



Research Report 192, Pt 1

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

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Appendix D. Analyses of Responders and of Relationships Between 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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INTRODUCTION

This Appendix includes the following post-hoc analyses:

- Section 1. Spaghetti plots of FEV₁ and PMN values for each MOSES subject
- Section 2. Scatter plots to describe correlations between respiratory outcomes, and between respiratory outcomes and cardiovascular outcomes
- Section 3. Analyses of responders

Section 1. Spaghetti Plots of FEV₁ and PMN as a Function of Ozone Exposure

The plots in Figures D.1a and D.1b below were constructed to graphically represent, by center, how 15 min post-exposure FEV₁ changes and PMN (%) progressed as ozone exposure levels increased. Figure D.1a shows that the small decrements in FEV₁ did not appear to be driven by a small subset of subjects. Only *one* subject had a decrease of at least 10% from pre-exposure to 15 minutes post-exposure, and *no* subject had a decrease of at least 10% from pre-exposure to 22 hours post-exposure. Figure D.1b does not show a consistent pattern of exposure-related changes in PMN across the subjects. These data do not provide evidence that there is a subset of subjects more responsive to ozone.

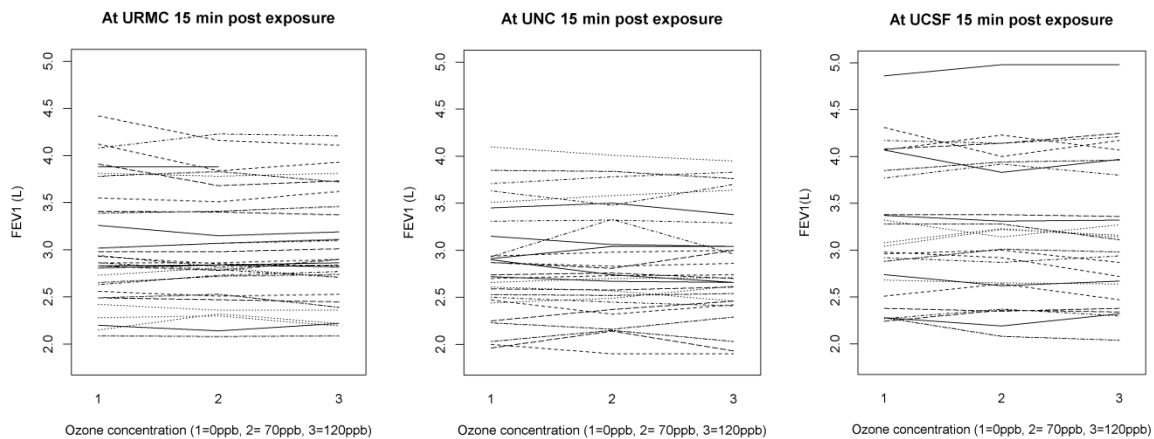


Figure D.1a. Spaghetti plots of FEV₁ at 15 min post-exposure for each ozone exposure by center.

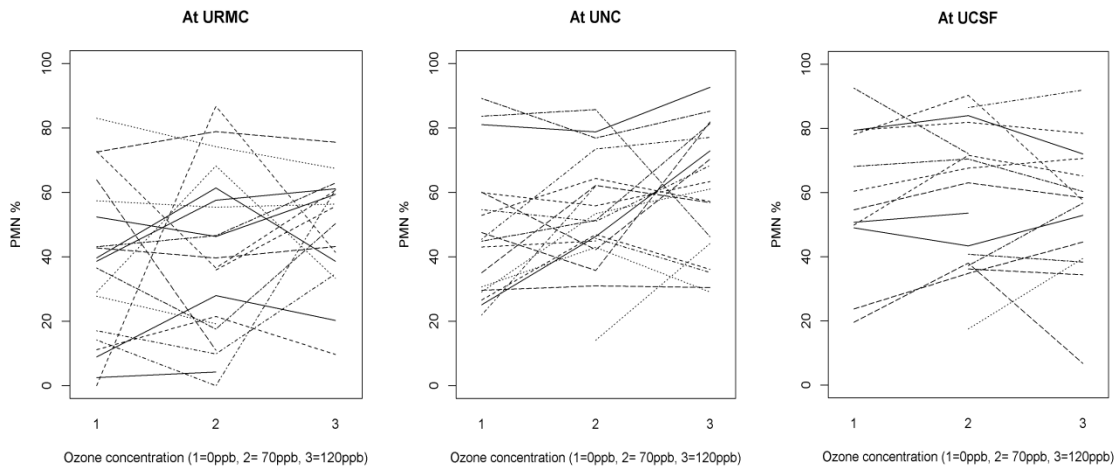


Figure D.1.b. Spaghetti plots of PMN (%) at 22 hours post-exposure for each ozone exposure.

Section 2. Scatter Plots

Figure D.2a shows the relationships between different outcomes and the Pearson correlation coefficients. The left panel shows that there is no significant correlation between changes from pre- to 15 minutes post-exposure in FEV₁ and changes from pre- to 4 hours post-exposure in CC16 (a marker of lung injury) at 120 ppb ozone exposure. The right panel shows no significant correlation between changes from pre- to 15 minutes post-exposure in FEV₁ at 120 ppb ozone exposure and changes in PMN percentage (a marker of lung inflammation) from 0 to 120 ppb ozone exposure at 22 hours post-exposure.

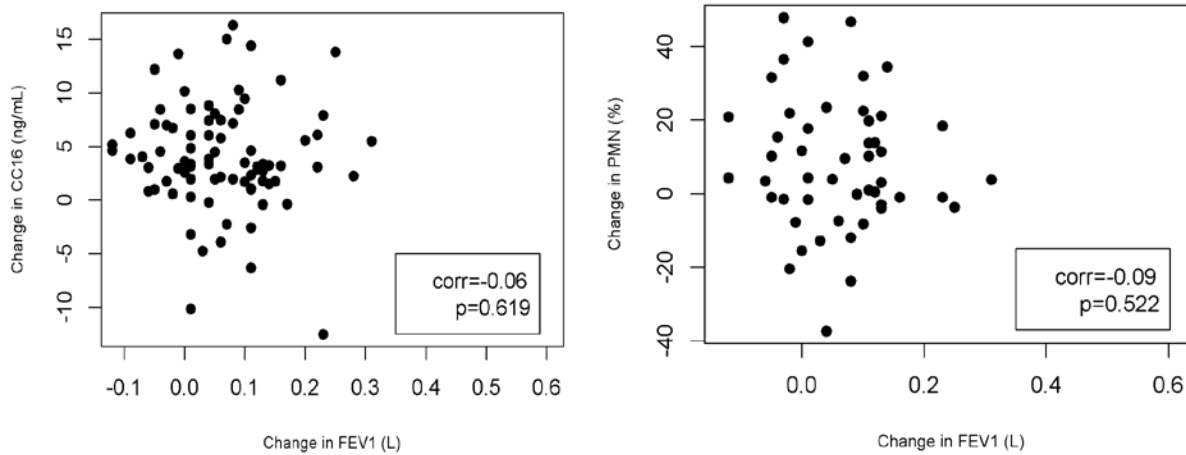


Figure D.2a. Scatter plot of (left) 15-minute post-exposure change in FEV₁ (L) vs. 4-hour post-exposure change in CC16 (mg/mL), both at 120 ppb ozone; and (right) 15-minute post-exposure change in FEV₁ (L) at 120 ppb ozone vs. 22-hour changes in PMN (%) from 0 ppb to 120 ppb ozone.

Figure D.2b shows that there is no correlation between the change from pre- to 4-hour post-exposure in CC16 at the 120 ppb ozone exposure and the change in PMN (%) from 0 to 120 ppb ozone exposure at 22 hours post-exposure.

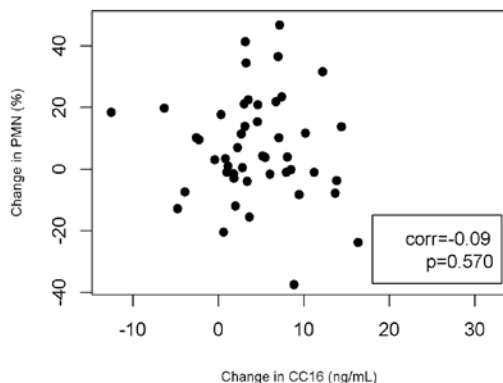


Figure D.2b. Scatter plot of 4-hour post-exposure change in CC16 (mg/mL) at 120 ppb ozone exposure vs. 22-hour change in PMN (%) from 0 to 120 ppb ozone exposure.

In Figure D.2c, the left panel shows the correlation between the 4-hour post-exposure change in CC16 and the 15-minute post-exposure change in HF (a marker of heart rate variability) at 120 ppb ozone exposure. The right panel shows the correlation between the 10-minute post-exposure change in FEV₁ and the 10-minute post-exposure change in HF at 120 ppb ozone exposure. The results indicate the changes in these pulmonary outcomes were not correlated with changes in HF.

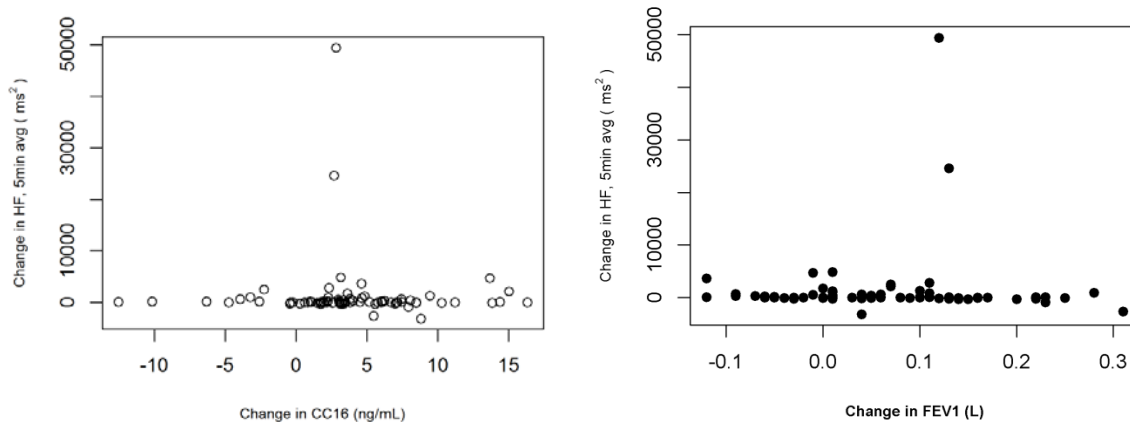


Figure D.2.c. Scatter plots of (left) 4-hour post-exposure change in CC16 (mg/mL) vs. 15-minute post-exposure change in 5-minute average HF (ms²), both at 120 ppb ozone exposure; and (right) 15-minute post-exposure change in FEV₁ (L) vs. 15-minute post-exposure change in 5-minute average HF (ms²), both at 120 ppb ozone exposure.

The plots in Figure D.2d show there is no significant correlation between the 4-hour post-exposure change in CC16 and endothelin 1 (ET-1) (a marker of vascular function) at 120 ppb ozone exposure.

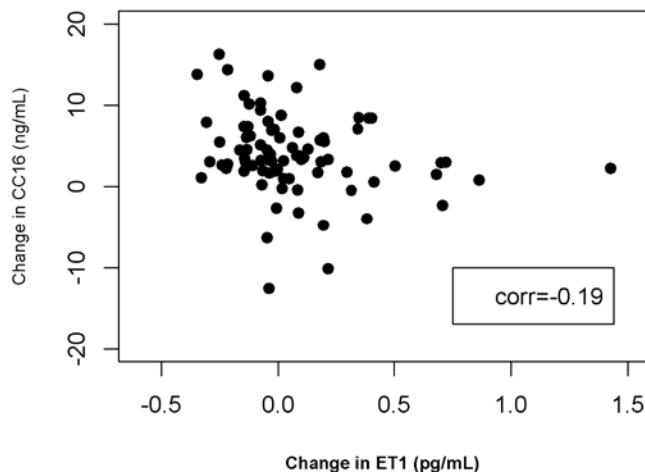


Figure D.2d. Scatter plot of post-exposure change in ET-1 (pg/mL) vs. post-exposure change in CC16 (mg/mL) — both at 4 hours and 120 ppb ozone exposure.

Section 3. Analyses of Responders

The goal of these analyses was to address the question of whether there were relationships between the cardiovascular and respiratory responses across ozone exposures in subgroups of respiratory “responders.” For each of the two respiratory variables, FEV₁ and PMN (%), subjects were divided into two subgroups based on level of response.

For FEV₁, the subgroups were (1) subjects with a change in FEV₁ greater than the median; and (2) subjects with a change in FEV₁ less than or equal to the median — at 15 minutes after 120 ppb ozone exposure for both groups.

For PMN, the groups were (1) subjects with a change in percentage of PMN greater than the median; and (2) subjects with a change in percentage of PMN less than or equal to the median — from 0 ppb to 120 ppb ozone exposure (at 22 hours post-exposure) for both groups.

The mixed effect linear model was applied separately to each subgroup to evaluate the impact of ozone on each of the primary cardiovascular outcomes. The results show that for each of these subgroups, none of the primary outcome variables were statistically significantly associated with ozone exposure according to the established 0.01 critical *P* value level. Only one outcome, monocyte–platelet conjugate counts, showed marginally significant ozone effects (*P* = 0.026) in the subgroup of subjects with change in FEV₁ less than or equal to the median. However, the ozone effect was greater for the 70 ppb than for 120 ppb ozone exposure.

**3.1. MIXED MODEL ANALYSES OF PRIMARY OUTCOMES STRATIFIED BY FEV₁:
SUBJECTS WITH CHANGE IN FEV₁ GREATER THAN THE MEDIAN**

Table D.3.1a. Summary Descriptive Data

	Greater than median change in FEV₁ (15 min, 120 ppb)
Male	22 (51.16%)
Female	21 (48.84%)
Mean ± SD age	60.40 ± 4.77
Mean ± SD change in FEV ₁ (15 min)	0.13 ± 0.06

Main Analyses of Ozone Effect

LF, 5-Min Average (ms²)

Table D.1.3b. Type III Sum of Squares for Change in LF, 5-Min Average (ms²), for Subjects with Change in FEV₁ Greater Than the Median (0.055 L) at 15 Minutes after 120 ppb Ozone Exposure

Effect	P Value
15-min vs. 4-hr vs. 22-hr change	0.2698
Ozone exposure	0.5093
Site	0.3777

Table D.3.1c. Mixed Model for Change in LF, 5-Min Average (ms²), for Subjects with Change in FEV₁ Greater Than the Median (0.055 L) at 15 Min after 120 ppb Ozone Exposure

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	-102.97	-633.32	427.39	0.6969
Change between pre- and post-exposure				
22-hr change	-73.1716	-380.46	234.12	0.6371
4-hr change	-246.10	-554.05	61.8577	0.1158
15-min change	0			
Ozone exposure				
120 ppb	131.61	-177.66	440.88	0.3998
70 ppb	-40.7658	-349.37	267.84	0.7934
0 ppb	0			
Site				
URMC	440.87	-190.70	1072.44	0.1660
UNC	255.62	-409.34	920.59	0.4418
UCSF	0			

HF, 5-Min Average (ms²)

Table D.3.1d. Type III Sum of Squares for Change in HF, 5-Min Average (ms²), for Subjects with Change in FEV₁ Greater Than the Median (0.055 L) at 15 Min after 120 ppb Ozone Exposure

Effect	P Value
15-min vs. 4-hr vs. 22-hr change	0.1234
Ozone exposure	0.2166
Site	0.1576

Table D.3.1e. Mixed Model for Change in HF, 5-Min Average (ms²), for Subjects with Change in FEV₁ Greater Than the Median (0.055 L) at 15 Min after 120 ppb Ozone Exposure

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	83.9497	-1461.90	1629.80	0.9132
Change between pre- and post-exposure				
22-hr change	-565.62	-1550.41	419.17	0.2566
4-hr change	-1026.09	-2012.99	-39.1870	0.0418
15-min change	0			
Ozone exposure				
120 ppb	783.10	-207.78	1773.98	0.1198
70 ppb	51.6042	-937.16	1040.37	0.9176
0 ppb	0			
Site				
URMC	1577.75	-200.64	3356.13	0.0805
UNC	199.20	-1673.43	2071.83	0.8309
UCSF	0			

ST in V5, 5-Min Average (µV)

Table D.3.1f. Type III Sum of Squares for Change in ST in V5, 5-Min Average (µV), for Subjects with Change in FEV₁ Greater Than the Median (0.055 L) at 15 Min after 120 ppb Ozone Exposure

Effect	P Value
15-min vs. 4-hr vs. 22-hr change	<0.0001
Ozone exposure	0.8723
Site	0.0267

Table D.3.1g. Mixed Model for Change in ST in V5, 5-Min Average (µV), for Subjects with Change in FEV₁ Greater Than the Median (0.055 L) at 15 Min after 120 ppb Ozone Exposure

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	13.3623	7.9541	18.7706	<0.0001
Change between pre- and post-exposure				
22-hr change	-5.8125	-8.5058	-3.1192	<0.0001
4-hr change	-4.9039	-7.6031	-2.2048	0.0005
15-min change	0			
Ozone exposure				
120 ppb	0.5972	-2.1142	3.3085	0.6625
70 ppb	-0.03302	-2.7385	2.6725	0.9807
0 ppb	0			
Site				
URMC	-9.1727	-15.8773	-2.4681	0.0086
UNC	-3.2535	-10.3117	3.8048	0.3571
UCSF	0			

T-Wave Amplitude, 5-Min Average (μV)

Table 3.1h. Type III Sum of Squares for Change in T-Wave Amplitude, 5-Min Average (μV), for Subjects with Change in FEV₁ Greater Than the Median (0.055 L) at 15 Min after 120 ppb Ozone Exposure

Effect	P Value
15-min vs. 4-hr vs. 22-hr change	<0.0001
Ozone exposure	0.7353
Site	0.1269

Table D.3.1i. Mixed Model for Change in T-Wave Amplitude, 5-Min Average (μV), for Subjects with Change in FEV₁ Greater Than the Median (0.055 L) at 15 Min after 120 ppb Ozone Exposure

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	195.42	151.13	239.70	<0.0001
Change between pre- and post-exposure				
22-hr change	-112.36	-134.57	-90.1461	<0.0001
4-hr change	-107.19	-129.45	-84.9343	<0.0001
15-min change	0			
Ozone exposure				
120 ppb	8.8042	-13.5545	31.1628	0.4357
70 ppb	5.0467	-17.2634	27.3568	0.6539
0 ppb	0			
Site				
URMC	-54.3390	-109.15	0.4710	0.0519
UNC	-43.2901	-100.99	14.4112	0.1373
UCSF	0			

T-Wave Amplitude, 24-Hr Average (μV)

Table D.3.1j. Type III Sum of Squares for T-Wave Amplitude, 24-Hr Average (μV), for Subjects with Change in FEV₁ Greater Than the Median (0.055 L) at 15 Min after 120 ppb Ozone Exposure

Effect	P Value
Ozone exposure	0.2343
Site	0.1638

Table D.3.1k. Mixed Model for T-Wave Amplitude, 24-Hr Average (μV), for Subjects with Change in FEV₁ Greater Than the Median (0.055 L) at 15 Min after 120 ppb Ozone Exposure

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	758.17	587.94	928.40	<0.0001
Ozone exposure				
120 ppb	-10.7102	-35.2898	13.8693	0.3886
70 ppb	-21.2399	-45.8194	3.3397	0.0894
0 ppb	0			
Site				
URMC	-173.50	-405.67	58.6748	0.1388
UNC	35.3587	-208.99	279.71	0.7714
UCSF	0			

Ln of RMSSD, 24-Hr Average (ms)

Table D.3.1l. Type III Sum of Squares for Ln of RMSSD, 24-Hr Average (ms), for Subjects with Change in FEV₁ Greater Than the Median (0.055 L) at 15 Min after 120 ppb Ozone Exposure

Effect	P Value
Ozone exposure	0.2226
Site	0.2135

Table D.3.1m. Mixed Model for Ln of RMSSD, 24-Hr Average (ms), for Subjects with Change in FEV₁ Greater Than the Median (0.055 L) at 15 Min after 120 ppb Ozone Exposure

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	3.2972	3.0303	3.5641	<0.0001
Ozone exposure				
120 ppb	-0.04575	-0.1374	0.04586	0.3234
70 ppb	0.03384	-0.05778	0.1255	0.4647
0 ppb	0			
Site				
URMC	-0.1831	-0.5404	0.1742	0.3065
UNC	0.1366	-0.2394	0.5126	0.4670
UCSF	0			

ST in V5, 24-Hr Average (μV)

Table D.3.1n. Type III Sum of Squares for ST in V5, 24-Hr Average (μV), for Subjects with Change in FEV₁ Greater Than the Median (0.055 L) at 15 Min after 120 ppb Ozone Exposure

Effect	P Value
Ozone exposure	0.6168
Site	0.4888

Table D.3.10. Mixed Model for ST in V5, 24-Hr Average (μV), for Subjects with Change in FEV₁ Greater Than the Median (0.055 L) at 15 Min after 120 ppb Ozone Exposure

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	30.0905	8.4048	51.7762	0.0077
Ozone exposure				
120 ppb	0.4350	-3.7081	4.5781	0.8351
70 ppb	-1.5069	-5.6500	2.6362	0.4715
0 ppb	0			
Site				
URMC	-11.1707	-40.6587	18.3173	0.4484
UNC	6.3950	-24.6396	37.4296	0.6793
UCSF	0			

FMD (%)

Table D.3.1p. Type III Sum of Squares for Change in FMD (%) for Subjects with Change in FEV₁ Greater Than the Median (0.055 L) at 15 Min after 120 ppb Ozone Exposure

Effect	P Value
Ozone exposure	0.4763
Site	0.2862

Table D.3.1q. Mixed Model for Change in FMD (%) for Subjects with Change in FEV₁ Greater Than the Median (0.055 L) at 15 Min after 120 ppb Ozone Exposure

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	0.5347	-0.4504	1.5197	0.2785
Ozone exposure				
120 ppb	-0.5568	-1.4747	0.3612	0.2308
70 ppb	-0.3530	-1.2710	0.5649	0.4461
0 ppb	0			
Site				
URMC	0.8139	-0.3357	1.9635	0.1598
UNC	0.8204	-0.4329	2.0737	0.1929
UCSF	0			

SBP (mmHg)

Table D.3.1r. Type III Sum of Squares for Change in SBP (mmHg) for Subjects with Change in FEV₁ Greater Than the Median (0.055 L) at 15 Min after 120 ppb Ozone Exposure

Effect	P Value
15-min vs. 4-hr vs. 22-hr change	0.0080
Ozone exposure	0.6024
Site	0.0081

Table D.3.1s. Mixed Model for Change in SBP (mmHg) for Subjects with Change in FEV₁ Greater Than the Median (0.055 L) at 15 Min after 120 ppb Ozone Exposure

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	-4.8398	-7.5819	-2.0977	0.0010
Change between pre- and post-exposure				
22-hr change	2.0698	0.03870	4.1008	0.0459
4-hr change	3.2248	1.1937	5.2559	0.0022
15-min change	0			
Ozone exposure				
120 ppb	-0.9457	-2.9768	1.0853	0.3571
70 ppb	-0.8295	-2.8605	1.2016	0.4190
0 ppb	0			
Site				
URMC	2.6111	-0.3506	5.5728	0.0824
UNC	5.0855	1.9684	8.2026	0.0021
UCSF	0			

CRP (mg/L)

Table D.3.1t. Type III Sum of Squares for Change in CRP (mg/L) for Subjects with Change in FEV₁ Greater Than the Median (0.055 L) at 15 Min after 120 ppb Ozone Exposure

Effect	P Value
4-hr vs. 22-hr change	0.5227
Ozone exposure	0.7169
Site	0.4835

Table D.3.1u. Mixed Model for Change in CRP (mg/L) for Subjects with Change in FEV₁ Greater Than the Median (0.055 L) at 15 Min after 120 ppb Ozone Exposure

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	-0.1063	-0.9832	0.7706	0.8077
Change between pre- and post-exposure				
4-hr change	0			
22-hr change	0.1864	-0.3973	0.7702	0.5227
Ozone exposure				
120 ppb	-0.2396	-0.9504	0.4713	0.5045
70 ppb	-0.2627	-0.9663	0.4410	0.4599
0 ppb	0			
Site				
URMC	0.1806	-0.8001	1.1613	0.7117
UNC	-0.4204	-1.4618	0.6209	0.4194
UCSF	0			

Monocyte–Platelet Conjugate Count

Table D.3.1v. Type III Sum of Squares for Change in Monocyte–Platelet Conjugate Count for Subjects with Change in FEV₁ Greater Than the Median (0.055 L) at 15 Min after 120 ppb Ozone Exposure

Effect	P Value
4-hr vs. 22-hr change	0.1253
Ozone exposure	0.3992
Site	0.2036

Table D.3.1w. Mixed Model for Change in Monocyte–Platelet Conjugate Count for Subjects with Change in FEV₁ Greater Than the Median (0.055 L) at 15 Min after 120 ppb Ozone Exposure

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	-10.3250	-25.3556	4.7057	0.1724
Change between pre- and post-exposure				
4-hr change	0			
22-hr change	-6.4157	-14.6977	1.8664	0.1253
Ozone exposure				
120 ppb	4.1390	-5.9253	14.2033	0.4152
70 ppb	6.8762	-3.2360	16.9884	0.1796
0 ppb	0			
Site				
URMC	14.6586	-3.2696	32.5867	0.1061
UNC	1.3025	-18.6305	21.2354	0.8955
UCSF	0			

MP-TFA (pg/mL)

Table D.3.1x. Type III Sum of Squares for Change in MP-TFA (pg/mL) for Subjects with Change in FEV₁ Greater Than the Median (0.055 L) at 15 Min after 120 ppb Ozone Exposure

Effect	P Value
4-hr vs. 22-hr change	0.6213
Ozone exposure	0.7003
Site	0.6929

Table D.3.1y. Mixed Model for Change in MP-TFA (pg/mL) for Subjects with Change in FEV₁ Greater Than the Median (0.055 L) at 15 Min after 120 ppb Ozone Exposure

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	0.02798	-0.04563	0.1016	0.4468
Change between pre- and post-exposure				
4-hr change	0			
22-hr change	-0.01302	-0.06580	0.03976	0.6213
Ozone exposure				
120 ppb	-0.01314	-0.07678	0.05051	0.6824
70 ppb	0.01394	-0.05023	0.07811	0.6668
0 ppb	0			
Site				
URMC	-0.03094	-0.1101	0.04820	0.4341
UNC	-0.02890	-0.1139	0.05609	0.4959
UCSF	0			

3.2. MIXED MODEL ANALYSES OF PRIMARY OUTCOMES STRATIFIED BY FEV₁: SUBJECTS WITH CHANGE IN FEV₁ LESS THAN OR EQUAL TO THE MEDIAN

Table D.3.2a. Summary Descriptive Table

	Less than or equal to median change in FEV ₁ (15 min, 120 ppb)
Male	12 (27.91%)
Female	31 (72.09%)
Mean ± SD age	59.33 ± 4.29
Mean ± SD change in FEV ₁ (15 min)	-0.01 ± 0.05

Main Analyses of Ozone Effect

LF, 5-Min Average (ms²)

Table D.3.2b. Type III Sum of Squares for Change in LF, 5-Min Average (ms²), for Subjects with Change in FEV₁ Less Than or Equal to the Median (0.055 L) at 15 Min after 120 ppb Ozone Exposure

Effect	P Value
15-min vs. 4-hr vs. 22-hr change	0.1882
Ozone exposure	0.1010
Site	0.2931

Table D.3.2c. Mixed Model for Change in LF, 5-Min Average (ms²), for Subjects with Change in FEV₁ Less Than or Equal to the Median (0.055 L) at 15 Min after 120 ppb Ozone Exposure

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	60.0231	-200.67	320.72	0.6442
Change between pre- and post-exposure				
22-hr change	-131.87	-307.08	43.3375	0.1382
4-hr change	18.3998	-152.31	189.11	0.8308
15-min change	0			
Ozone exposure				
120 ppb	159.00	-17.6477	335.65	0.0770
70 ppb	-16.3486	-187.61	154.91	0.8498
0 ppb	0			
Site				
URMC	156.79	-136.02	449.60	0.2856
UNC	-51.1137	-342.12	239.89	0.7245
UCSF	0			

HF, 5-Min Average (ms²)

Table D.3.2d. Type III Sum of Squares for Change in HF, 5-Min Average (ms²), for Subjects with Change in FEV₁ Less Than or Equal to the Median (0.055 L) at 15 Min after 120 ppb Ozone Exposure

Effect	P Value
15-min vs. 4-hr vs. 22-hr change	0.2120
Ozone exposure	0.1288
Site	0.2616

Table D.3.2e. Mixed Model for Change in HF, 5-Min Average (ms²), for Subjects with Change in FEV₁ Less Than or Equal to the Median (0.055 L) at 15 Min after 120 ppb Ozone Exposure

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	257.93	-175.50	691.36	0.2361
Change between pre- and post-exposure				
22-hr change	-219.11	-605.74	167.52	0.2630
4-hr change	123.36	-254.18	500.91	0.5176
15-min change	0			
Ozone exposure				
120 ppb	298.56	-89.1259	686.25	0.1293
70 ppb	-82.5195	-460.38	295.34	0.6650
0 ppb	0			
Site				
URMC	-153.44	-553.44	246.55	0.4427
UNC	-328.56	-729.82	72.6934	0.1058
UCSF	0			

ST in V5, 5-Min Average (μV)

Table D.3.2f. Type III Sum of Squares for Change in ST in V5, 5-Min Average (μV), for Subjects with Change in FEV₁ Less Than or Equal to the Median (0.055 L) at 15 Min after 120 ppb Ozone Exposure

Effect	P Value
15-min vs. 4-hr vs. 22-hr change	<0.0001
Ozone exposure	0.8656
Site	0.0192

Table D.3.2g. Mixed Model for Change in ST in V5, 5-Min Average (μV), for Subjects with Change in FEV₁ Less Than or Equal to the Median (0.055 L) at 15 Min after 120 ppb Ozone Exposure

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	11.8867	7.0652	16.7081	<0.0001
Change between pre- and post-exposure				
22-hr change	-4.4420	-6.9748	-1.9092	0.0008
4-hr change	-6.7920	-9.2579	-4.3261	<0.0001
15-min change	0			
Ozone exposure				
120 ppb	-0.06705	-2.6265	2.4924	0.9586
70 ppb	0.5480	-1.9282	3.0241	0.6608
0 ppb	0			
Site				
URMC	-7.3988	-13.2464	-1.5513	0.0144
UNC	-0.6083	-6.3995	5.1829	0.8330
UCSF	0			

T-Wave Amplitude, 5-Min Average (μV)

Table D.3.2h. Type III Sum of Squares for Change in T-Wave Amplitude, 5-Min Average (μV), for Subjects with Change in FEV₁ Less Than or Equal to the Median (0.055 L) at 15 Min after 120 ppb Ozone Exposure

Effect	P Value
15-min vs. 4-hr vs. 22-hr change	<0.0001
Ozone exposure	0.1370
Site	0.1315

Table D.3.2i. Mixed Model for Change in T-Wave Amplitude, 5-Min Average (μV), for Subjects with Change in FEV₁ Less Than or Equal to the Median (0.055 L) at 15 Min after 120 ppb Ozone Exposure

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	176.39	139.41	213.38	<0.0001
Change between pre- and post-exposure				
22-hr change	-101.62	-120.06	-83.1702	<0.0001
4-hr change	-116.07	-134.03	-98.1169	<0.0001
15-min change	0			
Ozone exposure				
120 ppb	1.7051	-16.9403	20.3505	0.8561
70 ppb	16.6761	-1.3566	34.7088	0.0694
0 ppb	0			
Site				
URMC	-45.5886	-90.9432	-0.2341	0.0489
UNC	-32.3529	-77.2487	12.5429	0.1531
UCSF	0			

T-Wave Amplitude, 24-Hr Average (μV)

Table D.3.2j. Type III Sum of Squares for T-Wave Amplitude, 24-Hr Average (μV), for Subjects with Change in FEV₁ Less Than or Equal to the Median (0.055 L) at 15 Min after 120 ppb Ozone Exposure

Effect	P Value
Ozone exposure	0.9978
Site	0.5994

Table D.3.2k. Mixed Model for T-Wave Amplitude, 24-Hr Average (μV), for Subjects with Change in FEV₁ Less Than or Equal to the Median (0.055 L) at 15 Min after 120 ppb Ozone Exposure

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	640.25	508.47	772.02	<0.0001
Ozone exposure				
120 ppb	-0.5942	-21.8639	20.6755	0.9558
70 ppb	0.05048	-20.8433	20.9443	0.9962
0 ppb	0			
Site				
URMC	-70.5435	-246.57	105.48	0.4228
UNC	4.5810	-169.00	178.16	0.9577
UCSF	0			

Ln of RMSSD, 24-Hr Average (ms)

Table D.3.2l. Type III Sum of Squares for Ln of RMSSD, 24-Hr Avg (ms), for Subjects with Change in FEV₁ Less Than or Equal to the Median (0.055 L) at 15 Min after 120 ppb Ozone Exposure

Effect	P Value
Ozone exposure	0.4987
Site	0.0077

Table D.3.2m. Mixed Model for Ln of RMSSD, 24-Hr Average (ms), for Subjects with Change in FEV₁ Less Than or Equal to the Median (0.055 L) at 15 Min after 120 ppb Ozone Exposure

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	3.4745	3.2571	3.6919	<0.0001
Ozone exposure				
120 ppb	0.02375	-0.05093	0.09843	0.5287
70 ppb	-0.02071	-0.09411	0.05268	0.5760
0 ppb	0			
Site				
URMC	-0.1937	-0.4796	0.09225	0.1786
UNC	-0.4560	-0.7381	-0.1740	0.0022
UCSF	0			

ST in V5, 24-Hr Average (μ V)

Table D.3.2n. Type III Sum of Squares for ST in V5, 24-Hr Average (μ V), for Subjects with Change in FEV₁ Less Than or Equal to the Median (0.055 L) at 15 Min after 120 ppb Ozone Exposure

Effect	P Value
Ozone exposure	0.7409
Site	0.7243

Table D.3.2o. Mixed Model for ST in V5, 24-Hr Average (μ V), for Subjects with Change in FEV₁ Less Than or Equal to the Median (0.055 L) at 15 Min after 120 ppb Ozone Exposure

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	13.9550	-4.8728	32.7828	0.1420
Ozone exposure				
120 ppb	0.5264	-2.7870	3.8398	0.7528
70 ppb	-0.7558	-4.0107	2.4991	0.6454
0 ppb	0			
Site				
URMC	9.8214	-15.3081	34.9510	0.4342
UNC	7.1008	-17.6804	31.8820	0.5658
UCSF	0			

FMD (%)

Table D.3.2p. Type III Sum of Squares for Change in FMD (%) for Subjects with Change in FEV₁ Less Than or Equal to the Median (0.055 L) at 15 Min after 120 ppb Ozone Exposure

Effect	P Value
Ozone exposure	0.8800
Site	0.7689

Table D.3.2q. Mixed Model for Change in FMD (%) for Subjects with Change in FEV₁ Less Than or Equal to the Median (0.055 L) at 15 Min after 120 ppb Ozone Exposure

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	0.3066	-1.1140	1.7271	0.6635
Ozone exposure				
120 ppb	0.1001	-1.2480	1.4483	0.8825
70 ppb	0.3351	-1.0235	1.6936	0.6240
0 ppb	0			
Site				
URMC	-0.01945	-1.6821	1.6432	0.9812
UNC	0.4574	-1.0838	1.9987	0.5501
UCSF	0			

SBP (mmHg)

Table D.3.2.r. Type III Sum of Squares for Change in SBP (mmHg) for Subjects with Change in FEV₁ Less Than or Equal to the Median (0.055 L) at 15 Min after 120 ppb Ozone Exposure

Effect	P Value
15-min vs. 4-hr vs. 22-hr change	0.0002
Ozone exposure	0.3135
Site	0.0058

Table D.3.2s. Mixed Model for Change in SBP (mmHg) for Subjects with Change in FEV₁ Less Than or Equal to the Median (0.055 L) at 15 Min after 120 ppb Ozone Exposure

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	-4.8867	-8.3861	-1.3874	0.0074
Change between pre- and post-exposure				
22-hr change	1.0465	-0.8714	2.9645	0.2810
4-hr change	4.0930	2.1751	6.0110	<0.0001
15-min change	0			
Ozone exposure				
120 ppb	1.4341	-0.4838	3.3521	0.1408
70 ppb	1.0310	-0.8869	2.9490	0.2881
0 ppb	0			
Site				
URMC	1.5963	-2.5849	5.7775	0.4449
UNC	6.5116	2.3888	10.6343	0.0027
UCSF	0			

CRP (mg/L)

Table D.3.2t. Type III Sum of Squares for Change in CRP (mg/L) for Subjects with Change in FEV₁ Less Than or Equal to the Median (0.055 L) at 15 Min after 120 ppb Ozone Exposure

Effect	P Value
4-hr vs. 22-hr change	0.0573
Ozone exposure	0.8976
Site	0.1250

Table D.3.2u. Mixed Model for Change in CRP (mg/L) for Subjects with Change in FEV₁ Less Than or Equal to the Median (0.055 L) at 15 Min after 120 ppb Ozone Exposure

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	-0.6744	-1.2567	-0.09201	0.0243
Change between pre- and post-exposure				
4-hr change	0			
22-hr change	0.2589	-0.00841	0.5262	0.0573
Ozone exposure				
120 ppb	-0.07569	-0.4004	0.2491	0.6440
70 ppb	-0.03273	-0.3562	0.2908	0.8409
0 ppb	0			
Site				
URMC	0.7276	0.008269	1.4470	0.0475
UNC	0.2688	-0.4445	0.9821	0.4508
UCSF	0			

Monocyte–Platelet Conjugate Count

Table D.3.2v. Type III Sum of Squares for Change in Monocyte–Platelet Conjugate Count for Subjects with Change in FEV₁ Less Than or Equal to the Median (0.055 L) at 15 Min after 120 ppb Ozone Exposure

Effect	P Value
4-hr vs. 22-hr change	0.8212
Ozone exposure	0.0255
Site	0.0590

Table D.3.2w. Mixed Model for Change in Monocyte–Platelet Conjugate Count for Subjects with Change in FEV₁ Less Than or Equal to the Median (0.055 L) at 15 Min after 120 ppb Ozone Exposure

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	7.4017	-2.4349	17.2383	0.1359
Change between pre- and post-exposure				
4-hr change	0			
22-hr change	0.7912	-6.2487	7.8311	0.8212
Ozone exposure				
120 ppb	-5.4594	-13.9506	3.0319	0.2036
70 ppb	-12.0029	-20.6064	-3.3993	0.0070
0 ppb	0			
Site				
URMC	-1.1491	-11.6788	9.3805	0.8262
UNC	-12.8062	-24.3942	-1.2182	0.0312
UCSF	0			

MP-TFA (pg/mL)

Table D.3.2x. Type III Sum of Squares for Change in MP-TFA (pg/mL) for Subjects with Change in FEV₁ Less Than or Equal to the Median (0.055 L) at 15 Min after 120 ppb Ozone Exposure

Effect	P Value
4-hr v 22-hr change	0.6535
Ozone exposure	0.0895
Site	0.3943

Table D.3.2y. Mixed Model for Change in MP-TFA (pg/mL) for Subjects with Change in FEV₁ Less Than or Equal to the Median (0.055 L) at 15 Min after 120 ppb Ozone Exposure

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	0.03258	-0.03495	0.1001	0.3353
Change between pre- and post-exposure				
4-hr change	0			
22-hr change	-0.00877	-0.04793	0.03039	0.6535
Ozone exposure				
120 ppb	0.02837	-0.01932	0.07605	0.2400
70 ppb	-0.02421	-0.07170	0.02328	0.3134
0 ppb	0			
Site				
URMC	-0.01448	-0.09210	0.06314	0.7082
UNC	-0.04991	-0.1268	0.02702	0.1973
UCSF	0			

3.3 MIXED MODEL ANALYSES OF PRIMARY OUTCOMES STRATIFIED BY PMN: SUBJECTS WITH CHANGE IN PMN GREATER THAN THE MEDIAN

Table D.3.3a. Descriptive Summary

	PMN (%) greater than median (at 120 ppb ozone exposure)
Male	9 (29.03%)
Female	22 (70.97%)
Mean ± SD age	60.16 ± 4.66
Mean ± SD PMN%	71.66 ± 10.32

Main Analyses of Ozone Effect

LF, 5-Min Average (ms²)

Table D.3.3b. Type III Sum of Squares for Change in LF, 5-Min Average (ms²), for Subjects with PMN (%) Greater Than the Median (57.35%) at 120 ppb Ozone Exposure

Effect	P Value
15-min vs. 4-hr vs. 22-hr change	0.0730
Ozone exposure	0.4802
Site	0.6643

Table D.3.3c. Mixed Model for Change in LF, 5-Min Average (ms²), for Subjects with PMN (%) Greater Than the Median (57.35%) at 120 ppb Ozone Exposure

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	130.40	-189.49	450.29	0.4108
Change between pre- and post-exposure				
22-hr change	-244.78	-457.09	-32.4564	0.0246
4-hr change	-83.6832	-293.34	125.98	0.4278
15-min change	0			
Ozone exposure				
120 ppb	126.66	-89.2074	342.52	0.2449
70 ppb	88.3983	-119.31	296.11	0.3977
0 ppb	0			
Site				
URMC	82.8549	-340.28	505.99	0.6914
UNC	-107.00	-497.12	283.11	0.5787
UCSF	0			

HF, 5-Min Average (ms²)

Table D.3.3d. Type III Sum of Squares for Change in HF, 5-Min Average (ms²), for Subjects with PMN (%) Greater Than the Median (57.35%) at 120 ppb Ozone Exposure

Effect	P Value
15-min vs. 4-hr vs. 22-hr change	0.1601
Ozone exposure	0.3390
Site	0.6572

Table D.3.3e. Mixed Model for Change in HF, 5-Min Average (ms²), for Subjects with PMN (%) Greater Than the Median (57.35%) at 120 ppb Ozone Exposure

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	-4.1087	-583.29	575.07	0.9885
Change between pre- and post-exposure				
22-hr change	-79.2883	-593.45	434.87	0.7588
4-hr change	385.10	-122.93	893.13	0.1347
15-min change	0			
Ozone exposure				
120 ppb	164.66	-355.10	684.41	0.5284
70 ppb	-217.82	-720.93	285.29	0.3896
0 ppb	0			
Site				
URMC	88.5754	-535.00	712.15	0.7732
UNC	-188.25	-768.97	392.48	0.5121
UCSF	0			

ST in V5, 5-Min Average (μV)

Table D.3.3f. Type III Sum of Squares for Change in ST in V5, 5-Min Average (μV), for Subjects with PMN (%) Greater Than the Median (57.35%) at 120 ppb Ozone Exposure

Effect	P Value
15-min vs. 4-hr vs. 22-hr change	0.0002
Ozone exposure	0.4910
Site	0.0926

Table D.3.3g. Mixed Model for Change in ST in V5, 5-Min Average (μV), for Subjects with PMN (%) Greater Than the Median (57.35%) at 120 ppb Ozone Exposure

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	10.4110	4.2959	16.5260	0.0016
Change between pre- and post-exposure				
22-hr change	-6.3749	-9.2224	-3.5273	<0.0001
4-hr change	-3.7667	-6.5779	-0.9555	0.0095
15-min change	0			
Ozone exposure				
120 ppb	0.8550	-2.0477	3.7577	0.5576
70 ppb	1.6695	-1.1161	4.4551	0.2350
0 ppb	0			
Site				
URMC	-9.2390	-18.1645	-0.3135	0.0430
UNC	-0.7073	-8.8988	7.4843	0.8609
UCSF	0			

T-Wave Amplitude, 5-Min Average (μV)

Table D.3.3h. Type III Sum of Squares for Change in T-Wave Amplitude, 5-Min Avg (μV), for Subjects with PMN (%) Greater Than the Median (57.35%) at 120 ppb Ozone Exposure

Effect	P Value
15-min vs. 4-hr vs. 22-hr change	<0.0001
Ozone exposure	0.3920
Site	0.3744

Table D.3.3i. Mixed Model for Change in T-Wave Amplitude, 5-Min Average (μV), for Subjects with PMN (%) Greater Than the Median (57.35%) at 120 ppb Ozone Exposure

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	155.30	105.26	205.34	<0.0001
Change between pre- and post-exposure				
22-hr change	-113.54	-139.67	-87.3991	<0.0001
4-hr change	-102.45	-128.26	-76.6486	<0.0001
15-min change	0			
Ozone exposure				
120 ppb	14.5632	-12.0634	41.1897	0.2780
70 ppb	16.1354	-9.4323	41.7032	0.2115
0 ppb	0			
Site				
URMC	-39.2921	-110.68	32.0945	0.2691
UNC	9.4362	-56.1483	75.0207	0.7704
UCSF	0			

T-Wave Amplitude, 24-Hr Average (μV)

Table D.3.3j. Type III Sum of Squares for T-Wave Amplitude, 24-Hr Average (μV), for Subjects with PMN (%) Greater Than the Median (57.35%) at 120 ppb Ozone Exposure

Effect	P Value
Ozone exposure	0.0744
Site	0.1808

Table D.3.3k. Mixed Model for T-Wave Amplitude, 24-Hr Average (μV), for Subjects with PMN (%) Greater Than the Median (57.35%) at 120 ppb Ozone Exposure

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	748.96	608.03	889.89	<0.0001
Ozone exposure				
120 ppb	-5.7024	-31.4981	20.0932	0.6598
70 ppb	-27.8279	-52.9856	-2.6703	0.0308
0 ppb	0			
Site				
URMC	-203.56	-425.13	18.0123	0.0703
UNC	-53.6646	-256.34	149.01	0.5918
UCSF	0			

Ln of RMSSD, 24-Hr Average (ms)

Table D.3.3l. Type III Sum of Squares for Ln of RMSSD, 24-Hr Average (ms), for Subjects with PMN (%) Greater Than the Median (57.35%) at 120 ppb Ozone Exposure

Effect	P Value
Ozone exposure	0.8435
Site	0.3192

Table D.3.3m. Mixed Model for Ln of RMSSD, 24-Hr Average (ms), for Subjects with PMN (%) Greater Than the Median (57.35%) at 120 ppb Ozone Exposure

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	3.2633	3.0417	3.4849	<0.0001
Ozone exposure				
120 ppb	0.02049	-0.07754	0.1185	0.6772
70 ppb	0.02677	-0.06891	0.1225	0.5776
0 ppb	0			
Site				
URMC	-0.1161	-0.4549	0.2226	0.4883
UNC	-0.2335	-0.5437	0.07664	0.1342
UCSF	0			

ST in V5, 24-Hr Average (µV)

Table D.3.3n. Type III Sum of Squares for ST in V5, 24-Hr Average (µV), for Subjects with PMN (%) Greater Than the Median (57.35%) at 120 ppb Ozone Exposure

Effect	P Value
Ozone exposure	0.4602
Site	0.8343

Table D.3.3o. Mixed Model for ST in V5, 24-Hr Average (µV), for Subjects with PMN (%) Greater Than the Median (57.35%) at 120 ppb Ozone Exposure

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	24.0940	2.7242	45.4639	0.0285
Ozone exposure				
120 ppb	1.5888	-3.6553	6.8330	0.5466
70 ppb	-1.6935	-6.8087	3.4216	0.5101
0 ppb	0			
Site				
URMC	-3.8508	-37.2978	29.5962	0.8153
UNC	-9.0099	-39.6087	21.5889	0.5513
UCSF	0			

FMD (%)

Table D.3.3p. Type III Sum of Squares for Change in FMD (%) for Subjects with PMN (%) Greater Than the Median (57.35%) at 120 ppb Ozone Exposure

Effect	P Value
Ozone exposure	0.9474
Site	0.9698

Table D.3.3q. Mixed Model for Change in FMD (%) for Subjects with PMN (%) Greater Than the Median (57.35%) at 120 ppb Ozone Exposure

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	0.7186	-0.5096	1.9468	0.2400
Ozone exposure				
120 ppb	0.03448	-1.2166	1.2856	0.9562
70 ppb	0.1949	-1.0687	1.4585	0.7584
0 ppb	0			
Site				
URMC	0.03218	-1.6644	1.7288	0.9692
UNC	0.1653	-1.2534	1.5839	0.8126
UCSF	0			

SBP (mmHg)

Table D.3.3r. Type III Sum of Squares for Change in SBP (mmHg) for Subjects with PMN (%) Greater Than the Median (57.35%) at 120 ppb Ozone Exposure

Effect	P Value
15-min vs. 4-hr vs. 22-hr change	<0.0001
Ozone exposure	0.6997
Site	0.0008

Table D.3.3s. Mixed Model for Change in SBP (mmHg) for Subjects with PMN (%) Greater Than the Median (57.35%) at 120 ppb Ozone Exposure

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	-6.5188	-9.3415	-3.6961	<0.0001
Change between pre- and post-exposure				
22-hr change	4.5054	2.3304	6.6803	0.0001
4-hr change	6.0323	3.8573	8.2072	<0.0001
15-min change	0			
Ozone exposure				
120 ppb	0.2473	-1.9277	2.4223	0.8208
70 ppb	-0.6452	-2.8201	1.5298	0.5552
0 ppb	0			
Site				
URMC	0.5278	-2.8857	3.9412	0.7538
UNC	6.1187	2.9970	9.2404	0.0004
UCSF	0			

CRP (mg/L)

Table D.3.3t. Type III Sum of Squares for Change in CRP (mg/L) for Subjects with PMN (%) Greater Than the Median (57.35%) at 120 ppb Ozone Exposure

Effect	P Value
4-hr vs. 22-hr change	0.5756
Ozone exposure	0.2295
Site	0.1894

Table D.3.3u. Mixed Model for Change in CRP (mg/L) for Subjects with PMN% Greater Than the Median at 120 ppb Ozone Exposure (57.35%)

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	-0.6421	-1.3248	0.04056	0.0642
Change between pre- and post-exposure				
4-hr change	0			
22-hr change	-0.1265	-0.5827	0.3298	0.5756
Ozone exposure				
120 ppb	-0.3744	-0.9328	0.1839	0.1847
70 ppb	0.07590	-0.4680	0.6198	0.7809
0 ppb	0			
Site				
URMC	0.7407	-0.1487	1.6302	0.0991
UNC	0.006285	-0.8038	0.8163	0.9874
UCSF	0			

Monocyte–Platelet Conjugate Count

Table D.3.3v. Type III Sum of Squares for Change in Monocyte–Platelet Conjugate Count for Subjects with PMN (%) Greater Than the Median (57.35%) at 120 ppb Ozone Exposure

Effect	P Value
4-hr vs. 22-hr change	0.7795
Ozone exposure	0.5081
Site	0.6084

Table D.3.3w. Mixed Model for Change in Monocyte–Platelet Conjugate Count for Subjects with PMN (%) Greater Than the Median (57.35%) at 120 ppb Ozone Exposure

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	-11.6228	-28.5820	5.3363	0.1711
Change between pre- and post-exposure				
4-hr change	0			
22-hr change	-1.4612	-12.0388	9.1164	0.7795
Ozone exposure				
120 ppb	7.5622	-5.5039	20.6283	0.2504
70 ppb	4.4475	-8.3014	17.1964	0.4866
0 ppb	0			
Site				
URMC	11.1161	-11.6344	33.8665	0.3250
UNC	3.5417	-18.4385	25.5220	0.7435
UCSF	0			

MP-TFA (pg/mL)

Table D.3.3x. Type III Sum of Squares for Change in MP-TFA (pg/mL) for Subjects with PMN (%) Greater Than the Median (57.35%) at 120 ppb Ozone Exposure

Effect	P Value
4-hr vs. 22-hr change	0.4516
Ozone exposure	0.9229
Site	0.2092

Table D.3.3y. Mixed Model for Change in MP-TFA (pg/mL) for Subjects with PMN (%) Greater Than the Median (57.35%) at 120 ppb Ozone Exposure

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	0.05558	-0.03888	0.1500	0.2382
Change between pre- and post-exposure				
4-hr change	0			
22-hr change	-0.02518	-0.09261	0.04225	0.4516
Ozone exposure				
120 ppb	-0.00305	-0.08510	0.07900	0.9409
70 ppb	-0.01530	-0.09688	0.06627	0.7085
0 ppb	0			
Site				
URMC	-0.03942	-0.1558	0.07694	0.4934
UNC	-0.09429	-0.2006	0.01201	0.0799
UCSF	0			

3.4 MIXED MODEL ANALYSES OF PRIMARY OUTCOMES STRATIFIED BY PMN: SUBJECTS WITH CHANGE IN PMN LESS OR EQUAL THAN THE MEDIAN

Table D.3.4a. Summary Descriptive Table

	PMN (%) less than or equal to median (at 120 ppb ozone exposure)
Male	17 (54.84%)
Female	14 (45.16%)
Mean \pm SD age	59.97 \pm 4.83
Mean \pm SD PMN (%)	40.83 \pm 12.57

Main Analyses of Ozone Effect

LF, 5-Min Average (ms²)

Table D.3.4b. Type III Sum of Squares for Change in LF, 5-Min Average (ms²), for Subjects with PMN (%) Less Than or Equal to the Median (57.35%) at 120 ppb Ozone Exposure

Effect	P Value
15-min vs. 4-hr vs. 22-hr change	0.1721
Ozone exposure	0.3457
Site	0.4307

Table D.3.4c. Mixed Model for Change in LF, 5-Min Average (ms²), for Subjects with PMN (%) Less Than or Equal to the Median (57.35%) at 120 ppb Ozone Exposure

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	278.20	-146.04	702.43	0.1900
Change between pre- and post-exposure				
22-hr change	-242.24	-578.00	93.5253	0.1542
4-hr change	-299.06	-632.79	34.6651	0.0781
15-min change	0			
Ozone exposure				
120 ppb	117.70	-219.43	454.84	0.4875
70 ppb	-128.26	-463.43	206.91	0.4469
0 ppb	0			
Site				
URMC	228.70	-182.76	640.16	0.2645
UNC	15.8184	-412.99	444.63	0.9403
UCSF	0			

HF, 5-Min Average (ms²)

Table D.3.4d. Type III Sum of Squares for Change in HF, 5-Min Average (ms²), for Subjects with PMN (%) Less Than or Equal to the Median (57.35%) at 120 ppb Ozone Exposure

Effect	P Value
15-min vs. 4-hr vs. 22-hr change	0.0540
Ozone exposure	0.3034
Site	0.2085

Table D.3.4e. Mixed Model for Change in HF, 5-Min Average (ms²), for Subjects with PMN (%) Less Than or Equal to the Median (57.35%) at 120 ppb Ozone Exposure

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	695.29	-1522.81	2913.38	0.5260
Change between pre- and post-exposure				
22-hr change	-1291.36	-2648.06	65.3333	0.0617
4-hr change	-1561.12	-2908.81	-213.43	0.0239
15-min change	0			
Ozone exposure				
120 ppb	986.41	-377.39	2350.21	0.1531
70 ppb	154.92	-1200.62	1510.45	0.8199
0 ppb	0			
Site				
URMC	1812.90	-678.91	4304.71	0.1473
UNC	-68.6517	-2664.98	2527.67	0.9572
UCSF	0			

ST in V5, 5-Min Average (μV)

Table D.3.4f. Type III Sum of Squares for Change in ST in V5, 5-Min Average (μV), for Subjects with PMN (%) Less Than or Equal to the Median (57.35%) at 120 ppb Ozone Exposure

Effect	P Value
15-min vs. 4-hr vs. 22-hr change	<0.0001
Ozone exposure	0.4211
Site	0.0034

Table D.3.4g. Mixed Model for Change in ST in V5, 5-Min Average (μV), for Subjects with PMN (%) Less Than or Equal to the Median (57.35%) at 120 ppb Ozone Exposure

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	16.4151	10.0259	22.8043	<0.0001
Change between pre- and post-exposure				
22-hr change	-7.6392	-11.0297	-4.2486	<0.0001
4-hr change	-9.4660	-12.8335	-6.0985	<0.0001
15-min change	0			
Ozone exposure				
120 ppb	2.1973	-1.2122	5.6068	0.2022
70 ppb	0.6615	-2.7271	4.0501	0.6975
0 ppb	0			
Site				
URMC	-13.0318	-20.5419	-5.5217	0.0014
UNC	-3.7242	-11.5492	4.1008	0.3380
UCSF	0			

T-Wave Amplitude, 5-Min Average (μV)

Table D.3.4h. Type III Sum of Squares for Change in T-Wave Amplitude, 5-Min Average (μV), for Subjects with PMN (%) Less Than or Equal to the Median (57.35%) at 120 ppb Ozone Exposure

Effect	P Value
15-min vs. 4-hr vs. 22-hr change	<0.0001
Ozone exposure	0.6863
Site	0.0002

Table D.3.4i. Mixed Model for Change in T-Wave Amplitude, 5-Min Average (μV), for Subjects with PMN (%) Less Than or Equal to the Median (57.35%) at 120 ppb Ozone Exposure

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	246.22	206.54	285.89	<0.0001
Change between pre- and post-exposure				
22-hr change	-125.38	-148.67	-102.10	<0.0001
4-hr change	-131.64	-154.76	-108.51	<0.0001
15-min change	0			
Ozone exposure				
120 ppb	7.7872	-15.6191	31.1935	0.5082
70 ppb	-1.7109	-24.9749	21.5531	0.8835
0 ppb	0			
Site				
URMC	-103.32	-148.56	-58.0776	<0.0001
UNC	-87.2105	-134.35	-40.0697	0.0007
UCSF	0			

T-Wave Amplitude, 24-Hr Average (μV)

Table D.3.4j. Type III Sum of Squares for T-Wave Amplitude, 24-Hr Average (μV), for Subjects with PMN (%) Less Than or Equal to the Median (57.35%) at 120 ppb Ozone Exposure

Effect	P Value
Ozone exposure	0.6072
Site	0.5169

Table D.3.4k. Mixed Model for T-Wave Amplitude, 24-Hr Average (μV), for Subjects with PMN (%) Less Than or Equal to the Median (57.35%) at 120 ppb Ozone Exposure

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	795.14	561.70	1028.57	<0.0001
Ozone exposure				
120 ppb	-12.9375	-42.7685	16.8934	0.3890
70 ppb	-0.1812	-30.0122	29.6497	0.9903
0 ppb	0			
Site				
URMC	-169.76	-477.54	138.02	0.2681
UNC	-61.1486	-381.84	259.54	0.6991
UCSF	0			

Ln of RMSSD, 24-Hr Average (ms)

Table D.3.4l. Type III Sum of Squares for Ln of RMSSD, 24-Hr Average (ms), for Subjects with PMN (%) Less Than or Equal to the Median (57.35%) at 120 ppb Ozone Exposure

Effect	P Value
Ozone exposure	0.1770
Site	0.8547

Table D.3.4m. Mixed Model for Ln of RMSSD, 24-Hr Average (ms), for Subjects with PMN (%) Less Than or Equal to the Median (57.35%) at 120 ppb Ozone Concentration

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	3.4071	3.0689	3.7454	<0.0001
Ozone exposure				
120 ppb	-0.08469	-0.1787	0.009309	0.0765
70 ppb	-0.02065	-0.1146	0.07334	0.6618
0 ppb	0			
Site				
URMC	-0.07827	-0.5187	0.3622	0.7186
UNC	-0.1249	-0.5838	0.3340	0.5815
UCSF	0			

ST in V5, 24-Hr Average (μ V)

Table D.3.4n. Type III Sum of Squares for ST in V5, 24-Hr Average (μ V), for Subjects with PMN (%) Less Than or Equal to the Median (57.35%) at 120 ppb Ozone Exposure

Effect	P Value
Ozone exposure	0.8771
Site	0.3073

Table D.3.4o. Mixed Model for ST in V5, 24-Hr Average (μ V), for Subjects with PMN (%) Less Than or Equal to the Median (57.35%) at 120 ppb Ozone Exposure

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	25.9463	-2.2894	54.1820	0.0702
Ozone exposure				
120 ppb	-0.7045	-4.4798	3.0709	0.7102
70 ppb	-0.9303	-4.7056	2.8451	0.6238
0 ppb	0			
Site				
URMC	-3.8181	-41.0347	33.3986	0.8351
UNC	22.4319	-16.3464	61.2103	0.2460
UCSF	0			

FMD (%)

Table D.3.4p. Type III Sum of Squares for Change in FMD (%) for Subjects with PMN (%) Less Than or Equal to the Median (57.35%) at 120 ppb Ozone Exposure

Effect	P Value
Ozone exposure	0.2602
Site	0.1942

Table D.3.4q. Mixed Model for Change in FMD (%) for Subjects with PMN (%) Less Than or Equal to the Median (57.35%) at 120 ppb Ozone Exposure

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	-0.2363	-1.6569	1.1843	0.7348
Ozone exposure				
120 ppb	-0.2492	-1.5110	1.0125	0.6933
70 ppb	0.7544	-0.5073	2.0162	0.2355
0 ppb	0			
Site				
URMC	1.2509	-0.3203	2.8220	0.1136
UNC	1.3853	-0.3396	3.1102	0.1106
UCSF	0			

SBP (mmHg)

Table D.3.4r. Type III Sum of Squares for Change in SBP (mmHg) for Subjects with PMN (%) Less Than or Equal to the Median (57.35%) at 120 ppb Ozone Exposure

Effect	P Value
15-min vs. 4-hr vs. 22-hr change	0.0951
Ozone exposure	0.2624
Site	0.0579

Table D.3.4s. Mixed Model for Change in SBP (mmHg) for Subjects with PMN (%) Less Than or Equal to the Median (57.35%) at 120 ppb Ozone Exposure

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	-3.9319	-7.2421	-0.6217	0.0216
Change between pre- and post-exposure				
22-hr change	2.0108	-0.3593	4.3808	0.0949
4-hr change	2.4624	0.09230	4.8324	0.0420
15-min change	0			
Ozone exposure				
120 ppb	-1.4409	-3.8109	0.9292	0.2287
70 ppb	0.4301	-1.9400	2.8002	0.7179
0 ppb	0			
Site				
URMC	3.6852	0.1776	7.1928	0.0402
UNC	4.0444	0.3896	7.6992	0.0313
UCSF	0			

CRP (mg/L)

Table D.3.4t. Type III Sum of Squares for Change in CRP (mg/L) for Subjects with PMN (%) Less Than or Equal to the Median (57.35%) at 120 ppb Ozone Exposure

Effect	P Value
4-hr vs. 22-hr change	0.4739
Ozone exposure	0.0623
Site	0.9473

Table D.3.4u. Mixed Model for Change in CRP (mg/L) for Subjects with PMN (%) Less Than or Equal to the Median (57.35%) at 120 ppb Ozone Exposure

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	0.03149	-0.9299	0.9929	0.9470
Change between pre- and post-exposure				
4-hr change	0			
22-hr change	0.1563	-0.2843	0.5969	0.4739
Ozone exposure				
120 ppb	-0.1957	-0.7283	0.3370	0.4650
70 ppb	-0.6227	-1.1528	-0.09262	0.0221
0 ppb	0			
Site				
URMC	0.02309	-1.1435	1.1896	0.9680
UNC	-0.1531	-1.3895	1.0834	0.8017
UCSF	0			

Monocyte–Platelet Conjugate Count

Table D.3.4v. Type III Sum of Squares for Change in Monocyte–Platelet Conjugate Count for Subjects with PMN (%) Less Than or Equal to the Median (57.35%) at 120 ppb Ozone Exposure

Effect	P Value
4-hr vs. 22-hr change	0.5613
Ozone exposure	0.0820
Site	0.4266

Table D.3.4w. Mixed Model for Change in Monocyte–Platelet Conjugate Count for Subjects with PMN (%) Less Than or Equal to the Median (57.35%) at 120 ppb Ozone Exposure

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	12.3688	-3.1036	27.8411	0.1120
Change between pre- and post-exposure				
4-hr change	0			
22-hr change	-2.9236	-13.1504	7.3032	0.5613
Ozone exposure				
120 ppb	-12.0706	-24.2995	0.1582	0.0529
70 ppb	-12.1185	-24.4274	0.1904	0.0535
0 ppb	0			
Site				
URMC	-0.6771	-17.2680	15.9138	0.9336
UNC	-12.2006	-32.9949	8.5938	0.2377
UCSF	0			

MP-TFA (pg/mL)

Table D.3.4x. Type III Sum of Squares for Change in MP-TFA (pg/mL) for Subjects with PMN (%) Less Than or Equal to the Median (57.35%) at 120 ppb Ozone Exposure

Effect	P Value
4-hr vs. 22-hr change	0.9201
Ozone exposure	0.5664
Site	0.5327

Table D.3.4y. Mixed Model for Change in MP-TFA (pg/mL) for Subjects with PMN (%) Less Than or Equal to the Median (57.35%) at 120 ppb Ozone Exposure

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	0.03421	-0.04398	0.1124	0.3778
Change between pre- and post-exposure				
4-hr change	0			
22-hr change	-0.00264	-0.05595	0.05067	0.9201
Ozone exposure				
120 ppb	0.03158	-0.03211	0.09527	0.3250
70 ppb	0.004978	-0.05952	0.06947	0.8777
0 ppb	0			
Site				
URMC	-0.04522	-0.1287	0.03831	0.2769
UNC	-0.01689	-0.1066	0.07280	0.7027
UCSF	0			

Abbreviations and Other Terms

CC16	club cell protein 16
CI	confidence interval
CRP	C-reactive protein
ET-1	endothelin-1
FEV ₁	forced expiratory volume in 1 second
FMD	flow-mediated dilatation
HF	high frequency (power band 0.15–0.40 Hz)
HR	heart rate
LF	low frequency (power band 0.04–0.15 Hz)
Ln	natural logarithm
MOSES	Multicenter Ozone Study of oldEr Subjects
MP	microparticle
MP-TFA	microparticle-associated tissue factor activity
ms	millisecond
PMN	polymorphonuclear neutrophils
ppb	part per billion
RMSSD	root mean square of successive differences in normal-to-normal sinus beat intervals
SBP	systolic blood pressure
SD	standard deviation
ST	ST segment
UCSF	University of California at San Francisco
UNC	University of North Carolina
URMC	University of Rochester Medical Center