



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**

Mark W. Frampton et al.

**Appendix C.1 Analyses of ECG Outcomes Measured During Exposure  
Exercise 6**

**Appendix C.2 Analyses of Blood Pressure Measured During Exposure  
Rest Periods 2 and 4**

These Appendices were reviewed solely for spelling, grammar, and cross-references to the main text. They have not been formatted or fully edited by HEI. This document was reviewed by the HEI MOSES Review Panel.

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## **APPENDIX C.1**

### **Analyses of ECG Outcomes Measured During Exposure Exercise 6**

## 1. Descriptive Statistics

**Table C.1.1. Descriptive Analyses of Primary\* and Secondary Cardiac Outcomes (5-Min Averages) at All Time Points, Including Exposure Exercise 6**

	0 ppb			70 ppb			120 ppb		
	<i>N</i>	Mean	SD	<i>N</i>	Mean	SD	<i>N</i>	Mean	SD
<b>HF, 5-min avg (ms<sup>2</sup>)</b>									
Pre-exposure	85	945.2	4052.9	87	664.7	1831.2	84	508.5	1064.4
During exposure (exercise period 6)	83	83.6	348.2	86	113.5	496.7	83	117.1	577.6
15 min post-exposure	85	1288.2	5496.9	87	903.4	2429.1	84	1693.2	6112.0
4 hr post-exposure	85	773.9	2317.7	87	897.2	3073.4	83	845.3	2530.2
22 hr post-exposure	83	1191.8	4760.9	84	542.5	1564.4	78	1066.8	4697.3
<b>HR, 5-min avg (beats/min)</b>									
Pre-exposure	85	67.5	8.6	87	67.6	8.2	84	67.6	9.3
During exposure (exercise period 6)	84	104.2	15.5	87	104.6	15.1	83	103.8	15.8
15 min post-exposure	85	67.6	10.5	87	67.2	9.5	84	66.8	10.3
4 hr post-exposure	85	67.4	9.5	87	66.6	9.0	83	66.1	9.2
22 hr post-exposure	83	64.0	8.8	84	64.4	8.4	78	64.7	10.1
<b>LF, 5-min avg (ms<sup>2</sup>)</b>									
Pre-exposure	85	593.7	1141.7	87	492.7	1001.5	84	542.8	1119.3
During exposure (exercise period 6)	83	133.7	460.5	86	155.9	645.1	83	135.9	496.2
15 min post-exposure	85	707.1	1083.2	87	565.4	648.5	84	821.8	1137.7
4 hr post-exposure	85	550.1	720.2	87	543.0	757.6	83	650.5	813.9
22 hr post-exposure	83	646.8	928.6	84	423.3	480.0	78	740.1	2023.7

	0 ppb			70 ppb			120 ppb		
	N	Mean	SD	N	Mean	SD	N	Mean	SD
<b>LF/HF, 5-min avg</b>									
Pre-exposure	85	2.66	3.72	87	2.04	2.81	84	2.44	3.37
During exposure (exercise period 6)	83	4.78	4.07	86	5.49	5.94	83	6.01	6.07
15 min post-exposure	85	3.21	6.05	87	2.03	2.44	84	2.54	4.49
4 hr post-exposure	85	2.78	3.52	87	2.41	3.12	83	2.44	2.93
22 hr post-exposure	83	2.47	2.51	84	2.51	3.43	78	2.63	4.63
<b>QTc, 5-min avg (ms)</b>									
Pre-exposure	85	425.4	16.3	87	426.8	16.4	84	425.1	17.2
During exposure (exercise period 6)	84	430.0	18.4	87	432.0	19.0	83	431.0	22.5
15 min post-exposure	85	421.8	18.0	87	422.7	17.9	84	419.9	18.5
4 hr post-exposure	85	424.7	19.9	87	424.4	17.5	83	423.1	18.0
22 hr post-exposure	83	416.4	18.9	84	419.5	16.7	78	418.3	19.8
<b>T amplitude, 5-min avg (<math>\mu</math>V)</b>									
Pre-exposure	85	661.9	295.7	87	652.6	282.3	84	662.4	295.3
During exposure (exercise period 6)	83	660.8	281.2	86	681.3	298.0	83	687.6	294.8
15 min post-exposure	85	808.2	329.4	87	819.1	316.8	84	827.8	344.5
4 hr post-exposure	85	697.7	313.7	87	708.8	300.9	83	714.2	319.8
22 hr post-exposure	83	728.6	313.5	84	708.4	301.4	78	716.5	326.8
<b>RMSSD, 5-min avg (ms)</b>									
Pre-exposure	85	28.5	24.4	87	28.0	24.9	84	26.8	19.7
During exposure (exercise period 6)	84	13.1	18.0	87	13.1	22.0	83	10.2	14.0
15 min post-exposure	85	29.6	21.1	87	32.0	21.9	84	33.6	24.9
4 hr post-exposure	85	28.3	23.2	87	29.5	23.6	83	29.0	21.0
22 hr post-exposure	83	30.1	24.8	84	28.1	20.4	78	29.0	23.2
<b>SDNN, 5-min avg (ms)</b>									
Pre-exposure	85	48.1	39.0	87	48.2	36.6	84	49.5	38.3
During exposure (exercise period 6)	84	21.5	22.1	87	21.5	26.0	83	21.7	28.2
15 min post-exposure	85	53.9	45.9	87	55.2	44.5	84	58.4	47.3

	<b>0 ppb</b>			<b>70 ppb</b>			<b>120 ppb</b>		
	<b>N</b>	<b>Mean</b>	<b>SD</b>	<b>N</b>	<b>Mean</b>	<b>SD</b>	<b>N</b>	<b>Mean</b>	<b>SD</b>
4 hr post-exposure	85	57.2	46.0	87	54.9	46.0	83	56.4	42.5
22 hr post-exposure	83	54.3	44.2	84	50.7	41.0	78	51.5	50.0
<b>ST in lead II, 5-min avg (<math>\mu</math>V)</b>									
Pre-exposure	85	30.3	43.5	87	31.8	41.5	84	32.8	42.9
During exposure (exercise period 6)	84	7.0	57.8	87	8.0	60.7	83	10.1	56.6
15 min post-exposure	85	41.8	44.5	87	45.0	44.0	84	43.9	43.5
4 hr post-exposure	85	34.4	43.6	87	37.1	42.4	83	38.7	42.7
22 hr post-exposure	83	38.1	41.9	84	38.7	40.9	78	36.4	43.9
<b>ST in V2, 5-min avg (<math>\mu</math>V)</b>									
Pre-exposure	85	92.6	63.7	87	94.4	63.4	84	98.7	61.7
During exposure (exercise period 6)	84	67.0	58.2	87	66.4	57.8	83	72.1	60.1
15 min post-exposure	85	97.2	67.4	87	98.7	64.9	84	107.4	68.5
4 hr post-exposure	85	92.2	70.2	87	95.7	70.7	83	97.1	66.3
22 hr post-exposure	83	97.6	62.0	84	97.5	62.4	78	105.0	63.0
<b>ST in V5, 5-min avg (<math>\mu</math>V)</b>									
Pre-exposure	85	24.9	37.5	87	23.4	34.2	84	24.6	34.5
During exposure (exercise period 6)	84	8.2	52.0	87	7.7	51.6	83	13.4	55.1
15 min post-exposure	85	33.1	39.8	87	32.5	37.9	84	34.0	38.6
4 hr post-exposure	85	27.4	37.2	87	26.1	33.7	83	28.2	34.7
22 hr post-exposure	83	30.6	37.7	84	28.4	35.9	78	27.8	36.2

\*Primary outcomes are in boldface.

## Ozone Effects on Primary ECG Outcomes Measured During Exercise 6

### 2. HF, 5-Min Average (ms<sup>2</sup>)

As we can see from the tables below,

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

**Table C.1.2a. Type III Sum of Squares for Change in HF, 5-Min Average (ms<sup>2</sup>)**

Effect	<i>P</i> Value
Ozone exposure	0.3902
Site	0.4317

**Table C.1.2b. Mixed Model for Change in HF, 5-Min Average (ms<sup>2</sup>)**

Effect	Estimate	Lower 95% CI	Upper 95% CI	<i>P</i> Value
Intercept	-1178.61	-2054.94	-302.27	0.0090
Ozone exposure				
120 ppb	474.71	-207.22	1156.64	0.1711
70 ppb	219.52	-454.89	893.93	0.5213
0 ppb	0			
Site				
URMC	266.64	-784.44	1317.72	0.6152
UNC	695.86	-382.44	1774.15	0.2029
UCSF	0			

### 3. LF, 5-Min Average (ms<sup>2</sup>)

As we can see from the tables below,

- there were no differences in LF across the ozone exposures; and
- there was no difference in LF across the 3 sites.

**Table C.1.3a. Type III Sum of Squares for Change in LF, 5-Min Average (ms<sup>2</sup>)**

Effect	<i>P</i> Value
Ozone exposure	0.5485
Site	0.5920

**Table C.1.3b. Mixed Model for Change in LF, 5-Min Average (ms<sup>2</sup>)**

Effect	Estimate	Lower 95% CI	Upper 95% CI	<i>P</i> Value
Intercept	-615.66	-1008.82	-222.49	0.0025
Ozone exposure				
120 ppb	64.8097	-122.30	251.92	0.4950
70 ppb	101.70	-83.0463	286.45	0.2786
0 ppb	0			
Site				
URMC	258.82	-249.66	767.30	0.3143
UNC	181.38	-339.29	702.04	0.4904
UCSF	0			



#### 4. T-Wave Amplitude, 5-Min Average ( $\mu\text{V}$ )

As we can see from the tables below,

- there were no differences in T-wave amplitude across the ozone exposures; and
- there were no differences in T-wave amplitude across the 3 sites.

**Table C.1.4a. Type III Sum of Squares for Change in T-Wave Amplitude, 5-Min Average ( $\mu\text{V}$ )**

<b>Effect</b>	<b>P Value</b>
Ozone exposure	0.0636
Site	0.3806

**Table C.1.4b. Mixed Model for Change in T-Wave Amplitude, 5-Min Average ( $\mu\text{V}$ )**

<b>Effect</b>	<b>Estimate</b>	<b>Lower 95% CI</b>	<b>Upper 95% CI</b>	<b>P Value</b>
Intercept	32.2767	-35.5281	100.08	0.3465
Ozone exposure				
120 ppb	22.2326	-6.5709	51.0362	0.1294
70 ppb	33.7189	5.1831	62.2546	0.0209
0 ppb	0			
Site				
URMC	-45.4066	-133.58	42.7623	0.3087
UNC	-61.4834	-151.74	28.7696	0.1791
UCSF	0			

## 5. ST in V5, 5-Min Average ( $\mu\text{V}$ )

As we can see from the tables below,

- there were no differences in ST in V5 across the ozone exposures; and
- there were no differences in ST in V5 across the 3 sites.

**Table C.1.5a. Type III Sum of Squares for Change in ST in V5, 5-Min Average ( $\mu\text{V}$ )**

Effect	<i>P</i> Value
Ozone exposure	0.1821
Site	0.0922

**Table C.1.5b. Mixed Model for Change in ST in V5, 5-Min Average ( $\mu\text{V}$ )**

Effect	Estimate	Lower 95% CI	Upper 95% CI	<i>P</i> Value
Intercept	-5.1050	-18.5519	8.3419	0.4524
Ozone exposure				
120 ppb	5.1594	-0.5735	10.8923	0.0774
70 ppb	1.2427	-4.3936	6.8790	0.6639
0 ppb	0			
Site				
URMC	-18.8577	-36.3882	-1.3273	0.0353
UNC	-14.7771	-32.7232	3.1690	0.1053
UCSF	0			

## Ozone Effects on Secondary ECG Outcomes Measured During Exercise 6

### 6. RMSSD, 5-Min Average (ms)

As we can see from the tables below,

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

**Table C.1.6a. Type III Sum of Squares for Change in RMSSD, 5-Min Average (ms)**

<b>Effect</b>	<b>P Value</b>
Ozone exposure	0.9141
Site	0.5501

**Table C.1.6b. Mixed Model for Change in RMSSD, 5-Min Average (ms)**

<b>Effect</b>	<b>Estimate</b>	<b>Lower 95% CI</b>	<b>Upper 95% CI</b>	<b>P Value</b>
Intercept	-18.9971	-28.2991	-9.6950	0.0001
Ozone exposure				
120 ppb	-0.6722	-5.6504	4.3060	0.7901
70 ppb	0.3724	-4.5246	5.2693	0.8808
0 ppb	0			
Site				
URMC	6.5525	-5.3403	18.4453	0.2764
UNC	3.9196	-8.2609	16.1000	0.5240
UCSF	0			

## 7. SDNN, 5-Min Average (ms)

As we can see from the tables below,

- there were no differences in SDNN across the ozone exposures; and
- there were no differences in SDNN from exercise period 6 to pre-exposure across the 3 sites.

**Table C.1.7a. Type III Sum of Squares for Change in SDNN, 5-Min Average (ms)**

<b>Effect</b>	<b>P Value</b>
Ozone exposure	0.9602
Site	0.1241

**Table C.1.7b. Mixed Model for Change in SDNN, 5-Min Average (ms)**

<b>Effect</b>	<b>Estimate</b>	<b>Lower 95% CI</b>	<b>Upper 95% CI</b>	<b>P Value</b>
Intercept	-35.2151	-46.8214	-23.6087	<0.0001
Ozone exposure				
120 ppb	-1.1611	-9.2418	6.9197	0.7770
70 ppb	-0.4747	-8.4319	7.4826	0.9064
0 ppb	0			
Site				
URMC	14.4277	0.1582	28.6973	0.0476
UNC	11.0111	-3.6169	25.6390	0.1382
UCSF	0			

## 8. HR, 5-Min Average (beats/min)

As we can see from the tables below,

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

**Table C.1.8a. Type III Sum of Squares for Change in HR, 5-Min Average (beats/min)**

<b>Effect</b>	<b>P Value</b>
Ozone exposure	0.7898
Site	0.1267

**Table C.1.8b. Mixed Model for Change in HR, 5-Min Average (beats/min)**

<b>Effect</b>	<b>Estimate</b>	<b>Lower 95% CI</b>	<b>Upper 95% CI</b>	<b>P Value</b>
Intercept	39.9137	35.3346	44.4928	<0.0001
Ozone exposure				
120 ppb	0.1336	-1.8523	2.1194	0.8945
70 ppb	0.6423	-1.3102	2.5947	0.5169
0 ppb	0			
Site				
URMC	-3.9082	-9.8710	2.0545	0.1960
UNC	-6.2757	-12.3800	-0.1714	0.0440
UCSF	0			

## 9. QTc, 5-Min Average (ms)

As we can see from the tables below,

- there were no differences in change in QTc from exercise period 6 to pre-exposure across the ozone exposures; and
- there were significant differences in QTc across the 3 sites.

**Table C.1.9a. Type III Sum of Squares for Change in QTc, 5-Min Average (ms)**

	<i>P Value</i>
Ozone exposure	0.6629
Site	0.0008

**Table C.1.9b. Mixed Model for Change in QTc, 5-Min Average (ms)**

<b>Effect</b>	<b>Estimate</b>	<b>Lower 95% CI</b>	<b>Upper 95% CI</b>	<b>P Value</b>
Intercept	-0.7685	-7.1070	5.5701	0.8101
Ozone exposure				
120 ppb	1.5835	-1.9653	5.1324	0.3796
70 ppb	1.1206	-2.3708	4.6120	0.5271
0 ppb	0			
Site				
URMC	13.4135	5.3513	21.4758	0.0014
UNC	-0.09894	-8.3572	8.1593	0.9810
UCSF	0			

## 10. ST in Lead II, 5-min Average ( $\mu\text{V}$ )

As we can see from the tables below,

- there were no differences in ST in Lead II across the ozone exposures; and
- there were no differences in ST in Lead II across the 3 sites.

**Table C.1.10a. Type III Sum of Squares for Change in ST in Lead II, 5-Min Average ( $\mu\text{V}$ )**

<b>Effect</b>	<b>P Value</b>
Ozone exposure	0.9821
Site	0.3540

**Table C.1.10b. Mixed Model for Change in ST in Lead II, 5-Min Average ( $\mu\text{V}$ )**

<b>Effect</b>	<b>Estimate</b>	<b>Lower 95% CI</b>	<b>Upper 95% CI</b>	<b>P Value</b>
Intercept	-13.9493	-30.2425	2.3439	0.0924
Ozone exposure				
120 ppb	0.2502	-4.1633	4.6637	0.9110
70 ppb	-0.1678	-4.5045	4.1690	0.9392
0 ppb	0			
Site				
URMC	-14.9741	-36.6318	6.6837	0.1728
UNC	-12.5911	-34.7522	9.5699	0.2618
UCSF	0			

## 11. ST in V2, 5-Min Average ( $\mu\text{V}$ )

As we can see from the tables below,

- there were no differences in ST in V2 across the ozone exposures; and
- there were no differences in ST in V2 across the 3 sites.

**Table C.1.11a. Type III Sum of Squares for Change in ST in V2, 5-Min Average ( $\mu\text{V}$ )**

<b>Effect</b>	<b>P Value</b>
Ozone exposure	0.7217
Site	0.3572

**Table C.1.11b. Mixed Model for Change in ST in V2, 5-Min Average ( $\mu\text{V}$ )**

<b>Effect</b>	<b>Estimate</b>	<b>Lower 95% CI</b>	<b>Upper 95% CI</b>	<b>P Value</b>
Intercept	-31.6050	-45.0904	-18.1196	<0.0001
Ozone exposure				
120 ppb	-1.3899	-6.8396	4.0597	0.6152
70 ppb	-2.1709	-7.5282	3.1864	0.4248
0 ppb	0			
Site				
URMC	12.2572	-5.3827	29.8970	0.1707
UNC	3.5785	-14.4782	21.6352	0.6945
UCSF	0			



## Ozone Effects on Arrhythmias Measured During 3-Hour Exposure Period

### 12. VE During Exposure

#### *VE Singles*

**Table C.1.12a. Number of Subjects with Any VE Singles by Ozone Exposure**

	No	Yes	Total
0 ppb	49 (58%)	36 (42%)	85
70 ppb	50 (58%)	36 (42%)	86
120 ppb	45 (54%)	38 (46%)	83

**Table C.1.12b. Mixed Model for VE Singles**

Effect	Odds Ratio	Lower 95% CI	Upper 95% CI	P Value
Intercept	1.36	0.63	2.94	0.4320
Ozone exposure				
120 ppb	1.19	0.59	2.39	0.6193
70 ppb	0.97	0.48	1.93	0.9227
0 ppb				
Site				
URMC	0.35	0.15	0.86	0.0220
UNC	0.421	0.17	1.04	0.0598
UCSF	—	—	—	—

**Table C.1.12c. Distribution of VE Singles by Ozone Exposure**

<b>0 ppb*</b>			<b>70 ppb*</b>			<b>120 ppb*</b>		
VE (count)	Subject (N)	Cum (%)	VE (count)	Subject (N)	Cum (%)	VE (count)	Subject (N)	Cum (%)
1	16	76.5	1	11	70.9	1	14	71.1
2	4	81.2	2	6	77.9	2	4	75.9
3	1	82.4	3	2	80.2	3	3	79.5
4	2	84.7	4	2	82.6	4	2	81.9
5	2	87.1	6	1	83.7	5	2	84.3
6	1	88.2	7	1	84.9	8	1	85.5
7	1	89.4	8	1	86.0	9	2	88.0
9	1	90.6	9	2	88.4	10	1	89.2
10	2	92.9	10	1	89.5	14	1	90.4
12	1	94.1	15	1	90.7	16	1	91.6
24	2	96.5	16	1	91.9	18	1	92.8
33	1	97.6	20	1	93.0	20	1	94.0
50	1	98.8	21	1	94.2	35	1	95.2
1362	1	100.0	22	1	95.3	56	1	96.4
			34	1	96.5	133	1	97.6
			44	1	97.7	146	1	98.8
			48	1	98.8	1239	1	100.0
			1328	1	100.0			

\* The percentages are based on the total number of subjects, including those without VE couplets or runs

*Subjects with Any VE Singles During Exposure*

**Table C.1.12d. Number of Subjects with Any VE Singles by Ozone Exposure**

	No	Yes	Total
0 ppb	49 (58%)	36 (42%)	85
70 ppb	50 (58%)	36 (42%)	86
120 ppb	45 (54%)	38 (46%)	83

**Table C.1.12e. Mixed Model for Any VE Single**

Effect	Odds Ratio	Lower 95% CI	Upper 95% CI	P Value
Intercept	1.36	0.63	2.94	0.4320
Ozone exposure				
120 ppb	1.19	0.59	2.39	0.6193
70 ppb	0.97	0.48	1.93	0.9227
0 ppb				
Site				
URMC	0.35	0.15	0.86	0.0220
UNC	0.42	0.17	1.04	0.0598
UCSF	—	—	—	—

*VE Couplets or Runs During Exposure*

**Table C.1.12f. Number of Subjects with Any VE Couplet or Run by Ozone Exposure**

	No	Yes	Total
<b>0 ppb</b>	82 (96%)	3 (4%)	85
<b>70 ppb</b>	78 (91%)	8 (9%)	86
<b>120 ppb</b>	79 (95%)	4 (5%)	83

**Table C.1.12g. Mixed Model for Any VE Couplet or Run**

Effect	Odds Ratio	Lower 95% CI	Upper 95% CI	P Value
Intercept	0.07	0.02	0.28	0.0003
Ozone exposure				
120 ppb	1.48	0.27	8.07	0.6489
70 ppb	3.7	0.8	17.22	0.0943
0 ppb				
Site				
URMC	0.14	0.03	0.64	0.0120
UNC	0.00	—	—	0.96
UCSF	—	—	—	—

**Table C.1.12h. Distribution of VE Couplets or Runs by Ozone Exposure**

0 ppb*			70 ppb*			120 ppb*		
VE (count)	Subject (N)	Cum (%)	VE (count)	Subject (N)	Cum (%)	VE (count)	Subject (N)	Cum (%)
1	1	97.6	1	3	94.2	1	1	96.4
11	1	98.8	2	2	96.5	3	1	97.6
32	1	100.0	3	1	97.7	6	1	98.8
			27	1	98.8	22	1	100.0
			82	1	100.0			

\* The percentages are based on the total number of subjects, including those without VE couplets or runs.

### 13. SE During Exposure

#### *SE Singles*

**Table C.1.13a. Number of Subjects with Any SE Single by Ozone Exposure**

	No	Yes	Total
0 ppb	26 (31%)	59 (69%)	85
70 ppb	27 (31%)	59 (69%)	86
120 ppb	31 (37%)	52 (63%)	83

**Table C.1.13b. Mixed Model for Any SE Single**

Effect	Odds Ratio	Lower 95% CI	Upper 95% CI	P Value
Intercept	2.85	1.27	6.36	0.0114
Ozone exposure				
120 ppb	0.69	0.34	1.43	0.3153
70 ppb	0.95	0.46	1.96	0.8837
0 ppb				
Site				
URMC	0.8	0.32	1.97	0.6229
UNC	1.16	0.45	2.97	0.7544
UCSF	—	—	—	—

**Table C.1.13c. Distribution of SE Singles by Ozone Exposure (Based on Data Collected During the 3-Hour Exposure Period)**

0 ppb*			70 ppb*			120 ppb*		
VE (count)	Subject (N)	Cum (%)	VE (count)	Subject (N)	Cum (%)	VE (count)	Subject (N)	Cum (%)
1	14	47.1	1	20	54.7	1	11	50.6
2	9	57.6	2	10	66.3	2	10	62.7
3	11	70.6	3	7	74.4	3	7	71.1
4	8	80.0	4	3	77.9	4	3	74.7
5	2	82.4	5	3	81.4	5	2	77.1
6	1	83.5	6	2	83.7	6	4	81.9
7	1	84.7	7	1	84.9	7	1	83.1
8	1	85.9	9	3	88.4	9	1	84.3
9	1	87.1	10	1	89.5	12	1	85.5
10	3	90.6	12	2	91.9	13	1	86.7
15	1	91.8	21	1	93.0	14	1	88.0
18	1	92.9	22	1	94.2	17	2	90.4
35	1	94.1	39	1	95.3	20	1	91.6
36	1	95.3	80	1	96.5	34	1	92.8
44	1	96.5	152	1	97.7	44	1	94.0
101	1	97.6	197	1	98.8	63	1	95.2
161	1	98.8	256	1	100.0	85	1	96.4
229	1	100.0				193	1	97.6
						217	1	98.8
						301	1	100.0

\*The percentages are based on the total number of subjects, including those without SE singles.

*More Than 1 SE Single (Median)*

**Table C.1.13d. Number of Subjects with More Than 1 SE Single (Median) by Ozone Exposure**

	No	Yes	Total
0 ppb	40 (47%)	45 (53%)	85
70 ppb	47 (55%)	39 (45%)	86
120 ppb	42 (51%)	41 (49%)	83

**Table C.1.13e. Mixed Model for More Than 1 (Median) SE Single**

Effect	Odds Ratio	Lower 95% CI	Upper 95% CI	P Value
Intercept	1.39	0.65	2.99	0.3962
Ozone exposure				
120 ppb	0.85	0.43	1.7	0.6495
70 ppb	0.68	0.34	1.35	0.2694
0 ppb				
Site				
URMC	0.7	0.29	1.68	0.4228
UNC	0.87	0.36	2.14	0.7667
UCSF	—	—	—	—

*SE Couplet or Run*

**Table C.1.13f. Number of Subjects with Any SE Couplet or Run by Ozone Exposure**

	No	Yes	Total
0 ppb	68 (80%)	17 (20%)	85
70 ppb	73 (85%)	13 (15%)	86
120 ppb	73 (88%)	10 (12%)	83

**Table C.1.13g. Mixed Model for Any SE Couplet or Run**

Effect	Odds Ratio	Lower 95% CI	Upper 95% CI	P Value
Intercept	0.15	0.06	0.4	0.0002
Ozone exposure				
120 ppb	0.49	0.19	1.26	0.1375
70 ppb	0.67	0.28	1.61	0.3608
0 ppb				
Site				
URMC	0.84	0.26	2.66	0.7596
UNC	2.10	0.70	6.29	0.1799
UCSF	—	—	—	—

**Table C.1.13h. Distribution of SE Couplets or Runs by Ozone Exposure**

0 ppb*			70 ppb*			120 ppb*		
VE (count)	Subject (N)	Cum (%)	VE (count)	Subject (N)	Cum (%)	VE (count)	Subject (N)	Cum (%)
1	12	94.1	1	7	93.0	1	7	96.4
2	3	97.6	2	1	94.2	16	1	97.6
30	1	98.8	3	2	96.5	31	1	98.8
62	1	100.0	9	1	97.7	198	1	100.0
			13	1	98.8			
			35	1	100.0			

\*The percentages are based on the total number of subjects, including those without SE couplets or runs.



## **APPENDIX C.2**

### **Analyses of Blood Pressure Measured During Exposure Rest Periods 2 and 4**

## 1. Descriptive Statistics: Systolic Blood Pressure (Primary Outcome) and Diastolic Blood Pressure (Secondary Outcome)

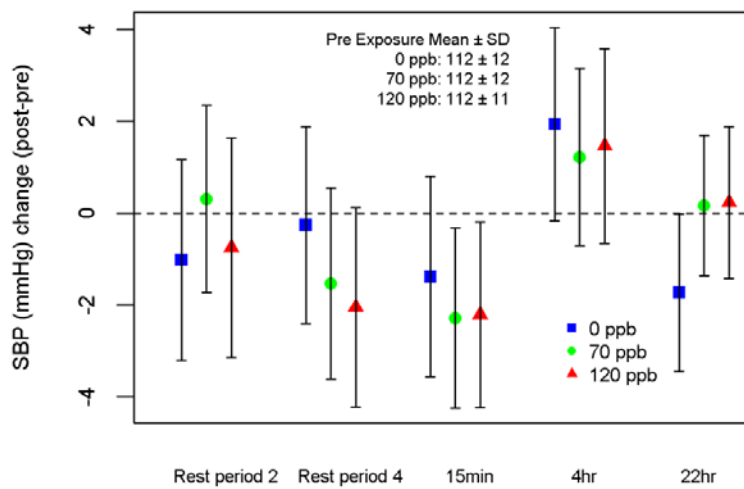
**Table C.2.1. Descriptive Analyses for Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP)**

	0 ppb			70 ppb			120 ppb		
	<i>N</i>	Mean	SD	<i>N</i>	Mean	SD	<i>N</i>	Mean	SD
<b>SBP (mmHg)</b>									
Pre-exposure	87	111.9	11.8	87	111.9	11.8	87	112.2	10.5
During exposure (rest period 2)	87	110.9	11.4	87	112.2	10.2	87	111.4	11.4
During exposure (rest period 4)	87	111.7	11.7	87	110.4	10.4	87	110.1	10.2
<b>DBP (mmHg)</b>									
Pre-exposure	87	67.3	8.4	87	67.3	8.0	87	67.7	7.1
During exposure (rest period 2)	87	70.9	7.4	87	71.1	7.5	87	70.8	7.2
During exposure (rest period 4)	87	71.6	7.2	87	72.0	7.1	87	71.9	6.7

# Ozone Effects on Blood Pressure Measured During Exposure Rest Periods 2 and 4

## 2. Systolic Blood Pressure

The following figure shows the change in SBP from pre- to during-exposure and from pre- to post-exposure over time. The data come from Table C.2.1.



**Figure C.2.2. Change in SBP (mmHg) at rest period 2 and 4 and after 15 minutes, 4 hours, and 22 hours at each ozone exposure.**

As we can see from the tables below,

- there were no differences in resting SBP across the two time intervals;
- there were no differences in resting SBP across the ozone exposures; and
- there was a significant difference in resting SBP across the 3 sites.

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

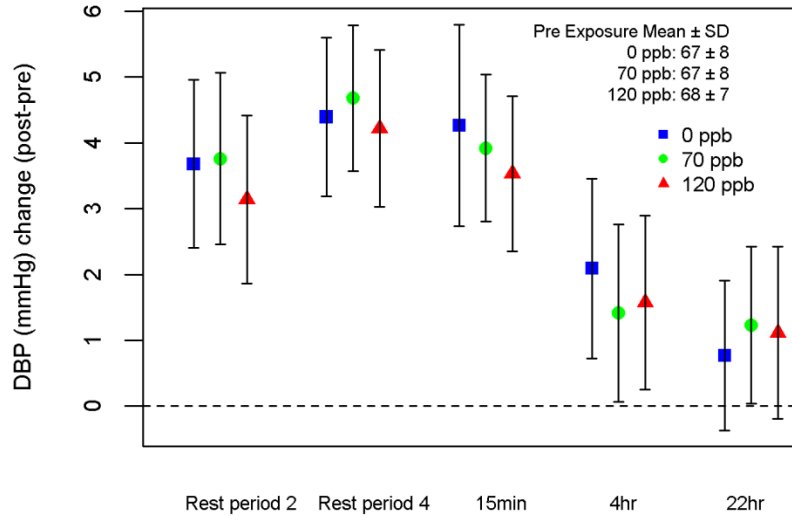
<b>Effect</b>	<b>P Value</b>
Rest Period 2 vs. Rest Period 4	0.2160
Ozone exposure	0.5182
Site	<0.0001

**Table C.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	-9.3135	-11.8172	-6.8098	<0.0001
Change between				
Rest period 4 and immediate pre-exposure	0			
Rest period 2 and immediate pre-exposure	0.7969	-0.4742	2.0680	0.2160
Ozone exposure				
0 ppb	0			
70 ppb	0.02874	-1.5170	1.5745	0.9708
120 ppb	-0.7644	-2.3101	0.7814	0.3304
Site				
URMC	10.8946	7.8675	13.9218	<0.0001
UNC	12.7924	9.6959	15.8890	<0.0001
UCSF	0			

### 3. Diastolic Blood Pressure

The following figure shows the change in DBP from pre- to during-exposure (rest periods 2 and 4) and from pre- to post-exposure over time. The data come from Table C.2.1.



**Figure C.2.3. Change in DBP (mmHg) at rest period 2 and 4, and after 15 minutes, 4 hours, and 22 hours at each ozone exposure.**

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

- there was a marginally significant difference in resting DBP across the two time intervals;
- there were no differences in resting DBP across the ozone exposures; and
- there was a significant difference in resting DBP across the 3 sites.

**Table C.2.3a. Type III Sum of Squares for Change in DBP (mmHg)**

<b>Effect</b>	<b>P Value</b>
Rest Period 2 vs. Rest Period 4	0.0289
Ozone exposure	0.5460
Site	<0.0001

**Table C.2.3b. Mixed model for change in DBP (mmHg)**

<b>Effect</b>	<b>Estimate</b>	<b>Lower 95% CI</b>	<b>Upper 95% CI</b>	<b>P-value</b>
Intercept	1.4519	-0.08983	2.9936	0.0646
Change between				
Rest period 4 and Immediate pre-exposure	0			
Rest period 2 and Immediate pre-exposure	-0.9042	-1.7133	-0.09512	0.0289
Ozone exposure				
0 ppb	0			
70 ppb	0.1839	-0.8000	1.1678	0.7126
120 ppb	-0.3563	-1.3402	0.6276	0.4757
Site				
URMC	4.2817	2.4330	6.1303	<0.0001
UNC	4.3795	2.4885	6.2706	<0.0001
UCSF	0			

## Abbreviations and Other Terms

DBP	diastolic blood pressure
ECG	electrocardiogram
HF	high frequency power (0.15–0.40 Hz)
HR	heart rate
LF	low frequency power (0.04–0.15 Hz)
MOSES	multicenter ozone study in elderly subjects
ppb	parts per billion
QTc	rate-corrected QT interval (based on QT:RR regression)
RMSSD	root mean square of successive differences in normal-to-normal sinus beat intervals
SBP	systolic blood pressure
SD	standard deviation
SDNN	standard deviation of normal-to-normal sinus beat intervals
SE	supraventricular ectopy
ST	ST segment
UCSF	University of California at San Francisco
UNC	University of North Carolina at Chapel Hill
URMC	University of Rochester Medical Center
VE	ventricular ectopy