (FMD) (%) of the brachial artery from pre- to post-exposure. The data come from Table B.2.1a.



**Figure B.2.4. Change in FMD (%) at 4 hours post-exposure at each ozone exposure.**



## Main Analysis of Ozone Effect

As we can see from the tables below,

- there were no differences in FMD (%) across the ozone exposures; and
- there were no differences in FMD (%) across the 3 sites.

**Table B.2.4a. Type III Sum of Squares for Change in FMD (%)**

Effect	P Value
Ozone exposure	0.7855
Site	0.3925

**Table B.2.4b. Mixed Model for Change in FMD (%)**

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	0.4331	-0.3743	1.2405	0.2887
Ozone exposure				
120 ppb	-0.2578	-1.0336	0.5179	0.5123
70 ppb	-0.05101	-0.8296	0.7276	0.8971
0 ppb	0			
Site				
URMC	0.4276	-0.5008	1.3559	0.3618
UNC	0.6381	-0.3030	1.5792	0.1808
UCSF	0			

## Analyses of Interactions

As we can see from the tables below, the ozone effect did not differ by age.

**Table B.2.4c. Type III Sum of Squares for Change in FMD (%), Including Ozone Exposure, by Age Interaction**

Effect	P Value
Ozone exposure	0.7761
Site	0.3999
Age	0.2191
Ozone exposure by age	0.8799

**Table B.2.4d. Mixed Model for Change in FMD (%), Including Ozone Exposure, by Age Interaction**

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	0.4501	-0.3571	1.2573	0.2700
Ozone exposure				
120 ppb	-0.2682	-1.0493	0.5129	0.4984
70 ppb	-0.05956	-0.8436	0.7245	0.8809
0 ppb	0			
Site				
URMC	0.3699	-0.5587	1.2986	0.4299
UNC	0.6382	-0.2989	1.5753	0.1789
UCSF	0			
Age	0.02691	-0.1004	0.1543	0.6748
Ozone exposure by age				
120 ppb by age	0.04170	-0.1260	0.2094	0.6239
70 ppb by age	0.02984	-0.1380	0.1977	0.7258
0 ppb by age	0			

As we can see from the tables below, the ozone effect did not differ by sex.

**Table B.2.4e. Type III Sum of Squares for Change in FMD (%), Including Ozone Exposure, by Sex Interaction**

<b>Effect</b>	<b>P Value</b>
Ozone exposure	0.6875
Site	0.5715
Sex	0.2129
Ozone exposure by sex	0.1564

**Table B.2.4f. Mixed Model for Change in FMD (%), Including Ozone Exposure, by Sex Interaction**

<b>Effect</b>	<b>Estimate</b>	<b>Lower 95% CI</b>	<b>Upper 95% CI</b>	<b>P Value</b>
Intercept	0.7119	-0.2946	1.7185	0.1629
Ozone exposure				
120 ppb	-0.9991	-2.1578	0.1596	0.0905
70 ppb	-0.7761	-1.9347	0.3826	0.1876
0 ppb	0			
Site				
URMC	0.3694	-0.5637	1.3025	0.4327
UNC	0.4948	-0.4748	1.4644	0.3125
UCSF	0			
Sex				
Female	-0.3816	-1.5796	0.8164	0.5275
Male	0			
Ozone exposure by sex				
120 ppb by female	1.3269	-0.2235	2.8773	0.0929
70 ppb by female	1.3099	-0.2451	2.8648	0.0981
0 ppb by female	0			
120 ppb by male	0			
70 ppb by male	0			
0 ppb by male	0			

As we can see from the tables below, the ozone effect did not differ by GSTM1 status.

**Table B.2.4g. Type III Sum of Squares for Change in FMD (%), Including Ozone Exposure, by GSTM1 Status Interaction**

Effect	P Value
Ozone exposure	0.6367
Site	0.4446
GSTM1 status	0.2376
Ozone exposure by GSTM1 status	0.1208

**Table B.2.4h. Mixed Model for Change in FMD (%), Including Ozone Exposure, by GSTM1 Status Interaction**

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	0.3977	-0.5349	1.3303	0.3981
Ozone exposure				
120 ppb	-0.1327	-1.1314	0.8659	0.7932
70 ppb	-0.5556	-1.5605	0.4493	0.2763
0 ppb	0			
Site				
URMC	0.3931	-0.5342	1.3203	0.4010
UNC	0.5942	-0.3461	1.5346	0.2119
UCSF	0			
GSTM1 status				
Sufficient	0.1488	-1.0426	1.3402	0.8041
Null	0			
Ozone exposure by GSTM1 status				
120 ppb by sufficient	-0.3106	-1.8788	1.2575	0.6960
70 ppb by sufficient	1.2489	-0.3232	2.8211	0.1186
0 ppb by sufficient	0			
120 ppb by null	0			
70 ppb by null	0			
0 ppb by null	0			

## Sensitivity Analysis

As we can see from the tables below, there are no statistically significant results for change from pre- to post-exposure in FMD in subjects with all three pre-exposure FMD values >5%. This means that:

- there were no differences in FMD across the ozone exposures; and
- there were no differences in FMD across the 3 sites.

**Table B.2.4i. Type III Sum of Squares for Change in FMD (%), in Subjects Where FMD Was >5% in All Three Pre-Exposures (N = 21)**

Effect	P Value
Ozone exposure	0.8993
Site	0.8442

**Table B.2.4j. Mixed Model for Change in FMD (%), in Subjects Where FMD Was >5% in All Three Pre-Exposures**

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	0.4613	-1.3667	2.2893	0.6025
Ozone exposure				
120 ppb	-0.2276	-1.7220	1.2667	0.7598
70 ppb	-0.3338	-1.8282	1.1605	0.6541
0 ppb	0			
Site				
URMC	0.6258	-2.4242	3.6759	0.6715
UNC	-0.1995	-2.3365	1.9375	0.8467
UCSF	0			

As we can see from the tables below, there are no statistically significant results for change from pre- to post-exposure in FMD in subjects with all three CRP pre-exposure values less than the overall median CRP pre-exposure value. This means that:

- there were no differences in FMD across the ozone exposures; and
- there were no differences in FMD across the 3 sites.

**Table B.2.4k. Type III Sum of Squares for Change in FMD (%) in Subjects Where All Pre-Exposure CRP Values Were Less Than the Overall Median of All CRP Pre-Exposure Values (1.799 mg/L)\* (N = 24)**

Effect	P Value
Ozone exposure	0.7893
Site	0.3438

\*The median is the average of two middle observations.

**Table B.2.4l. Mixed Model for Change in FMD (%) in Subjects Where All Three Pre-Exposure CRP Values Were Less Than Overall Median of All CRP Pre-Exposure Values (1.799 mg/L)\* (N = 24)**

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	0.07291	-1.3935	1.5394	0.9184
Ozone exposure				
120 ppb	0.3771	-0.9264	1.6807	0.5620
70 ppb	0.3873	-0.8980	1.6725	0.5460
0 ppb	0			
Site				
URMC	0.4382	-1.3785	2.2549	0.6203
UNC	1.2301	-0.5002	2.9604	0.1537
UCSF	0			

\*The median is the average of two middle observations.

As we can see from the tables below, there are no statistically significant results for change from pre-to post-exposure in FMD in subjects with at least 1 pre-exposure CRP value greater than overall median CRP pre-exposure value. This means that:

- there were no differences in FMD across the ozone exposures; and
- there were no differences in FMD across the 3 sites.

**Table B.2.4m. Type III Sum of Squares for Change in FMD (%) in Subjects Where at Least 1 Pre-Exposure CRP Value Was Greater Than the Overall Median of All CRP Pre-Exposure Values (1.799 mg/L)\* (N = 52)**

Effect	P Value
Ozone exposure	0.5992
Site	0.7011

\*The median is the average of two middle observations.

**Table B.2.4n. Mixed Model for Change in FMD (%) in Subjects Where at Least 1 Pre-Exposure CRP Value Was Greater Than the Overall Median of All CRP Pre-Exposure Values (1.799 mg/L)\* (N = 52)**

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	0.5664	-0.4417	1.5746	0.2646
Ozone exposure				
120 ppb	-0.4920	-1.4546	0.4707	0.3132
70 ppb	-0.2292	-1.2022	0.7439	0.6414
0 ppb	0			
Site				
URMC	0.4534	-0.6886	1.5953	0.4291
UNC	0.3888	-0.7940	1.5717	0.5122
UCSF	0			

\*The median is the average of two middle observations

## Secondary Endpoints

### 5. Descriptive Statistics

**Table B.2.5. Descriptive Statistics of Secondary Endpoints**

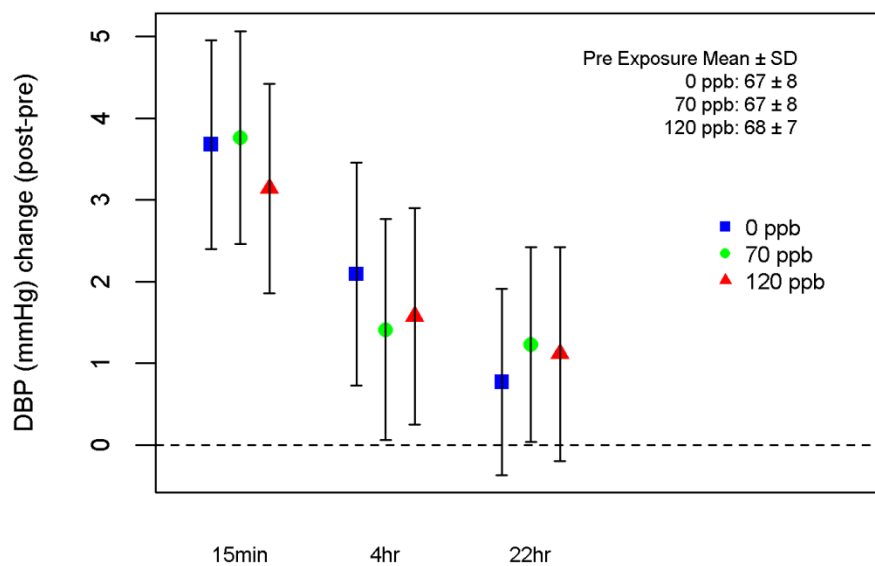
	0 ppb			70 ppb			120 ppb		
	<i>N</i>	Mean	SD	<i>N</i>	Mean	SD	<i>N</i>	Mean	SD
DBP (mmHg)									
Pre-exposure	87	67.3	8.4	87	67.3	8.0	87	67.7	7.1
15 min post-exposure	87	71.5	7.4	87	71.2	7.1	87	71.2	6.3
4 hr post-exposure	87	69.3	8.7	87	68.7	7.7	87	69.2	7.5
22 hr post-exposure	87	68.0	9.0	87	68.5	8.0	87	68.8	8.4
VTI (cm)									
Pre-exposure	83	77.8	27.3	84	77.1	25.1	78	75.5	25.0
4 hr post-exposure	83	75.2	24.1	84	75.7	25.9	78	76.6	23.6
BAD (mm)									
Pre-exposure	80	3.5	0.7	81	3.5	0.7	80	3.5	0.7
4 hr post-exposure	80	3.4	0.7	81	3.4	0.7	80	3.4	0.7
8-Isoprostane (pg/mL)									
Pre-exposure	85	61.7	30.1	85	61.1	31.5	84	62.0	33.7
4 hr post-exposure	85	58.0	27.1	85	55.4	25.1	84	59.5	30.9
22 hr post-exposure	82	63.0	32.7	85	59.9	28.7	82	60.4	26.3
Nitrotyrosine (nM)									
Pre-exposure	85	621.6	885.8	85	641.0	1066.7	84	606.5	807.2
4 hr post-exposure	85	629.3	905.2	85	659.1	1169.0	84	592.9	758.6
22 hr post-exposure	82	678.0	1010.3	85	647.6	1138.5	82	514.9	437.0
IL-6 (pg/mL)									



	0 ppb			70 ppb			120 ppb		
	<i>N</i>	Mean	SD	<i>N</i>	Mean	SD	<i>N</i>	Mean	SD
Pre-exposure	85	3.25	3.14	85	3.26	3.03	84	3.03	2.65
4 hr post-exposure	85	3.28	2.85	85	2.84	2.21	84	2.83	2.34
22 hr post-exposure	82	3.34	2.80	85	3.31	3.33	82	2.89	2.73
ET-1 (pg/mL)									
Pre-exposure	85	1.27	0.42	85	1.26	0.35	84	1.18	0.40
4 hr post-exposure	85	1.24	0.43	85	1.22	0.36	84	1.24	0.47
22 hr post-exposure	82	1.23	0.51	85	1.17	0.40	82	1.20	0.44
P-selectin (ng/mL)									
Pre-exposure	85	68.6	76.9	85	69.9	69.9	84	65.4	55.6
4 hr post-exposure	85	63.1	48.7	85	55.6	35.0	84	62.1	41.3
22 hr post-exposure	82	116.7	286.0	85	77.1	85.6	82	84.3	141.1
WBC count (1000/uL)									
Pre-exposure	85	5.9	1.4	86	5.9	1.4	86	5.9	1.5
4 hr post-exposure	85	6.3	1.6	86	6.2	1.6	85	6.3	1.7
22 hr post-exposure	81	5.0	1.4	86	5.0	1.5	82	4.9	1.3

## 6. Diastolic Blood Pressure (mmHg)

The following figure shows the change in diastolic blood pressure (DBP) from pre- to post-exposure over time. The data come from Table B.2.5.



**Figure B.2.6. Change in DBP at different post- exposure times at each ozone exposure.**

## Main Analysis of Ozone Effect

As we can see from the tables below, time and site are statistically significant. This means that:

- there were differences between the 15-minute, 4-hour, and 22-hour post-exposure DBP;
- there were no differences in DBP across the ozone exposures; and
- there were differences in DBP across the 3 sites.

**Table B.2.6a. Type III Sum of Squares for Change in DBP (mmHg)**

Effect	<i>P</i> Value
15-min vs. 4-hr vs. 22-hr change	<0.0001
Ozone exposure	0.8163
Site	0.0048

**Table B.2.6b. Mixed Model for Change in DBP (mmHg)**

Effect	Estimate	Lower 95% CI	Upper 95% CI	<i>P</i> Value
Intercept	3.4839	2.0506	4.9172	<0.0001
Change between pre- and post-exposure				
22-hr change	-2.8659	-3.8121	-1.9197	<0.0001
4-hr change	-2.2107	-3.1570	-1.2645	<0.0001
15-min change	0			
Ozone exposure				
120 ppb	-0.3027	-1.2489	0.6436	0.5286
70 ppb	-0.1877	-1.1340	0.7585	0.6958
0 ppb	0			
Site				
URMC	-0.3608	-1.9811	1.2594	0.6590
UNC	2.1496	0.4922	3.8070	0.0116
UCSF	0			

## Analyses of Interactions

As we can see from the tables below, the ozone effect did not differ by age.

**Table B.2.6c. Type III Sum of Squares for Change in DBP (mmHg), including Ozone Exposure, by Age Interaction**

Effect	P Value
Ozone exposure	0.8349
15-min vs. 4-hr vs. 22-hr change	<0.0001
Site	0.0071
Age	0.1464
Ozone exposure by age	0.6433

**Table B.2.6d. Mixed Model for Change in DBP (mmHg), Including Ozone Exposure, by Age Interaction**

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	3.4578	2.0303	4.8854	<0.0001
22-hr change	-2.8659	-3.8129	-1.9189	<0.0001
4-hr change	-2.2107	-3.1577	-1.2637	<0.0001
15-min change	0			
Ozone exposure				
120 ppb	-0.2885	-1.2375	0.6605	0.5492
70 ppb	-0.1586	-1.1076	0.7904	0.7420
0 ppb	0			
Site				
URMC	-0.2299	-1.8492	1.3894	0.7783
UNC	2.1344	0.4878	3.7810	0.0117
UCSF	0			
Age	-0.05835	-0.2490	0.1323	0.5443
Ozone exposure by age				
120 ppb by age	-0.04856	-0.2574	0.1603	0.6482
70 ppb by age	-0.09995	-0.3088	0.1089	0.3478
0 ppb by age	0			

As we can see from the tables below, the ozone effect did not differ by sex.

**Table B.2.6e. Type III Sum of Squares for Change in DBP (mmHg), Including Ozone Exposure, by Sex Interaction**

<b>Effect</b>	<b>P Value</b>
Ozone exposure	0.7206
15-min vs. 4-hr vs. 22-hr change	<0.0001
Site	0.0044
Sex	0.5779
Ozone exposure by sex	0.1821

**Table B.2.6f. Mixed Model for Change in DBP (mmHg), Including Ozone Exposure, by Sex Interaction**

<b>Effect</b>	<b>Estimate</b>	<b>Lower 95% CI</b>	<b>Upper 95% CI</b>	<b>P Value</b>
Intercept	4.0571	2.3494	5.7647	<0.0001
22-hr change	-2.8659	-3.8112	-1.9206	<0.0001
4-hr change	-2.2107	-3.1560	-1.2655	<0.0001
15-min change	0			
Ozone exposure				
120 ppb	-0.4762	-1.9666	1.0143	0.5291
70 ppb	-1.2000	-2.6904	0.2904	0.1138
0 ppb	0			
Site				
URMC	-0.2978	-1.9404	1.3448	0.7193
UNC	2.2375	0.5438	3.9312	0.0102
UCSF	0			
Sex				
Female	-1.0468	-2.8190	0.7255	0.2434
Male	0			
Ozone exposure by sex				
120 ppb by female	0.2903	-1.6376	2.2181	0.7666
70 ppb by female	1.6936	-0.2343	3.6214	0.0847
0 ppb by female	0			
120 ppb by male	0			
70 ppb by Male	0			
0 ppb by Male	0			

As we can see from the tables below, the ozone effect did not differ by GSTM1 status.

**Table B.2.6g. Type III Sum of Squares for Change in DBP (mmHg), Including Ozone Exposure, by GSTM1 Status Interaction**

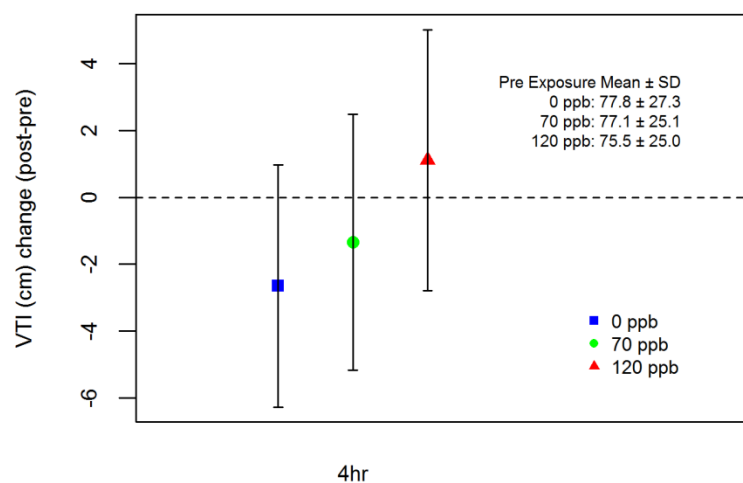
Effect	P Value
Ozone exposure	0.6692
15-min vs. 4-hr vs. 22-hr change	<0.0001
Site	0.0050
GSTM1 status	0.7321
Ozone exposure by GSTM1 status	0.1495

**Table B.2.6h. Mixed Model for Change in DBP (mmHg), Including Ozone Exposure, by GSTM1 Status Interaction**

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	3.2764	1.6923	4.8605	<0.0001
22-hr change	-2.8659	-3.8109	-1.9209	<0.0001
4-hr change	-2.2107	-3.1557	-1.2657	<0.0001
15-min change	0			
Ozone exposure				
120 ppb	0.4467	-0.8000	1.6933	0.4804
70 ppb	-0.07333	-1.3200	1.1733	0.9077
0 ppb	0			
Site				
URMC	-0.3324	-1.9698	1.3051	0.6875
UNC	2.1733	0.5012	3.8454	0.0115
UCSF	0			
GSTM1 status				
Sufficient	0.4446	-1.3010	2.1902	0.6138
Null	0			
Ozone exposure by GSTM1 status				
120 ppb by sufficient	-1.7620	-3.6736	0.1496	0.0706
70 ppb by sufficient	-0.2690	-2.1806	1.6426	0.7815
0 ppb by sufficient	0			
120 ppb by null	0			
70 ppb by null	0			
0 ppb by null	0			

## 7. Velocity Time Interval (cm)

The following figure shows the change in velocity time interval (VTI) from pre- to post-exposure. The data come from Table B.2.5.



**Figure B.2.7. Change in VTI at 4 hours post-exposure at each ozone exposure.**

## Main Analysis of Ozone Effect

As we can see from the tables below, there are no statistically significant results. This means that:

- there were no differences in VTI across the ozone exposures; and
- there were no differences in VTI across the 3 sites.

**Table B.2.7a. Type III Sum of Squares for Change in VTI (cm)**

Effect	<i>P</i> Value
Ozone exposure	0.3422
Site	0.2641

**Table B.2.7b. Mixed Model for Change in VTI (cm)**

Effect	Estimate	Lower 95% CI	Upper 95% CI	<i>P</i> Value
Intercept	-2.5582	-7.7546	2.6381	0.3303
Ozone exposure				
120 ppb	3.8629	-1.4152	9.1411	0.1503
70 ppb	1.2627	-3.9147	6.4402	0.6307
0 ppb	0			
Site				
URMC	-2.1899	-7.8393	3.4595	0.4429
UNC	2.4341	-3.5053	8.3736	0.4173
UCSF	0			



## Analyses of Interactions

As we can see from the tables below, there was a marginally significant difference in the ozone effect on VTI by age — an increase in age was associated with an increase in VTI from pre-exposure to post-exposure when comparing 70 ppb and 120 ppb versus 0 ppb ozone.

**Table B.2.7c. Type III Sum of Squares for Change in VTI (cm), Including Ozone Exposure, by Age Interaction**

Effect	P Value
Ozone exposure	0.2769
Site	0.3186
Age	0.2228
Ozone exposure by age	0.0437

**Table B.2.7d. Mixed Model for Change in VTI (cm), Including Ozone Exposure, by Age Interaction**

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	-2.8431	-8.0107	2.3246	0.2770
Ozone exposure				
120 ppb	4.2393	-0.9837	9.4623	0.1109
70 ppb	1.7342	-3.3904	6.8588	0.5048
0 ppb	0			
Site				
URMC	-1.8565	-7.5225	3.8095	0.5163
UNC	2.4369	-3.4834	8.3572	0.4153
UCSF	0			
Age	0.5100	-0.3213	1.3412	0.2258
Ozone exposure by age				
120 ppb by age	-1.1503	-2.2972	-0.00331	0.0494
70 ppb by age	-1.3328	-2.4569	-0.2086	0.0205
0 ppb by age	0			

As we can see from the tables below, the ozone effect did not differ by sex.

**Table B.2.7e. Type III Sum of Squares for Change in VTI (cm), Including Ozone Exposure, by Sex Interaction**

<b>Effect</b>	<b>P Value</b>
Ozone exposure	0.4013
Site	0.2728
Sex	0.8736
Ozone exposure by sex	0.5887

**Table B.2.7f. Mixed Model for Change in VTI (cm), Including Ozone Exposure, by Sex Interaction**

<b>Effect</b>	<b>Estimate</b>	<b>Lower 95% CI</b>	<b>Upper 95% CI</b>	<b>P Value</b>
Intercept	-0.9532	-7.6544	5.7480	0.7779
Ozone exposure				
120 ppb	1.6695	-6.6010	9.9400	0.6906
70 ppb	-1.9374	-10.0804	6.2056	0.6390
0 ppb	0			
Site				
URMC	-2.2358	-7.9789	3.5073	0.4409
UNC	2.3584	-3.7369	8.4536	0.4437
UCSF	0			
Sex				
Female	-2.6493	-10.4736	5.1750	0.5025
Male	0			
Ozone exposure by sex				
120 ppb by female	3.7158	-7.0507	14.4823	0.4964
70 ppb by female	5.4013	-5.1736	15.9763	0.3146
0 ppb by female	0			
120 ppb by male	0			
70 ppb by male	0			
0 ppb by male	0			

As we can see from the tables below, the ozone effect did not differ by GSTM1 status.

**Table B.2.7g. Type III Sum of Squares for Change in VTI (cm), Including Ozone Exposure, by GSTM1 Status Interaction**

<b>Effect</b>	<b>P Value</b>
Ozone exposure	0.4440
Site	0.2837
GSTM1 status	0.6424
Ozone exposure by GSTM1 status	0.3225

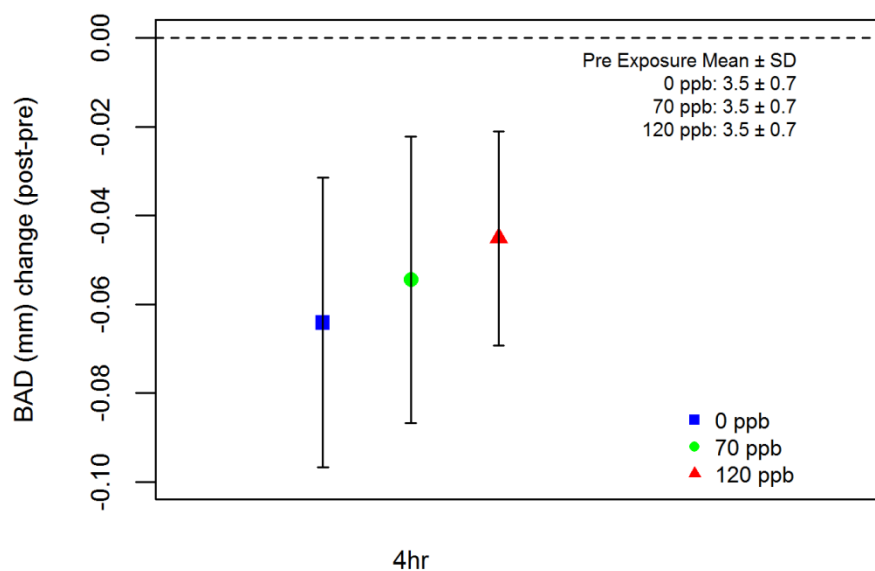
**Table B.2.7h. Mixed Model for Change in VTI (cm), Including Ozone Exposure, by GSTM1 Status Interaction**

<b>Effect</b>	<b>Estimate</b>	<b>Lower 95% CI</b>	<b>Upper 95% CI</b>	<b>P Value</b>
Intercept	-3.8594	-9.9691	2.2503	0.2125
Ozone exposure				
120 ppb	7.4251	0.3748	14.4754	0.0391
70 ppb	2.8193	-4.0830	9.7216	0.4210
0 ppb	0			
Site				
URMC	-2.0476	-7.7523	3.6572	0.4772
UNC	2.4761	-3.5150	8.4673	0.4134
UCSF	0			
GSTM1 status				
Sufficient	2.7627	-4.9114	10.4369	0.4759
Null	0			
Ozone exposure by GSTM1 status				
120 ppb by sufficient	-8.1054	-18.7274	2.5165	0.1337
70 ppb by sufficient	-3.5118	-13.9443	6.9206	0.5071
0 ppb by sufficient	0			
120 ppb by null	0			
70 ppb by null	0			
0 ppb by null	0			

## 8. Brachial Artery Diameter (mm)

The BAU lab reported that 5 subjects were missing BAD data because of poor image quality. Three subjects had images that could not be read for one of their exposures and were included only in the analyses for the other two exposures. In total there were 82 subjects included in the analysis. Of these, 80 subjects had pre- and post-exposure data for the 0 ppb exposure; 81 subjects had pre-and post-exposure data for the 70 ppb exposure; and 80 subjects had pre- and post-exposure data for the 120 ppb exposure.

The following figure shows the descriptive analysis of the change in BAD between pre- and post-exposure at 4 hours. The data come from Table B.2.5.



**Figure B.2.8. Change in BAD at 4 hours post-exposure at each ozone exposure.**

## Main Analysis of Ozone Effect

As we can see from the tables below, there are no statistically significant results. This means that:

- there were no differences in BAD across the ozone exposures; and
- there were no differences in BAD across the 3 sites.

**Table B.2.8a. Type III Sum of Squares for Change in BAD (mm)**

Effect	<i>P</i> Value
Ozone exposure	0.5233
Site	0.9814

**Table B.2.8b. Mixed Model for Change in BAD (mm)**

Effect	Estimate	Lower 95% CI	Upper 95% CI	<i>P</i> Value
Intercept	-0.06070	-0.1078	-0.01361	0.0122
Ozone exposure				
120 ppb	0.01889	-0.01383	0.05161	0.2559
70 ppb	0.00915	-0.02351	0.04181	0.5808
0 ppb	0			
Site				
URMC	-0.00537	-0.06378	0.05303	0.8552
UNC	-0.00457	-0.06465	0.05552	0.8801
UCSF	0			

## Analyses of Interactions

As we can see from the tables below, the ozone effect did not differ by age.

**Table B.2.8c. Type III Sum of Squares for Change in BAD (mm), Including Ozone Exposure, by Age Interaction**

Effect	P Value
Ozone exposure	0.5445
Site	0.9892
Age	0.3885
Ozone exposure by age	0.9466

**Table B.2.8d. Mixed Model for Change in BAD (mm), Including Ozone Exposure, by Age Interaction**

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	-0.06083	-0.1081	-0.01361	0.0123
Ozone exposure				
120 ppb	0.01846	-0.01455	0.05146	0.2710
70 ppb	0.008992	-0.02397	0.04195	0.5907
0 ppb	0			
Site				
URMC	-0.00277	-0.06158	0.05604	0.9255
UNC	-0.00442	-0.06461	0.05576	0.8840
UCSF	0			
Age	-0.00265	-0.00934	0.004041	0.4327
Ozone exposure by age				
120 ppb by age	0.001065	-0.00608	0.008210	0.7688
70 ppb by age	0.000060	-0.00706	0.007176	0.9868
0 ppb by age	0			

As we can see from the tables below,

- there was a marginally significant difference in the ozone effect on BAD by sex — BAD in women increased from pre- to post-exposure relative to men, independent of ozone exposure; and
- the ozone effect did not differ by sex.

**Table B.2.8e. Type III Sum of Squares for Change in BAD (mm), Including Ozone Exposure, by Sex Interaction**

Effect	P Value
Ozone exposure	0.4821
Site	0.7582
Sex	0.0122
Ozone exposure by sex	0.5855

**Table B.2.8f. Mixed Model for Change in BAD (mm), Including Ozone Exposure, by Sex Interaction**

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	-0.09791	-0.1533	-0.04249	0.0007
Ozone exposure				
120 ppb	0.02818	-0.02279	0.07916	0.2765
70 ppb	0.02987	-0.02088	0.08063	0.2467
0 ppb	0			
Site				
URMC	-0.01520	-0.07225	0.04184	0.5972
UNC	-0.02180	-0.08145	0.03784	0.4690
UCSF	0			
Sex				
Female	0.07897	0.01705	0.1409	0.0131
Male	0			
Ozone exposure by sex				
120 ppb by female	-0.01592	-0.08251	0.05067	0.6374
70 ppb by female	-0.03480	-0.1012	0.03161	0.3022
0 ppb by female	0			
120 ppb by male	0			
70 ppb by male	0			
0 ppb by male	0			

As we can see from the tables below, the ozone effect did not differ by GSTM1 status.

**Table B.2.8g. Type III Sum of Squares for Change in BAD (mm), Including Ozone Exposure, by GSTM1 Status Interaction**

<b>Effect</b>	<b>P Value</b>
Ozone exposure	0.4649
Site	0.9927
GSTM1 status	0.3634
Ozone exposure by GSTM1 status	0.1617

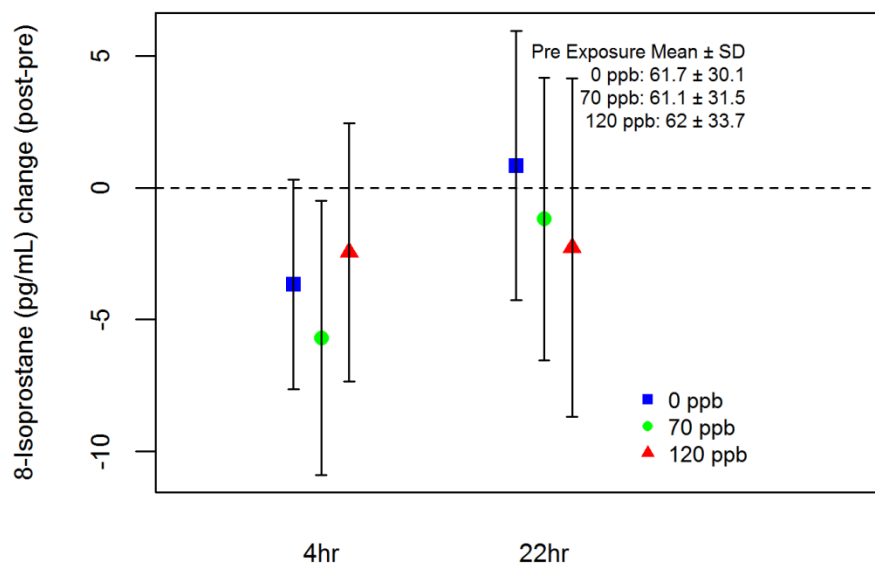
**Table B.2.8h. Mixed Model for Change in BAD (mm), Including Ozone Exposure, by GSTM1 Status Interaction**

<b>Effect</b>	<b>Estimate</b>	<b>Lower 95% CI</b>	<b>Upper 95% CI</b>	<b>P Value</b>
Intercept	-0.05647	-0.1093	-0.00368	0.0364
Ozone exposure				
120 ppb	0.01174	-0.03110	0.05458	0.5891
70 ppb	0.02858	-0.01443	0.07160	0.1913
0 ppb	0			
Site				
URMC	-0.00328	-0.06196	0.05540	0.9118
UNC	-0.00303	-0.06333	0.05726	0.9205
UCSF	0			
GSTM1 status				
Sufficient	-0.01298	-0.07488	0.04892	0.6775
Null	0			
Ozone exposure by GSTM1 status				
120 ppb by sufficient	0.01690	-0.04899	0.08279	0.6131
70 ppb by sufficient	-0.04479	-0.1104	0.02086	0.1797
0 ppb by sufficient	0			
120 ppb by null	0			
70 ppb by null	0			
0 ppb by null	0			



## 9. 8-Isoprostane (pg/mL)

The following figure shows the change in 8-isoprostane from pre- to post-exposure over time. The data come from Table B.2.5.



**Figure B.2.9. Change in 8-isoprostane at different post-exposure times and at each ozone exposure.**

## Main Analysis of Ozone Effect

As we can see from the tables below, none of the variables were statistically significant. This means that:

- there were no differences between the 4 hour and 22 hour post-exposure 8-isoprostane;
- there were no differences in 8-isoprostane across the ozone exposures; and
- there were no differences in 8-isoprostane across the 3 sites.

**Table B.2.9a. Type III Sum of Squares for Change in 8-Isoprostane (pg/mL)**

Effect	P Value
4-hr vs. 22-hr change	0.1350
Ozone exposure	0.7489
Site	0.6810

**Table B.2.9b. Mixed Model for Change in 8-Isoprostane (pg/mL)**

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	-1.4207	-7.3808	4.5395	0.6367
Change between pre- and post-exposure				
4-hr change	-3.0913	-7.1645	0.9820	0.1350
22-hr change	0			
Ozone exposure				
120 ppb	-0.8832	-5.8653	4.0989	0.7268
70 ppb	-1.9056	-6.8543	3.0430	0.4481
0 ppb	0			
Site				
URMC	2.8493	-3.6324	9.3310	0.3845
UNC	1.3043	-5.3878	7.9964	0.6993
UCSF	0			

## Analyses of Interactions

As we can see from the tables below, the ozone effect did not differ by age.

**Table B.2.9c. Type III Sum of Squares for Change in 8-Isoprostane (pg/mL), Including Ozone Exposure, by Age Interaction**

Effect	P Value
Ozone exposure	0.6837
4-hr vs. 22-hr change	0.1371
Site	0.6655
Age	0.6480
Ozone exposure by age	0.1140

**Table B.2.9d. Mixed Model for Change in 8-Isoprostane (pg/mL), Including Ozone Exposure, by Age Interaction**

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	-1.3889	-7.3699	4.5920	0.6454
4-hr change	-3.0655	-7.1264	0.9953	0.1371
22-hr change	0			
Ozone exposure				
120 ppb	-0.8057	-5.7770	4.1656	0.7494
70 ppb	-2.1613	-7.1045	2.7819	0.3892
0 ppb	0			
Site				
URMC	2.9543	-3.6075	9.5162	0.3731
UNC	1.2186	-5.5162	7.9534	0.7198
UCSF	0			
Age	-0.3496	-1.2238	0.5245	0.4286
Ozone exposure by age				
120 ppb by age	-0.2258	-1.3141	0.8626	0.6836
70 ppb by age	0.8631	-0.2227	1.9489	0.1189
0 ppb by age	0			

As we can see from the tables below, the ozone effect did not differ by sex.

**Table B.2.9e. Type III Sum of Squares for change in 8-Isoprostane (pg/mL), Including Ozone Exposure by Sex Interaction**

Effect	P Value
Ozone exposure	0.5967
4-hr vs. 22-hr change	0.1367
Site	0.6848
Sex	0.8741
Ozone exposure by sex	0.1335

**Table B.2.9f. Mixed Model for Change in 8-Isoprostane (pg/mL), Including Ozone Exposure, by Sex Interaction**

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	-1.0063	-8.3263	6.3138	0.7852
4-hr change	-3.0698	-7.1328	0.9931	0.1367
22-hr change	0			
Ozone exposure				
120 ppb	1.8027	-5.8415	9.4470	0.6421
70 ppb	-5.2563	-12.9661	2.4536	0.1801
0 ppb	0			
Site				
URMC	2.8695	-3.7167	9.4557	0.3887
UNC	1.3211	-5.5133	8.1556	0.7016
UCSF	0			
Sex				
Female	-0.7537	-8.7886	7.2812	0.8525
Male	0			
Ozone exposure by sex				
120 ppb by female	-4.6610	-14.7222	5.4001	0.3617
70 ppb by female	5.5990	-4.4400	15.6380	0.2724
0 ppb by female	0			
120 ppb by male	0			
70 ppb by male	0			
0 ppb by male	0			

As we can see from the tables below, the ozone effect did not differ by GSTM1 status.

**Table B.2.9g. Type III Sum of Squares for Change in 8-Isoprostane (pg/mL), Including Ozone Exposure, by GSTM1 Status Interaction**

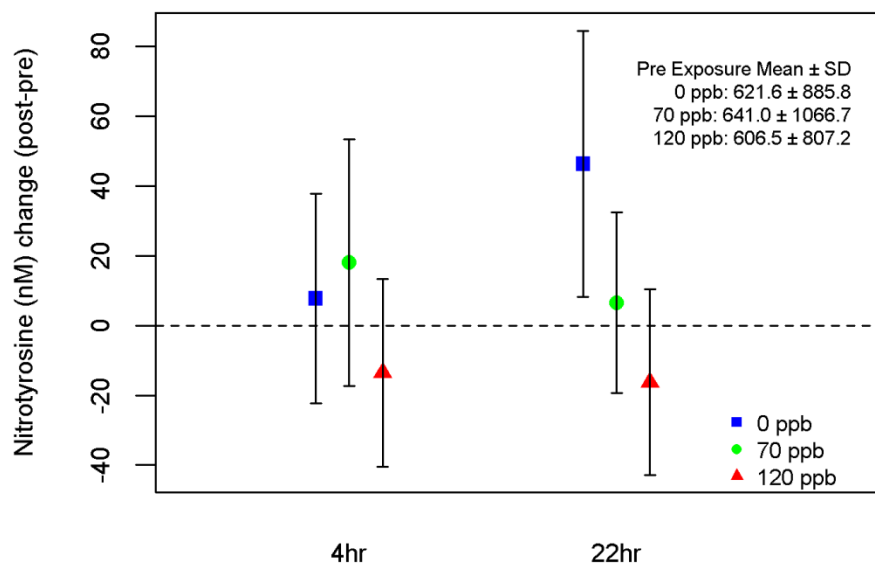
Effect	P Value
Ozone exposure	0.7962
4-hr vs. 22-hr change	0.1388
Site	0.6384
GSTM1 status	0.4684
Ozone exposure by GSTM1 status	0.6427

**Table B.2.9h. Mixed Model for Change in 8-Isoprostane (pg/mL), Including Ozone Exposure, by GSTM1 Status Interaction**

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	0.2778	-6.4333	6.9889	0.9346
4-hr change	-3.0653	-7.1436	1.0130	0.1388
22-hr change	0			
Ozone exposure				
120 ppb	-2.8767	-9.3913	3.6380	0.3845
70 ppb	-2.9807	-9.4763	3.5150	0.3662
0 ppb	0			
Site				
URMC	3.1111	-3.4318	9.6540	0.3470
UNC	1.4479	-5.2847	8.1805	0.6699
UCSF	0			
GSTM1 status				
Sufficient	-4.4753	-12.4865	3.5360	0.2697
Null	0			
Ozone exposure by GSTM1 status				
120 ppb by sufficient	4.8227	-5.3066	14.9520	0.3485
70 ppb by sufficient	2.6354	-7.4108	12.6816	0.6052
0 ppb by sufficient	0			
120 ppb by null	0			
70 ppb by null	0			
0 ppb by null	0			

## 10. Nitrotyrosine (nM)

The following figure shows the change in nitrotyrosine (nM) from pre- to post-exposure over time. The data come from Table B.2.5.



**Figure B.2.10. Change in nitrotyrosine at different post-exposure times and at each ozone exposure.**

## Main Analysis of Ozone Effect

As we can see from the tables below, the ozone effect is marginally statistically significant. This means that:

- there were no differences between the 4-hour and 22-hour post-exposure nitrotyrosine;
- there were marginally significant differences in nitrotyrosine across the ozone exposures; and
- there were no differences in nitrotyrosine across the 3 sites.

**Table B.2.10a. Type III Sum of Squares for Change in Nitrotyrosine (nM)**

Effect	P Value
4-hr vs. 22-hr change	0.4780
Ozone exposure	0.0165
Site	0.6298

**Table B.2.10b. Mixed Model for Change in Nitrotyrosine (nM)**

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	41.0278	3.7788	78.2768	0.0313
Change between pre- and post-exposure				
4-hr change	-8.3957	-31.8187	15.0273	0.4780
22-hr change	0			
Ozone exposure				
120 ppb	-41.4511	-70.1239	-12.7783	0.0049
70 ppb	-14.2489	-42.7215	14.2236	0.3245
0 ppb	0			
Site				
URMC	-8.7146	-50.8430	33.4137	0.6819
UNC	-20.9205	-64.3724	22.5314	0.3411
UCSF	0			

## Analyses of Interactions

As we can see from the tables below, the ozone effect did not differ by age.

**Table B.2.10c. Type III Sum of Squares for Change in Nitrotyrosine (nM), Including Ozone Exposure, by Age Interaction**

Effect	P Value
Ozone exposure	0.0169
4-hr vs. 22-hr change	0.4808
Site	0.6215
Age	0.7412
Ozone exposure by age	0.6570

**Table B.2.10d. Mixed Model for Change in Nitrotyrosine (nM), Including Ozone Exposure, by Age Interaction**

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	41.2092	3.7855	78.6329	0.0313
4-hr change	-8.3550	-31.8121	15.1022	0.4808
22-hr change	0			
Ozone exposure				
120 ppb	-41.5710	-70.3080	-12.8340	0.0048
70 ppb	-14.9425	-43.5105	13.6255	0.3032
0 ppb	0			
Site				
URMC	-8.1190	-50.7355	34.4976	0.7057
UNC	-21.2266	-64.9226	22.4693	0.3368
UCSF	0			
Age	-2.0259	-7.3759	3.3241	0.4535
Ozone exposure by age				
120 ppb by age	1.2318	-5.0582	7.5217	0.7005
70 ppb by age	2.9136	-3.3614	9.1885	0.3619
0 ppb by age	0			



As we can see from the tables below, the ozone effect did not differ by sex.

**Table B.2.10e. Type III Sum of Squares for Change in Nitrotyrosine (nM), Including Ozone Exposure, by Sex Interaction**

<b>Effect</b>	<b>P Value</b>
Ozone exposure	0.0085
4-hr vs. 22-hr change	0.4819
Site	0.6895
Sex	0.6693
Ozone exposure by sex	0.1828

**Table B.2.10f. Mixed Model for Change in Nitrotyrosine (nM), Including Ozone Exposure, by Sex Interaction**

<b>Effect</b>	<b>Estimate</b>	<b>Lower 95% CI</b>	<b>Upper 95% CI</b>	<b>P Value</b>
Intercept	61.8474	16.6249	107.07	0.0079
4-hr change	-8.3073	-31.6886	15.0740	0.4819
22-hr change	0			
Ozone exposure				
120 ppb	-72.0553	-116.04	-28.0713	0.0015
70 ppb	-35.5419	-79.9222	8.8384	0.1157
0 ppb	0			
Site				
URMC	-7.6695	-50.4392	35.1001	0.7222
UNC	-19.0636	-63.4171	25.2898	0.3951
UCSF	0			
Sex				
Female	-37.6478	-86.7734	11.4777	0.1312
Male	0			
Ozone exposure by sex				
120 ppb by female	53.0667	-4.8639	111.00	0.0723
70 ppb by female	36.7061	-21.0915	94.5037	0.2116
0 ppb by female	0			
120 ppb by male	0			
70 ppb by male	0			
0 ppb by male	0			

As we can see from the tables below, the ozone effect did not differ by GSTM1 status.

**Table B.2.10g. Type III Sum of Squares for Change in Nitrotyrosine (nM), Including Ozone Exposure, by GSTM1 Status Interaction**

Effect	P Value
Ozone exposure	0.0138
4-hr vs. 22-hr change	0.4827
Site	0.6415
GSTM1 status	0.7818
Ozone exposure by GSTM1 status	0.2605

**Table B.2.10h. Mixed Model for Change in Nitrotyrosine (nM), Including Ozone Exposure, by GSTM1 Status Interaction**

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	46.4121	4.7761	88.0482	0.0293
4-hr change	-8.3028	-31.7168	15.1112	0.4827
22-hr change	0			
Ozone exposure				
120 ppb	-37.4676	-74.8883	-0.04686	0.0497
70 ppb	-29.4106	-66.7204	7.8992	0.1215
0 ppb	0			
Site				
URMC	-8.2794	-50.7983	34.2396	0.6995
UNC	-20.5597	-64.2749	23.1555	0.3523
UCSF	0			
GSTM1 status	-13.7645	-62.6146	35.0856	0.5767
Sufficient	0			
Null				
Ozone exposure by GSTM1 status				
120 ppb by sufficient	-9.5100	-67.7176	48.6977	0.7474
70 ppb by sufficient	36.0291	-21.6809	93.7391	0.2194
0 ppb by sufficient	0			
120 ppb by null	0			
70 ppb by null	0			
0 ppb by null	0			

There is no interaction between ozone and time (see tables below), suggesting that the ozone effect is not different at 4 hours and 22 hours.

**Table B.2.10i Type III Sum of Squares for Change in Nitrotyrosine (nM), Including Ozone Exposure, by Time Interaction**

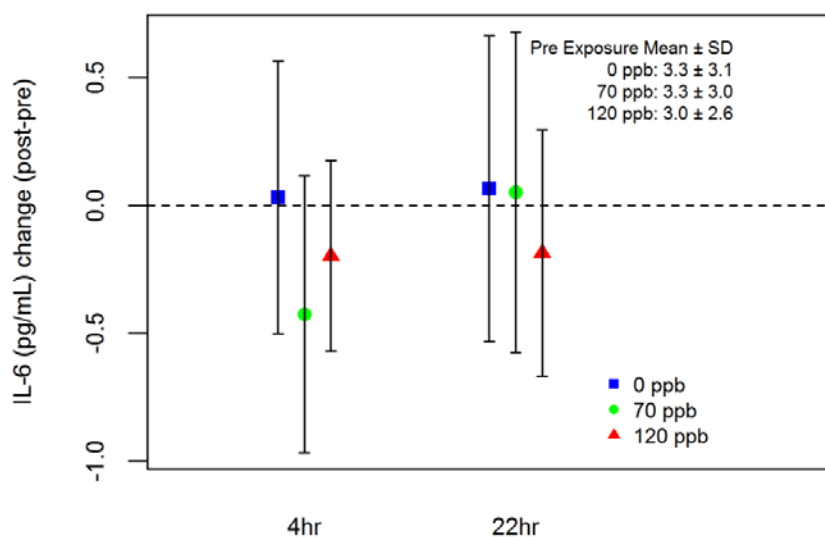
<b>Effect</b>	<b>P Value</b>
4-hr vs. 22-hr change	0.6332
Ozone exposure	0.0046
Site	0.7616
Ozone exposure by time	0.5101

**Table B.2.10j. Mixed Model for Change in Nitrotyrosine (nM), Including Ozone Exposure, By Time Interaction**

<b>Effect</b>	<b>Estimate</b>	<b>Lower 95% CI</b>	<b>Upper 95% CI</b>	<b>P Value</b>
Intercept	-4.2549	-66.7508	58.2411	0.8926
Change between post- and pre-exposure				
22-hr change	38.7301	-25.3448	102.80	0.2328
4-hr change	0			
Ozone exposure				
120 ppb	-52.4989	-115.79	10.7879	0.1034
70 ppb	10.3713	-52.7037	73.4462	0.7459
0 ppb	0			
Site				
URMC	23.5526	-40.1148	87.2200	0.4640
UNC	10.8656	-54.8249	76.5561	0.7430
UCSF	0			
Ozone exposure by time (change at 4 hr vs. 22 hr)				
120 ppb	-39.2653	-129.38	50.8478	0.3908
70 ppb	-50.2588	-139.81	39.2931	0.2694
0 ppb	0			

## 11. IL-6 (serum) (pg/mL)

The following figure shows the change in IL-6 from pre- to post-exposure over time. The data come from Table B.2.5.



**Figure B.2.11. Change in IL-6 at different post-exposure times and at each ozone exposure.**

## Main Analysis of Ozone Effect

As we can see from the tables below, none of the variables are statistically significant. This means that:

- there were no differences between the 4 hour and 22 hour post-exposure IL-6;
- there were no differences in IL-6 across the ozone exposures; and
- there were no differences in IL-6 across the 3 sites.

**Table B.2.11a. Type III Sum of Squares for Change in IL-6 (pg/mL)**

Effect	P Value
4-hr vs. 22-hr change	0.3905
Ozone exposure	0.5668
Site	0.7899

**Table B.2.11b. Mixed Model for Change in IL-6 (pg/mL)**

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	0.002003	-0.6160	0.6200	0.9949
Change between pre- and post-exposure				
4-hr change	-0.1806	-0.5966	0.2354	0.3905
22-hr change	0			
Ozone exposure				
120 ppb	-0.2244	-0.7332	0.2845	0.3853
70 ppb	-0.2486	-0.7541	0.2568	0.3328
0 ppb	0			
Site				
URMC	0.2021	-0.4754	0.8796	0.5546
UNC	0.2143	-0.4850	0.9136	0.5439
UCSF	0			

## Analyses of Interactions

As we can see from the tables below, the ozone effect did not differ by age.

**Table B.2.11c. Type III Sum of Squares for Change in IL-6 (pg/mL), Including Ozone Exposure, by Age Interaction**

Effect	P Value
Ozone exposure	0.5692
4-hr vs. 22-hr change	0.3899
Site	0.8027
Age	0.6143
Ozone exposure by age	0.9843

**Table B.2.11d. Mixed Model for Change in IL-6 (pg/mL), Including Ozone Exposure, by Age Interaction**

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	0.003974	-0.6172	0.6251	0.9899
4-hr change	-0.1812	-0.5981	0.2357	0.3899
22-hr change	0			
Ozone exposure				
120 ppb	-0.2246	-0.7350	0.2858	0.3862
70 ppb	-0.2483	-0.7558	0.2592	0.3354
0 ppb	0			
Site				
URMC	0.1837	-0.5019	0.8692	0.5955
UNC	0.2181	-0.4854	0.9216	0.5392
UCSF	0			
Age	0.02005	-0.07043	0.1105	0.6606
Ozone exposure by age				
120 ppb by age	-0.00287	-0.1146	0.1089	0.9597
70 ppb by age	-0.00979	-0.1213	0.1017	0.8630
0 ppb by age	0			

As we can see from the tables below, there was a marginally significant difference in the ozone effect on IL-6 by sex — IL-6 in women increased from pre- to post-exposure relative to men at 70 ppb ozone exposure, but not at 120 ppb ozone exposure.

**Table B.2.11e. Type III Sum of Squares for Change in IL-6 (pg/mL), Including Ozone Exposure, by Sex Interaction**

Effect	<i>P</i> Value
Ozone exposure	0.3285
4-hr vs. 22-hr change	0.3937
Site	0.8791
Sex	0.4178
Ozone exposure by sex	0.0276

**Table B.2.11f. Mixed Model for Change in IL-6 (pg/mL), Including Ozone Exposure, by Sex Interaction**

Effect	Estimate	Lower 95% CI	Upper 95% CI	<i>P</i> Value
Intercept	0.2643	-0.4911	1.0197	0.4884
4-hr change	-0.1781	-0.5912	0.2350	0.3937
22-hr change	0			
Ozone exposure				
120 ppb	-0.5205	-1.2977	0.2567	0.1879
70 ppb	-1.0698	-1.8537	-0.2858	0.0078
0 ppb	0			
Site				
URMC	0.1529	-0.5346	0.8404	0.6593
UNC	0.1611	-0.5522	0.8744	0.6545
UCSF	0			
Sex				
Female	-0.3968	-1.2241	0.4304	0.3428
Male	0			
Ozone exposure by sex				
120 ppb by female	0.5133	-0.5098	1.5364	0.3233
70 ppb by female	1.3849	0.3641	2.4057	0.0081
0 ppb by female	0			
120 ppb by male	0			
70 ppb by male	0			
0 ppb by male	0			

As we can see from the tables below, there was a marginally significant difference in the ozone effect on IL-6 by GSTM1 status — IL-6 increased after 70 ppb, but not 120 ppb, ozone exposure in GSTM1-sufficient subjects relative to GSTM1-null subjects.

**Table B.2.11g. Type III Sum of Squares for Change in IL-6 (pg/mL), Including Ozone Exposure, by GSTM1 Status Interaction**

Effect	P Value
Ozone exposure	0.7639
4-hr vs. 22-hr change	0.4040
Site	0.7184
GSTM1 status	0.1544
Ozone exposure by GSTM1 status	0.0310

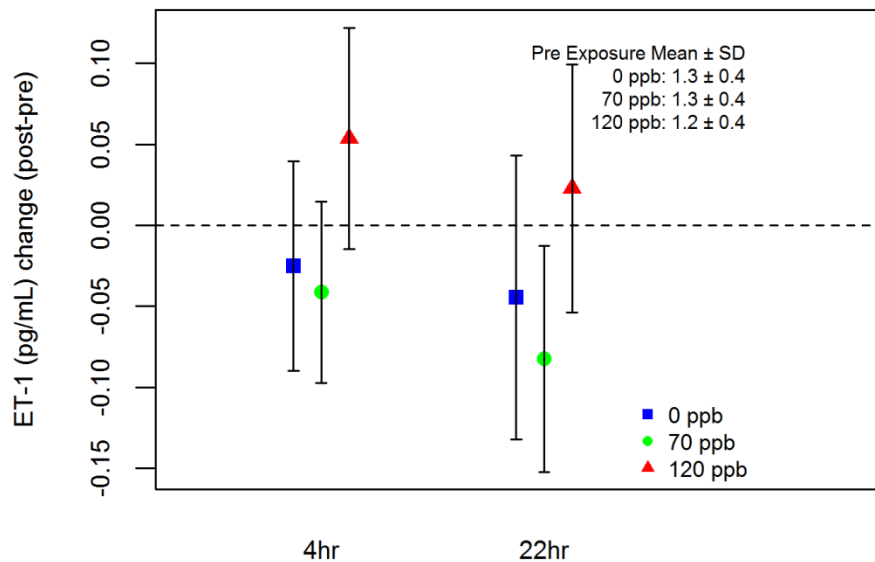
**Table B.2.11h. Mixed Model for Change in IL-6 (pg/mL), Including Ozone Exposure, by GSTM1 Status Interaction**

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	0.3899	-0.3007	1.0804	0.2647
4-hr change	-0.1743	-0.5874	0.2388	0.4040
22-hr change	0			
Ozone exposure				
120 ppb	-0.4114	-1.0713	0.2486	0.2202
70 ppb	-0.8111	-1.4691	-0.1530	0.0160
0 ppb	0			
Site				
URMC	0.2500	-0.4302	0.9302	0.4668
UNC	0.2442	-0.4556	0.9440	0.4896
UCSF	0			
GSTM1 status				
Sufficient	-1.0093	-1.8305	-0.1880	0.0166
Null	0			
Ozone exposure by GSTM1 status				
120 ppb by sufficient	0.4562	-0.5701	1.4824	0.3814
70 ppb by sufficient	1.3478	0.3301	2.3656	0.0098
0 ppb by sufficient	0			
120 ppb by null	0			
70 ppb by null	0			
0 ppb by null	0			



## 12. ET-1 (pg/mL)

The following figure shows the change in ET-1 from pre- to post-exposure over time. The data come from Table B.2.5.



**Figure B.2.12. Change in ET-1 at different post-exposure times and at each ozone exposure.**

## Main Analysis of Ozone Effect

As we can see from the tables below, ozone is statistically significant. This means that:

- there were no differences between the 4 hour and 22 hour post-exposure ET-1;
- there were differences in ET-1 across the ozone exposures; and
- there were no differences in ET-1 across the 3 sites.

**Table B.2.12a. Type III Sum of Squares for Change in ET-1 (pg/mL)**

<b>Effect</b>	<b>P Value</b>
4-hr vs. 22-hr change	0.2584
Ozone exposure	0.0080
Site	0.8426

**Table B.2.12b. Mixed Model for Change in ET-1 (pg/mL)**

<b>Effect</b>	<b>Estimate</b>	<b>Lower 95% CI</b>	<b>Upper 95% CI</b>	<b>P Value</b>
Intercept	-0.03674	-0.1216	0.04809	0.3915
Change between pre- and post-exposure				
4-hr change	0.03092	-0.02311	0.08495	0.2584
22-hr change	0			
Ozone exposure				
120 ppb	0.07408	0.007951	0.1402	0.0284
70 ppb	-0.02767	-0.09334	0.03800	0.4067
0 ppb	0			
Site				
URMC	-0.02751	-0.1229	0.06792	0.5680
UNC	-0.00997	-0.1084	0.08847	0.8409
UCSF	0			

## Analyses of Interactions

As we can see from the tables below,

- there was a marginally significant effect of age on ET-1 — ET-1 increased slightly with increasing age independent of ozone exposure; and
- the ozone effect did not differ by age.

**Table B.2.12c. Type III Sum of Squares for Change in ET-1 (pg/mL), Including Ozone Exposure, by Age Interaction**

Effect	P Value
Ozone exposure	0.0101
4-hr vs. 22-hr change	0.2581
Site	0.9393
Age	0.0405
Ozone exposure by age	0.7610

**Table B.2.12d. Mixed Model for Change in ET-1 (pg/mL), Including Ozone Exposure, by Age Interaction**

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	-0.03849	-0.1222	0.04519	0.3629
4-hr change	0.03100	-0.02314	0.08515	0.2581
22-hr change	0			
Ozone exposure				
120 ppb	0.07390	0.007592	0.1402	0.0292
70 ppb	-0.02527	-0.09119	0.04066	0.4503
0 ppb	0			
Site				
URMC	-0.01648	-0.1105	0.07750	0.7281
UNC	-0.01138	-0.1078	0.08502	0.8150
UCSF	0			
Age	-0.00856	-0.02062	0.003509	0.1621
Ozone exposure by age				
120 ppb by age	0.002140	-0.01238	0.01666	0.7721
70 ppb by age	-0.00324	-0.01772	0.01124	0.6599
0 ppb by age	0			

As we can see from the tables below, the ozone effect did not differ by sex.

**Table B.2.12e. Type III Sum of Squares for Change in ET-1 (pg/mL), Including Ozone Exposure, by Sex Interaction**

Effect	<i>P</i> Value
Ozone exposure	0.0050
4-hr vs. 22-hr change	0.2615
Site	0.8006
Sex	0.4107
Ozone exposure by sex	0.1022

**Table B.2.12f. Mixed Model for Change in ET-1 (pg/mL), Including Ozone Exposure, by Sex Interaction**

Effect	Estimate	Lower 95% CI	Upper 95% CI	<i>P</i> Value
Intercept	-0.09784	-0.2007	0.005049	0.0621
4-hr change	0.03062	-0.02324	0.08448	0.2615
22-hr change	0			
Ozone exposure				
120 ppb	0.1565	0.05515	0.2578	0.0027
70 ppb	0.02710	-0.07512	0.1293	0.6013
0 ppb	0			
Site				
URMC	-0.03241	-0.1290	0.06413	0.5062
UNC	-0.01770	-0.1178	0.08243	0.7260
UCSF	0			
Sex				
Female	0.1128	0.000838	0.2248	0.0483
Male	0			
Ozone exposure by sex				
120 ppb by female	-0.1428	-0.2762	-0.00935	0.0361
70 ppb by female	-0.09473	-0.2279	0.03840	0.1619
0 ppb by female	0			
120 ppb by male	0			
0 ppb by male	0			

As we can see from the tables below, the ozone effect did not differ by GSTM1 status.

**Table B.2.12g. Type III Sum of Squares for Change in ET-1 (pg/mL), Including Ozone Exposure, by GSTM1 Status Interaction**

Effect	<i>P</i> Value
Ozone exposure	0.0068
4-hr vs. 22-hr change	0.2606
Site	0.7995
GSTM1 status	0.3628
Ozone exposure by GSTM1 status	0.8030

**Table B.2.12h. Mixed Model for Change in ET-1 (pg/mL), Including Ozone Exposure, by GSTM1 Status Interaction**

Effect	Estimate	Lower 95% CI	Upper 95% CI	<i>P</i> Value
Intercept	-0.04297	-0.1377	0.05180	0.3697
4-hr change	0.03084	-0.02330	0.08499	0.2606
22-hr change	0			
Ozone exposure				
120 ppb	0.05697	-0.02956	0.1435	0.1954
70 ppb	-0.02977	-0.1160	0.05650	0.4966
0 ppb	0			
Site				
URMC	-0.03192	-0.1279	0.06403	0.5100
UNC	-0.01312	-0.1118	0.08555	0.7921
UCSF	0			
GSTM1 status				
Sufficient	0.02114	-0.09043	0.1327	0.7073
Null	0			
Ozone exposure by GSTM1 status				
120 ppb by sufficient	0.04136	-0.09323	0.1759	0.5448
70 ppb by sufficient	0.005067	-0.1284	0.1385	0.9403
0 ppb by sufficient	0			
120 ppb by null	0			
70 ppb by null	0			
0 ppb by null	0			

There is no interaction between ozone and time (see tables below), suggesting that the ozone effect is not different at 4 hours and 22 hours.

**Table B.2.12i. Type III Sum of Squares for Change in ET-1 (pg/mL), Including Ozone Exposure, by Time Interaction**

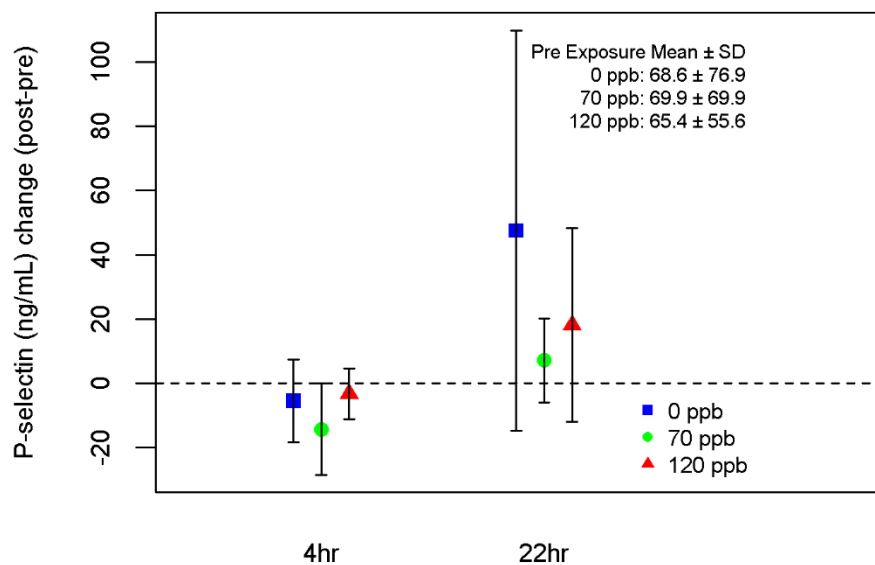
<b>Effect</b>	<b>P Value</b>
4-hr vs. 22-hr change	0.2607
Ozone exposure	0.0082
Site	0.8427
Ozone exposure by time	0.9546

**Table B.2.12j. Mixed Model for Change in ET-1 (pg/mL), Including Ozone Exposure, by Time Interaction**

<b>Effect</b>	<b>Estimate</b>	<b>Lower 95% CI</b>	<b>Upper 95% CI</b>	<b>P Value</b>
Intercept	-0.01079	-0.1036	0.08205	0.8178
Change between pre- and post-exposure				
22-hr change	-0.02086	-0.1149	0.07318	0.6602
4-hr change	0			
Ozone exposure				
120 ppb	0.07882	-0.01406	0.1717	0.0957
70 ppb	-0.01762	-0.1102	0.07496	0.7076
0 ppb	0			
Site				
URMC	-0.02748	-0.1229	0.06795	0.5684
UNC	-0.00989	-0.1083	0.08855	0.8421
UCSF	0			
Ozone exposure by time (change at 4 hr vs. 22 hr)				
120 ppb	-0.00967	-0.1419	0.1226	0.8854
70 ppb	-0.02027	-0.1517	0.1112	0.7611
0 ppb	0			

### 13. P-selectin (ng/mL)

The following figure shows the change in P-selectin from pre- to post-exposure over time. The data come from Table B.2.5.



**Figure B.2.13. Change in P-selectin at different post-exposure times and at each ozone exposure.**

## Main Analysis of Ozone Effect

As we can see from the tables below, time is statistically significant. This means that:

- there were differences between the 4-hour and 22-hour post-exposure P-selectin;
- there were no differences in P-selectin across the ozone exposures; and
- there were no differences in P-selectin across the 3 sites.

**Table B.2.13a. Type III Sum of Squares for Change in P-selectin (ng/mL)**

Effect	P Value
4-hr vs. 22-hr change	0.0077
Ozone exposure	0.2345
Site	0.2172

**Table B.2.13b. Mixed Model for Change in P-selectin (ng/mL)**

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	56.1380	22.8777	89.3983	0.0012
Change between pre- and post-exposure				
4-hr change	-31.8182	-54.9756	-8.6608	0.0077
22-hr change	0			
Ozone exposure				
120 ppb	-14.0550	-42.3738	14.2639	0.3286
70 ppb	-24.2839	-52.4143	3.8465	0.0902
0 ppb	0			
Site				
URMC	-26.6794	-62.4839	9.1251	0.1421
UNC	-29.6612	-66.6367	7.3144	0.1144
UCSF	0			



## Analyses of Interactions

As we can see from the tables below, the ozone effect did not differ by age.

**Table B.2.13c. Type III Sum of Squares for Change in P-selectin (ng/mL), Including Ozone Exposure, by Age Interaction**

Effect	P Value
Ozone exposure	0.2665
4-hr vs. 22-hr change	0.0074
Site	0.2099
Age	0.3468
Ozone exposure by age	0.0956

**Table B.2.13d. Mixed Model for Change in P-selectin (ng/mL), Including Ozone Exposure, by Age Interaction**

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	55.6557	22.3882	88.9233	0.0013
4-hr change	-31.8521	-54.9322	-8.7719	0.0074
22-hr change	0			
Ozone exposure				
120 ppb	-13.1711	-41.4194	15.0772	0.3586
70 ppb	-23.1669	-51.2580	4.9241	0.1054
0 ppb	0			
Site				
URMC	-28.2124	-64.2873	7.8626	0.1236
UNC	-29.0273	-66.0638	8.0093	0.1228
UCSF	0			
Age	5.5032	0.6100	10.3964	0.0280
Ozone exposure by age				
120 ppb by age	-5.7773	-11.9620	0.4074	0.0670
70 ppb by age	-6.0589	-12.2293	0.1115	0.0543
0 ppb by age	0			

As we can see from the tables below, the ozone effect did not differ by sex.

**Table B.2.13e. Type III Sum of Squares for Change in P-selectin (ng/mL), Including Ozone Exposure, by Sex Interaction**

Effect	P Value
Ozone exposure	0.1783
4-hr vs. 22-hr change	0.0078
Site	0.2360
Sex	0.9438
Ozone exposure by sex	0.3245

**Table B.2.13f. Mixed Model for Change in P-selectin (ng/mL), Including Ozone Exposure, by Sex Interaction**

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	70.4303	29.4498	111.41	0.0010
4-hr change	-31.7621	-54.9176	-8.6067	0.0078
22-hr change	0			
Ozone exposure				
120 ppb	-38.8533	-82.4208	4.7143	0.0801
70 ppb	-40.9463	-84.8824	2.9899	0.0676
0 ppb	0			
Site				
URMC	-26.6716	-63.0080	9.6647	0.1481
UNC	-29.2797	-66.9923	8.4328	0.1263
UCSF	0			
Sex				
Female	-24.9286	-70.0364	20.1792	0.2749
Male	0			
Ozone exposure by sex				
120 ppb by female	42.9081	-14.4228	100.24	0.1414
70 ppb by female	28.6270	-28.5793	85.8334	0.3246
0 ppb by female	0			
120 ppb by male	0			
70 ppb by male	0			
0 ppb by male	0			

As we can see from the tables below, the ozone effect did not differ by GSTM1 status.

**Table B.2.13g. Type III Sum of Squares for Change in P-selectin (ng/mL), Including Ozone Exposure, by GSTM1 Status Interaction**

Effect	P Value
Ozone exposure	0.3319
4-hr vs. 22-hr change	0.0081
Site	0.2571
GSTM1 status	0.2691
Ozone exposure by GSTM1 status	0.5017

**Table B.2.13h. Mixed Model for Change in P-selectin (ng/mL), Including Ozone Exposure, by GSTM1 Status Interaction**

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	68.3782	31.0031	105.75	0.0005
4-hr change	-31.6151	-54.7964	-8.4337	0.0081
22-hr change	0			
Ozone exposure				
120 ppb	-19.7032	-56.7269	17.3205	0.2949
70 ppb	-38.3309	-75.2472	-1.4147	0.0419
0 ppb	0			
Site				
URMC	-24.6497	-60.5707	11.2714	0.1760
UNC	-28.4156	-65.3876	8.5564	0.1302
UCSF	0			
GSTM1 status				
Sufficient	-32.5450	-77.3783	12.2884	0.1526
Null	0			
Ozone exposure by GSTM1 status				
120 ppb by sufficient	13.7613	-43.7976	71.3202	0.6375
70 ppb by sufficient	33.8090	-23.2842	90.9023	0.2440
0 ppb by sufficient	0			
120 ppb by null	0			
70 ppb by null	0			
0 ppb by null	0			

## 14. White Blood Cells (1000/ $\mu$ L)

### Main Analysis of Ozone Effect

As we can see from the tables below, time is statistically significant. This means that:

- there were differences between the 4-hour and 22-hour post-exposure white blood cell (WBC) count;
- there were no differences in WBC across the ozone exposures; and
- there were no differences in WBC across the 3 sites;

**Table B.2.14a. Type III Sum of Squares for Change in WBC (1000/uL)**

Effect	<i>P</i> Value
4-hr vs. 22-hr change	<0.0001
Ozone exposure	0.9112
Site	0.1835

**Table 1 B.2.4b. Mixed model for change in WBC (1000/uL)**

Effect	Estimate	Lower 95% CI	Upper 95% CI	<i>P</i> Value
Intercept	-0.8136	-1.0727	-0.5546	<0.0001
Change between pre- and post-exposure				
4-hr change	1.2665	1.1148	1.4182	<0.0001
22-hr change	0			
Ozone exposure				
120 ppb	-0.02247	-0.2084	0.1634	0.8117
70 ppb	-0.04020	-0.2245	0.1441	0.6673
0 ppb	0			
Site				
URMC	-0.00125	-0.3017	0.2991	0.9934
UNC	-0.2456	-0.5551	0.06389	0.1183
UCSF	0			

## Analyses of Interactions

As we can see from the tables below, the ozone effect did not differ by age.

**Table B.2.14c. Type III Sum of Squares for Change in WBC (1000/uL), including Ozone Exposure, by Age Interaction**

Effect	<i>P</i> Value
Ozone exposure	0.8992
4-hr vs. 22-hr change	<0.0001
Site	0.2018
Age	0.6495
Ozone exposure by age	0.7584

**Table B.2.14d. Mixed Model for Change in WBC (1000/uL), Including Ozone Exposure, by Age Interaction**

Effect	Estimate	Lower 95% CI	Upper 95% CI	<i>P</i> Value
Intercept	-0.8114	-1.0716	-0.5511	<0.0001
4-hr change	1.2668	1.1149	1.4188	<0.0001
22-hr change	0			
Ozone exposure				
120 ppb	-0.02494	-0.2113	0.1614	0.7919
70 ppb	-0.04305	-0.2279	0.1418	0.6464
0 ppb	0			
Site				
URMC	-0.00924	-0.3130	0.2945	0.9519
UNC	-0.2448	-0.5559	0.06637	0.1215
UCSF	0			
Age	-0.00250	-0.03894	0.03394	0.8917
Ozone exposure by age				
120 ppb by age	0.01431	-0.02651	0.05512	0.4912
70 ppb by age	0.01214	-0.02835	0.05263	0.5558
0 ppb by age	0			

As we can see from the tables below, the ozone effect did not differ by sex.

**Table B.2.14e. Type III Sum of Squares for Change in WBC (1000/uL), Including Ozone Exposure, by Sex Interaction**

Effect	P Value
Ozone exposure	0.8319
4-hr vs. 22-hr change	<0.0001
Site	0.2330
Sex	0.2718
Ozone exposure by sex	0.5146

**Table B.2.14f. Mixed Model for Change in WBC (1000/uL), Including Ozone Exposure, by Sex Interaction**

Effect	Estimate	Lower 95% CI	Upper 95% CI	P-value
Intercept	-0.6811	-0.9916	-0.3706	<0.0001
4-hr change	1.2678	1.1160	1.4197	<0.0001
22-hr change	0			
Ozone exposure				
120 ppb	-0.1014	-0.3873	0.1845	0.4847
70 ppb	-0.1657	-0.4516	0.1202	0.2541
0 ppb	0			
Site				
URMC	0.02037	-0.2823	0.3231	0.8938
UNC	-0.2159	-0.5297	0.09796	0.1750
UCSF	0			
Sex				
Female	-0.2590	-0.5945	0.07643	0.1284
Male	0			
Ozone exposure by sex				
120 ppb by female	0.1376	-0.2389	0.5142	0.4715
70 ppb by female	0.2166	-0.1576	0.5909	0.2548
0 ppb by female	0			
120 ppb by male	0			
70 ppb by male	0			
0 ppb by male	0			

As we can see from the tables below, the ozone effect did not differ by GSTM1 status.

**Table B.2.14g. Type III Sum of Squares for Change in WBC (1000/uL), Including Ozone Exposure, by GSTM1 Status Interaction**

<b>Effect</b>	<b>P Value</b>
Ozone exposure	0.9492
4-hr vs. 22-hr change	<0.0001
Site	0.1992
GSTM1 status	0.6982
Ozone exposure by GSTM1 status	0.0562

**Table B.2.14h. Mixed Model for Change in WBC (1000/uL), Including Ozone Exposure, by GSTM1 Status Interaction**

<b>Effect</b>	<b>Estimate</b>	<b>Lower 95% CI</b>	<b>Upper 95% CI</b>	<b>P Value</b>
Intercept	-0.7684	-1.0573	-0.4796	<0.0001
4-hr change	1.2687	1.1177	1.4197	<0.0001
22-hr change	0			
Ozone exposure				
120 ppb	0.02570	-0.2183	0.2697	0.8355
70 ppb	-0.1762	-0.4172	0.06475	0.1507
0 ppb	0			
Site				
URMC	0.004303	-0.2996	0.3082	0.9776
UNC	-0.2379	-0.5503	0.07446	0.1336
UCSF	0			
GSTM1 status				
Sufficient	-0.1198	-0.4532	0.2137	0.4770
Null	0			
Ozone exposure by GSTM1 status				
120 ppb by sufficient	-0.1125	-0.4868	0.2618	0.5536
70 ppb by sufficient	0.3243	-0.04730	0.6959	0.0867
0 ppb by sufficient	0			
120 ppb by null	0			
70 ppb by null	0			
0 ppb by null	0			

## Abbreviations and Other Terms

BAD	brachial artery diameter
BAU	brachial artery ultrasound
CRP	C-reactive protein
DBP	diastolic blood pressure
ET-1	endothelin 1
FMD	flow-mediated dilatation
GSTM1	glutathione S-transferase Mu 1
IL-6	interleukin 6
MOSES	Multicenter Ozone Study in oldEr Subjects
ppb	part per billion
SBP	systolic blood pressure
SD	standard deviation
UCSF	University of California at San Francisco
UNC	University of North Carolina at Chapel Hill
URMC	University of Rochester Medical Center
WBC	white blood cell