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 B.1 Analyses of Cardiac Rhythm Outcomes

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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Contents

Primary Endpoints

1. Descriptive Statistics

Table B.1.1a. Descriptive Statistics of Primary Outcomes

	0 ppb			70 ppb			120 ppb		
	N	**Mean**	**SD**	***N***	**Mean**	**SD**	***N***	**Mean**	**SD**
HF, 5-min avg (ms^2)									
Pre-exposure	85	945.2	4052.9	87	664.7	1831.2	84	508.5	1064.4
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
LF, 5-min avg (ms^2)									
Pre-exposure	85	593.7	1141.7	87	492.7	1001.5	84	542.8	1119.3
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
Ln of RMSSD, 24 hr (ms)	86	3.3	0.5	87	3.3	0.4	85	3.2	0.5
T-wave amplitude, 5 min (μV)									
Pre-exposure	85	661.9	295.7	87	652.6	282.3	84	662.4	295.3
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
T–wave amplitude, 24 hr (μV)	86	651.4	278.8	87	648.5	273.9	85	652.6	280.9
ST in V5, 5 min (μV)									
Pre-exposure	85	24.9	37.5	87	23.4	34.2	84	24.6	34.5
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
ST in V5, 24 hr (μV)	86	23.7	37.7	87	22.8	35.7	85	24.4	35.8

Table B.1.1b. Median and IQR of Skewed Data

	0 ppb			70 ppb			120 ppb		
	N	**Median**	**IQR**	***N***	**Median**	**IQR**	***N***	**Median**	**IQR**
LF, 24-hr avg (ms^2)	86	591.1	(352.1, 934.5)	87	580.4	(370.5, 867.8)	85	598.9	(389.1, 901.9)
HF, 24-hr avg (ms^2)	86	207.2	(117.9, 412.4)	87	218.2	(115.4, 364.9)	85	213.2	(107.6, 406.7)
RMSSD, 24 hr (ms)	86	25.0	(18.0, 34.0)	87	26.0	(20.0, 31.0)	85	25.0	(20.0, 33.0)

2. HF, 5-Min Average (ms^2)

The following figure shows the change in high-frequency (HF) power from pre- to post-exposure over time. The data come from Table B.1.1a.

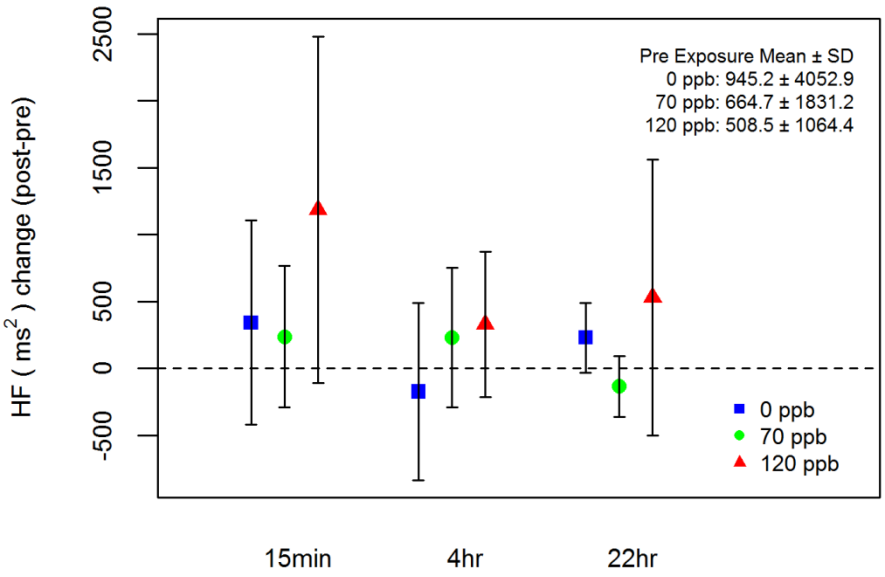

Figure B.1.2. Change in 5-min average HF at different post-exposure times and at each ozone exposure.

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

Table B.1.2a. Type III Sum of Squares for Change in HF 5-Min Average (ms^2)

Effect	*P* Value
15-min v 4-hr vs. 22-hr change	0.1915
Ozone exposure	0.0667
Site	0.1578

Table B.1.2b. Mixed Model for Change in HF 5-Min. Average (ms^2)

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	146.37	-667.13	959.86	0.7214
Change between post- and pre-exposure				
22-hr change	-384.57	-916.99	147.86	0.1558
4-hr change	-452.67	-979.11	73.7689	0.0915
15-min change	0			
Ozone exposure				
120 ppb	545.25	9.1474	1081.35	0.0463
70 ppb	-12.9727	-540.64	514.69	0.9613
0 ppb	0			
Site				
URMC	736.44	-184.74	1657.62	0.1156
UNC	-39.1709	-985.83	907.48	0.9346
UCSF	0			

Analyses of Interactions

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

Table B.1.2c. Type III Sum of Squares for Change in HF 5-Min. Average (ms^2), Including Ozone Exposure, by Age Interaction

Effect	*P* value
Ozone exposure	0.0992
15-min vs. 4-hr vs. 22-hr change	0.1881
Site	0.1753
Age	0.6845
Ozone exposure by age	0.2204

Table B.1.2d. Mixed Model for Change in HF 5-Min Average (ms^2), Including Ozone Exposure, by Age Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* value
Intercept	162.57	-654.68	979.81	0.6934
22-hr change	-386.64	-918.70	145.42	0.1533
4-hr change	-454.65	-980.72	71.4157	0.0898
15-min change	0			
Ozone exposure				
120 ppb	508.10	-30.5984	1046.80	0.0643
70 ppb	-6.9162	-535.79	521.96	0.9794
0 ppb	0			
Site				
URMC	714.13	-216.83	1645.09	0.1309
UNC	-56.8348	-1008.54	894.87	0.9057
UCSF	0			
Age	2.0531	-107.93	112.04	0.9705
Ozone exposure by age				
120 ppb by age	74.2277	-46.6198	195.08	0.2282
70 ppb by age	-28.3431	-145.88	89.1980	0.6360
0 ppb by age	0			

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

Table B.1.2e. Type III Sum of Squares for Change in HF 5-Min Average (ms^2), Including Ozone Exposure, by Sex Interaction

Effect	*P* Value
Ozone exposure	0.0902
15-min vs. 4-hr vs. 22-hr change	0.1904
Site	0.1558
Sex	0.5690
Ozone exposure by sex	0.3732

Table B.1.2f. Mixed Model for Change in HF 5-Min Average (ms^2), Including Ozone Exposure, by Sex Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	520.33	-449.92	1490.58	0.2892
22-hr change	-385.96	-918.40	146.47	0.1543
4-hr change	-452.99	-979.43	73.4485	0.0912
15-min change	0			
Ozone exposure				
120 ppb	152.05	-683.66	987.75	0.7199
70 ppb	-415.66	-1246.98	415.66	0.3250
0 ppb	0			
Site				
URMC	768.09	-166.19	1702.38	0.1058
UNC	6.5691	-960.06	973.20	0.9892
UCSF	0			
Sex				
Female	-670.21	-1672.47	332.06	0.1872
Male	0			
Ozone exposure by sex				
120 ppb by female	662.78	-426.75	1752.31	0.2314
70 ppb by female	674.60	-401.28	1750.48	0.2175
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.1.2g. Type III Sum of Squares for Change in HF 5-Min Average (ms^2), Including Ozone Exposure, by GSTM1 Status Interaction

Effect	*P* Value
Ozone exposure	0.0767
15-min vs. 4-hr vs. 22-hr change	0.1916
Site	0.1719
GSTM1 status	0.5671
Ozone exposure by GSTM1 status	0.6161

Table B.1.2h. Mixed Model for Change in HF 5-Min Average (ms^2), Including Ozone Exposure, by GSTM1 Status Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	-56.6197	-952.86	839.62	0.9003
22-hr change	-385.20	-918.05	147.65	0.1554
4-hr change	-452.63	-979.48	74.2223	0.0917
15-min change	0			
Ozone exposure				
120 ppb	717.45	6.5664	1428.33	0.0479
70 ppb	203.38	-495.33	902.08	0.5663
0 ppb	0			
Site				
URMC	706.66	-223.75	1637.07	0.1347
UNC	-67.0820	-1021.86	887.69	0.8892
UCSF	0			
GSTM1 status				
Sufficient	524.38	-464.04	1512.80	0.2944
Null	0			
Ozone exposure by GSTM1 status				
120 ppb by sufficient	-403.24	-1486.92	680.43	0.4636
70 ppb by sufficient	-506.13	-1573.30	561.04	0.3504
0 ppb by sufficient	0			
120 ppb by null	0			
70 ppb by null	0			
0 ppb by null	0			

3. LF, 5-Min Average (ms^2)

The following figure shows the change in low-frequency (LF) power from pre- to post-exposure over time. The data come from Table B.1.1a.

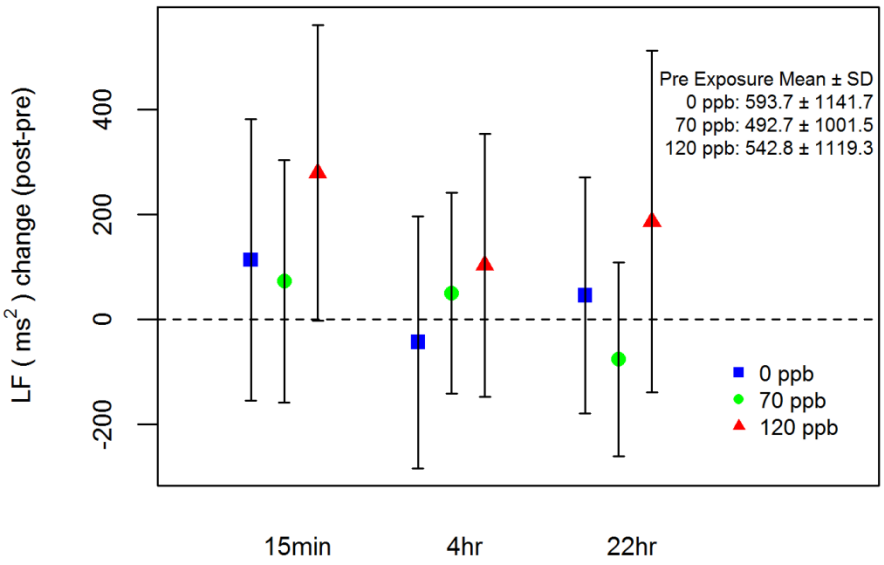

Figure B.1.3. Change in 5-min average LF at different post-exposure times and at each ozone exposure.

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

Table B.1.3a. Type III Sum of Squares for Change in LF 5-Min Average (ms^2)

Effect	*P* Value
15-min vs. 4-hr vs. 22-hr change	0.3669
Ozone exposure	0.1094
Site	0.2145

Table B.1.3b. Mixed Model for Change in LF 5-Min Average (ms^2)

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	-33.7371	-326.72	259.25	0.8194
Change between post- and pre-exposure				
22-hr change	-99.6598	-276.09	76.7659	0.2664
4-hr change	-116.21	-290.63	58.2105	0.1902
15-min change	0			
Ozone exposure				
120 ppb	150.77	-26.9703	328.50	0.0959
70 ppb	-25.3677	-200.24	149.50	0.7749
0 ppb	0			
Site				
URMC	298.06	-44.0279	640.15	0.0868
UNC	110.84	-240.41	462.09	0.5320
UCSF	0			

Analyses of Interactions

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

Table B.1.3c. Type III Sum of Squares for Change in LF 5-Min Average (ms^2), Including Ozone Exposure, by Age Interaction

Effect	*P* Value
Ozone exposure	0.1404
15-min vs. 4-hr vs. 22-hr change	0.3638
Site	0.2052
Age	0.7477
Ozone exposure by age	0.2269

Table B.1.3d. Mixed Model for Change in LF 5-Min Average (ms^2), Including Ozone Exposure, by Age Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	-35.3727	-329.85	259.10	0.8118
22-hr change	-100.08	-276.38	76.2257	0.2641
4-hr change	-116.58	-290.88	57.7080	0.1885
15-min change	0			
Ozone exposure				
120 ppb	146.22	-32.3997	324.84	0.1079
70 ppb	-18.0395	-193.31	157.24	0.8392
0 ppb	0			
Site				
URMC	304.81	-41.1176	650.73	0.0834
UNC	107.27	-246.02	460.56	0.5476
UCSF	0			
Age	0.5425	-38.5693	39.6544	0.9781
Ozone exposure by age				
120 ppb by age	7.9311	-32.1591	48.0213	0.6978
70 ppb by age	-24.8508	-63.8172	14.1156	0.2109
0 ppb by age	0			

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

Table B.1.3e. Type III Sum of Squares for Change in LF 5-Min Average (ms^2), Including Ozone Exposure, by Sex Interaction

Effect	*P* Value
Ozone exposure	0.1669
15-min vs. 4-hr vs. 22-hr change	0.3655
Site	0.1580
Sex	0.1298
Ozone exposure by sex	0.5003

Table B.1.3f. Mixed Model for Change in LF 5-Min Average (ms^2), Including Ozone Exposure, by Sex Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	127.46	-216.65	471.57	0.4634
22-hr change	-100.14	-276.64	76.3549	0.2643
4-hr change	-116.33	-290.82	58.1546	0.1899
15-min change	0			
Ozone exposure				
120 ppb	24.2133	-252.87	301.29	0.8632
70 ppb	-73.1107	-348.72	202.50	0.6012
0 ppb	0			
Site				
URMC	333.06	-9.7927	675.92	0.0568
UNC	159.61	-194.92	514.13	0.3732
UCSF	0			
Sex				
Female	-318.37	-672.64	35.9062	0.0775
Male	0			
Ozone exposure by sex				
120 ppb by female	213.74	-147.56	575.05	0.2445
70 ppb by female	80.1708	-276.52	436.86	0.6578
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.1.3g. Type III Sum of Squares for Change in LF 5-Min Average (ms^2), Including Ozone Exposure, by GSTM1 Status Interaction

Effect	*P* Value
Ozone exposure	0.1830
15-min vs. 4-hr vs. 22-hr change	0.3662
Site	0.2379
GSTM1 status	0.6340
Ozone exposure by GSTM1 status	0.1394

Table B.1.3h. Mixed Model for Change in LF 5-Min Average (ms^2), Including Ozone Exposure, by GSTM1 Status Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	-120.03	-441.89	201.83	0.4603
22-hr change	-100.05	-276.19	76.0827	0.2637
4-hr change	-115.86	-289.99	58.2680	0.1908
15-min post change	0			
Ozone exposure				
120 ppb	301.27	66.1393	536.40	0.0123
70 ppb	13.0973	-217.90	244.09	0.9110
0 ppb	0			
Site				
URMC	289.80	-56.3358	635.94	0.0996
UNC	103.82	-251.05	458.69	0.5622
UCSF	0			
GSTM1 status				
Sufficient	215.25	-136.63	567.13	0.2272
Null	0			
Ozone exposure by GSTM1 status				
120 ppb by sufficient	-349.71	-708.11	8.6846	0.0557
70 ppb by sufficient	-90.7663	-443.57	262.04	0.6122
0 ppb by sufficient	0			
120 ppb by null	0			
70 ppb by null	0			
0 ppb by null	0			

4. Ln of RMSSD, 24-Hr Average (ms)

The following figure shows the natural logarithm (Ln) of the root mean square of successive differences (RMSSD) in normal-to-normal sinus beat intervals (24-hour average) by ozone exposure. The data come from Table B.1.1a.

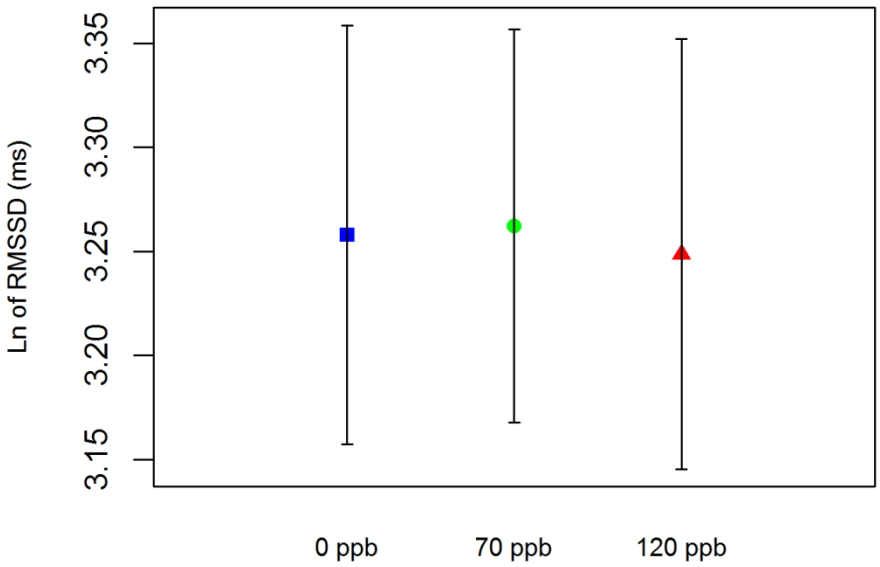

Figure B.1.4. Change in natural logarithm of 24-hour average RMSSD by ozone exposure.

Main Analysis of Ozone Effect

As we can see from the tables below, neither variable was statistically significant. This means that:

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

Table B.1.4a. TYPE III Sum of Squares for LN of RMSSD 24-Hr Average (ms)

Effect	*P* Value
Ozone exposure	0.8108
Site	0.2447

Table B.1.4b. Mixed Model for Ln of RMSSD 24-Hr Average (ms)

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	3.3787	3.2030	3.5544	<0.0001
Ozone exposure				
120 ppb	-0.01239	-0.07084	0.04605	0.6760
70 ppb	0.006433	-0.05152	0.06439	0.8268
0 ppb	0			
Site				
URMC	-0.1763	-0.4082	0.05560	0.1343
UNC	-0.1737	-0.4109	0.06358	0.1492
UCSF	0			

Analyses of Interactions

As we can see from the tables below,

- there was a marginally significant age effect on the pre-exposure to post-exposure change in Ln of RMSSD (24-hour average), independent of ozone exposure; and
- there was a significant difference in the ozone effect by age — an increase in age was associated with an increase in RMSSD from pre-exposure to post-exposure when comparing 70 ppb to 0 ppb ozone.

Table B.1.4c. Type III Sum of Squares for Ln of RMSSD 24-Hr Average (ms), Including Ozone Exposure, by Age Interaction

Effect	*P* Value
Ozone exposure	0.6583
Site	0.1808
Age	0.0401
Ozone exposure by age	0.0084

Table B.1.4d. Mixed Model for Ln of RMSSD 24-Hr Average (ms), Including Ozone Exposure, by Age Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	3.3817	3.2090	3.5545	<.0001
Ozone exposure				
120 ppb	-0.01679	-0.07418	0.04060	0.5643
70 ppb	0.009360	-0.04747	0.06619	0.7455
0 ppb	0			
Site				
URMC	-0.2029	-0.4322	0.02637	0.0820
UNC	-0.1727	-0.4059	0.06058	0.1447
UCSF	0			
Age	0.02134	-0.00077	0.04345	0.0583
Ozone exposure by age				
120 ppb by age	0.01072	-0.00231	0.02374	0.1061
70 ppb by age	-0.00951	-0.02229	0.003273	0.1438
0 ppb by age	0			

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

- there were no differences in Ln of RMSSD across the ozone exposures;
- there were no differences in Ln of RMSSD between the sexes;
- there were no differences in Ln of RMSSD across the 3 sites; and
- the ozone effect did not differ by sex.

Table B.1.4e. Type III Sum of Squares for Ln of RMSSD 24-Hr Average (ms), Including Ozone Exposure, by Sex Interaction

Effect	*P* Value
Ozone exposure	0.7253
Site	0.3148
Sex	0.4523
Ozone exposure by sex	0.4658

Table B.1.4f. Mixed Model for Ln of RMSSD 24-Hr Average (ms), Including Ozone Exposure, by Sex Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	3.4363	3.2337	3.6389	<0.0001
Ozone exposure				
120 ppb	-0.05713	-0.1492	0.03498	0.2225
70 ppb	-0.01670	-0.1088	0.07541	0.7208
0 ppb	0			
Site				
Sex				
Female	-0.1120	-0.3199	0.09589	0.2870
Male	0			
Ozone exposure by sex				
120 ppb by female	0.07488	-0.04444	0.1942	0.2171
70 ppb by female	0.03801	-0.08063	0.1567	0.5279
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.1.4g. Type III Sum of Squares for Ln of RMSSD 24-Hr Average (ms), Including Ozone Exposure, by GSTM1 Status Interaction

Effect	*P* Value
Ozone exposure	0.7769
Site	0.2651
GSTM1 status	0.7623
Ozone exposure by GSTM1 status	0.5406

Table B.1.4h. Mixed Model for Ln of RMSSD 24-Hr Average (ms), Including Ozone Exposure, by GSTM1 Status Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	3.3729	3.1822	3.5637	<0.0001
Ozone exposure				
120 ppb	0.01312	-0.06377	0.09000	0.7366
70 ppb	0.02896	-0.04736	0.1053	0.4549
0 ppb	0			
Site				
URMC	-0.1728	-0.4071	0.06151	0.1462
UNC	-0.1706	-0.4100	0.06870	0.1599
UCSF	0			
GSTM1 status				
Sufficient	0.008879	-0.1956	0.2134	0.9314
Null	0			
Ozone exposure by GSTM1 status				
120 ppb by sufficient	-0.06098	-0.1797	0.05778	0.3122
70 ppb by sufficient	-0.05379	-0.1715	0.06392	0.3683
0 ppb by sufficient	0			
120 ppb by null	0			

5. T-wave Amplitude, 5-Min Average (μV)

The following figure shows the change in T-wave amplitude from pre- to post-exposure over time. The data come from Table B.1.1a.

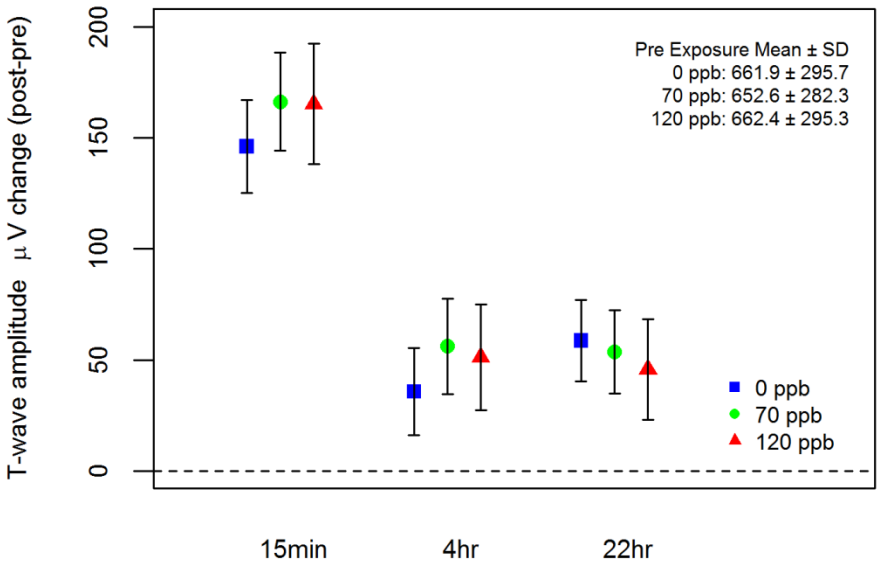

Figure B.1.5. Change in 5-min average T-wave amplitude at different post-exposure times and at each ozone exposure.

Main Analysis of Ozone Effect

As we can see from the tables below, time is statistically significant, but ozone exposure is not. This means that:

- there were differences among the 15-minute post-exposure, 4-hour post exposure, and 22-hour post-exposure T-wave amplitudes — the 4 hr and 22 hr values were lower than the 15-minute value;
- there were no differences in T-wave amplitude across the ozone exposures; and
- there were marginally significant differences in T-wave amplitude across the 3 sites.

Table B.1.5a. Type III Sum of Squares for Change in T-wave Amplitude, 5-Min Average (μV)

Effect	*P* Value
15-min vs. 4-hr vs. 22-hr change	<0.0001
Ozone exposure	0.3325
Site	0.0112

Table B.1.5b. Mixed Model for Change in T-wave Amplitude, 5-Min Average (μV)

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	186.25	158.18	214.33	<0.0001
Change between post- and pre-exposure				
22-hr change	-106.94	-121.21	-92.6726	<0.0001
4-hr change	-111.43	-125.54	-97.3326	<0.0001
15-min change	0			
Ozone exposure				
120 ppb	6.3550	-8.0289	20.7389	0.3843
70 ppb	10.6098	-3.5340	24.7535	0.1405
0 ppb	0			
Site				
URMC	-51.8143	-86.1101	-17.5185	0.0035
UNC	-38.7959	-73.9673	-3.6245	0.0310
UCSF	0			

Analyses of Interactions

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

Table B.1.5c. Type III Sum of Squares for Change in T-wave Amplitude 5-Min Average (μV), Including Ozone Exposure, by Age Interaction

Effect	*P* Value
Ozone exposure	0.3221
15-min vs. 4-hr vs. 22-hr change	<0.0001
Site	0.0111
Age	0.7864
Ozone exposure by age	0.4926

Table B.1.5d. Mixed Model for Change in T-wave Amplitude 5-Min Average (μV), Including Ozone Exposure, by Age Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	186.44	158.22	214.65	<0.0001
22-hr change	-106.97	-121.25	-92.6976	<0.0001
4-hr change	-111.47	-125.58	-97.3567	<0.0001
15-min change	0			
Ozone exposure				
120 ppb	5.8146	-8.6621	20.2913	0.4289
70 ppb	10.8559	-3.3397	25.0515	0.1330
0 ppb	0			
Site				
URMC	-52.3313	-86.9878	-17.6749	0.0035
UNC	-39.0442	-74.3888	-3.6996	0.0308
UCSF	0			
Age	0.3979	-3.2688	4.0646	0.8297
Ozone exposure by age				
120 ppb by age	1.0128	-2.2388	4.2644	0.5410
70 ppb by age	-0.9180	-4.0753	2.2393	0.5683
0 ppb by age	0			

As we can see from the tables below,

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

Table B.1.5e. Type III Sum of Squares for Change in T-wave Amplitude 5-Min Average (μV), Including Ozone Exposure, by Sex Interaction

Effect	*P* Value
Ozone exposure	0.4163
15-min vs. 4-hr vs. 22-hr change	<0.0001
Site	0.0276
Sex	0.0110
Ozone exposure by sex	0.6976

Table B.1.5f. Mixed Model for Change in T-wave Amplitude 5-Min Average (μV), Including Ozone Exposure, by Sex Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	207.48	175.54	239.41	<0.0001
22-hr change	-106.99	-121.26	-92.7076	<0.0001
4-hr change	-111.43	-125.54	-97.3161	<0.0001
15-min change	0			
Ozone exposure				
120 ppb	-0.6755	-23.0976	21.7466	0.9526
70 ppb	4.8651	-17.4371	27.1672	0.6672
0 ppb	0			
Site				
URMC	-45.8617	-79.3846	-12.3389	0.0079
UNC	-30.6293	-65.2643	4.0057	0.0823
UCSF	0			
Sex				
Female	-43.7521	-76.4490	-11.0551	0.0093
Male	0			
Ozone exposure by sex				
120 ppb by female	11.7505	-17.4961	40.9971	0.4288
70 ppb by female	9.6630	-19.1990	38.5251	0.5095
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.1.5g. Type III Sum of Squares for Change in T-wave Amplitude, 5-Min Average (μV), Including Ozone Exposure, by GSTM1 Status Interaction

Effect	*P* Value
Ozone exposure	0.4723
15-min vs. 4-hr vs. 22-hr change	<0.0001
Site	0.0154
GSTM1 status	0.3337
Ozone exposure by GSTM1 status	0.0599

Table B.1.5h. Mixed Model for Change in T-wave Amplitude, 5-Min Average (μV), Including Ozone Exposure, by GSTM1 Status Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	187.12	156.58	217.66	<0.0001
22-hr change	-106.87	-121.09	-92.6400	<0.0001
4-hr change	-111.45	-125.51	-97.3880	<0.0001
15-min post change	0			
Ozone exposure				
120 ppb	5.8064	-13.2003	24.8131	0.5472
70 ppb	23.2061	4.5456	41.8666	0.0151
0 ppb	0			
Site				
URMC	-50.1940	-84.7103	-15.6776	0.0049
UNC	-37.5261	-72.8685	-2.1836	0.0377
UCSF	0			
GSTM1 status				
Sufficient	-4.5023	-37.4387	28.4341	0.7864
Null	0			
Ozone exposure by GSTM1 status				
120 ppb by sufficient	1.1781	-27.7894	30.1456	0.9361
70 ppb by sufficient	-29.3147	-57.8144	-0.8149	0.0439
0 ppb by sufficient	0			
120 ppb by null	0			
70 ppb by null	0			
0 ppb by null	0			

6. T-wave Amplitude, 24-Hr Average (μV)

The following figure shows T-wave amplitude by ozone exposure. The data come from Table B.1.1a.

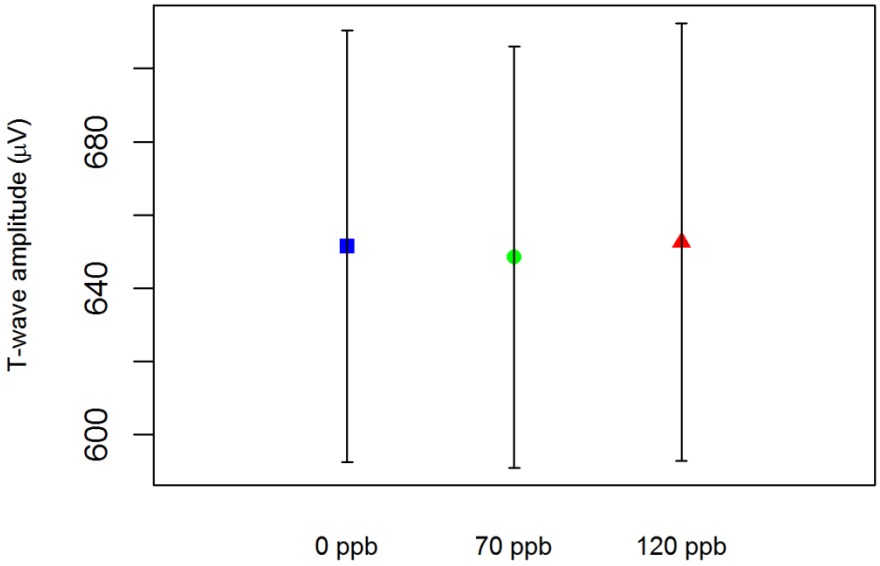

Figure B.1.6. The 24-hour average T-wave amplitude by ozone exposure.

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

Table B.1.6a. Type III Sum of Squares for T-wave Amplitude, 24-Hr Average (μV)

Effect	*P* Value
Ozone exposure	0.4770
Site	0.0935

Table B.1.6b. Mixed Model for T-wave Amplitude, 24-Hr Average (μV)

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	702.51	596.33	808.70	<0.0001
Ozone exposure				
120 ppb	-4.3177	-20.3459	11.7105	0.5956
70 ppb	-9.7892	-25.6783	6.1000	0.2256
0 ppb	0			
Site				
URMC	-128.26	-270.65	14.1253	0.0768
UNC	8.8397	-136.82	154.50	0.9042
UCSF	0			

Analyses of Interactions

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

Table B.1.6c. Type III Sum of Squares for T-wave Amplitude, 24-Hr Average (μV), Including Ozone Exposure, by Age Interaction

Effect	*P* Value
Ozone exposure	0.4963
Site	0.1147
Age	0.6220
Ozone exposure by age	0.9489

Table B.1.6d. Mixed Model for T-wave Amplitude, 24-Hr Average (μV), Including Ozone Exposure, by Age Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	702.08	595.38	808.78	<0.0001
Ozone exposure				
120 ppb	-4.3092	-20.5126	11.8941	0.6002
70 ppb	-9.6168	-25.6578	6.4241	0.2382
0 ppb	0			
Site				
URMC	-124.31	-268.22	19.6019	0.0895
UNC	8.3864	-137.96	154.73	0.9095
UCSF	0			
Age	-3.0644	-16.2506	10.1218	0.6451
Ozone exposure by age				
120 ppb by age	-0.00485	-3.6844	3.6747	0.9979
70 ppb by age	-0.5104	-4.1193	3.0986	0.7804
0 ppb by age	0			

As we can see from the tables below,

- there was a significant difference in T-wave amplitude by sex — T-wave amplitude in women decreased from pre-exposure to post-exposure relative to men, independent of ozone exposure; and
- the ozone effect did not differ by sex.

Table B.1.6e. Type III Sum of Squares for T-wave Amplitude, 24-Hr Average (μV), Including Ozone Exposure, by Sex Interaction

Effect	*P* Value
Ozone exposure	0.2549
Site	0.0661
Sex	0.0002
Ozone exposure by sex	0.0497

Table B.1.6f. Mixed Model for T-wave Amplitude, 24-Hr Average (μV), Including Ozone Exposure, by Sex Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	815.98	704.17	927.79	<0.0001
Ozone exposure				
120 ppb	-25.4559	-50.3647	-0.5471	0.0452
70 ppb	-30.7983	-55.7071	-5.8894	0.0157
0 ppb	0			
Site				
URMC	-93.5103	-226.89	39.8697	0.1669
UNC	57.5305	-80.0035	195.06	0.4078
UCSF	0			
Sex				
Female	-237.96	-350.96	-124.96	<0.0001
Male	0			
Ozone exposure by sex				
120 ppb by female	35.1464	2.8775	67.4154	0.0330
70 ppb by female	34.7333	2.6536	66.8130	0.0340
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.1.6g. Type III Sum of Squares for T-wave Amplitude, 24-Hr Average (μV), Including Ozone Exposure, by GSTM1 Status Interaction

Effect	*P* Value
Ozone exposure	0.4837
Site	0.0975
GSTM1 status	0.9722
Ozone exposure by GSTM1 status	0.5936

Table B.1.6h. Mixed Model for T-wave Amplitude 24-Hr Average (μV), Including Ozone Exposure, by GSTM1 Status Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	705.51	590.86	820.16	<0.0001
Ozone exposure				
120 ppb	-10.6468	-31.7377	10.4440	0.3204
70 ppb	-10.1435	-31.0757	10.7887	0.3401
0 ppb	0			
Site				
URMC	-128.05	-272.02	15.9158	0.0806
UNC	8.9341	-138.09	155.96	0.9041
UCSF	0			
GSTM1 status				
Sufficient	-7.4211	-127.23	112.39	0.9023
Null	0			
Ozone exposure by GSTM1 status				
120 ppb by sufficient	15.0677	-17.5173	47.6527	0.3626
70 ppb by sufficient	0.9576	-31.3305	33.2458	0.9534
0 ppb by sufficient	0			
120 ppb by null	0			
70 ppb by null	0			
0 ppb by null	0			

7. ST Segment in V5, 5-Min Average (μV)

The following figure shows the change in ST segment in V5 from pre- to post-exposure over time. The data come from Table B.1.1a.

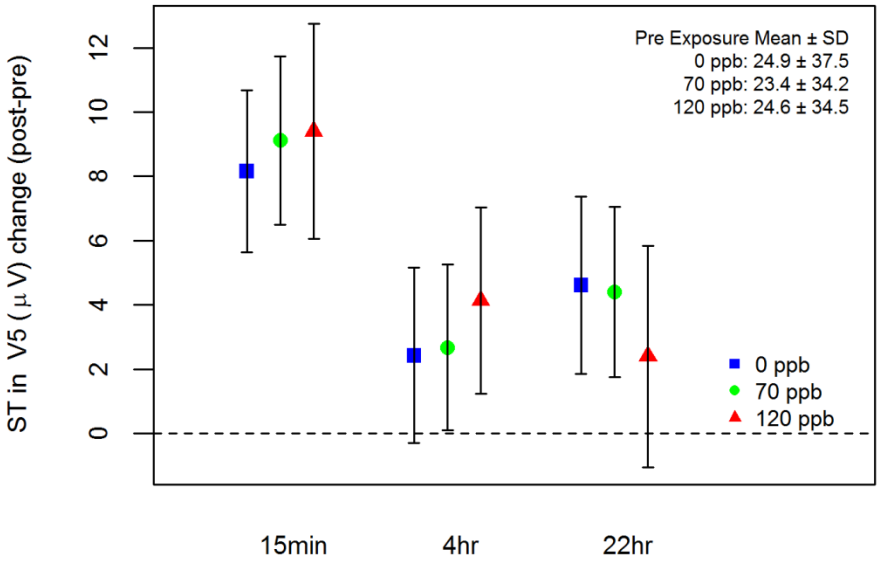

Figure B.1.7. Change in 5-min average ST segment in V5 at different post-exposure times and at each ozone exposure.

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 among 15-minute post-exposure, 4-hour post-exposure, and 22-hour post-exposure ST in V5 — the 4-hour and 22-hour values tended to be lower than the 15-minute value;
- there were no differences in ST in V5 across the ozone exposures; and
- there were significant differences in ST in V5 across the 3 sites.

Table B.1.7a. Type III Sum of Squares for Change in ST in V5, 5-Min Average (μV)

Effect	*P* Value
15-min vs. 4-hr vs. 22-hr change	<0.0001
Ozone exposure	0.9319
Site	0.0002

Table B.1.7b. Mixed Model for Change in ST in V5, 5-Min Average (μV)

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	7.5575	3.9920	11.1230	<0.0001
Change between post- and pre-exposure				
22-hr change	-5.0903	-6.9083	-3.2723	<0.0001
4-hr change	-5.8352	-7.6322	-4.0382	<0.0001
15-min change	0			
Ozone exposure				
120 ppb	0.3075	-1.5254	2.1405	0.7409
70 ppb	0.2911	-1.5112	2.0935	0.7502
0 ppb	0			
Site				
URMC	-8.7917	-13.1330	-4.4503	0.0001
UNC	-1.9635	-6.4159	2.4889	0.3830
UCSF	0			

Analyses of Interactions

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

Table B.1.7c. Type III Sum of Squares for Change in ST in V5, 5-Min Average (μV), Including Ozone Exposure, by Age Interaction

Effect	*P* Value
Ozone exposure	0.9135
15-min v 4-hr v 22-hr change	<0.0001
Site	0.0002
Age	0.4835
Ozone exposure by age	0.6144

Table B.1.7d. Mixed Model for Change in ST in V5, 5-Min Average (μV), Including Ozone Exposure, by Age Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	12.6222	9.0517	16.1927	<0.0001
22-hr change	-5.0894	-6.9090	-3.2699	<0.0001
4-hr change	-5.8370	-7.6354	-4.0385	<0.0001
15-min change	0			
Ozone exposure				
120 ppb	0.3199	-1.5253	2.1651	0.7326
70 ppb	0.3574	-1.4520	2.1668	0.6970
0 ppb	0			
Site				
URMC	-8.9469	-13.3265	-4.5674	0.0001
UNC	-1.9416	-6.4083	2.5251	0.3898
UCSF	0			
Age	0.2192	-0.2452	0.6837	0.3506
Ozone exposure by age				
120 ppb by age	-0.04391	-0.4583	0.3705	0.8353
70 ppb by age	-0.1921	-0.5946	0.2103	0.3488
0 ppb by age	0			

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

Table B.1.7e. Type III Sum of Squares for Change in ST in V5, 5-Min Average (μV), Including Ozone Exposure, by Sex Interaction

Effect	*P* Value
Ozone exposure	0.9775
15-min vs. 4-hr vs. 22-hr change	<0.0001
Site	0.0003
Sex	0.6366
Ozone exposure by sex	0.4109

Table B.1.7f. Mixed Model for Change in ST in V5, 5-Min Average (μV), Including Ozone Exposure, by Sex Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	13.7546	9.5874	17.9217	<0.0001
22-hr change	-5.0922	-6.9104	-3.2740	<0.0001
4-hr change	-5.8382	-7.6353	-4.0410	<0.0001
15-min change	0			
Ozone exposure				
120 ppb	-1.1638	-4.0191	1.6915	0.4221
70 ppb	-0.2831	-3.1231	2.5569	0.8442
0 ppb	0			
Site				
URMC	-8.6666	-13.0731	-4.2600	0.0002
UNC	-1.7744	-6.3266	2.7778	0.4404
UCSF	0			
Sex				
Female	-2.0325	-6.2952	2.2301	0.3457
Male	0			
Ozone exposure by sex				
120 ppb by female	2.5019	-1.2226	6.2264	0.1866
70 ppb by female	0.9624	-2.7129	4.6377	0.6058
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.1.7g. Type III Sum of Squares for Change in ST in V5, 5-Min Average (μV), Including Ozone Exposure, by GSTM1 Status Interaction

Effect	*P* Value
Ozone exposure	0.8969
15-min vs. 4-hr vs. 22-hr change	<0.0001
Site	0.0003
GSTM1 status	0.8509
Ozone exposure by GSTM1 status	0.5449

Table B.1.7h. Mixed Model for Change in ST in V5, 5-Min Average (μV), Including Ozone Exposure, by GSTM1 Status Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	13.0088	9.1181	16.8994	<0.0001
22-hr change	-5.0882	-6.9072	-3.2691	<0.0001
4-hr change	-5.8373	-7.6353	-4.0394	<0.0001
15-min post change	0			
Ozone exposure				
120 ppb	-0.4490	-2.8793	1.9814	0.7158
70 ppb	0.3252	-2.0609	2.7113	0.7882
0 ppb	0			
Site				
URMC	-8.7539	-13.1467	-4.3611	0.0002
UNC	-1.9350	-6.4330	2.5630	0.3947
UCSF	0			
GSTM1 status				
Sufficient	-0.9026	-5.0994	3.2943	0.6699
Null	0			
Ozone exposure by GSTM1 status				
120 ppb by sufficient	1.7543	-1.9497	5.4583	0.3511
70 ppb by sufficient	-0.07432	-3.7186	3.5699	0.9679
0 ppb by sufficient	0			
120 ppb by null	0			
70 ppb by null	0			
0 ppb by null	0			

8. ST in V5, 24-Hr Average (μV)

The following figure shows ST segment in V5 by ozone exposure. The data come from Table B.1.1a.

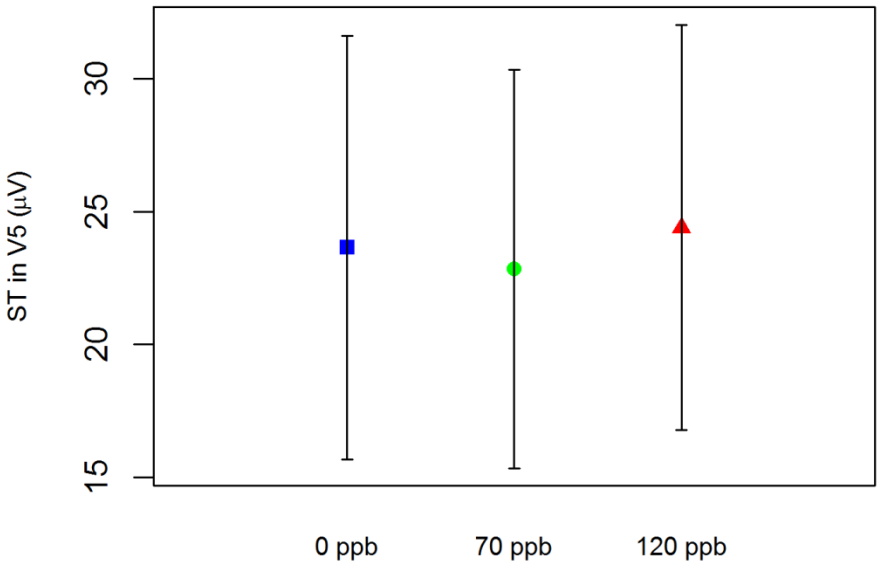

Figure B.1.8. The 24-hour average ST segment in V5 (μV) by ozone exposure.

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 in ST in V5 (24 h) across the ozone exposures; and
- there were no differences in ST in V5 (24 h) across the 3 sites.

Table B.1.8a. TYPE III Sum of Squares for ST in V5, 24-Hr Average (μV)

Effect	*P* Value
Ozone exposure	0.4912
Site	0.7521

Table B.1.8b. Mixed Model for ST in V5, 24-Hr Average (μV)

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	22.7019	8.6140	36.7899	0.0019
Ozone exposure				
120 ppb	0.3111	-2.2929	2.9150	0.8139
70 ppb	-1.1723	-3.7537	1.4092	0.3713
0 ppb	0			
Site				
URMC	-1.2950	-20.1474	17.5573	0.8917
UNC	5.3574	-13.9285	24.6433	0.5821
UCSF	0			

Analyses of Interactions

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

Table B.1.8c. Type III Sum of Squares for ST in V5, 24-Hr Average (μV), Including Ozone Exposure, by Age Interaction

Effect	*P* Value
Ozone exposure	0.4910
Site	0.7409
Age	0.7893
Ozone exposure by age	0.9887

Table B.1.8d. Mixed Model for ST in V5, 24-Hr Average (μV), Including Ozone Exposure, by Age Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	22.7315	8.5593	36.9037	0.0020
Ozone exposure				
120 ppb	0.3122	-2.3208	2.9451	0.8152
70 ppb	-1.1842	-3.7908	1.4225	0.3711
0 ppb	0			
Site				
URMC	-1.5782	-20.6542	17.4978	0.8697
UNC	5.3907	-14.0084	24.7897	0.5820
UCSF	0			
Age	0.2213	-1.5385	1.9811	0.8031
Ozone exposure by age				
120 ppb by age	-0.00327	-0.6011	0.5946	0.9914
70 ppb by age	0.03663	-0.5498	0.6231	0.9020
0 ppb by age	0			

As we can see from the tables below,

- there was a significant difference in ST in V5 (24 hr) by sex — ST in V5 in women decreased from pre-exposure to post-exposure relative to men, independent of ozone exposure; and
- the ozone effect did not differ by sex.

Table B.1.8e. Type III Sum of Squares for ST in V5, 24-Hr Average (μV), Including Ozone Exposure, by Sex Interaction

Effect	*P* Value
Ozone exposure	0.4353
Site	0.3684
Sex	<0.0001
Ozone exposure by sex	0.2403

Table B.1.8f. Mixed Model for ST in V5, 24-Hr Average (μV), Including Ozone Exposure, by Sex Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	38.4482	23.7879	53.1086	<0.0001
Ozone exposure				
120 ppb	-2.2459	-6.3316	1.8398	0.2794
70 ppb	-3.3031	-7.3887	0.7826	0.1124
0 ppb	0			
Site				
URMC	3.6738	-13.7250	21.0726	0.6756
UNC	12.3148	-5.6263	30.2558	0.1759
UCSF	0			
Sex				
Female	-33.2323	-48.0901	-18.3745	<0.0001
Male	0			
Ozone exposure by sex				
120 ppb by female	4.2499	-1.0430	9.5428	0.1148
70 ppb by female	3.5146	-1.7474	8.7766	0.1891
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.1.8g. Type III Sum of Squares for ST in V5, 24-Hr Average (μV), Including Ozone Exposure, by GSTM1 Status Interaction

Effect	*P* Value
Ozone exposure	0.4222
Site	0.7518
GSTM1 status	0.6994
Ozone exposure by GSTM1 status	0.4206

Table B.1.8h. Mixed Model for ST in V5, 24-Hr Average (μV), Including Ozone Exposure, by GSTM1 Status Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	24.2099	9.0007	39.4190	0.0022
Ozone exposure				
120 ppb	-0.9911	-4.4105	2.4284	0.5680
70 ppb	-1.2000	-4.5938	2.1938	0.4861
0 ppb	0			
Site				
URMC	-0.9305	-19.9759	18.1150	0.9228
UNC	5.6453	-13.8048	25.0954	0.5653
UCSF	0			
GSTM1 status				
Sufficient	-4.1129	-20.0618	11.8359	0.6094
Null	0			
Ozone exposure by GSTM1 status				
120 ppb by sufficient	3.1002	-2.1826	8.3831	0.2483
70 ppb by sufficient	0.09140	-5.1435	5.3262	0.9725
0 ppb by sufficient	0			
120 ppb by null	0			
70 ppb by null	0			
0 ppb by null	0			

9. Secondary Endpoints

Descriptive Statistics

Table B.1.9a. Descriptive Statistics of Secondary Cardiac Outcomes

	0 ppb			70 ppb			120 ppb		
	N	**Mean**	**SD**	***N***	**Mean**	**SD**	***N***	**Mean**	**SD**
LF/HF, 5 min									
Pre-exposure	85	2.66	3.72	87	2.04	2.81	84	2.44	3.37
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
RMSSD, 5 min (ms)									
Pre-exposure	85	28.5	24.4	87	28.0	24.9	84	26.8	19.7
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
SDNN, 5 min (ms)									
Pre-exposure	85	48.1	39.0	87	48.2	36.6	84	49.5	38.3
15-min post-exposure	85	53.9	45.9	87	55.2	44.5	84	58.4	47.3
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
SDNN, 24 hr (ms)	86	154.3	34.6	87	155.0	38.2	85	156.4	37.6
Ln of LF, 24 hr (ms^2)	86	6.353	0.776	87	6.340	0.727	85	6.354	0.808
Ln of HF, 24 hr (ms^2)	86	5.450	1.099	87	5.421	1.029	85	5.458	1.123
HR, 5-min avg (beats/min)									
Pre-exposure	85	67.5	8.6	87	67.6	8.2	84	67.6	9.3
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
HR, 24 hr (beats/min)	86	70.6	7.8	87	70.9	8.1	85	70.7	8.3
QTc, 5 min (ms)									
Pre-exposure	85	425.4	16.3	87	426.8	16.4	84	425.1	17.2
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
ST in lead II, 5 min (μV)									

	0 ppb			70 ppb			120 ppb		
	N	**Mean**	**SD**	***N***	**Mean**	**SD**	***N***	**Mean**	**SD**
Pre-exposure	85	30.3	43.5	87	31.8	41.5	84	32.8	42.9
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
ST in lead II, 24 hr (μV)	86	28.6	41.7	87	30.7	41.8	85	30.2	42.0
ST in V2, 5 min (μV)									
Pre-exposure	85	92.6	63.7	87	94.4	63.4	84	98.7	61.7
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
ST in V2, 24 hr (μV)	86	79.0	56.8	87	79.6	54.0	85	84.7	55.8

10. LF/HF, 5-Min Average

The following figure shows the change in LF/HF ratio from pre- to post-exposure over time. The data come from Table B.1.9a.

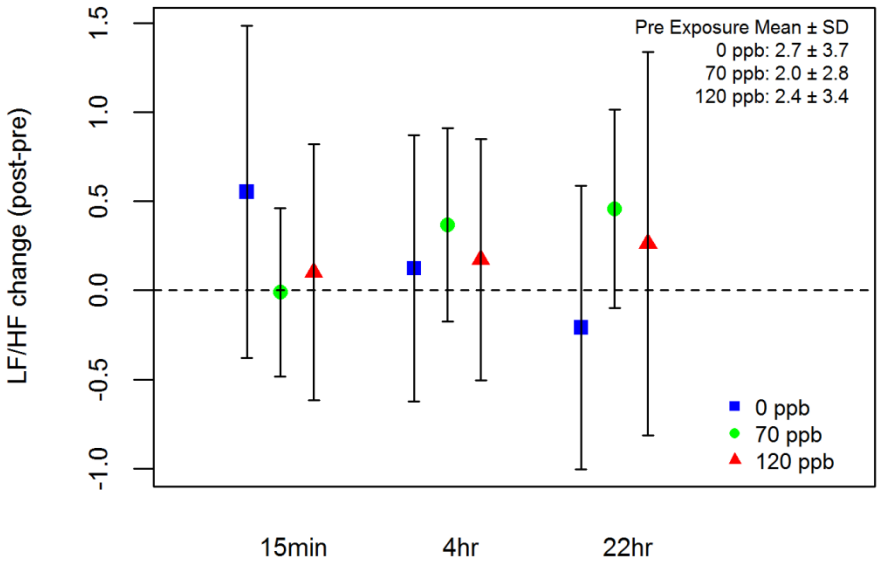

Figure B.1.10. Change in 5-min average LF/HF ratio at different post-exposure times and at each ozone exposure.

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

Table B.1.10a. Type III Sum of Squares for Change in LF/HF, 5-Min Average

Effect	*P* Value
15-min vs. 4-hr vs. 22-hr change	0.9797
Ozone exposure	0.9206
Site	0.4388

Table B.1.10b. Mixed Model for Change in LF/HF, 5-Min Average

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* value
Intercept	0.07346	-0.6802	0.8271	0.8468
Change between post- and pre-exposure				
22-hr change	-0.05035	-0.6348	0.5341	0.8652
4-hr change	0.003383	-0.5748	0.5815	0.9908
15-min change	0			
Ozone exposure				
120 ppb	0.04432	-0.5433	0.6319	0.8818
70 ppb	0.1180	-0.4610	0.6970	0.6880
0 ppb	0			
Site				
URMC	0.3436	-0.4359	1.1232	0.3832
UNC	-0.1305	-0.9336	0.6727	0.7475
UCSF	0			

Analyses of Interactions

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

Table B.1.10c. Type III Sum of Squares for Change in LF/HF, 5-Min Average, Including Ozone Exposure, by Age Interaction

Effect	*P* Value
Ozone exposure	0.9413
15-min vs. 4-hr vs. 22-hr change	0.9799
Site	0.5488
Age	0.0640
Ozone exposure by age	0.1318

Table B.1.10d. Mixed Model for Change in LF/HF, 5-Min Average, Including Ozone Exposure, by Age Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	0.1202	-0.6249	0.8654	0.7491
22-hr change	-0.05117	-0.6352	0.5329	0.8629
4-hr change	0.001252	-0.5765	0.5790	0.9966
15-min change	0			
Ozone exposure				
120 ppb	-0.01326	-0.6033	0.5768	0.9647
70 ppb	0.08141	-0.4988	0.6617	0.7821
0 ppb	0			
Site				
URMC	0.2589	-0.5080	1.0259	0.5038
UNC	-0.1482	-0.9348	0.6384	0.7088
UCSF	0			
Age	-0.01140	-0.1153	0.09251	0.8278
Ozone exposure by age				
120 ppb by age	0.1203	-0.01183	0.2525	0.0743
70 ppb by age	0.1120	-0.01684	0.2408	0.0883
0 ppb by age	0			

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

Table B.1.10e. Type III Sum of Squares for Change in LF/HF, 5-Min Average, Including Ozone Exposure, by Sex Interaction

Effect	*P* Value
Ozone exposure	0.9175
15-min vs. 4-hr vs. 22-hr change	0.9811
Site	0.4381
Sex	0.2999
Ozone exposure by sex	0.7287

Table B.1.10f. Mixed Model for Change in LF/HF, 5-Min Average, Including Ozone Exposure, by Sex Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	0.01720	-0.8977	0.9321	0.9703
22-hr change	-0.04919	-0.6341	0.5357	0.8683
4-hr change	0.002174	-0.5764	0.5808	0.9941
15-min change	0			
Ozone exposure				
120 ppb	-0.2151	-1.1327	0.7024	0.6440
70 ppb	0.07858	-0.8343	0.9914	0.8653
0 ppb	0			
Site				
URMC	0.2829	-0.5060	1.0717	0.4777
UNC	-0.2077	-1.0254	0.6100	0.6148
UCSF	0			
Sex				
Female	0.1749	-0.7792	1.1291	0.7163
Male	0			
Ozone exposure by sex				
120 ppb by female	0.4467	-0.7487	1.6421	0.4617
70 ppb by female	0.06556	-1.1159	1.2470	0.9129
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.1.10g. Type III Sum of Squares for Change in LF/HF, 5-Min Average, Including Ozone Exposure, by GSTM1 Status Interaction

Effect	*P* Value
Ozone exposure	0.9466
15-min vs. 4-hr vs. 22-hr change	0.9804
Site	0.4406
GSTM1 status	0.9247
Ozone exposure by GSTM1 status	0.8363

Table B.1.10h. Mixed Model for Change in LF/HF, 5-Min Average, Including Ozone Exposure, by GSTM1 Status Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	0.05161	-0.7875	0.8907	0.9029
22-hr change	-0.04971	-0.6350	0.5355	0.8670
4-hr change	0.003138	-0.5758	0.5820	0.9915
15-min post change	0			
Ozone exposure				
120 ppb	0.02337	-0.7560	0.8028	0.9529
70 ppb	0.2387	-0.5283	1.0058	0.5398
0 ppb	0			
Site				
URMC	0.3466	-0.4422	1.1355	0.3846
UNC	-0.1287	-0.9404	0.6830	0.7532
UCSF	0			
GSTM1 status				
Sufficient	0.04646	-0.8982	0.9911	0.9223
Null	0			
Ozone exposure, by GSTM1 status				
120 ppb by sufficient	0.04852	-1.1399	1.2370	0.9358
70 ppb by sufficient	-0.2808	-1.4525	0.8908	0.6367
0 ppb by sufficient	0			
120 ppb by null	0			
70 ppb by null	0			
0 ppb by null	0			

11. RMSSD, 5-Min Average (ms)

The following figure shows the change in RMSSD from pre- to post-exposure across the ozone exposures. The data come from Table B.1.9a.

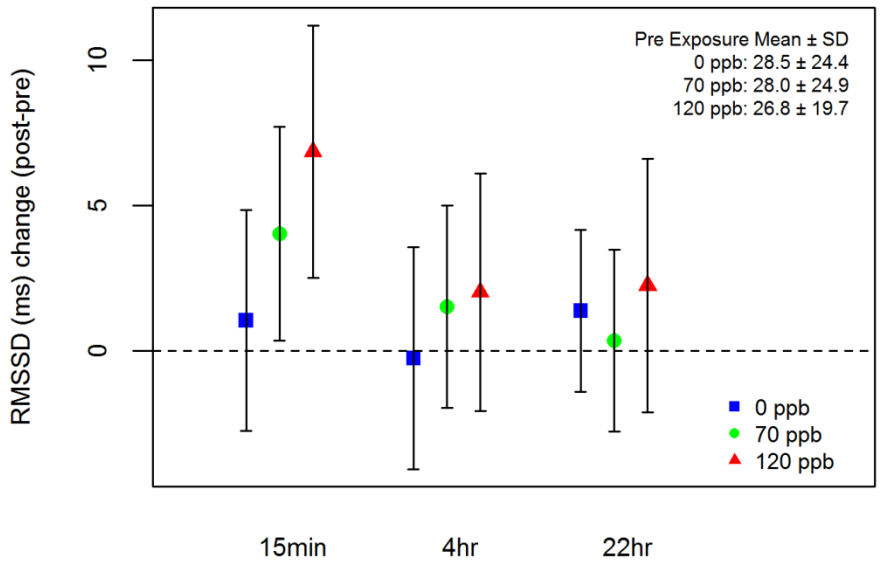

Figure B.1.11. Change in RMSSD, 5-min average.

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

Table B.1.11a. Type III Sum of Squares for Change in RMSSD, 5-Min Average (ms)

Effect	*P* Value
15-min vs. 4-hr vs. 22-hr change	0.0713
Ozone exposure	0.1158
Site	0.2260

Table B.1.11b. Mixed Model for Change in RMSSD, 5-Min Average (ms)

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	1.1198	-3.2816	5.5212	0.6142
Change between post- and pre-exposure				
22-hr change	-2.6272	-5.3584	0.1040	0.0593
4-hr change	-2.8593	-5.5595	-0.1590	0.0381
15-min change	0			
Ozone exposure				
120 ppb	2.9090	0.1580	5.6601	0.0383
70 ppb	1.3176	-1.3895	4.0246	0.3380
0 ppb	0			
Site				
URMC	3.7537	-1.3330	8.8403	0.1460
UNC	0.01258	-5.2118	5.2369	0.9962
UCSF	0			

Analyses of Interactions

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

Table B.1.11c. Type III Sum of Squares for Change in RMSSD, 5-Min Average (ms), Including Ozone Exposure, by Age Interaction

Effect	*P* Value
Ozone exposure	0.1788
15-min vs. 4-hr vs. 22-hr change	0.0682
Site	0.2216
Age	0.9415
Ozone exposure by age	0.0510

Table B.1.11d. Mixed Model for Change in RMSSD, 5-Min Average (ms), Including Ozone Exposure, by Age Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	1.2673	-3.1569	5.6915	0.5704
22-hr change	-2.6453	-5.3684	0.07776	0.0568
4-hr change	-2.8727	-5.5648	-0.1805	0.0366
15-min change	0			
Ozone exposure				
120 ppb	2.6054	-0.1529	5.3637	0.0640
70 ppb	1.3108	-1.3963	4.0179	0.3405
0 ppb	0			
Site				
URMC	3.7492	-1.3993	8.8978	0.1513
UNC	-0.1505	-5.4102	5.1092	0.9548
UCSF	0			
Age	-0.1996	-0.7897	0.3905	0.5029
Ozone exposure by age				
120 ppb by age	0.6223	0.003343	1.2413	0.0488
70 ppb by age	-0.07543	-0.6772	0.5263	0.8057
0 ppb by age	0			

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

Table B.1.11e. Type III Sum of Squares for Change in RMSSD, 5-Min Average (ms), Including Ozone Exposure, by Sex Interaction

Effect	*P* Value
Ozone exposure	0.1636
15-min vs. 4-hr vs. 22-hr change	0.0711
Site	0.1687
Sex	0.0370
Ozone exposure by sex	0.5480

Table B.1.11f. Mixed Model for Change in RMSSD, 5-Min Average (ms), Including Ozone Exposure, by Sex Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	3.4598	-1.6782	8.5978	0.1841
22-hr change	-2.6342	-5.3671	0.09873	0.0588
4-hr change	-2.8601	-5.5621	-0.1582	0.0381
15-min change	0			
Ozone exposure				
120 ppb	1.6262	-2.6638	5.9161	0.4553
70 ppb	1.8197	-2.4476	6.0871	0.4010
0 ppb	0			
Site				
URMC	4.4827	-0.5477	9.5131	0.0800
UNC	1.0164	-4.1867	6.2195	0.6986
UCSF	0			
Sex				
Female	-4.9231	-10.2221	0.3759	0.0682
Male	0			
Ozone exposure by sex				
120 ppb by female	2.1666	-3.4269	7.7600	0.4455
70 ppb by female	-0.8381	-6.3608	4.6846	0.7648
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.1.11g. Type III Sum of Squares for Change in RMSSD, 5-Min Average (ms), Including Ozone Exposure, by GSTM1 Status Interaction

Effect	*P* Value
Ozone exposure	0.1281
15-min vs. 4-hr vs. 22-hr change	0.0715
Site	0.2338
GSTM1 status	0.9231
Ozone exposure by GSTM1 status	0.3944

Table B.1.11h. Mixed Model for Change in RMSSD, 5-Min Average (ms), Including Ozone Exposure, by GSTM1 Status Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	0.4299	-4.4129	5.2728	0.8603
22-hr change	-2.6235	-5.3551	0.1081	0.0597
4-hr change	-2.8605	-5.5611	-0.1599	0.0380
15-min change	0			
Ozone exposure				
120 ppb	3.2584	-0.3873	6.9042	0.0795
70 ppb	2.8674	-0.7148	6.4496	0.1159
0 ppb	0			
Site				
URMC	3.7144	-1.4319	8.8607	0.1549
UNC	-0.03615	-5.3140	5.2417	0.9892
UCSF	0			
GSTM1 status				
Sufficient	1.6876	-3.6230	6.9983	0.5291
Null	0			
Ozone exposure by GSTM1 status				
120 ppb by sufficient	-0.8302	-6.3875	4.7271	0.7684
70 ppb by sufficient	-3.6141	-9.0853	1.8572	0.1940
0 ppb by Sufficient	0			
120 ppb by null	0			
70 ppb by null	0			
0 ppb by null	0			

12. SDNN, 5-Min Average (ms)

The following figure shows the change in SDNN from pre- to post-exposure over time. The data come from Table B.1.9a.

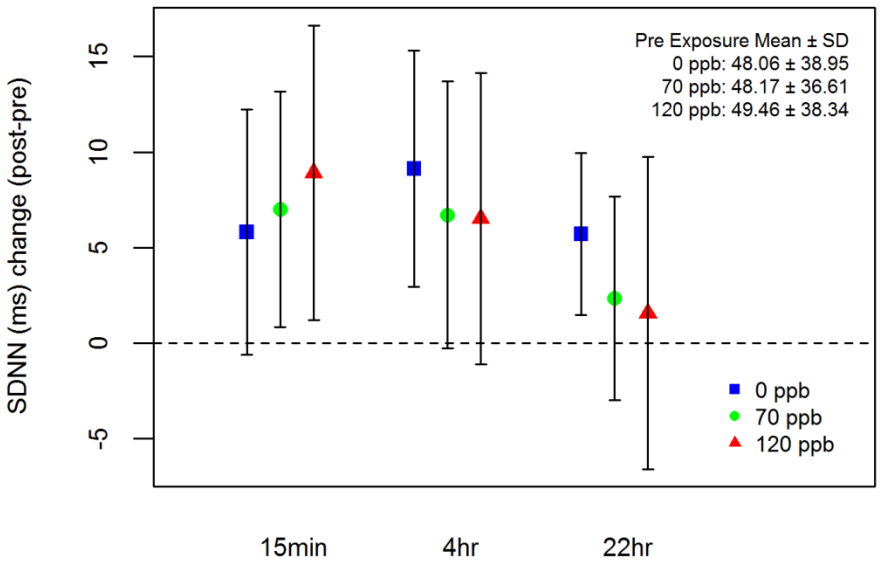

Figure B.1.12. Change in 5-min average SDNN at different post-exposure times and at each ozone exposure.

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

Table B.1.12a. Type III Sum of Squares for Change in SDNN, 5-Min Average (ms)

Effect	*P* Value
15-min vs. 4-hr vs. 22-hr change	0.1013
Ozone exposure	0.7572
Site	0.3266

Table B.1.12b. Mixed Model for Change in SDNN, 5-Min Average (ms)

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	5.3154	-3.0466	13.6774	0.2097
Change between post- and pre-exposure				
22-hr change	-4.1548	-8.6925	0.3829	0.0725
4-hr change	0.2928	-4.1926	4.7783	0.8976
15-min change	0			
Ozone exposure				
120 ppb	-1.2632	-5.8369	3.3106	0.5863
70 ppb	-1.6266	-6.1249	2.8717	0.4763
0 ppb	0			
Site				
URMC	6.8162	-3.2440	16.8764	0.1815
UNC	0.8332	-9.4881	11.1545	0.8728
UCSF	0			

Analyses of Interactions

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

Table B.1.12c. Type III Sum of Squares for Change in SDNN, 5-Min Average (ms), Including Ozone Exposure, by Age Interaction

Effect	*P* Value
Ozone exposure	0.7361
15-min vs. 4-hr vs. 22-hr change	0.1022
Site	0.3949
Age	0.3975
Ozone exposure by age	0.5339

Table B.1.12d. Mixed Model for Change in SDNN, 5-Min Average (ms), Including Ozone Exposure, by Age Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	5.3847	-2.9975	13.7668	0.2049
22-hr change	-4.1462	-8.6865	0.3941	0.0732
4-hr change	0.2971	-4.1909	4.7851	0.8962
15-min change	0			
Ozone exposure				
120 ppb	-1.2124	-5.8152	3.3904	0.6037
70 ppb	-1.7549	-6.2695	2.7597	0.4439
0 ppb	0			
Site				
URMC	6.3339	-3.8012	16.4690	0.2174
UNC	0.9206	-9.4209	11.2620	0.8599
UCSF	0			
Age	0.2754	-0.8229	1.3736	0.6193
Ozone exposure by age				
120 ppb by age	-0.09042	-1.1240	0.9431	0.8637
70 ppb by age	0.4438	-0.5601	1.4478	0.3857
0 ppb by age	0			

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

Table B.1.12e. Type III Sum of Squares for Change in SDNN, 5-Min Average (ms), Including Ozone Exposure, by Sex Interaction

Effect	*P* Value
Ozone exposure	0.8006
15-min vs. 4-hr vs. 22-hr change	0.1009
Site	0.2664
Sex	0.1278
Ozone exposure by sex	0.9163

Table B.1.12f. Mixed Model for Change in SDNN, 5-Min Average (ms), Including Ozone Exposure, by Sex Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	7.6709	-2.0664	17.4083	0.1210
22-hr change	-4.1613	-8.7053	0.3827	0.0724
4-hr change	0.2984	-4.1933	4.7902	0.8958
15-min change	0			
Ozone exposure				
120 ppb	-0.1480	-7.2831	6.9870	0.9674
70 ppb	-0.8555	-7.9525	6.2415	0.8122
0 ppb	0			
Site				
URMC	7.9083	-2.1680	17.9847	0.1223
UNC	2.3084	-8.1045	12.7214	0.6604
UCSF	0			
Sex				
Female	-5.4379	-15.4226	4.5468	0.2818
Male	0			
Ozone exposure by sex				
120 ppb by female	-1.9323	-11.2382	7.3736	0.6824
70 ppb by female	-1.2873	-10.4718	7.8972	0.7823
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.1.12g. Type III Sum of Squares for Change in SDNN, 5-Min Average (ms), Including Ozone Exposure, by GSTM1 Status Interaction

Effect	*P* Value
Ozone exposure	0.7002
15-min vs. 4-hr vs. 22-hr change	0.1028
Site	0.3192
GSTM1 status	0.7177
Ozone exposure by GSTM1 status	0.5241

Table B.1.12h. Mixed Model for Change in SDNN, 5-Min Average (ms), Including Ozone Exposure, by GSTM1 Status Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	5.3282	-3.8203	14.4767	0.2500
22-hr change	-4.1445	-8.6850	0.3960	0.0733
4-hr change	0.2903	-4.1979	4.7784	0.8986
15-min change	0			
Ozone exposure				
120 ppb	-1.5075	-7.5722	4.5572	0.6242
70 ppb	0.1983	-5.7572	6.1539	0.9477
0 ppb	0			
Site				
URMC	6.9897	-3.1739	17.1533	0.1751
UNC	0.9642	-9.4472	11.3755	0.8543
UCSF	0			
GSTM1 status				
Sufficient	-0.2930	-10.2075	9.6215	0.9533
Null	0			
Ozone exposure by GSTM1 status				
120 ppb by sufficient	0.5519	-8.6915	9.7953	0.9063
70 ppb by sufficient	-4.2473	-13.3432	4.8485	0.3579
0 ppb by sufficient	0			
120 ppb by null	0			
70 ppb by null	0			
0 ppb by null	0			

13. SDNN, 24-Hr Average (ms)

The following figure shows SDNN across the ozone exposure. The data come from Table B.1.9a.

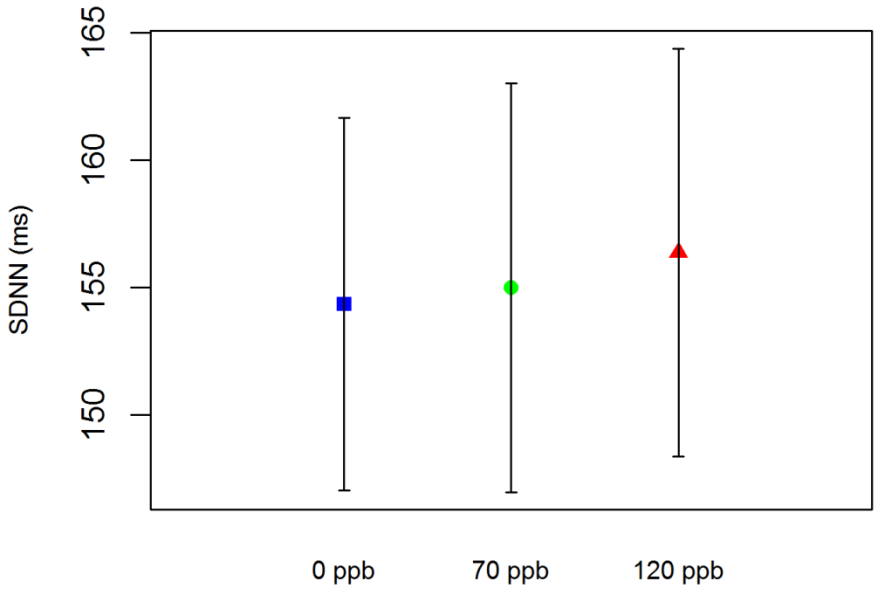

Figure B.1.13. Change in SDNN (ms), 24-hour average.

Main Analysis of Ozone Effect

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

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

Table B.1.13a. Type III Sum of Squares for SDNN, 24-Hr Average (ms)

Effect	*P* Value
Ozone exposure	0.5140
Site	0.0084

Table B.1.13b. Mixed Model for SDNN, 24-Hr Average (ms)

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	171.41	158.11	184.71	<0.0001
Ozone exposure				
120 ppb	2.3872	-1.7000	6.4744	0.2505
70 ppb	1.0378	-3.0146	5.0903	0.6138
0 ppb	0			
Site				
URMC	-26.0102	-43.6198	-8.4005	0.0043
UNC	-23.6776	-41.6943	-5.6609	0.0106
UCSF	0			

Analyses of Interactions

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

Table B.1.13c. Type III Sum of Squares for SDNN, 24-Hr Average (ms), Including Ozone Exposure, by Age Interaction

Effect	*P* Value
Ozone exposure	0.5914
Site	0.0048
Age	0.0522
Ozone exposure by age	0.1996

Table B.1.13d. Mixed Model for SDNN, 24-Hr Average (ms), Including Ozone Exposure, by Age Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	171.68	158.59	184.78	<0.0001
Ozone exposure				
120 ppb	2.1283	-1.9651	6.2218	0.3061
70 ppb	1.0792	-2.9741	5.1326	0.5998
0 ppb	0			
Site				
Ozone exposure by age				
120 ppb by age	0.6149	-0.3141	1.5440	0.1931
70 ppb by age	-0.1834	-1.0951	0.7282	0.6917
0 ppb by age	0			

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

Table B.1.13e. Type III Sum of Squares for SDNN, 24-Hr Avg (ms), Including Ozone Exposure, by Sex Interaction

Effect	*P* Value
Ozone exposure	0.5506
Site	0.0123
Sex	0.6798
Ozone exposure by sex	0.3642

Table B.1.13f. Mixed Model for SDNN, 24-Hr Avg (ms), Including Ozone Exposure, by Sex Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	174.38	159.05	189.71	<0.0001
Ozone exposure				
120 ppb	1.3430	-5.0884	7.7745	0.6807
70 ppb	-2.4570	-8.8884	3.9745	0.4518
0 ppb	0			
Site				
URMC	-25.5234	-43.3839	-7.6628	0.0056
UNC	-22.9967	-41.4152	-4.5781	0.0150
UCSF	0			
Sex				
Female	-5.6015	-21.2891	10.0862	0.4796
Male	0			
Ozone exposure by sex				
120 ppb by female	1.6794	-6.6522	10.0111	0.6912
70 ppb by female	5.8031	-2.4805	14.0868	0.1685
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.1.13g. Type III Sum of Squares for SDNN, 24-Hr Avg (ms), Including Ozone Exposure, by GSTM1 Status Interaction

Effect	*P* Value
Ozone exposure	0.6856
Site	0.0116
GSTM1 status	0.3784
Ozone exposure by GSTM1 status	0.1555

Table B.1.13h. Mixed Model for SDNN, 24-Hr Avg (ms), Including Ozone Exposure, by GSTM1 Status Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	171.74	157.38	186.09	<0.0001
Ozone exposure				
120 ppb	5.5621	0.2246	10.8995	0.0412
70 ppb	3.6400	-1.6581	8.9381	0.1768
0 ppb	0			
Site				
URMC	-25.2241	-42.9366	-7.5116	0.0058
UNC	-23.0007	-41.0918	-4.9096	0.0133
UCSF	0			
GSTM1 status				
Sufficient	-1.8821	-17.2047	13.4405	0.8076
Null	0			
Ozone exposure by GSTM1 status				
120 ppb by sufficient	-7.5830	-15.8280	0.6620	0.0712
70 ppb by sufficient	-6.2140	-14.3854	1.9574	0.1352
0 ppb by sufficient	0			
120 ppb by null	0			
70 ppb by null	0			
0 ppb by null	0			

14. Ln of HF, 24-Hr Average (ms^2)

The following figure shows the natural logarithm of HF across the ozone exposures. The data come from Table B.1.9a.

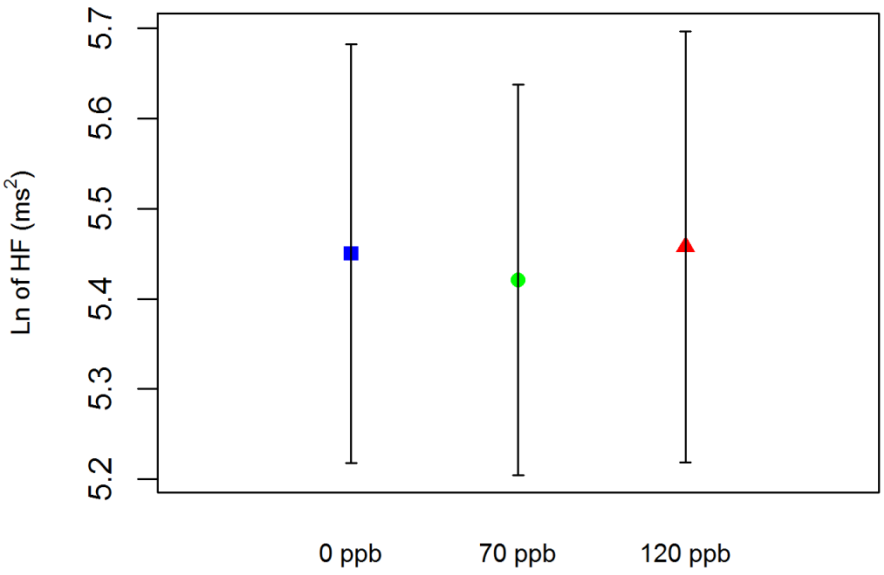

Figure B.1.14. Change in the natural logarithm of HF (ms^2), 24-hour average.

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

Table B.1.14a Type III Sum of Squares for Ln of HF, 24-Hr Average (ms^2)

Effect	*P* Value
Ozone exposure	0.7297
Site	0.1702

Table B.1.14b. Mixed Model for Ln of HF, 24-Hr Average (ms^2)

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	5.7393	5.3296	6.1489	<0.0001
Ozone exposure				
120 ppb	0.003006	-0.09220	0.09821	0.9504
70 ppb	-0.03131	-0.1257	0.06307	0.5135
0 ppb	0			
Site				
URMC	-0.2964	-0.8426	0.2499	0.2837
UNC	-0.5342	-1.0930	0.02467	0.0608
UCSF	0			

Analyses of Interactions

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

Table B.1.14c. Type III Sum of Squares for Ln of HF, 24-Hr Average (ms^2), Including Ozone Exposure, by Age Interaction

Effect	*P* Value
Ozone exposure	0.8185
Site	0.1536
Age	0.0301
Ozone exposure by age	0.0614

Table B.1.14d. Mixed Model for Ln of HF, 24-Hr Average (ms^2), Including Ozone Exposure, by Age Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	5.7450	5.3440	6.1460	<0.0001
Ozone exposure				
120 ppb	-0.00142	-0.09609	0.09324	0.9763
70 ppb	-0.02669	-0.1204	0.06703	0.5747
0 ppb	0			
Site				
Ozone exposure by age				
120 ppb by age	0.01098	-0.01051	0.03247	0.3146
70 ppb by age	-0.01425	-0.03534	0.006831	0.1838
0 ppb by age	0			

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

Table B.1.14e. Type III Sum of Squares for Ln of HF, 24-Hr Average (ms^2), Including Ozone Exposure, by Sex Interaction

Effect	*P* Value
Ozone exposure	0.6120
Site	0.1917
Sex	0.8906
Ozone exposure by sex	0.3195

Table B.1.14f. Mixed Model for Ln of HF, 24-Hr Average (ms^2), Including Ozone Exposure, by Sex Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	5.8065	5.3370	6.2760	<0.0001
Ozone exposure				
120 ppb	-0.06760	-0.2173	0.08206	0.3738
70 ppb	-0.1143	-0.2640	0.03535	0.1335
0 ppb	0			
Site				
URMC	-0.2923	-0.8471	0.2624	0.2976
UNC	-0.5278	-1.0999	0.04421	0.0700
UCSF	0			
Sex				
Female	-0.1171	-0.5940	0.3599	0.6267
Male	0			
Ozone exposure by sex				
120 ppb by female	0.1174	-0.07650	0.3113	0.2337
70 ppb by female	0.1374	-0.05535	0.3301	0.1612
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.1.14g. Type III Sum of Squares for Ln of HF, 24-Hr Average (ms^2), Including Ozone Exposure, by GSTM1 Status Interaction

Effect	*P* Value
Ozone exposure	0.6522
Site	0.1675
GSTM1 status	0.7769
Ozone exposure by GSTM1 status	0.5857

Table B.1.14h. Mixed Model for Ln of HF, 24-Hr Average (ms^2), Including Ozone Exposure, by GSTM1 Status Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	5.6971	5.2540	6.1403	<0.0001
Ozone exposure				
120 ppb	0.02164	-0.1036	0.1469	0.7335
70 ppb	0.01089	-0.1134	0.1352	0.8629
0 ppb	0			
Site				
URMC	-0.3050	-0.8572	0.2473	0.2752
UNC	-0.5414	-1.1054	0.02251	0.0596
UCSF	0			
GSTM1 status				
Sufficient	0.1133	-0.3542	0.5808	0.6310
Null	0			
Ozone exposure by GSTM1 status				
120 ppb by sufficient	-0.04497	-0.2385	0.1485	0.6470
70 ppb by sufficient	-0.1004	-0.2922	0.09136	0.3028
0 ppb by sufficient	0			
120 ppb by null	0			
70 ppb by null	0			
0 ppb by null	0			

15. Ln of LF, 24-Hr Average (ms^2)

The following figure shows the natural logarithm of LF by ozone exposure. The data come from Table B.1.9a.

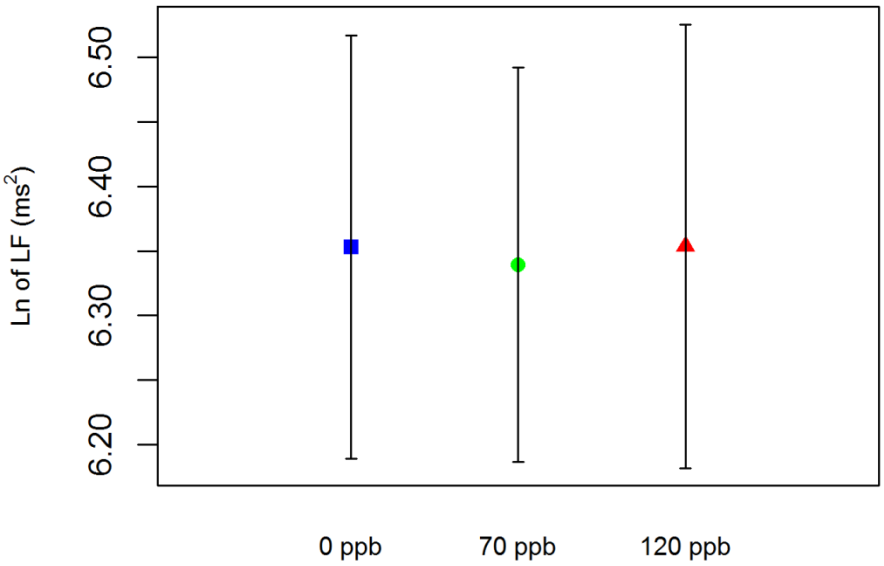

Figure B.1.15. Change in the natural logarithm of 24-hour average LF by ozone exposure.

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

Table B.1.15a. Type III Sum of Squares for LN of LF, 24-Hr Average (ms^2)

Effect	*P* Value
Ozone exposure	0.9295
Site	0.0932

Table B.1.15b. Mixed Model for Ln of LF, 24-Hr Average (ms^2)

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	6.5231	6.2330	6.8132	<0.0001
Ozone exposure				
120 ppb	0.000358	-0.06357	0.06428	0.9912
70 ppb	-0.01045	-0.07383	0.05292	0.7452
0 ppb	0			
Site				
URMC	-0.09554	-0.4827	0.2917	0.6249
UNC	-0.4140	-0.8101	-0.01791	0.0407
UCSF	0			

Analyses of Interactions

As we can see from the tables below,

- there was a marginally significant difference in LF by age, independent of ozone exposure; and
- there was a marginally significant difference in the ozone effect by age — an increase in age was associated with an increase in LF from pre-exposure to post-exposure when comparing 70 ppb and 120 ppb versus 0 ppb ozone.

Table B.1.15c. Type III Sum of Squares for Ln of LF, 24-Hr Average (ms^2), Including Ozone Exposure, by Age Interaction

Effect	*P* Value
Ozone exposure	0.9846
Site	0.1022
Age	0.0039
Ozone exposure by age	0.0276

Table B.1.15d. Mixed Model for Ln of LF, 24-Hr Average (ms^2), Including Ozone Exposure, by Age Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	6.5252	6.2473	6.8031	<0.0001
Ozone exposure				
120 ppb	0.000889	-0.06237	0.06415	0.9779
70 ppb	-0.00433	-0.06696	0.05830	0.8916
0 ppb	0			
Site				
URMC	-0.1556	-0.5285	0.2173	0.4091
UNC	-0.4068	-0.7861	-0.02761	0.0358
UCSF	0			
Age	0.05609	0.02134	0.09084	0.0019
Ozone exposure by age				
120 ppb by age	-0.00040	-0.01476	0.01396	0.9563
70 ppb by age	-0.01678	-0.03087	-0.00269	0.0199
0 ppb by age	0			

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

Table B.1.15e. Type III Sum of Squares for Ln of LF, 24-Hr Average (ms^2), Including Ozone Exposure, by Sex Interaction

Effect	*P* Value
Ozone exposure	0.8733
Site	0.1693
Sex	0.0372
Ozone exposure by sex	0.1121

Table B.1.15f. Mixed Model for Ln of LF, 24-Hr Avg (ms^2), Including Ozone Exposure, by Sex Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	6.7190	6.3953	7.0427	<0.0001
Ozone exposure				
120 ppb	-0.08102	-0.1809	0.01885	0.1111
70 ppb	-0.04135	-0.1412	0.05853	0.4149
0 ppb	0			
Site				
URMC	-0.04115	-0.4241	0.3418	0.8313
UNC	-0.3371	-0.7320	0.05774	0.0932
UCSF	0			
Sex				
Female	-0.4028	-0.7315	-0.07420	0.0169
Male	0			
Ozone exposure by sex				
120 ppb by female	0.1364	0.007059	0.2658	0.0389
70 ppb by female	0.05049	-0.07814	0.1791	0.4395
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.1.15g. Type III Sum of Squares for Ln of LF, 24-Hr Average (ms^2), Including Ozone Exposure, by GSTM1 Status Interaction

Effect	*P* Value
Ozone exposure	0.8850
Site	0.1007
GSTM1 status	0.6519
Ozone exposure by GSTM1 status	0.7415

Table B.1.15h. Mixed Model for Ln of LF, 24-Hr Average (ms^2), Including Ozone Exposure by GSTM1 Status Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	6.5420	6.2285	6.8555	<0.0001
Ozone exposure				
120 ppb	0.001446	-0.08278	0.08567	0.9730
70 ppb	0.008583	-0.07501	0.09218	0.8396
0 ppb	0			
Site				
URMC	-0.08684	-0.4780	0.3043	0.6599
UNC	-0.4069	-0.8063	-0.00745	0.0460
UCSF	0			
GSTM1 status				
Sufficient	-0.05721	-0.3874	0.2730	0.7312
Null	0			
Ozone exposure by GSTM1 status				
120 ppb by sufficient	-0.00282	-0.1329	0.1273	0.9660
70 ppb by sufficient	-0.04507	-0.1740	0.08387	0.4911
0 ppb by sufficient	0			
120 ppb by null	0			
70 ppb by null	0			
0 ppb by null	0			

16. HR (NN Interval) 5-Min Average (beats/min)

The following figure shows the change in HR from pre- to post-exposure over time. The data come from Table B.1.9a.

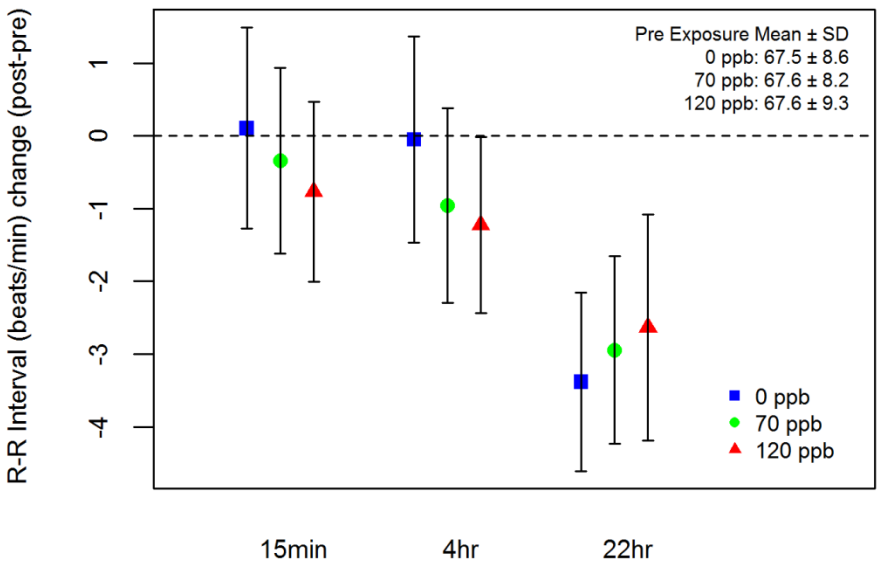

Figure B.1.16. Change in 5-min average HR at different post-exposure times and at each ozone exposure.

Main Analysis of Ozone Effect

As we can see from the tables below,

- there were differences among the 15-minute post-exposure, 4-hour post exposure, and 22-hour post-exposure changes in HR, but only the change from pre-exposure to 22-hour post-exposure was statistically significant;
- there were no differences in HR across the ozone exposures; and
- there were no differences in HR across the 3 sites.

Table B.1.16a Type III Sum of Squares for Change in HR, 5-Min Average (beats/min)

Effect	*P* Value
15-min vs. 4-hr vs. 22-hr change	<0.0001
Ozone exposure	0.6496
Site	0.2842

Table B.1.16b. Mixed Model for Change in HR, 5-Min Average (beats/min)

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	-1.1451	-2.8618	0.5716	0.1883
Change between post- and pre-exposure				
22-hr change	-2.7231	-3.6100	-1.8361	<0.0001
4-hr change	-0.4075	-1.2842	0.4691	0.3601
15-min change	0			
Ozone exposure				
120 ppb	-0.4105	-1.3047	0.4837	0.3660
70 ppb	-0.2822	-1.1615	0.5971	0.5272
0 ppb	0			
Site				
URMC	1.3988	-0.6907	3.4883	0.1867
UNC	1.5765	-0.5666	3.7195	0.1472
UCSF	0			

Analyses of Interactions

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

Table B.1.16c. Type III Sum of Squares for Change in HR, 5-Min Average (beats/min), Including Ozone Exposure, by Age Interaction

Effect	*P* Value
Ozone exposure	0.7929
15-min vs. 4-hr vs. 22-hr change	<0.0001
Site	0.2774
Age	0.5777
Ozone exposure by age	0.0538

Table B.1.16d. Mixed Model for Change in HR, 5-Min Average (beats/min), Including Ozone Exposure, by Age Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	-1.2234	-2.9476	0.5008	0.1619
22-hr change	-2.7165	-3.6009	-1.8322	<0.0001
4-hr change	-0.4039	-1.2780	0.4702	0.3630
15-min change	0			
Ozone exposure				
120 ppb	-0.2936	-1.1903	0.6032	0.5190
70 ppb	-0.2277	-1.1070	0.6517	0.6099
0 ppb	0			
Site				
URMC	1.3536	-0.7583	3.4655	0.2059
UNC	1.6443	-0.5097	3.7984	0.1327
UCSF	0			
Age	0.1790	-0.04542	0.4035	0.1164
Ozone exposure by age				
120 ppb by age	-0.2485	-0.4499	-0.04705	0.0157
70 ppb by age	-0.1272	-0.3228	0.06838	0.2021
0 ppb by age	0			

As we can see from the tables below,

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

Table B.1.16e. Type III Sum of Squares for Change in HR, 5-Min Average (beats/min), Including Ozone Exposure, by Sex Interaction

Effect	*P* Value
Ozone exposure	0.8337
15-min vs. 4-hr vs. 22-hr change	<0.0001
Site	0.5197
Sex	0.0095
Ozone exposure by sex	0.2342

Table B.1.16f. Mixed Model for Change in HR, 5-Min Average (beats/min), Including Ozone Exposure, by Sex Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	-2.6835	-4.6351	-0.7319	0.0076
22-hr change	-2.7183	-3.6045	-1.8320	<0.0001
4-hr change	-0.4069	-1.2829	0.4692	0.3606
15-min change	0			
Ozone exposure				
120 ppb	0.5206	-0.8710	1.9122	0.4612
70 ppb	0.2219	-1.1623	1.6061	0.7520
0 ppb	0			
Site				
URMC	1.0358	-1.0024	3.0741	0.3151
UNC	1.0715	-1.0346	3.1775	0.3145
UCSF	0			
Sex				
Female	3.0783	1.0792	5.0774	0.0030
Male	0			
Ozone exposure by sex				
120 ppb by female	-1.5714	-3.3865	0.2438	0.0893
70 ppb by female	-0.8458	-2.6371	0.9456	0.3526
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 HR by GSTM1 status — HR decreased after 120 ppb but not 70 ppb ozone exposure in GSTM1-sufficient subjects relative to GSTM1-null subjects.

Table B.1.16g. Type III Sum of Squares for Change in HR, 5-Min Average (beats/min), Including Ozone Exposure, by GSTM1 Status Interaction

Effect	*P* Value
Ozone exposure	0.4383
15-min vs. 4-hr vs. 22-hr change	<0.0001
Site	0.2896
GSTM1 status	0.9770
Ozone exposure by GSTM1 status	0.0115

Table B.1.16h. Mixed Model for Change in HR, 5-Min Average (beats/min), Including Ozone Exposure, by GSTM1 Status Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	-1.5702	-3.4440	0.3037	0.0994
22-hr change	-2.7251	-3.6074	-1.8428	<0.0001
4-hr change	-0.4046	-1.2767	0.4675	0.3611
15-min change	0			
Ozone exposure				
120 ppb	0.6866	-0.4922	1.8653	0.2518
70 ppb	-0.1363	-1.2936	1.0210	0.8164
0 ppb	0			
Site				
URMC	1.4016	-0.7103	3.5135	0.1904
UNC	1.5828	-0.5798	3.7454	0.1492
UCSF	0			
GSTM1 status				
Sufficient	0.9882	-1.0342	3.0106	0.3339
Null	0			
Ozone exposure by GSTM1 status				
120 ppb by sufficient	-2.5437	-4.3403	-0.7472	0.0058
70 ppb by sufficient	-0.3452	-2.1127	1.4224	0.7003
0 ppb by sufficient	0			
120 ppb by null	0			
70 ppb by null	0			
0 ppb by null	0			

17. HR (NN interval), 24-Hr Average (beats/min)

The following figure shows HR by ozone exposure. The data come from Table B.1.9a.

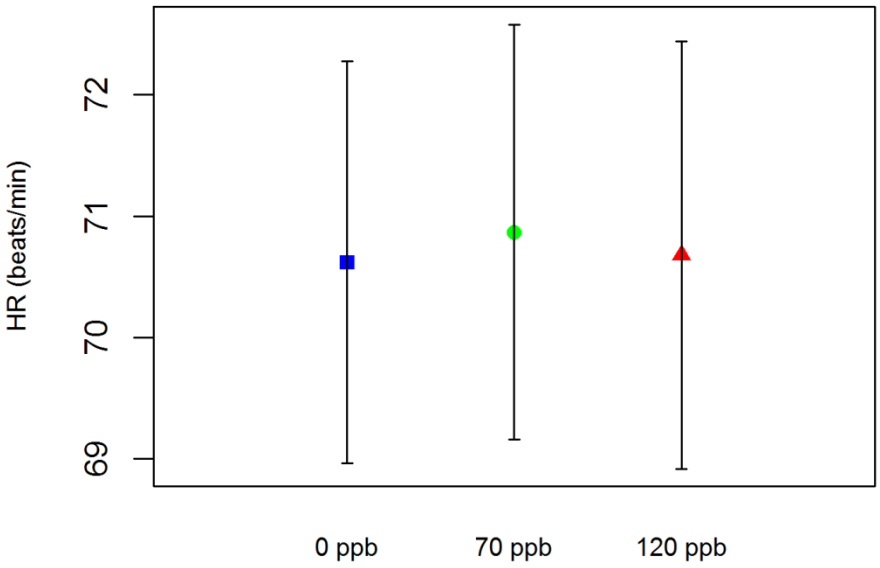

Figure B.1.17. The 24-hour average HR by ozone exposure.

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

Table B.1.17a. Type III Sum of Squares for HR, 24-Hr Average (beats/min)

Effect	*P* Value
Ozone exposure	0.7363
Site	0.2350

Table B.1.17b. Mixed Model for HR, 24-Hr Average (beats/min)

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	68.9528	65.9098	71.9958	<0.0001
Ozone exposure				
120 ppb	0.2666	-0.6016	1.1348	0.5452
70 ppb	0.3194	-0.5414	1.1801	0.4649
0 ppb	0			
Site				
URMC	1.1871	-2.8506	5.2249	0.5603
UNC	3.4782	-0.6528	7.6092	0.0978
UCSF	0			

Analyses of Interactions

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

Table B.1.17c. Type III Sum of Squares for HR, 24-Hr Average (beats/min), Including Ozone Exposure, by Age Interaction

Effect	*P* Value
Ozone exposure	0.7766
Site	0.2091
Age	0.2081
Ozone exposure by age	0.1294

Table B.1.17d. Mixed Model for HR, 24-Hr Avg (beats/min), Including Ozone Exposure, by Age Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	68.9988	65.9663	72.0313	<0.0001
Ozone exposure				
120 ppb	0.2728	-0.5944	1.1401	0.5354
70 ppb	0.2662	-0.5925	1.1248	0.5414
0 ppb	0			
Site				
Ozone exposure by age				
120 ppb by age	-0.01884	-0.2157	0.1780	0.8503
70 ppb by age	0.1606	-0.03252	0.3538	0.1025
0 ppb by age	0			

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

Table B.1.17e. Type III Sum of Squares for HR, 24-Hr Average (beats/min), Including Ozone Exposure, by Sex Interaction

Effect	*P* Value
Ozone exposure	0.5123
Site	0.3793
Sex	0.0544
Ozone exposure by sex	0.0632

Table B.1.17f. Mixed Model for HR, 24-Hr Average (beats/min), Including Ozone Exposure, by Sex Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	66.8245	63.3961	70.2529	<0.0001
Ozone exposure				
120 ppb	1.5147	0.1630	2.8664	0.0283
70 ppb	0.8488	-0.5029	2.2005	0.2168
0 ppb	0			
Site				
URMC	0.6696	-3.3403	4.6794	0.7406
UNC	2.7414	-1.3936	6.8765	0.1909
UCSF	0			
Sex				
Female	4.2716	0.7704	7.7727	0.0174
Male	0			
Ozone exposure by sex				
120 ppb by female	-2.0914	-3.8424	-0.3403	0.0195
70 ppb by female	-0.8671	-2.6080	0.8738	0.3269
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.1.17g. Type III Sum of Squares for HR, 24-Hr Average (beats/min), Including Ozone Exposure, by GSTM1 Status Interaction

Effect	*P* Value
Ozone exposure	0.7366
Site	0.2285
GSTM1 status	0.7066
Ozone exposure by GSTM1 status	0.5830

Table B.1.17h. Mixed Model for HR, 24-Hr Average (beats/min), Including Ozone Exposure, by GSTM1 Status Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	69.1294	65.8332	72.4256	<0.0001
Ozone exposure				
120 ppb	0.5178	-0.6247	1.6603	0.3722
70 ppb	0.1839	-0.9501	1.3180	0.7492
0 ppb	0			
Site				
URMC	1.2703	-2.8086	5.3493	0.5373
UNC	3.5521	-0.6139	7.7182	0.0937
UCSF	0			
GSTM1 status				
Sufficient	-0.5439	-4.0490	2.9612	0.7584
Null	0			
Ozone exposure by GSTM1 status				
120 ppb by sufficient	-0.5952	-2.3601	1.1697	0.5064
70 ppb by sufficient	0.3171	-1.4320	2.0662	0.7209
0 ppb by sufficient	0			
120 ppb by null	0			
70 ppb by null	0			
0 ppb by null	0			

18. QTc, 5-Min Average (ms)

The following figure shows the change in QTc from pre- to post-exposure over time. The data come from Table B.1.9a.

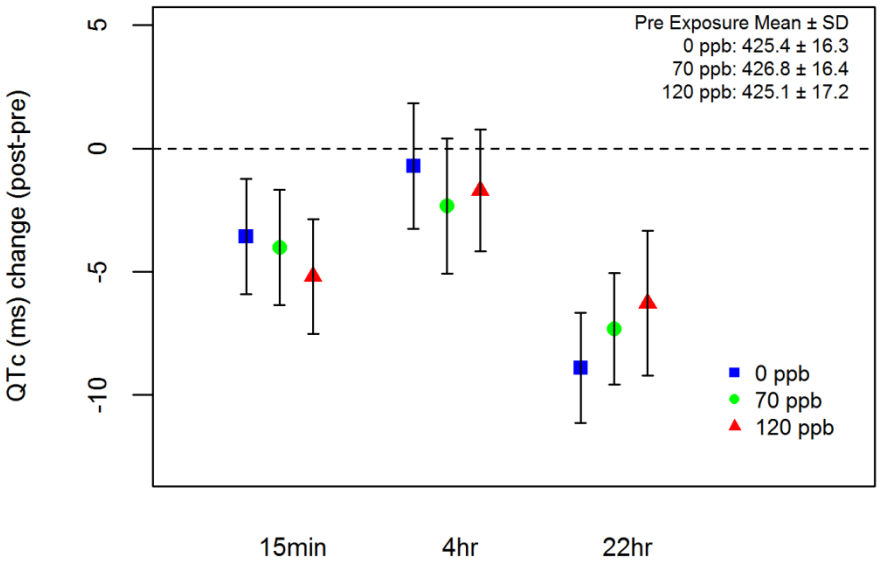

Figure B.1.18a. Change in 5-min average QTc at different post-exposure times and at each ozone exposure.

Main Analysis of Ozone Effect

As we can see from the tables below,

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

Table B.1.18a. Type III Sum of Squares for Change in QTC, 5-Min Avg (ms)

Effect	*P* Value
15-min vs. 4-hr vs. 22-hr change	<0.0001
Ozone exposure	0.9846
Site	<0.0001

Table B.1.18b. Mixed Model for Change in QTc, 5-Min Average (ms)

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	-10.0788	-13.1406	-7.0169	<0.0001
Change between post- and pre-exposure				
22-hr change	-3.2529	-4.8376	-1.6681	<0.0001
4-hr change	2.6742	1.1077	4.2407	0.0009
15-min change	0			
Ozone exposure				
120 ppb	0.09428	-1.5034	1.6920	0.9074
70 ppb	-0.04506	-1.6162	1.5261	0.9549
0 ppb	0			
Site				
URMC	7.8490	4.1238	11.5742	<0.0001
UNC	8.5531	4.7324	12.3739	<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.1.18c. Type III Sum of Squares for Change in QTc, 5-Min Average (ms), Including Ozone Exposure, by Age Interaction

Effect	*P* Value
Ozone exposure	0.9806
15-min vs. 4-hr vs. 22-hr change	<0.0001
Site	<0.0001
Age	0.4107
Ozone exposure by age	0.8383

Table B.1.18d. Mixed Model for Change in QTc, 5-Min Average (ms), Including Ozone Exposure, by Age Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	-10.1045	-13.1779	-7.0310	<0.0001
22-hr change	-3.2497	-4.8362	-1.6631	<0.0001
4-hr change	2.6745	1.1063	4.2427	0.0009
15-min change	0			
Ozone exposure				
120 ppb	0.1355	-1.4733	1.7443	0.8682
70 ppb	-0.00816	-1.5858	1.5695	0.9919
0 ppb	0			
Site				
URMC	7.6902	3.9310	11.4494	0.0001
UNC	8.5926	4.7583	12.4269	<0.0001
UCSF	0			
Age	0.2040	-0.1963	0.6044	0.3137
Ozone exposure by age				
120 ppb by age	-0.09567	-0.4570	0.2657	0.6033
70 ppb by age	-0.09134	-0.4422	0.2595	0.6094
0 ppb by age	0			

The following figures show the change in QTc from pre- to post-exposure over time by sex and are derived from the data in Table B.1.9a.

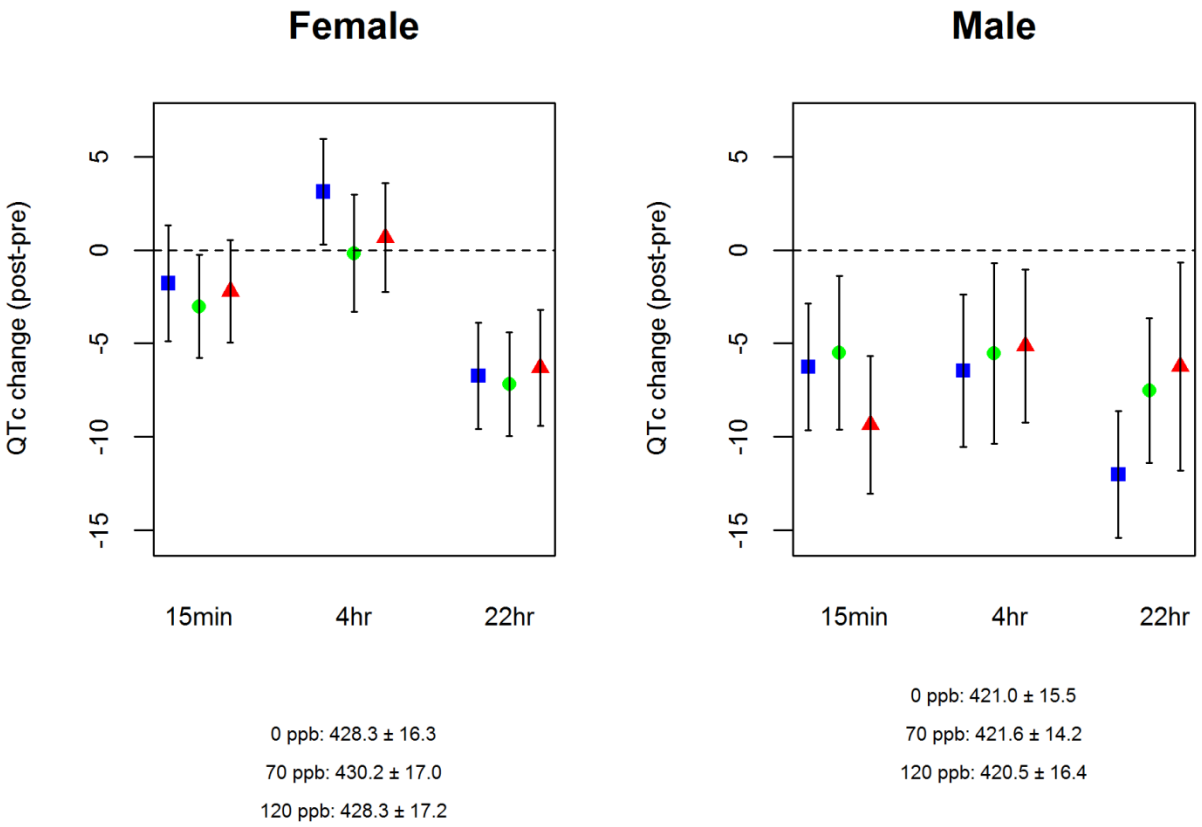

Figure B.1.18b. Change in 5-min average QTc at different post-exposure times and at each ozone exposure by sex. (The data shown here are the averages of the pre-exposure measurements at each ozone exposure.)

As we can see from the tables below,

- there was a marginally significant difference in QTc by sex — QTc in women increased from pre-exposure to post-exposure relative to men, independent of ozone exposure; and
- there was a marginally significant difference in the ozone effect on QTc by sex — QTc in women decreased from pre-exposure to post-exposure relative to men, at 70 ppb, but not at 120 ppb, relative to 0 ppb ozone exposure.

Table B.1.18e. Type III Sum of Squares for Change in QTc, 5-Min Average (ms), Including Ozone Exposure, by Sex Interaction

Effect	*P* Value
Ozone exposure	0.8775
15-min vs. 4-hr vs. 22-hr change	<0.0001
Site	<0.0001
Sex	0.0387
Ozone exposure by sex	0.0338

Table B.1.18f. Mixed Model for Change in QTc, 5-Min Average (ms), Including Ozone Exposure, by Sex Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	-12.9787	-16.5012	-9.4562	<0.0001
22-hr change	-3.2427	-4.8212	-1.6641	<0.0001
4-hr change	2.6735	1.1131	4.2339	0.0009
15-min change	0			
Ozone exposure				
120 ppb	1.7082	-0.7707	4.1871	0.1755
70 ppb	2.4626	-0.00304	4.9282	0.0503
0 ppb	0			
Site				
URMC	7.3370	3.6424	11.0316	0.0002
UNC	7.8452	4.0280	11.6625	0.0001
UCSF	0			
Sex				
Female	5.5606	1.9540	9.1672	0.0029
Male	0			
Ozone exposure by sex				
120 ppb by female	-2.6983	-5.9317	0.5351	0.1013
70 ppb by female	-4.2018	-7.3927	-1.0110	0.0102
0 ppb by female	0			
120 ppb by male	0			
70 ppb by male	0			
0 ppb by male	0			

Table B.1.18g. Pre-Exposure (mean ± SD) QTc, 5-Min Average (ms), by Ozone Concentration and Sex

0 ppb		70 ppb		120 ppb	
Male *N* = 34	Female *N* = 51	Male *N* = 35	Female *N* = 52	Male *N* = 35	Female *N* = 49
421.0 ± 15.5	428.3 ± 16.3	421.6 ± 14.2	430.2 ± 17.0	420.5 ± 16.4	428.3 ± 17.2

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

Table B.1.18h. Type III Sum of Squares for Change in QTc, 5-Min Average (ms), Including Ozone Exposure, by GSTM1 Status Interaction

Effect	*P* Value
Ozone exposure	0.9458
15-min vs. 4-hr vs. 22-hr change	<0.0001
Site	<0.0001
GSTM1 status	0.5842
Ozone exposure by GSTM1 status	0.0089

Table B.1.18i. Mixed Model for Change in QTc, 5-Min Average (ms), Including Ozone Exposure, by GSTM1 Status Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	-10.8268	-14.1696	-7.4839	<0.0001
22-hr change	-3.2519	-4.8274	-1.6764	<0.0001
4-hr change	2.6793	1.1221	4.2366	0.0008
15-min change	0			
Ozone exposure				
120 ppb	2.2725	0.1676	4.3774	0.0345
70 ppb	0.9043	-1.1623	2.9710	0.3888
0 ppb	0			
Site				
URMC	7.9632	4.1966	11.7298	<0.0001
UNC	8.6526	4.7955	12.5096	<0.0001
UCSF	0			
GSTM1 status				
Sufficient	1.5688	-2.0392	5.1769	0.3896
Null	0			
Ozone exposure by GSTM1 status				
120 ppb by sufficient	-5.0543	-8.2623	-1.8462	0.0022
70 ppb by sufficient	-2.2195	-5.3758	0.9369	0.1669
0 ppb by sufficient	0			
120 ppb by null	0			
70 ppb by null	0			
0 ppb by null	0			

The following figures show the change in QTc from pre- to post-exposure by GSTM1 status.

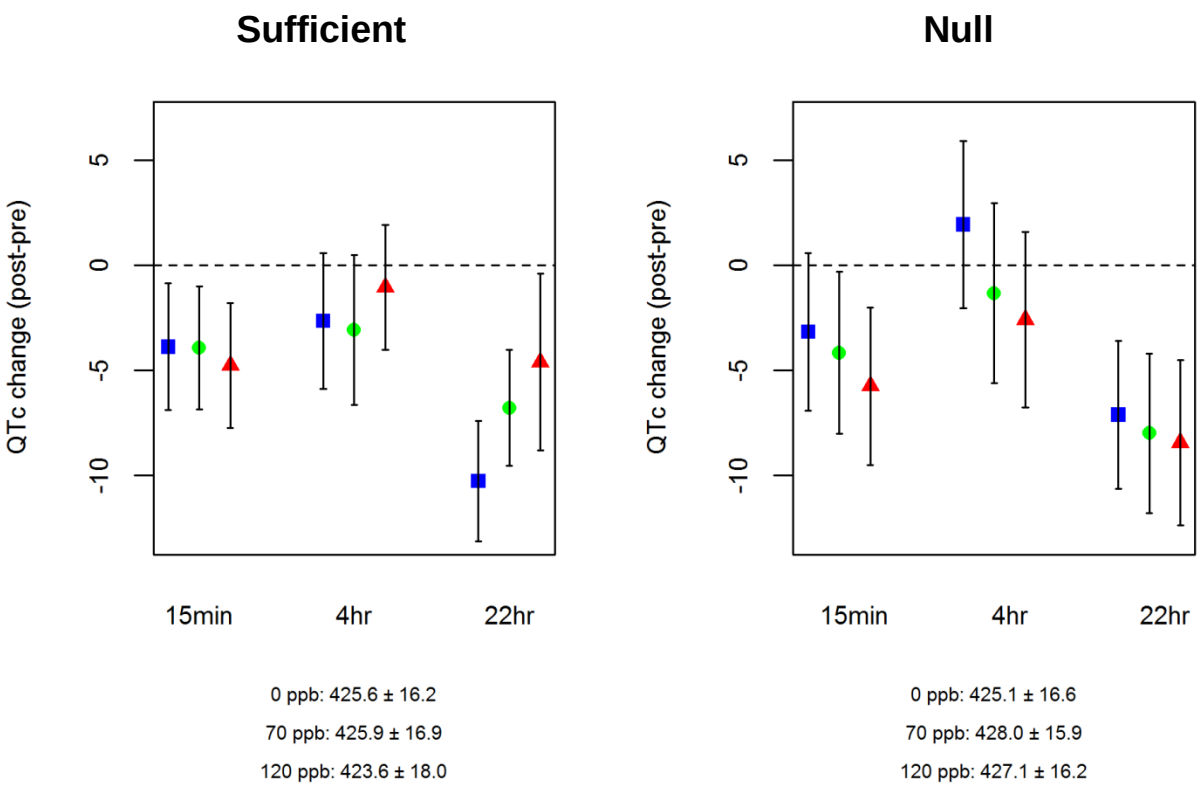

Figure B.1.18c. Change in 5-min average QTc at different post-exposure times and at each ozone exposure by GSTM1 status. (The data in the box are the averages of the pre-exposure measurements at each ozone exposure.)

19. ST in Lead II, 5-Min Average (μV)

The following figure shows the change in ST in Lead II from pre- to post-exposure over time. The data come from Table B.1.9a.

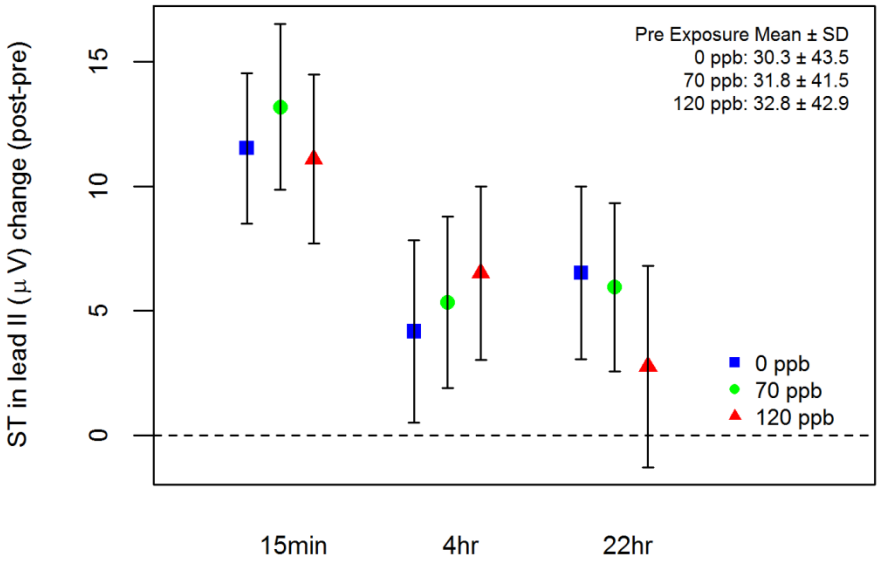

Figure B.1.19. Change in 5-min average ST in Lead II (μV) at different post-exposure times and at each ozone exposure.

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

Table B.1.19a. Type III Sum of Squares for Change in ST in Lead II, 5-Min Average (μV)

Effect	*P* Value
15-min vs. 4-hr vs. 22-hr change	<0.0001
Ozone exposure	0.5717
Site	0.0014

Table B.1.19b. Mixed Model for Change in ST in Lead II, 5-Min Average (μV)

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	17.7882	13.2058	22.3706	<0.0001
Change between post- and pre-exposure				
22-hr change	-6.7872	-8.9146	-4.6598	<0.0001
4-hr change	-6.6499	-8.7525	-4.5473	<0.0001
15-min change	0			
Ozone exposure				
120 ppb	-0.3971	-2.5426	1.7484	0.7153
70 ppb	0.7250	-1.3842	2.8342	0.4983
0 ppb	0			
Site				
URMC	-10.8202	-16.5160	-5.1243	0.0003
UNC	-5.5925	-11.4311	0.2461	0.0602
UCSF	0			

Analyses of Interactions

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

Table B.1.19c. Type III Sum of Squares for Change in ST in Lead II, 5-Min Average (μV), Including Ozone Exposure, by Age Interaction

Effect	*P* Value
Ozone exposure	0.5426
15-min vs. 4-hr vs. 22-hr change	<0.0001
Site	0.0017
Age	0.8089
Ozone exposure by age	0.8030

Table B.1.19d. Mixed Model for Change in ST in Lead II, 5-Min Average (μV), Including Ozone Exposure, by Age Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	17.8032	13.1948	22.4117	<0.0001
22-hr change	-6.7910	-8.9210	-4.6610	<0.0001
4-hr change	-6.6525	-8.7576	-4.5473	<0.0001
15-min change	0			
Ozone exposure				
120 ppb	-0.4497	-2.6106	1.7112	0.6817
70 ppb	0.7355	-1.3828	2.8539	0.4940
0 ppb	0			
Site				
URMC	-10.7472	-16.5085	-4.9860	0.0004
UNC	-5.6308	-11.5032	0.2417	0.0600
UCSF	0			
Age	-0.08115	-0.6746	0.5123	0.7863
Ozone exposure by age				
120 ppb by age	0.1054	-0.3800	0.5909	0.6699
70 ppb by age	-0.05301	-0.5242	0.4182	0.8253
0 ppb by age	0			

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

Table B.1.19e. Type III Sum of Squares for Change in ST in Lead II, 5-Min Average (μV), Including Ozone Exposure, by Sex Interaction

Effect	*P* Value
Ozone exposure	0.4303
15-min vs. 4-hr vs. 22-hr change	<0.0001
Site	0.0018
Sex	0.7315
Ozone exposure by sex	0.2821

Table B.1.19f. Mixed Model for Change in ST in Lead II, 5-Min Average (μV), Including Ozone Exposure, by Sex Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	18.4766	13.1350	23.8182	<0.0001
22-hr change	-6.7853	-8.9116	-4.6590	<0.0001
4-hr change	-6.6546	-8.7561	-4.5530	<0.0001
15-min change	0			
Ozone exposure				
120 ppb	-1.8209	-5.1605	1.5186	0.2832
70 ppb	1.2971	-2.0245	4.6187	0.4418
0 ppb	0			
Site				
URMC	-10.6984	-16.4847	-4.9120	0.0004
UNC	-5.4008	-11.3763	0.5746	0.0759
UCSF	0			
Sex				
Female	-1.3328	-6.7813	4.1158	0.6279
Male	0			
Ozone exposure by sex				
120 ppb by female	2.4446	-1.9122	6.8014	0.2695
70 ppb by female	-0.9572	-5.2557	3.3414	0.6608
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.1.19g. Type III Sum of Squares for Change in ST in Lead II, 5-Min Average (μV), Including Ozone Exposure, by GSTM1 Status Interaction

Effect	*P* Value
Ozone exposure	0.5793
15-min vs. 4-hr vs. 22-hr change	<0.0001
Site	0.0018
GSTM1 status	0.6991
Ozone exposure by GSTM1 status	0.8629

Table B.1.19h. Mixed Model for Change in ST in Lead II, 5-Min Average (μV), Including Ozone Exposure, by GSTM1 Status Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	18.3870	13.3922	23.3818	<0.0001
22-hr change	-6.7857	-8.9158	-4.6556	<0.0001
4-hr change	-6.6506	-8.7559	-4.5453	<0.0001
15-min change	0			
Ozone exposure				
120 ppb	-0.8891	-3.7361	1.9580	0.5384
70 ppb	0.3648	-2.4297	3.1592	0.7969
0 ppb	0			
Site				
URMC	-10.7037	-16.4606	-4.9467	0.0004
UNC	-5.4907	-11.3825	0.4011	0.0674
UCSF	0			
GSTM1 status				
Sufficient	-1.5874	-6.9417	3.7669	0.5570
Null	0			
Ozone exposure by GSTM1 status				
120 ppb by sufficient	1.1480	-3.1908	5.4869	0.6021
70 ppb by sufficient	0.8442	-3.4237	5.1120	0.6966
0 ppb by sufficient	0			
120 ppb by null	0			
70 ppb by null	0			
0 ppb by null	0			

20. ST in Lead II, 24-Hr Average (μV)

The following figure shows ST in Lead II by ozone exposure. The data come from Table B.1.9a.

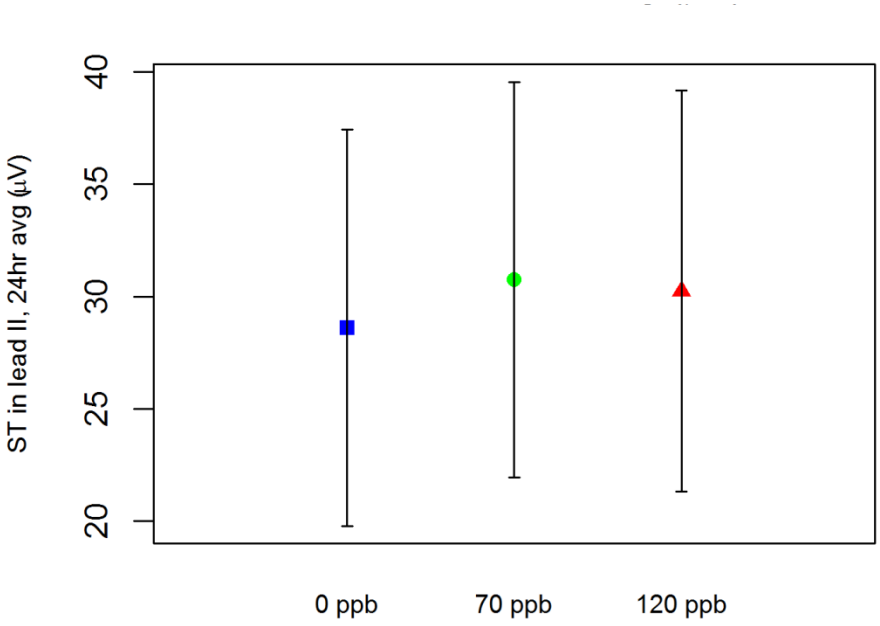

Figure B.1.20. The 24-hour average ST in Lead II (μV) by ozone exposure.

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

Table B.1.20a. Type III Sum of Squares for ST in Lead II, 24-Hr Average (μV)

Effect	*P* Value
Ozone exposure	0.6720
Site	0.3344

Table B.1.20b. Mixed Model for ST in Lead II, 24-Hr Average (μV)

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	29.9067	14.0065	45.8068	0.0003
Ozone exposure				
120 ppb	1.0791	-2.7970	4.9552	0.5833
70 ppb	1.7208	-2.1220	5.5636	0.3779
0 ppb	0			
Site				
URMC	6.0402	-15.1415	27.2220	0.5722
UNC	-9.3062	-30.9761	12.3637	0.3955
UCSF	0			

Analyses of Interactions

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

Table B.1.20c. Type III Sum of Squares for ST in Lead II, 24-Hr Average (μV), Including Ozone Exposure, by Age Interaction

Effect	*P* Value
Ozone exposure	0.6996
Site	0.3381
Age	0.9278
Ozone exposure by age	0.9042

Table B.1.20d. Mixed Model for ST in Lead II, 24-Hr Average (μV), Including Ozone Exposure, by Age Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	29.9725	13.9678	45.9772	0.0004
Ozone exposure				
120 ppb	0.9973	-2.9194	4.9140	0.6158
70 ppb	1.6517	-2.2262	5.5296	0.4016
0 ppb	0			
Site				
URMC	6.1227	-15.3214	27.5668	0.5716
UNC	-9.3537	-31.1626	12.4553	0.3961
UCSF	0			
Age	-0.2045	-2.2126	1.8036	0.8400
Ozone exposure by age				
120 ppb by age	0.1817	-0.7075	1.0709	0.6871
70 ppb by age	0.1660	-0.7063	1.0383	0.7076
0 ppb by age	0			

As we can see from the tables below,

- there were significant differences in ST in lead II by sex — ST in lead II in women decreased from pre- to post-exposure relative to men, independent of ozone exposure; and
- the ozone effect did not differ by sex.

Table B.1.20e. Type III Sum of Squares for ST in Lead II, 24-Hr Average (μV), Including Ozone Exposure, by Sex Interaction

Effect	*P* Value
Ozone exposure	0.5556
Site	0.3507
Sex	0.0017
Ozone exposure by sex	0.3655

Table B.1.20f. Mixed Model for ST in Lead II, 24-Hr Average (μV), Including Ozone Exposure, by Sex Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	41.9064	24.6731	59.1397	<0.0001
Ozone exposure				
120 ppb	0.5936	-5.5041	6.6913	0.8478
70 ppb	4.3650	-1.7327	10.4627	0.1594
0 ppb	0			
Site				
URMC	10.5476	-9.7240	30.8193	0.3037
UNC	-3.0078	-23.9119	17.8964	0.7755
UCSF	0			
Sex				
Female	-26.3736	-43.9208	-8.8264	0.0037
Male	0			
Ozone exposure by sex				
120 ppb by female	0.8460	-7.0534	8.7453	0.8328
70 ppb by female	-4.4131	-12.2666	3.4404	0.2689
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.1.20g. Type III Sum of Squares for ST in Lead II, 24-Hr Average (μV), Including Ozone Exposure, by GSTM1 Status Interaction

Effect	*P* Value
Ozone exposure	0.7640
Site	0.3388
GSTM1 status	0.9211
Ozone exposure by GSTM1 status	0.5846

Table B.1.20h. Mixed Model for ST in Lead II, 24-Hr Average (μV), Including Ozone Exposure, by GSTM1 Status Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	28.9688	11.7516	46.1860	0.0012
Ozone exposure				
120 ppb	1.4189	-3.6804	6.5183	0.5835
70 ppb	3.3600	-1.7014	8.4214	0.1918
0 ppb	0			
Site				
URMC	5.9062	-15.5185	27.3309	0.5850
UNC	-9.4279	-31.3089	12.4531	0.3939
UCSF	0			
GSTM1 status				
Sufficient	2.4541	-15.7365	20.6447	0.7891
Null	0			
Ozone exposure by GSTM1 status				
120 ppb by sufficient	-0.8323	-8.7100	7.0455	0.8350
70 ppb by sufficient	-3.8918	-11.6986	3.9149	0.3264
0 ppb by sufficient	0			
120 ppb by null	0			
70 ppb by null	0			
0 ppb by null	0			

21. ST in V2, 5-Min Average (µV)

The following figure shows the change in ST in V2 from pre- to post-exposure over time. The data come from Table B.1.9a.

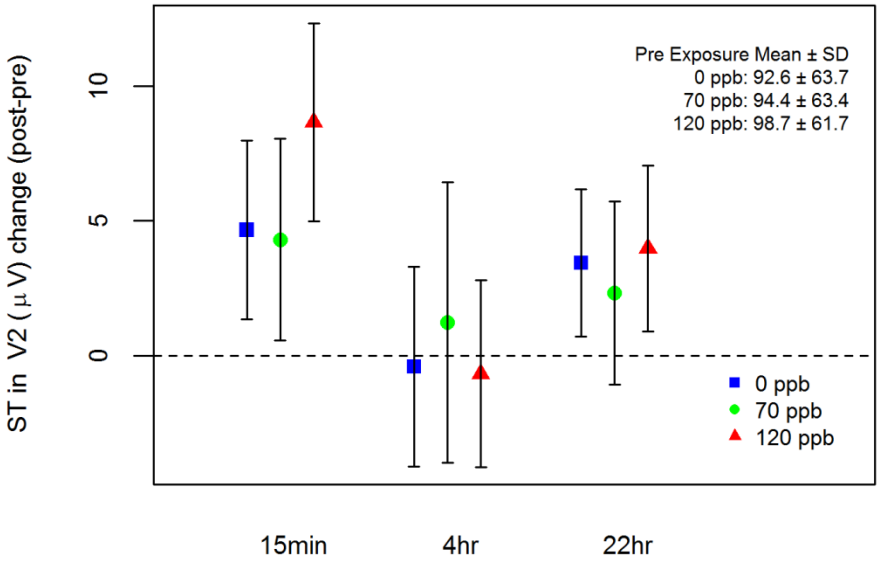

Figure B.1.21. Change in 5-min average ST in V2 at different post-exposure times and at each ozone exposure.

Main Analysis of Ozone Effect

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

- there were differences among the 15-minute post-exposure, 4-hour post exposure, and 22-hour post-exposure ST in V2;
- 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 B.1.21a. Type III Sum of Squares for Change in ST in V2, 5-Min Average (μV)

Effect	*P* Value
15-min vs. 4-hr vs. 22-hr change	<0.0001
Ozone exposure	0.4026
Site	0.4491

Table B.1.21b. Mixed Model for Change in ST in V2, 5-Min Average (μV)

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	3.5714	-1.0742	8.2169	0.1301
Change between post- and pre-exposure				
22-hr change	-2.6311	-5.1656	-0.09666	0.0420
4-hr change	-5.7590	-8.2643	-3.2536	<0.0001
15-min change	0			
Ozone exposure				
120 ppb	1.4489	-1.1057	4.0034	0.2644
70 ppb	-0.1247	-2.6372	2.3877	0.9220
0 ppb	0			
Site				
URMC	3.5673	-2.0141	9.1487	0.2072
UNC	1.9055	-3.8209	7.6319	0.5100
UCSF	0			

Analyses of Interactions

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

Table B.1.21c. Type III Sum of Squares for Change in ST in V2, 5-Min Average (μV), Including Ozone Exposure, by Age Interaction

Effect	*P* Value
Ozone exposure	0.5146
15-min vs. 4-hr vs. 22-hr change	<0.0001
Site	0.4428
Age	0.7340
Ozone exposure by age	0.1568

Table B.1.21d. Mixed Model for Change in ST in V2, 5-Min Average (μV), Including Ozone Exposure, by Age Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	3.7200	-0.9564	8.3964	0.1174
22-hr change	-2.6466	-5.1772	-0.1160	0.0405
4-hr change	-5.7684	-8.2699	-3.2669	<0.0001
15-min change	0			
Ozone exposure				
120 ppb	1.1936	-1.3719	3.7591	0.3597
70 ppb	-0.1876	-2.7039	2.3287	0.8832
0 ppb	0			
Site				
URMC	3.6377	-2.0180	9.2934	0.2044
UNC	1.7565	-4.0143	7.5273	0.5466
UCSF	0			
Age	-0.2993	-0.9120	0.3133	0.3340
Ozone exposure by age				
120 ppb by age	0.5323	-0.04379	1.1084	0.0701
70 ppb by age	0.1018	-0.4578	0.6614	0.7211
0 ppb by age	0			

As we can see from the tables below,

- there were marginally significant differences in ST in V2 by sex — ST in V2 in women decreased from pre- to post-exposure relative to men, independent of ozone exposure; and
- the ozone effect did not differ by sex.

Table B.1.21e. Type III Sum of Squares for Change in ST in V2, 5-Min Average (μV), Including Ozone Exposure, by Sex Interaction

Effect	*P* Value
Ozone exposure	0.4401
15-min vs. 4-hr vs. 22-hr change	<0.0001
Site	0.2198
Sex	0.0045
Ozone exposure by sex	0.7234

Table B.1.21f. Mixed Model for Change in ST in V2, 5-Min Average (μV), Including Ozone Exposure, by Sex Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	6.0344	0.7617	11.3070	0.0254
22-hr change	-2.6371	-5.1742	-0.09991	0.0417
4-hr change	-5.7557	-8.2637	-3.2476	<0.0001
15-min change	0			
Ozone exposure				
120 ppb	1.9013	-2.0824	5.8849	0.3474
70 ppb	1.1211	-2.8413	5.0836	0.5772
0 ppb	0			
Site				
URMC	4.6854	-0.7098	10.0807	0.0878
UNC	3.4177	-2.1588	8.9941	0.2263
UCSF	0			
Sex				
Female	-5.6645	-11.0777	-0.2513	0.0405
Male	0			
Ozone exposure by sex				
120 ppb by female	-0.7953	-5.9906	4.4001	0.7629
70 ppb by female	-2.0714	-7.1994	3.0566	0.4263
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.1.21g. Type III Sum of Squares for Change in ST in V2, 5-Min Average (μV), Including Ozone Exposure, by GSTM1 Status Interaction

Effect	*P* Value
Ozone exposure	0.4299
15-min vs. 4-hr vs. 22-hr change	<0.0001
Site	0.4521
GSTM1 status	0.9078
Ozone exposure by GSTM1 status	0.5757

Table B.1.21h. Mixed Model for Change in ST in V2, 5-Min Average (μV), Including Ozone Exposure, by GSTM1 Status Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	3.0045	-2.0868	8.0958	0.2439
22-hr change	-2.6288	-5.1648	-0.09274	0.0423
4-hr change	-5.7577	-8.2645	-3.2508	<0.0001
15-min change	0			
Ozone exposure				
120 ppb	2.3817	-1.0056	5.7689	0.1669
70 ppb	0.9494	-2.3770	4.2758	0.5738
0 ppb	0			
Site				
URMC	3.5953	-2.0549	9.2455	0.2092
UNC	1.9232	-3.8649	7.7113	0.5105
UCSF	0			
GSTM1 status				
Sufficient	1.2892	-4.2300	6.8084	0.6434
Null	0			
Ozone exposure by GSTM1 status				
120 ppb by sufficient	-2.1730	-7.3357	2.9897	0.4071
70 ppb by sufficient	-2.5088	-7.5891	2.5715	0.3310
0 ppb by sufficient	0			
120 ppb by null	0			
70 ppb by null	0			
0 ppb by null	0			

22. ST in V2, 24-Hr Average (μV)

The following figure shows ST in V2 by ozone exposure. The data come from Table B.1.9a.

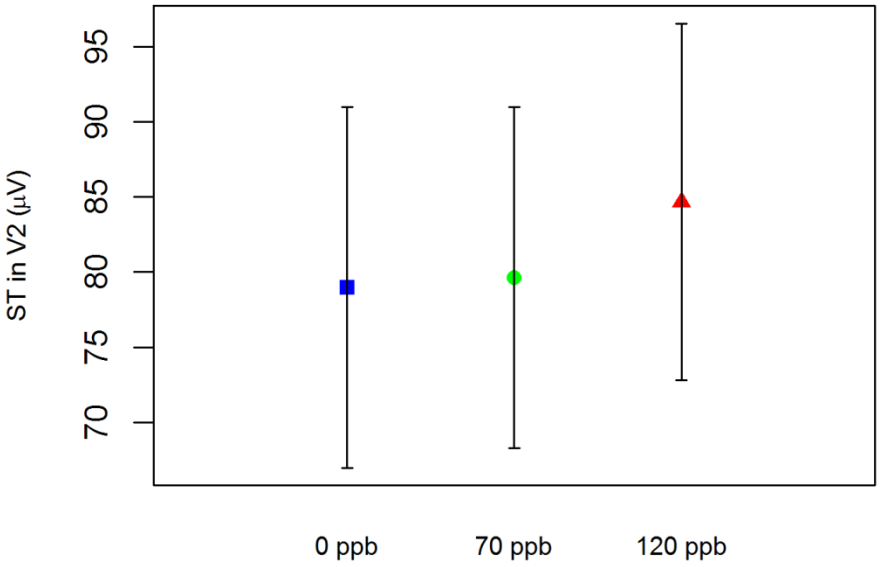

Figure B.1.22. The 24-hour average ST in V2 by ozone exposure.

Main Analysis of Ozone Effect

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

- there were marginally significant differences in ST in V2 across the ozone exposures; and
- there were differences in ST in V2 across the 3 sites.

Table B.1.22a. Type III Sum of Squares for ST in V2, 24-Hr Average (μV)

Effect	*P* Value
Ozone exposure	0.0186
Site	0.0002

Table B.1.22b. Mixed Model for ST in V2, 24-Hr Average (μV)

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	97.8898	78.3876	117.39	<0.0001
Ozone exposure				
120 ppb	4.7337	1.0103	8.4571	0.0130
70 ppb	0.1351	-3.5561	3.8264	0.9425
0 ppb	0			
Site				
URMC	-48.9294	-75.0166	-22.8423	0.0003
UNC	-1.1872	-27.8743	25.4999	0.9297
UCSF	0			

Analyses of Interactions

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

Table B.1.22c. Type III Sum of Squares for ST in V2, 24-Hr Average (μV), Including Ozone Exposure, by Age Interaction

Effect	*P* Value
Ozone exposure	0.0223
Site	0.0001
Age	0.2644
Ozone exposure by age	0.8047

Table B.1.22d. Mixed Model for ST in V2, 24-Hr Average (μV), Including Ozone Exposure, by Age Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	98.0266	78.5467	117.51	<0.0001
Ozone exposure				
120 ppb	4.6907	0.9304	8.4511	0.0148
70 ppb	0.1916	-3.5313	3.9144	0.9192
0 ppb	0			
Site				
URMC	-50.5514	-76.7587	-24.3441	0.0002
UNC	-1.0203	-27.6716	25.6310	0.9395
UCSF	0			
Age	1.3572	-1.0644	3.7789	0.2682
Ozone exposure by age				
120 ppb by age	0.1100	-0.7438	0.9639	0.7995
70 ppb by age	-0.1662	-1.0038	0.6713	0.6957
0 ppb by age	0			

As we can see from the tables below,

- there were statistically significant differences in ST in V2 by sex — ST in V2 in women decreased from pre- to post-exposure relative to men, independent of ozone exposure; and
- the ozone effect did not differ by sex.

Table B.1.22e. Type III Sum of Squares for ST in V2, 24-Hr Average (μV), Including Ozone Exposure, by Sex Interaction

Effect	*P* Value
Ozone exposure	0.0262
Site	<0.0001
Sex	<0.0001
Ozone exposure by sex	0.2812

Table B.1.22f. Mixed Model for ST in V2, 24-Hr Average (μV), Including Ozone Exposure, by Sex Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	120.56	100.47	140.65	<0.0001
Ozone exposure				
120 ppb	2.0456	-3.8025	7.8938	0.4908
70 ppb	-3.4115	-9.2596	2.4366	0.2511
0 ppb	0			
Site				
URMC	-41.7014	-65.5130	-17.8898	0.0008
UNC	8.9210	-15.6328	33.4748	0.4719
UCSF	0			
Sex				
Female	-47.9405	-68.3154	-27.5656	<0.0001
Male	0			
Ozone exposure by sex				
120 ppb by female	4.4319	-3.1442	12.0080	0.2498
70 ppb by female	5.8634	-1.6685	13.3953	0.1262
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.1.22g. Type III Sum of Squares for ST in V2, 24-Hr Average (μV), Including Ozone Exposure, by GSTM1 Status Interaction

Effect	*P* Value
Ozone exposure	0.0115
Site	0.0002
GSTM1 status	0.8619
Ozone exposure by GSTM1 status	0.3600

Table B.1.22h. Mixed Model for ST in V2, 24-Hr Average (μV), Including Ozone Exposure, by GSTM1 Status Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	97.5120	76.4389	118.59	<0.0001
Ozone exposure				
120 ppb	3.2183	-1.6665	8.1032	0.1951
70 ppb	0.8900	-3.9582	5.7382	0.7175
0 ppb	0			
Site				
URMC	-49.1894	-75.5639	-22.8148	0.0004
UNC	-1.4301	-28.3651	25.5049	0.9162
UCSF	0			
GSTM1 status				
Sufficient	1.2905	-20.8219	23.4029	0.9079
Null	0			
Ozone exposure by GSTM1 status				
120 ppb by sufficient	3.5943	-3.9524	11.1411	0.3484
70 ppb by sufficient	-1.7619	-9.2402	5.7164	0.6424
0 ppb by sufficient	0			
120 ppb by null	0			
70 ppb by null	0			
0 ppb by null	0			

23. VE, 24-Hr Total

VE Singles

Initially, we analyzed ventricular ectopic (VE) beats to determine whether there was an association between ozone exposure and having any SE single versus none. We see from Table B.1.23a below that when subjects were exposed to 0 ppb ozone, 88% experienced at least one VE single. When subjects were exposed to 70 ppb ozone, 81% experienced at least one VE single. Last, when subjects were exposed to 120 ppb ozone, 88% experienced at least one VE single. This difference was not statistically significant (chi-square test, *P* value = 0.3217). The mixed model results are presented below in Table B.1.23b, which shows that ozone exposure was not statistically significantly associated with whether a subject had a VE single caused by ozone exposure. Table B.1.23c shows the distribution of VE singles among subjects by ozone exposure.

Table B.1.23a. Number (%) of Subjects with Any VE Single by Ozone Exposure

	No	Yes	Total
0 ppb	10 (12%)	76 (88%)	86
70 ppb	16 (19%)	70 (81%)	86
120 ppb	10 (12%)	75 (88%)	85
Total	36	221	257

Table B.1.23b. Mixed Model for Any VE Single

Effect	Odds Ratio	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	28.61	8.35	98.04	<0.0001
Ozone exposure				
120 ppb	0.99	0.36	2.73	0.9821
70 ppb	0.50	0.2	1.28	0.1485
0 ppb				
Site				
URMC	0.23	0.07	0.81	0.0224
UNC	0.40	0.11	1.47	0.1637
UCSF				

Table B.1.23c. Distribution of VE Singles Among Subjects, 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	9	22.1	1	14	34.9	1	9	22.4
2	11	34.9	2	11	47.7	2	11	35.3
3	13	50.0	3	4	52.3	3	12	49.4
4	6	57.0	4	4	57.0	4	3	52.9
5	1	58.1	5	1	58.1	5	2	55.3
6	5	64.0	7	1	59.3	6	4	60.0
7	1	65.1	8	3	62.8	7	1	61.2
8	2	67.4	10	1	64.0	8	3	64.7
10	1	68.6	11	1	65.1	9	2	67.1
11	1	69.8	13	3	68.6	10	1	68.2
13	2	72.1	14	1	69.8	12	1	69.4
14	1	73.3	15	3	73.3	15	1	70.6
16	2	75.6	17	2	75.6	18	1	71.8
19	1	76.7	21	1	76.7	20	1	72.9
25	2	79.1	25	1	77.9	22	1	74.1
26	1	80.2	26	1	79.1	26	1	75.3
33	1	81.4	34	1	80.2	27	1	76.5
41	1	82.6	39	2	82.6	31	1	77.6
44	1	83.7	73	1	83.7	33	2	80.0
56	1	84.9	100	1	84.9	45	1	81.2
60	1	86.0	101	1	86.0	49	1	82.4
61	1	87.2	105	1	87.2	68	1	83.5
75	1	88.4	122	2	89.5	72	1	84.7
104	1	89.5	126	1	90.7	77	1	85.9
133	1	90.7	163	1	91.9	78	1	87.1
135	1	91.9	189	1	93.0	81	1	88.2
140	1	93.0	191	1	94.2	97	1	89.4
156	1	94.2	217	1	95.3	121	1	90.6
212	1	95.3	551	1	96.5	134	1	91.8
300	1	96.5	764	1	97.7	162	1	92.9
614	1	97.7	1292	1	98.8	333	1	94.1
2063	1	98.8	11533	1	100.0	354	1	95.3
10373	1	100.0				640	1	96.5
						768	1	97.6
						1472	1	98.8
						11371	1	100.0

*Percentages are based on the total number of subjects, including those without VE singles.

Three (Median) or More VE Singles

Then, we analyzed whether there was an association between ozone exposure and having at least the median number of VE singles (which was 3). We see from Table B.1.23d below that when subjects were exposed to 0 ppb of ozone, 65% experienced 3 or more VE singles. When subjects were exposed to 70 ppb of ozone, 52% experienced 3 or more VE singles. Last, when subjects were exposed to 120 ppb of ozone, 65% experienced 3 or more VE singles. This difference was not statistically significant (chi-square test, *P* value = 0.1493).

Table B.1.23d. Number (%) of Subjects with 3 (Median) or More VE Singles, by Ozone Exposure

	No	Yes	Total
0 ppb	30 (35%)	56 (65%)	86
70 ppb	41 (48%)	45 (52%)	86
120 ppb	30 (35%)	55 (65%)	85
Total	101	156	257

One Hundred or More VE Singles

Next, we analyzed whether there was an association between ozone exposure and having at least 100 VE singles. We see from Table B.1.23e below that when subjects were exposed to 0 ppb of ozone, 12% experienced at least 100 VE singles. When subjects were exposed to 70 ppb of ozone, 16% experienced at least 100 VE singles. Last, when subjects were exposed to 120 ppb of ozone, 11% experienced at least 100 VE singles. This difference was not statistically significant (chi-square test, *P* value = 0.4949). The mixed model results are presented below in Table B.1.23f, which illustrates that ozone exposure is not statistically significant, but site is.

Table B.1.23e. Number (%) of Subjects with 100 or More VE Singles, by Ozone Exposure

	No	Yes	Total
0 ppb	76 (88%)	10 (12%)	86
70 ppb	72 (84%)	14 (16%)	86
120 ppb	76 (89%)	9 (11%)	85
Total	224	33	257

Table B.1.23f. Mixed Model for 100 or More VE Singles

Effect	Odds Ratio	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	0.24	0.1	0.57	0.0015
Ozone exposure				
120 ppb	0.88	0.29	2.66	0.8197
70 ppb	1.57	0.56	4.39	0.3845
0 ppb				
Site				
URMC	0.23	0.08	0.63	0.0045
UNC	0.18	0.06	0.55	0.0025
UCSF				

Any VE Couplet or Run

Next, we analyzed whether there was an association between ozone exposure and having any couplet or run. We see from Table B.1.23g below that when subjects were exposed to 0 ppb of ozone, 15% experienced at least one couplet or run. When subjects were exposed to 70 ppb of ozone, 27% experienced at least one couplet or run. Last, when subjects were exposed to 120 ppb of ozone, 21% experienced at least one couplet or run. This difference was not statistically significant (chi-square test, *P* value = 0.1733). The mixed model results are presented below in Table B.1.23h, which shows that ozone exposure was not a statistically significant predictor of having a VE couplet or run, but site was. Table B.1.23i shows the frequency of subjects with any VE couplet or run, by ozone exposure.

Table B.1.23g. Number (%) of Subjects with Any VE Couplet or Run, by Ozone Exposure

	No	Yes	Total
0 ppb	73 (85%)	13 (15%)	86
70 ppb	63 (73%)	23 (27%)	86
120 ppb	67 (79%)	18 (21%)	85
Total	203	54	257

Table B.1.23h. Mixed Model for Any VE Couplet or Run

Effect	Odds Ratio	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	0.39	0.16	0.92	0.0313
Ozone exposure				
120 ppb	1.71	0.69	4.26	0.2429
70 ppb	2.51	1.03	6.07	0.0421
0 ppb				
Site				
URMC	0.21	0.08	0.55	0.0018
UNC	0.11	0.04	0.32	0.0001
UCSF				

Table B.1.23i. Distribution of VE Couplets or Runs Among Subjects, 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	8	94.2	1	12	87.2	1	10	90.6
2	1	95.3	2	6	94.2	2	3	94.1
3	1	96.5	3	2	96.5	3	1	95.3
11	1	97.7	27	1	97.7	6	2	97.6
27	1	98.8	34	1	98.8	7	1	98.8
59	1	100.0	185	1	100.0	103	1	100.0

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

24. SE, 24-Hr Total

SE Singles

We analyzed supraventricular ectopic (SE) beats to determine whether there was an association between ozone exposure and having any SE single versus none. We see from B.1.Table 24a below that when subjects were exposed to 0 ppb of ozone, 98% experienced at least one SE single. When subjects were exposed to 70 ppb of ozone, 97% experienced at least one SE single. Last, when subjects were exposed to 120 ppb of ozone, 96% experienced at least one SE single. This difference was not statistically significant (Fisher exact test, *P* value = 0.9116). The mixed model results are presented below in Table B.1.24b, which illustrates that neither the ozone exposure nor site is statistically significant. Table B.1.24c shows the frequency of subjects with any SE single, by ozone exposure.

Table B.1.24a. Number (%) of Subjects with Any SE Single, by Ozone Exposure

	No	Yes	Total
0 ppb	2 (2%)	84 (98%)	86
70 ppb	3 (3%)	83 (97%)	86
120 ppb	3 (4%)	82 (96%)	85
Total	8	249	257

Table B.1.24b. Mixed Model for Any SE Single

Effect	Odds Ratio	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	1.29 E9	0		0.9938
Ozone exposure				
120 ppb	0.63	0.09	4.26	0.6306
70 ppb	0.59	0.09	3.98	0.5831
0 ppb				
Site				
URMC	0	0		0.9949
UNC	0	0		0.9950
UCSF				

Table B.1.24c. Distribution of SE Singles Among Subjects, by Ozone Exposure*

0 ppb*			70 ppb*			120 ppb*		
SE (count)	Subject (N)	Cum (%)	SE (count)	Subject (N)	Cum (%)	SE (count)	Subject (N)	Cum (%)
1	2	4.7	1	3	7.0	1	4	8.2
2	3	8.1	2	2	9.3	2	2	10.6
3	2	10.5	3	3	12.8	3	3	14.1
4	3	14.0	4	3	16.3	4	6	21.2
5	3	17.4	5	3	19.8	5	4	25.9
6	3	20.9	6	3	23.3	6	1	27.1
7	4	25.6	7	2	25.6	7	1	28.2
8	2	27.9	8	4	30.2	8	1	29.4
9	3	31.4	9	3	33.7	10	3	32.9
10	2	33.7	10	2	36.0	11	1	34.1
12	2	36.0	11	1	37.2	12	3	37.6
13	2	38.4	12	4	41.9	13	3	41.2
14	5	44.2	13	2	44.2	14	2	43.5
15	3	47.7	14	1	45.3	15	3	47.1
16	1	48.8	15	2	47.7	16	2	49.4
17	3	52.3	17	1	48.8	17	2	51.8
19	2	54.7	18	2	51.2	18	1	52.9
21	1	55.8	19	2	53.5	20	1	54.1
22	1	57.0	21	1	54.7	21	2	56.5
23	1	58.1	24	1	55.8	22	1	57.6
25	1	59.3	25	3	59.3	23	2	60.0
27	2	61.6	27	2	61.6	24	1	61.2
28	2	64.0	31	2	64.0	25	1	62.4
31	1	65.1	34	1	65.1	26	1	63.5
34	1	66.3	35	2	67.4	27	1	64.7
39	1	67.4	36	1	68.6	29	1	65.9
40	1	68.6	37	1	69.8	30	2	68.2
41	1	69.8	38	1	70.9	37	1	69.4
42	1	70.9	41	1	72.1	40	2	71.8
43	2	73.3	42	1	73.3	42	1	72.9
45	1	74.4	43	1	74.4	45	1	74.1
58	1	75.6	46	1	75.6	53	2	76.5
60	1	76.7	59	1	76.7	54	1	77.6
63	2	79.1	67	1	77.9	63	1	78.8
64	2	81.4	70	2	80.2	75	3	82.4
65	1	82.6	73	1	81.4	86	1	83.5
71	1	83.7	76	1	82.6	111	1	84.7
78	2	86.0	77	1	83.7	113	1	85.9
82	1	87.2	80	1	84.9	127	1	87.1
91	1	88.4	81	2	87.2	150	1	88.2
122	1	89.5	93	1	88.4	166	1	89.4
135	1	90.7	127	1	89.5	201	1	90.6
140	1	91.9	140	1	90.7	204	1	91.8
632	1	93.0	167	1	91.9	210	1	92.9
637	1	94.2	209	1	93.0	333	1	94.1
870	1	95.3	239	1	94.2	1073	1	95.3
1253	1	96.5	1302	1	95.3	1900	1	96.5
2271	1	97.7	1424	1	96.5	3131	1	97.6
4560	1	98.8	2334	1	97.7	3673	1	98.8
7285	1	100.0	4214	1	98.8	8563	1	100.0
			8197	1	100.0			

*Percentages are based on the total number of subjects including those without SE singles.

17 (Median) or More SE Singles

We analyzed whether there was an association between ozone exposure and having at least the median number of SE singles (which was 17). We see from Table B.1.24d below that when subjects were exposed to 0 ppb of ozone, 51% experienced 17 or more SE singles. When subjects were exposed to 70 ppb of ozone, 52% experienced 17 or more SE singles. Last, when subjects were exposed to 120 ppb of ozone, 51% experienced 17 or more SE singles. This difference was not statistically significant (chi-square test, *P* value = 0.9735).

Table B.1.24d. Number (%) of Subjects with 17 (Median) or More SE Singles, by Ozone Exposure

	No	Yes	Total
0 ppb	42 (49%)	44 (51%)	86
70 ppb	41 (48%)	45 (52%)	86
120 ppb	42 (49%)	43 (51%)	85
Total	125	132	257

100 or More SE Singles

Next, we analyzed whether there was an association between ozone exposure and having at least 100 SE singles. We see from B.1.Table 24e below that when subjects were exposed to 0 ppb of ozone, 12% experienced at least 100 SE singles. When subjects were exposed to 70 ppb of ozone, 11% experienced at least 100 SE singles. Last, when subjects were exposed to 120 ppb of ozone, 16% experienced at least 100 SE singles. This difference was not statistically significant (*P* = 0.5593). The mixed model results are presented below in Table B.1.24f, which shows that neither ozone exposure nor site is statistically significant.

Table B.1.24e. Number (%) of Subjects with 100 or More SE Singles, by Ozone Exposure

	No	Yes	Total
0 ppb	76 (88%)	10 (12%)	86
70 ppb	77 (89%)	10 (11%)	87
120 ppb	71 (84%)	14 (16%)	85
Total	224	34	258

Table B.1.24f. Mixed Model for 100 or More SE Singles

Effect	Odds Ratio	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	0.09	0.03	0.24	<0.0001
Ozone exposure				
120 ppb	1.58	0.59	4.25	0.3630
70 ppb	1.00	0.35	2.85	0.9999
0 ppb				
Site				
URMC	1.05	0.39	2.88	0.9201
UNC	0.97	0.34	2.74	0.9525
UCSF				

25. SE Couplets or Runs

This analysis explored whether there was a relationship between ozone exposure and whether the subject experienced any SE couplet or run. We see from Table B.1.24g below that when subjects were exposed to 0 ppb of ozone, 63% experienced at least one SE couplet or run. When subjects were exposed to 70 ppb of ozone, 65% experienced at least one SE couplet or run. Last, when subjects were exposed to 120 ppb of ozone, 53% experienced at least one SE couplet or run. This difference was not statistically significant (chi-square test, *P* value = 0.2255). The mixed model results are presented below in Table B.1.24h, which illustrates that neither ozone exposure nor site is statistically significant. Table B.1.24i shows the frequency of subjects with any SE couplet or run, by ozone exposure.

Table B.1.24g. Number (%) of Subjects with Any SE Couplet or Run, by Ozone Exposure

	No	Yes	Total
0 ppb	32 (37%)	54 (63%)	86
70 ppb	30 (35%)	56 (65%)	86
120 ppb	40 (47%)	45 (53%)	85
Total	102	155	257

Table B.1.24h. Mixed Model for Any SE Couplet or Run

Effect	Odds Ratio	Lower 95% CI	Upper 95% CI	*P* Value
Intercept	2.74	1.25	5.99	0.0119
Ozone exposure				
120 ppb	0.61	0.30	1.21	0.1579
70 ppb	1.11	0.55	2.22	0.7766
0 ppb				
Site				
URMC	0.47	0.19	1.14	0.0944
UNC	0.79	0.31	1.94	0.598
UCSF				

Table B.1.24i. Distribution of SE Couplets or Runs Among Subjects, by Ozone Exposure*

0 ppb*			70 ppb*			120 ppb*		
SE (count)	Subject (N)	Cum (%)	SE (count)	Subject (N)	Cum (%)	SE (count)	Subject (N)	Cum (%)
1	17	57.0	1	17	54.7	1	12	61.2
2	7	65.1	2	11	67.4	2	8	70.6
3	5	70.9	3	5	73.3	3	4	75.3
4	5	76.7	5	5	79.1	4	3	78.8
5	3	80.2	6	3	82.6	5	2	81.2
6	3	83.7	8	1	83.7	6	2	83.5
7	3	87.2	9	1	84.9	7	2	85.9
8	1	88.4	10	1	86.0	8	2	88.2
9	2	90.7	11	1	87.2	9	1	89.4
10	1	91.9	12	1	88.4	10	1	90.6
11	1	93.0	13	2	90.7	11	1	91.8
13	1	94.2	16	1	91.9	15	1	92.9
15	1	95.3	20	1	93.0	16	1	94.1
39	2	97.7	21	1	94.2	31	1	95.3
271	1	98.8	30	1	95.3	43	1	96.5
1520	1	100.0	58	1	96.5	472	1	97.6
			150	1	97.7	528	1	98.8
			240	1	98.8	1091	1	100.0
			1344	1	100.0			

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

Abbreviations and Other Terms

GSTM1	glutathione S-transferase Mu 1
HF	high frequency power (0.15–0.40 Hz)
HR	heart rate
LF	low frequency power (0.04–0.15 Hz)
Ln	natural logarithm
MOSES	multicenter ozone study in elderly subjects
NERI	New England Research Institute
ppb	part 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
R-R interval	R-wave-to-R-wave interval
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
V_E	minute ventilation