HE

Research Report 192

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.4. Analyses of Airway Inflammation and Lung Function 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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1. Descriptive Statistics: Secondary Endpoints

		0 ppb			70 ppb			120 ppb	
Outcome	N	Mean	SD	N	Mean	SD	N	Mean	SD
Ln of IL-6 (pg/mL)	77	-0.6	1.9	80	-0.4	2.0	76	-0.6	2.3
Ln of IL-8 (pg/mL)	78	4.6	1.9	80	5.0	1.5	76	4.7	2.4
Ln of TNF-α (pg/mL)	78	-2.3	2.0	80	-2.4	2.4	76	-2.2	2.2
Ln of total protein (µg/mL)	77	5.6	0.9	80	5.5	1.1	76	5.4	1.0
PMN % of total cell count	61	46.8	23.7	62	50.7	22.8	62	56.2	19.3
Ln of PMN (count/mg)	61	6.0	2.7	61	6.5	2.2	62	6.8	1.5
CC16 (ng/mL)									
Pre-exposure	85	16.4	8.1	85	16.6	8.0	84	16.5	7.6
4-hr post-exposure	85	16.7	8.1	85	17.8	7.9	84	20.5	8.8
22-hr post-exposure	82	19.1	8.6	85	20.0	9.3	82	19.8	8.9
FEV ₁ (L)									
Pre-exposure	87	2.95	0.63	87	2.95	0.62	87	2.96	0.64
15-min post-exposure	87	3.03	0.65	87	3.03	0.64	86	3.01	0.65
22-hr post-exposure	87	2.99	0.63	87	2.97	0.62	87	2.97	0.64
FVC (L)									
Pre-exposure	87	3.90	0.87	87	3.90	0.87	87	3.91	0.87
15-min post-exposure	87	3.98	0.89	87	3.97	0.89	86	3.94	0.87
22-hr post-exposure	87	3.93	0.88	87	3.90	0.85	87	3.89	0.87
FEV₁/FVC (%)									
Pre-exposure	87	75.7	4.8	87	75.8	4.9	87	76.0	4.8

Table B.4.1a. Descriptive Statistics

		0 ppb			70 ppb			120 ppb	
Outcome	N	Mean	SD	N	Mean	SD	Ν	Mean	SD
15-min post-exposure	87	76.5	4.7	87	76.6	4.7	86	76.7	4.5
22-hr post-exposure	87	76.4	4.9	87	76.4	4.4	87	76.5	4.6
FEF ₂₅₋₇₅ (L/sec)									
Pre-exposure	87	2.48	0.78	87	2.51	0.79	87	2.53	0.81
15-min post-exposure	87	2.66	0.78	87	2.68	0.84	86	2.65	0.84
22-hr post-exposure	87	2.59	0.78	87	2.58	0.78	87	2.60	0.79

	0 ppb				70 ppb		120 ppb		ppb
	N	Median	IQR	N	Median	IQR	N	Median	IQR
IL-6 (sputum) (pg/mL)	77	0.75	(0.29, 1.93)	80	0.97	(0.29, 2.37)	76	1.04	(0.48, 1.92)
IL-8 (pg/mL)	78	117.7	(55.5, 281.1)	80	165.8	(74.8, 355.9)	76	153.5	(65.5, 294.1)
TNF-α (pg/mL)	78	0.15	(0.04, 0.33)	80	0.18	(0.04, 0.49)	76	0.18	(0.05, 0.34)
Total protein (µg/mL)	77	277.2	(165.4, 529.2)	80	220.4	(132.0, 479.2)	76	242.7	(117.6, 434.4)
PMN (count/mg)	61	594.6	(253.9, 1116.8)	61	839.1	(465.6, 1690.4)	62	1138.2	(509.0, 1800.1)

Table B.4.1b. Median and IQR of Skewed Data

2. IL-6 (sputum) (pg/mL)

The following figure shows the natural logarithm of IL-6 (sputum) level at 22 hours by ozone exposure. The data come from Table B.4.1a.



Figure B.4.2. Natural logarithm of IL-6 at 22 hours by ozone exposure.

Main Analysis of Ozone Effect

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

- there were no differences in Ln of IL-6 across the ozone exposures; and
- there were differences in Ln of IL-6 across the 3 sites.

(pg/mL)	
Effect	P Value
Ozone exposure	0.6096
Site	0.0009

Table B.4.2a. Type III sum of squares for Ln of IL-6 (sputum)

(F 3/····=/				
Effect	Estimate	Lower 95% Cl	Upper 95% Cl	P Value
Intercept	0.1473	-0.5373	0.8318	0.6698
Ozone exposure				
120 ppb	0.1049	-0.4073	0.6171	0.6863
70 ppb	0.2517	-0.2508	0.7542	0.3239
0 ppb	0			
Site				
URMC	-1.6472	-2.4863	-0.8082	0.0002
UNC	-0.7885	-1.6612	0.08431	0.0760
UCSF	0			

Table B.4.2b. Mixed model for Ln of IL-6 (sputum) (pg/mL)

Analyses of Interactions

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

Table B.4.2c. Type III Sum of Squares for Ln of IL-6 (sputum) (pg/mL), Including
Ozone Exposure, by Age Interaction

Effect	P Value
Ozone exposure	0.6369
Site	0.0014
Age	0.1380
Ozone exposure by age	0.4138

Table B.4.2d. Mixed Model for Ln of IL-6 (sputum) (pg/mL), Including Ozone Exposure, by Age Interaction

		Lower	Upper	
Effect	Estimate	95% CI	95% CI	P Value
Intercept	0.1419	-0.5373	0.8211	0.6787
Ozone exposure				
120 ppb	0.1111	-0.4029	0.6250	0.6699
70 ppb	0.2423	-0.2623	0.7468	0.3442
0 ppb	0			
Site				
URMC	-1.5859	-2.4210	-0.7508	0.0003
UNC	-0.7986	-1.6628	0.06556	0.0696
UCSF	0			
Age	-0.05028	-0.1515	0.05099	0.3262
Ozone exposure by age				
120 ppb by age	-0.04876	-0.1630	0.06544	0.4001
70 ppb by age	0.02640	-0.08581	0.1386	0.6426
0 ppb by age	0			

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

Table B.4.2e. Type III Sum of Squares for Ln of IL-6 (sputum) (pg/mL), Including Ozone Exposure, by Sex Interaction

Effect	P Value	
Ozone exposure	0.5951	
Site	0.0015	
Sex	0.2989	
Ozone exposure by sex	0.4263	

Table B.4.2f. Mixed Model for Ln of IL-6 (sputum) (pg/mL), Including Ozone Exposure, by Sex Interaction

		Lower	Upper		
Effect	Estimate	95% CI	95% CI	P Value	
Intercept	0.1662	-0.6691	1.0015	0.6933	
Ozone exposure					
120 ppb	0.4840	-0.3051	1.2731	0.2274	
70 ppb	0.3399	-0.4296	1.1094	0.3841	
0 ppb	0				
Site					
URMC	-1.5942	-2.4424	-0.7460	0.0003	
UNC	-0.7122	-1.6015	0.1770	0.1149	
UCSF	0				
Sex					
Female	-0.1055	-1.0424	0.8314	0.8233	
Male	0				
Ozone exposure by sex					
120 ppb by female	-0.6568	-1.6939	0.3804	0.2127	
70 ppb by female	-0.1572	-1.1731	0.8587	0.7601	
0 ppb by female	0				
120 ppb by male	0				
70 ppb by male	0				
0 ppb by male	0				

Table B.4.2g. Type III Sum of Squares for Ln of IL-6 (sputum) (pg/mL), Including
Ozone Exposure, by GSTM1 Status Interaction

Effect	<i>P</i> Value
Ozone exposure	0.6482
Site	0.0012
GSTM1 status	0.3508
Ozone exposure by GSTM1 status	0.8720

Table B.4.2h. Mixed Model for Ln of IL-6 (sputum) (pg/mL), Including OzoneExposure, by GSTM1 Status Interaction

		Lower	Upper	
Effect	Estimate	95% CI	95% CI	P Value
Intercept	0.2052	-0.5628	0.9732	0.5965
Ozone exposure				
120 ppb	0.1528	-0.5239	0.8296	0.6560
70 ppb	0.3741	-0.2950	1.0432	0.2709
0 ppb	0			
Site				
URMC	-1.6088	-2.4498	-0.7678	0.0003
UNC	-0.7346	-1.6114	0.1421	0.0993
UCSF	0			
GSTM1 status				
Sufficient	-0.2065	-1.1380	0.7251	0.6604
Null	0			
Ozone exposure by GSTM1 status				
120 ppb by sufficient	-0.1081	-1.1551	0.9388	0.8385
70 ppb by sufficient	-0.2689	-1.2945	0.7567	0.6051
0 ppb by sufficient	0			
120 ppb by null	0			
70 ppb by null	0			
0 ppb by null	0			

3. IL-8 (pg/mL)

The following figure shows the natural logarithm of IL-8 level at 22 hours by ozone exposure The data come from Table B.4.1a.



Figure B.4.3. Natural logarithm of IL-8 at 22 hours by ozone exposure.

Main Analysis of Ozone Effect

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

- there were no differences in Ln of IL-8 across the ozone exposures; and
- there were differences in Ln of IL-8 across the 3 sites.

Table B.4.3a. Type III Sum of Squares for Ln of IL-8 (pg/mL)		
Effect	<i>P</i> Value	
Ozone exposure	0.3297	
Site	<0.0001	

		Lower	Upper	
Effect	Estimate	95% CI	95% CI	P Value
Intercept	5.4691	4.9078	6.0303	<0.0001
Ozone exposure				
120 ppb	0.02318	-0.5560	0.6024	0.9371
70 ppb	0.3849	-0.1862	0.9560	0.1849
0 ppb	0			
Site				
URMC	-1.4224	-2.0345	-0.8103	<0.0001
UNC	-1.1022	-1.7500	-0.4545	0.0011
UCSF	0			

Table B.4.3b. Mixed Model for Ln of IL-8 (pg/mL)

Analyses of Interactions

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

Table B.4.3c.	Type III Sum of Squares for Ln of IL-8 (pg/mL), Including Ozone
Exposure, by	Age Interaction

<i>P</i> Value
0.3109
<0.0001
0.7261
0.4313

Table B.4.3d. Mixed Model for Ln of IL-8 (pg/mL), Including Ozone Exposure, by Age Interaction

		Lower	Upper	
Effect	Estimate	95% CI	95% CI	P Value
Intercept	5.4726	4.9076	6.0376	<0.0001
Ozone exposure				
120 ppb	0.01067	-0.5693	0.5906	0.9710
70 ppb	0.3894	-0.1826	0.9614	0.1805
0 ppb	0			
Site				
URMC	-1.4270	-2.0487	-0.8054	<0.0001
UNC	-1.1034	-1.7571	-0.4496	0.0012
UCSF	0			
Age	-0.00371	-0.09778	0.09037	0.9377
Ozone exposure by age				
120 ppb by age	0.06142	-0.06718	0.1900	0.3467
70 ppb by age	-0.01964	-0.1466	0.1073	0.7603
0 ppb by age	0			

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

Table B.4.3e. Type III Sum of Squares for Ln of IL-8 (pg/mL), Including Ozone Exposure, by Sex Interaction

Effect	P Value	
Ozone exposure	0.3703	
Site	0.0001	
Sex	0.3014	
Ozone exposure by sex	0.7243	

Table B.4.3f. Mixed Model for Ln of IL-8 (pg/mL), Including Ozone Exposure, by Sex Interaction

		Lower	Upper	
Effect	Estimate	95% CI	95% CI	P Value
Intercept	5.7540	5.0237	6.4842	<0.0001
Ozone exposure				
120 ppb	-0.2427	-1.1433	0.6579	0.5951
70 ppb	0.1695	-0.7163	1.0553	0.7058
0 ppb	0			
Site				
URMC	-1.3743	-1.9939	-0.7547	<0.0001
UNC	-1.0361	-1.6966	-0.3756	0.0025
UCSF	0			
Sex				
Female	-0.5477	-1.4129	0.3174	0.2114
Male	0			
Ozone exposure by sex				
120 ppb by female	0.4512	-0.7275	1.6298	0.4505
70 ppb by female	0.3618	-0.7997	1.5234	0.5391
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 Ln IL-8 by GSTM1 status — Ln IL-8 increased after 120 ppb, but not 70 ppb, ozone exposure in GSTM1-sufficient subjects relative to GSTM1-null subjects.

Table B.4.3g. Type III Sum of Squares for Ln of IL-8 (pg/mL), Including Ozone Exposure, by GSTM1 Status Interaction

Effect	<i>P</i> Value
Ozone exposure	0.3170
Site	<0.0001
GSTM1 status	0.8329
Ozone exposure by GSTM1 status	0.0313

Table B.4.3h. Mixed Model for Ln of IL-8 (pg/mL), Including Ozone Exposure, by GSTM1 Status Interaction

		Lower	Upper	
Effect	Estimate	95% CI	95% CI	P Value
Intercept	5.7111	5.0583	6.3640	<0.0001
Ozone exposure				
120 ppb	-0.6116	-1.3618	0.1385	0.1092
70 ppb	0.2445	-0.5003	0.9893	0.5175
0 ppb	0			
Site				
URMC	-1.4305	-2.0507	-0.8102	<0.0001
UNC	-1.1301	-1.7870	-0.4731	0.0010
UCSF	0			
GSTM1 status				
Sufficient	-0.5620	-1.4122	0.2882	0.1921
Null	0			
Ozone exposure by GSTM1 status				
120 ppb by sufficient	1.4903	0.3356	2.6449	0.0118
70 ppb by sufficient	0.3631	-0.7740	1.5002	0.5289
0 ppb by sufficient	0			
120 ppb by null	0			
70 ppb by null	0			
0 ppb by null	0			

4. TNF-α (pg/mL)

The following figure shows the natural logarithm of TNF- α level at 22 hours by ozone exposure. The data come from Table B.4.1a.



Figure B.4.4. Natural logarithm of TNF- α at 22 hours by ozone exposure.

Main Analysis of Ozone Effect

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

- there were no differences in Ln of TNF- α across the ozone exposures; and
- there were marginally significant differences in Ln of TNF-α across the 3 sites.

Table B.4.4a. Type III Sum of Squares for Ln TNF- α (pg/mL)

Effect	P Value	
Ozone exposure	0.9264	
Site	0.0101	

Table B.4.4b. Mixed Model for Ln TNF- α (pg/mL)

		Lower	Upper	
Effect	Estimate	95% CI	95% CI	P Value
Intercept	-1.4532	-2.2103	-0.6962	0.0003
Ozone exposure				
120 ppb	0.08766	-0.3934	0.5687	0.7193
70 ppb	0.01224	-0.4589	0.4834	0.9591
0 ppb	0			
Site				
URMC	-1.2863	-2.2424	-0.3301	0.0090
UNC	-1.3759	-2.3670	-0.3848	0.0071
UCSF	0			

Analyses of Interactions

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

Table B.4.4c. Type III Sum of Squares for Ln TNF- α (pg/mL), Including Ozone Exposure, by Age Interaction

Effect	<i>P</i> Value
Ozone exposure	0.9127
Site	0.0106
Age	0.0591
Ozone exposure by age	0.6807

Table B.4.4d. Mixed Model for Ln TNF- α (pg/mL), Including Ozone Exposure, by Age Interaction

		Lower	Upper	
Effect	Estimate	95% CI	95% CI	<i>P</i> Value
Intercept	-1.4659	-2.2123	-0.7195	0.0002
Ozone exposure				
120 ppb	0.09670	-0.3873	0.5807	0.6935
70 ppb	0.01418	-0.4604	0.4887	0.9530
0 ppb	0			
Site				
URMC	-1.1937	-2.1391	-0.2483	0.0140
UNC	-1.3978	-2.3725	-0.4230	0.0055
UCSF	0			
Age	-0.06322	-0.1695	0.04303	0.2399
Ozone exposure by age				
120 ppb by age	-0.04646	-0.1539	0.06096	0.3940
70 ppb by age	-0.01349	-0.1189	0.09191	0.8007
0 ppb by age	0			

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

Table B.4.4e. Type III Sum of Squares for Ln TNF- α (pg/mL), Including Ozone Exposure, by Sex Interaction

Effect	P Value	
Ozone exposure	0.8383	
Site	0.0209	
Sex	0.2486	
Ozone exposure by sex	0.1485	

Table B.4.4f. Mixed Model for Ln TNF- α (pg/mL), Including Ozone Exposure, by Sex Interaction

		Lower	Upper	
Effect	Estimate	95% CI	95% CI	P Value
Intercept	-1.1048	-2.0096	-0.2001	0.0173
Ozone exposure				
120 ppb	0.1358	-0.6024	0.8739	0.7167
70 ppb	-0.4305	-1.1483	0.2874	0.2378
0 ppb	0			
Site				
URMC	-1.2074	-2.1736	-0.2413	0.0150
UNC	-1.2668	-2.2757	-0.2578	0.0145
UCSF	0			
Sex				
Female	-0.7025	-1.6905	0.2855	0.1610
Male	0			
Ozone exposure by sex				
120 ppb by female	-0.08505	-1.0527	0.8827	0.8623
70 ppb by female	0.7654	-0.1806	1.7114	0.1120
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.4.4g. Type III Sum of Squares for Ln TNF-α (pg/mL), Including Ozone Exposure, by GSTM1 Status Interaction

Effect	P Value
Ozone exposure	0.8726
Site	0.0116
GSTM1 status	0.7824
Ozone exposure by GSTM1 status	0.6117

Table B.4.4h. Mixed Model for Ln TNF- α (pg/mL), Including Ozone Exposure, by GSTM1 Status Interaction

		Lower	Upper	
Effect	Estimate	95% CI	95% CI	P Value
Intercept	-1.3010	-2.1456	-0.4564	0.0030
Ozone exposure				
120 ppb	-0.1154	-0.7515	0.5207	0.7205
70 ppb	-0.1186	-0.7465	0.5092	0.7094
0 ppb	0			
Site				
URMC	-1.2763	-2.2428	-0.3097	0.0103
UNC	-1.3771	-2.3805	-0.3737	0.0078
UCSF	0			
GSTM1 status				
Sufficient	-0.3788	-1.3621	0.6045	0.4456
Null	0			
Ozone exposure by GSTM1 status				
120 ppb by sufficient	0.4829	-0.4943	1.4601	0.3304
70 ppb by sufficient	0.3167	-0.6389	1.2724	0.5134
0 ppb by sufficient	0			
120 ppb by null	0			
70 ppb by null	0			
0 ppb by null	0			

5. Total Protein (µg/mL)

The following figure shows the natural logarithm of total protein at 22 hours by ozone exposure. The data come from Table B.4.1a.





Main Analysis of Ozone Effect

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

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

Table B.4.5a. Type III Sum of Squares for Ln of Total Protein				
Effect	P Value			
Ozone exposure	0.2753			
Site	<0.0001			

Table B.4.5a.	Type III S	um of Sa	uares for L	n of Total P	Protein

		Lower	Upper	
Effect	Estimate	95% CI	95% CI	P Value
Intercept	6.1096	5.8117	6.4075	<0.0001
Ozone exposure				
120 ppb	-0.2240	-0.4996	0.05152	0.1102
70 ppb	-0.09477	-0.3662	0.1767	0.4913
0 ppb	0			
Site				
URMC	-0.7011	-1.0428	-0.3594	0.0001
UNC	-0.7673	-1.1266	-0.4079	<0.0001
UCSF	0			

Table B.4.5b. Mixed Model for Ln of Total Protein (µg/mL)

Analyses of Interactions

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

Table B.4.5c. Type III Sum of Squares for Ln of Total Protein (µg/mL), Including Ozone Exposure, by Age Interaction

Effect	P Value
Ozone exposure	0.2827
Site	<0.0001
Age	0.9892
Ozone exposure by age	0.4213

Table B.4.5d. Mixed Model for Ln of Total Protein (µg/mL), Including Ozone Exposure, by Age Interaction

		Lower	Upper	
Effect	Estimate	95% CI	95% CI	P Value
Intercept	6.1106	5.8109	6.4103	<0.0001
Ozone exposure				
120 ppb	-0.2227	-0.4989	0.05346	0.1131
70 ppb	-0.1004	-0.3724	0.1715	0.4666
0 ppb	0			
Site				
URMC	-0.7007	-1.0470	-0.3544	0.0001
UNC	-0.7636	-1.1257	-0.4015	<0.0001
UCSF	0			
Age	-0.00888	-0.05673	0.03896	0.7128
Ozone exposure by age				
120 ppb by age	-0.00530	-0.06638	0.05579	0.8642
70 ppb by age	0.03129	-0.02843	0.09102	0.3021
0 ppb by age	0			

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

Table B.4.5e. Type III Sum of Squares for Ln of Total Protein (µg/mL), Including Ozone Exposure, by Sex Interaction

Effect	<i>P</i> Value	
Ozone exposure	0.2673	
Site	0.0001	
Sex	0.2605	
Ozone exposure by sex	0.9329	

Table B.4.5f. Mixed Model for Ln of Total Protein (μ g/mL), Including Ozone Exposure, by Sex Interaction

		Lower	Upper	
Effect	Estimate	95% CI	95% CI	P Value
Intercept	6.2194	5.8426	6.5962	<0.0001
Ozone exposure				
120 ppb	-0.2696	-0.6979	0.1587	0.2154
70 ppb	-0.1544	-0.5743	0.2655	0.4686
0 ppb	0			
Site				
URMC	-0.6732	-1.0179	-0.3285	0.0002
UNC	-0.7282	-1.0935	-0.3628	0.0002
UCSF	0			
Sex				
Female	-0.2257	-0.6649	0.2134	0.3094
Male	0			
Ozone exposure by sex				
120 ppb by female	0.07614	-0.4857	0.6380	0.7892
70 ppb by female	0.1005	-0.4524	0.6533	0.7199
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.4.5g. Type III Sum of Squares for Ln of Total Protein (µg/mL), Including Ozone Exposure, by GSTM1 Status Interaction

Effect	P Value	
Ozone exposure	0.3123	
Site	<0.0001	
GSTM1 status	0.6827	
Ozone exposure by GSTM1 status	0.8746	

Table B.4.5h. Mixed Model for Ln of Total Protein (µg/mL), Including Ozone Exposure, by GSTM1 Status Interaction

		Lower	Upper	
Effect	Estimate	95% CI	95% CI	P Value
Intercept	6.1356	5.7907	6.4805	<0.0001
Ozone exposure				
120 ppb	-0.2634	-0.6290	0.1023	0.1567
70 ppb	-0.07170	-0.4325	0.2891	0.6950
0 ppb	0			
Site				
URMC	-0.6934	-1.0384	-0.3484	0.0001
UNC	-0.7603	-1.1234	-0.3973	<0.0001
UCSF	0			
GSTM1 status				
Sufficient	-0.07429	-0.5112	0.3626	0.7360
Null	0			
Ozone exposure by GSTM1 status				
120 ppb by sufficient	0.09302	-0.4684	0.6544	0.7438
70 ppb by sufficient	-0.04962	-0.6025	0.5032	0.8594
0 ppb by sufficient	0			
120 ppb by null	0			
70 ppb by null	0			
0 ppb by null	0			

6. PMN % of Total Cell Count



The following figure shows PMN % at 22 hours by ozone exposure. The data come from Table B.4.1a.

Figure B.4.6. PMN % of total cell count at 22 hours by ozone exposure.

Main Analysis of Ozone Effect

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

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

Table B.4.6a. Type III Sum of Squares for PMN % of Total Cell Count			
Effect	<i>P</i> Value		
Ozone exposure	0.0119		
Site	0.0238		

Table B.4.6b. Mixed Model for PMIN % of Total Cell Could	able B.4.6b	6b. Mixed Mode	I for PMN	% of Total	Cell Coun
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		Lower	Upper	
Effect	Estimate	95% CI	95% CI	P Value
Intercept	55.0711	46.7438	63.3984	<0.0001
Ozone exposure				
120 ppb	8.1592	2.8396	13.4787	0.0030
70 ppb	4.0670	-1.2672	9.4012	0.1336
0 ppb	0			
Site				
URMC	-14.6802	-25.1135	-4.2469	0.0064
UNC	-8.0021	-18.5182	2.5141	0.1338
UCSF	0			

Analyses of Interactions

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

Table B.4.6c. Type III Sum of Squares for PMN % of Total, Including Ozone Exposure, by Age Interaction

Effect	P Value
Ozone exposure	0.0130
Site	0.0337
Age	0.3861
Ozone exposure by age	0.4822

Table B.4.6d. Mixed Model for PMN % of Total, Including Ozone Exposure,by Age Interaction

		Lower	Upper	
Effect	Estimate	95% CI	95% CI	P Value
Intercept	55.0852	46.7022	63.4683	<0.0001
Ozone exposure				
120 ppb	8.0739	2.7435	13.4043	0.0033
70 ppb	3.6087	-1.7974	9.0148	0.1885
0 ppb	0			
Site				
URMC	-14.0632	-24.5977	-3.5286	0.0096
UNC	-8.0627	-18.6717	2.5463	0.1342
UCSF	0			
Age	-0.6705	-1.8197	0.4787	0.2488
Ozone exposure by age				
120 ppb by age	0.1020	-1.0455	1.2495	0.8604
70 ppb by age	0.6840	-0.5046	1.8726	0.2564
0 ppb by age	0			

Table B.4.6e. Type III Sum	of Squares for PMIN % of 101	ai, including Ozone Exposure
by Sex Interaction		
Effect	P Value	
Ozone exposure	0.0264	

Table B.4.6e. Type III Sum of Squares for PMN % of Total, Including Ozone Expo	sure,
by Sex Interaction	

		• •
Ozone exposure by sex	0.3989	
Sex	0.9205	
Site	0.0249	

Table B.4.6f. Mixed Model for PMN % of Total, Including Ozone Exposure, by Sex Interaction

		Lower	Upper	
Effect	Estimate	95% CI	95% CI	P Value
Intercept	56.4312	46.1884	66.6740	<0.0001
Ozone exposure				
120 ppb	4.5967	-3.9322	13.1256	0.2876
70 ppb	4.8886	-4.1480	13.9252	0.2858
0 ppb	0			
Site				
URMC	-14.8214	-25.4159	-4.2268	0.0067
UNC	-7.9466	-18.7064	2.8132	0.1454
UCSF	0			
Sex				
Female	-2.0509	-13.0394	8.9376	0.7110
Male	0			
Ozone exposure by sex				
120 ppb by female	5.8965	-5.0161	16.8091	0.2864
70 ppb by female	-1.0846	-12.2889	10.1197	0.8481
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.4.6g. Type III Sum of	Squares for PMN % of	Total, Including C	zone Exposure,
by GSTM1 Status Interaction	-	_	

Effect	<i>P</i> Value
Ozone exposure	0.0173
Site	0.0287
GSTM1 status	0.6623
Ozone exposure by GSTM1 status	0.4481

		Lower	Upper	
Effect	Estimate	95% CI	95% CI	P Value
Intercept	54.0363	44.6936	63.3791	<0.0001
Ozone exposure				
120 ppb	9.8619	2.7657	16.9581	0.0069
70 ppb	6.9243	-0.05231	13.9009	0.0517
0 ppb	0			
Site				
URMC	-14.3614	-24.8459	-3.8769	0.0079
UNC	-7.4363	-18.0791	3.2065	0.1680
UCSF	0			
GSTM1 status				
Sufficient	1.7369	-9.0287	12.5025	0.7488
Null	0			
Ozone exposure by GSTM1 status				
120 ppb by sufficient	-3.9925	-14.7486	6.7635	0.4633
70 ppb by sufficient	-6.9573	-17.8453	3.9308	0.2079
0 ppb by sufficient	0			
120 ppb by null	0			
70 ppb by null	0			
0 ppb by null	0			

 Table B.4.6h. Mixed Model for PMN % of Total, Including Ozone Exposure, by GSTM1

 Status Interaction

7. PMN (count/mg)

The following figure shows natural log of PMN (count/mg) at 22 hours by ozone exposure. The data come from Table B.4.1a.



Figure B.4.7. Natural log of PMN at 22 hours by ozone exposure

Main Analysis of Ozone Effect

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

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

Table B.4.7a. Type III Sum of Squares for Ln of PMIN (count/mg)			
Effect	<i>P</i> Value		
Ozone exposure	0.1600		
Site	0.0070		

	Table B.4.7a. T	vpe III Sum of	Squares for	Ln of PMN	(count/mg)
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	\ <u></u>			
Fffect	Fstimate	Lower 95% CI	Upper 95% CI	P Value
	Lotiniato	007001		
Intercept	6.8423	6.0743	7.6103	<0.0001
Ozone exposure				
120 ppb	0.6829	-0.03173	1.3976	0.0609
70 ppb	0.4620	-0.2553	1.1794	0.2044
0 ppb	0			
Site				
URMC	-1.3018	-2.1461	-0.4575	0.0030
UNC	-1.0897	-1.9370	-0.2425	0.0124
UCSF	0			

Table B.4.7b. Mixed Model for Ln of PMN (count/mg)

Analyses of Interactions

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

Table B.4.7c. Type III Sum of Squares for Ln of PMN (count/mg), Including Ozone Exposure, by Age Interaction

Effect	<i>P</i> Value	
Ozone exposure	0.1814	
Site	0.0082	
Age	0.6809	
Ozone exposure by age	0.7628	

Table B.4.7d. Mixed Model for Ln of PMN (count/mg), Including Ozone Exposure, by Age Interaction

		Lower	Upper	
Effect	Estimate	95% CI	95% CI	P Value
Intercept	6.8542	6.0791	7.6293	<0.0001
Ozone exposure				
120 ppb	0.6695	-0.05101	1.3900	0.0682
70 ppb	0.4270	-0.3061	1.1602	0.2507
0 ppb	0			
Site				
URMC	-1.2825	-2.1348	-0.4301	0.0037
UNC	-1.0965	-1.9537	-0.2393	0.0129
UCSF	0			
Age	-0.04547	-0.1628	0.07186	0.4425
Ozone exposure by age				
120 ppb by age	0.02895	-0.1254	0.1833	0.7107
70 ppb by age	0.06022	-0.1020	0.2224	0.4631
0 ppb by age	0			

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

Table B.4.7e. Type III Sum of Squares for Ln of PMN (count/mg), Including Ozone Exposure, by Sex Interaction

Effect	<i>P</i> Value	
Ozone exposure	0.1641	
Site	0.0089	
Sex	0.9733	
Ozone exposure by sex	0.7982	

Table B.4.7f. Mixed Model for Ln of PMN (count/mg), Including Ozone Exposure, by Sex Interaction

		Lower	Upper	
Effect	Estimate	95% CI	95% CI	P Value
Intercept	6.7724	5.7649	7.7799	<0.0001
Ozone exposure				
120 ppb	0.6634	-0.4790	1.8057	0.2521
70 ppb	0.7343	-0.4712	1.9397	0.2298
0 ppb	0			
Site				
URMC	-1.3045	-2.1674	-0.4416	0.0035
UNC	-1.0905	-1.9642	-0.2168	0.0151
UCSF	0			
Sex				
Female	0.1137	-1.0113	1.2388	0.8410
Male	0			
Ozone exposure by sex				
120 ppb by female	0.04089	-1.4257	1.5074	0.9560
70 ppb by female	-0.4185	-1.9216	1.0845	0.5820
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.4.7g. Type III Sum of Squares for Ln of PMN (count/mg), Including Ozone Exposure, by GSTM1 Status Interaction

Effect	<i>P</i> Value
Ozone exposure	0.2487
Site	0.0073
GSTM1 status	0.2861
Ozone exposure by GSTM1 status	0.2540

Table B.4.7h. Mixed Model for Ln of PMN (count/mg), Including Ozone Exposure, by GSTM1 Status Interaction

		Lower	Upper	
Effect	Estimate	95% CI	95% CI	P Value
Intercept	6.4221	5.5398	7.3045	<0.0001
Ozone exposure				
120 ppb	0.9558	0.006591	1.9050	0.0485
70 ppb	0.9606	0.03015	1.8911	0.0432
0 ppb	0			
Site				
URMC	-1.2840	-2.1214	-0.4466	0.0031
UNC	-1.0879	-1.9341	-0.2418	0.0124
UCSF	0			
GSTM1 status				
Sufficient	1.0098	-0.08003	2.0996	0.0689
Null	0			
Ozone exposure by GSTM1 status				
120 ppb by sufficient	-0.6890	-2.1311	0.7530	0.3455
70 ppb by sufficient	-1.2291	-2.6962	0.2381	0.0997
0 ppb by sufficient	0			
120 ppb by null	0			
70 ppb by null	0			
0 ppb by null	0			

8. CC16 (ng/mL)

The following figure shows the change from pre- to post-exposure in club cell protein 16 (CC16) (ng/mL) at 4 and 22 hours. The data come from Table B.4.1a.



Figure B.4.8. Change in CC16t 4 and 22 hours post-exposure at each ozone exposure

Main Analysis of Ozone Effect

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

- there were differences between the 4-hour and 22-hour post-exposure CC16;
- there were differences in CC16 across the ozone exposures; and
- there were no differences in CC16 across the 3 sites.

Table D.4.0a. Type III Sulli Ol	Squares for change in CC to (ng/mic)
Effect	P Value
4-hr vs. 22-hr change	0.0004
Ozone exposure	0.0002
Site	0.1218

Table B.4.8a. Type III Sum of Squares for Change in CC16 (ng/mL)

v		Lower	Upper	
Effect	Estimate	95% CI	95% CI	P Value
Intercept	2.0354	0.7502	3.3207	0.0023
Change between pre- and post-exposure				
4-hr change	-1.4000	-2.1519	-0.6482	0.0004
22-hr change	0			
Ozone exposure				
120 ppb	1.9772	1.0563	2.8981	<0.0001
70 ppb	0.6890	-0.2252	1.6033	0.1386
0 ppb	0			
Site				
URMC	-0.2802	-1.7740	1.2136	0.7101
UNC	1.1865	-0.3531	2.7260	0.1291
UCSF	0			

Table B.4.8b. Mixed model for change in CC16 (ng/mL)

Analyses of Interactions

As we can see from the tables below, there was a marginally significant difference in the ozone effect on CC16 by age — an increase in age was associated with an increase from pre- to post-exposure in CC16 when comparing 70 ppb, but not 120 ppb, versus 0 ppb ozone exposure.

Table B.4.8c. Type III Sum of Squares for Change in CC16 (ng/mL), Including Ozone Exposure, by Age Interaction

Effect	P Value	
Ozone exposure	0.0001	
4-hr vs. 22-hr change	0.0003	
Site	0.1391	
Age	0.5399	
Ozone exposure by age	0.0365	

		Lower	Upper	
Effect	Estimate	95% CI	95% CI	P Value
Intercept	2.0017	0.7163	3.2871	0.0027
4-hr change	-1.4019	-2.1499	-0.6539	0.0003
22-hr change	0			
Ozone exposure				
120 ppb	1.9936	1.0767	2.9105	<0.0001
70 ppb	0.7629	-0.1484	1.6743	0.1002
0 ppb	0			
Site				
URMC	-0.2116	-1.7166	1.2935	0.7805
UNC	1.1971	-0.3448	2.7390	0.1264
UCSF	0			
Age	0.08550	-0.09490	0.2659	0.3486
Ozone exposure by age				
120 ppb by age	-0.1205	-0.3212	0.08014	0.2384
70 ppb by age	-0.2627	-0.4628	-0.06251	0.0102
0 ppb by age	0			

Table B.4.8d. Mixed Model for Change in CC16 (ng/mL), Including Ozone Exposure, by Age Interaction

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

Table B.4.8e. Type III Sum of Squares for Change in CC16 (ng/m	L), Including Ozone
Exposure, by Sex Interaction	

Effect	P Value
Ozone exposure	0.0002
4-hr vs. 22-hr change	0.0004
Site	0.1100
Sex	0.4883
Ozone exposure by sex	0.6940

		Lower	Upper	
Effect	Estimate	95% CI	95% CI	P Value
Intercept	2.4700	0.9223	4.0177	0.0021
4-hr change	-1.3965	-2.1493	-0.6437	0.0004
22-hr change	0			
Ozone exposure				
120 ppb	1.7549	0.3389	3.1708	0.0155
70 ppb	0.2173	-1.2118	1.6465	0.7644
0 ppb	0			
Site				
URMC	-0.2142	-1.7294	1.3010	0.7793
UNC	1.2794	-0.2911	2.8500	0.1090
UCSF	0			
Sex				
Female	-0.8413	-2.5091	0.8265	0.3186
Male	0			
Ozone exposure by sex				
120 ppb by female	0.3849	-1.4810	2.2508	0.6843
70 ppb by female	0.8063	-1.0551	2.6678	0.3936
0 ppb by female	0			
120 ppb by male	0			
70 ppb by male	0			
0 ppb by male	0			

Table B.4.8f. Mixed Model for Change in CC16 (ng/mL), Including Ozone Exposure, by Sex Interaction

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

Table B.4.8g. Type III Sum of Squares for	Change in C	C16 (ng/mL),	Including (Ozone
Exposure, by GSTM1 Status Interaction				

Effect	P Value	
Ozone exposure	0.0002	
4-hr vs. 22-hr change	0.0004	
Site	0.1231	
GSTM1 status	0.3666	
Ozone exposure by GSTM1 status	0.4695	

		Lower	Upper	
Effect	Estimate	95% CI	95% CI	P Value
Intercept	2.1219	0.6947	3.5491	0.0040
4-hr change	-1.4000	-2.1523	-0.6477	0.0004
22-hr change	0			
Ozone exposure				
120 ppb	1.9176	0.7148	3.1204	0.0020
70 ppb	1.0793	-0.1199	2.2785	0.0774
0 ppb	0			
Site				
URMC	-0.2047	-1.7081	1.2987	0.7872
UNC	1.2361	-0.3087	2.7808	0.1153
UCSF	0			
GSTM1 status				
Sufficient	-0.3077	-1.9605	1.3451	0.7121
Null	0			
Ozone exposure by GSTM1 status				
120 ppb by sufficient	0.1406	-1.7309	2.0121	0.8823
70 ppb by sufficient	-0.9226	-2.7777	0.9325	0.3275
0 ppb by sufficient	0			
120 ppb by null	0			
70 ppb by null	0			
0 ppb by null	0			

Table B.4.8h. Mixed Model for Change in CC16 (ng/mL), Including Ozone Exposure,by GSTM1 Status Interaction

As we can see from the tables below, there is an interaction between ozone and time after 120 ppb ozone, but not 70 ppb, ozone exposure, suggesting that the ozone effect is different at 22 hours relative to 4 hours after exposure.

Table B.4.8i. Type III Sum of Squares for Change in CC16 (ng/mL), Including OzoneExposure, by Time Interaction

Effect	P Value	
4-hr vs. 22-hr change	0.0003	
Ozone exposure	0.0001	
Site	0.1201	
Ozone exposure by time	0.0002	

		Lower	Upper	
Effect	Estimate	95% CI	95% CI	P Value
Intercept	-0.03838	-1.4165	1.3397	0.9560
Change between post- and pre-exposure				
4-hr change	0			
22-hr change	2.7718	1.4904	4.0531	<.0001
Ozone exposure				
120 ppb	3.7471	2.4812	5.0130	<.0001
70 ppb	0.9540	-0.3076	2.2155	0.1373
0 ppb	0			
Site				
URMC	-0.2823	-1.7762	1.2117	0.7081
UNC	1.1896	-0.3499	2.7291	0.1281
UCSF	0			
Ozone exposure by time (change at 4 hr				
vs. 22 hr)				
120 ppb	-3.5918	-5.3936	-1.7899	0.0001
70 ppb	-0.5507	-2.3411	1.2398	0.5445
0 ppb	0			

Table B.4.8j. Mixed Model* for Change in CC16 (ng/mL), Including Ozone Exposure, by Time Interaction

* Time, ozone exposure, and site treated as fixed effects, and subject treated as a random effect. Pre-exposure measurement taken the day before.

9. FEV₁ (L)

The following figure shows the change from pre- to post-exposure in FEV_1 (L) at 15 minutes and 22 hours. The data come from Table B.4.1a.



Figure B.4.9. Change in \mbox{FeV}_1 at 15 minutes and 22 hours post-exposure at each ozone exposure

Main Analysis of Ozone Effect

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

- there were differences between the 15-minute post-exposure and 22-hour postexposure FEV₁;
- there were differences in FEV₁ across the ozone exposures; and
- there was no difference in FEV₁ across the 3 sites.

Table 9 B.4.a. Type III Sum of Squares for Change in FEV₁ (L)

P Value	
<0.0001	
0.0027	
0.3830	
	<i>P</i> Value <0.0001 0.0027 0.3830

Table 9 B.4.b. Mixed Model for Change from in FEV₁(L)

		Lower	Upper	
Effect	Estimate	95% CI	95% CI	P Value
Intercept	0.05148	0.02640	0.07657	0.0001
Change between pre- and post-exposure				
15-min change	0.05124	0.03611	0.06637	<0.0001
22-hr change	0			
Ozone exposure				
120 ppb	-0.03256	-0.05097	-0.01415	0.0006
70 ppb	-0.01471	-0.03309	0.003667	0.1159
0 ppb	0			
Site				
URMC	-0.01965	-0.04846	0.009153	0.1785
UNC	-0.01479	-0.04425	0.01466	0.3207
UCSF	0			

Analyses of Interactions

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

Table 9 B.4.c. Type III Sum of Squares for Change in FEV1 (L), Including OzoneExposure, by Age Interaction

Effect	<i>P</i> Value
Ozone exposure	0.0034
15-min vs. 22-hr change	< 0.0001
Site	0.4574
Age	0.0519
Ozone exposure by age	0.6979

Table B.4.9d. Mixed Model for Change in FEV_1 (L), Including Ozone Exposure, by Age Interaction

		Lower	Upper	
Effect	Estimate	95% CI	95% CI	P Value
Intercept	0.05088	0.02607	0.07570	0.0001
15-min change	0.05128	0.03612	0.06643	<0.0001
22-hr change	0			
Ozone exposure				
120 ppb	-0.03203	-0.05050	-0.01355	0.0008
70 ppb	-0.01433	-0.03277	0.004117	0.1271
0 ppb	0			
Site				
URMC	-0.01651	-0.04502	0.01200	0.2528
UNC	-0.01515	-0.04413	0.01382	0.3012
UCSF	0			
Age	-0.00156	-0.00506	0.001942	0.3780
Ozone exposure by age				
120 ppb by age	-0.00166	-0.00573	0.002407	0.4225
70 ppb by age	-0.00132	-0.00539	0.002743	0.5232
0 ppb by age	0			

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

Table B.4.9e. Type III Sum of Squares for Change in FEV_1 (L), Including Ozone Exposure, by Sex Interaction

Effect	<i>P</i> Value	
Ozone exposure	0.0031	
15-min vs. 22-hr change	<0.0001	
Site	0.5480	
Sex	0.0562	
Ozone exposure by sex	0.7771	

Table B.4.9f. Mixed Model for Change in FEV₁ (L), Including Ozone Exposure, by Sex Interaction

		Lower	Upper	
Effect	Estimate	95% CI	95% CI	P Value
Intercept	0.06067	0.03054	0.09080	0.0001
15-min change	0.05126	0.03610	0.06641	<0.0001
22-hr change	0			
Ozone exposure				
120 ppb	-0.03403	-0.06318	-0.00489	0.0224
70 ppb	-0.00857	-0.03760	0.02046	0.5608
0 ppb	0			
Site				
URMC	-0.01583	-0.04446	0.01279	0.2745
UNC	-0.00948	-0.03898	0.02001	0.5243
UCSF	0			
Sex				
Female	-0.02069	-0.05307	0.01168	0.2072
Male	0			
Ozone exposure by sex				
120 ppb by female	0.002496	-0.03514	0.04014	0.8960
70 ppb by female	-0.01027	-0.04782	0.02727	0.5898
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.4.9g. Type III Sum of Squares for Change in FEV_1 (L), Including Ozone Exposure, by GSTM1 Status Interaction

Effect	<i>P</i> Value
Ozone exposure	0.0036
15-min vs. 22-hr change	<0.0001
Site	0.3422
GSTM1 status	0.3884
Ozone exposure by GSTM1 status	0.9753

Table B.4.9h. Mixed Model for Change in FEV₁ (L), Including Ozone Exposure, by GSTM1 Status Interaction

		Lower	Upper	
Effect	Estimate	95% CI	95% CI	P Value
Intercept	0.04885	0.02084	0.07686	0.0008
15-min change	0.05126	0.03610	0.06642	<0.0001
22-hr change	0			
Ozone exposure				
120 ppb	-0.03430	-0.05860	-0.01000	0.0059
70 ppb	-0.01590	-0.04020	0.008401	0.1982
0 ppb	0			
Site				
URMC	-0.02091	-0.04991	0.008095	0.1554
UNC	-0.01586	-0.04546	0.01375	0.2899
UCSF	0			
GSTM1 status				
Sufficient	0.008078	-0.02413	0.04029	0.6192
Null	0			
Ozone exposure by GSTM1 status				
120 ppb by sufficient	0.004147	-0.03320	0.04149	0.8268
70 ppb by sufficient	0.002792	-0.03447	0.04005	0.8826
0 ppb by sufficient	0			
120 ppb by null	0			
70 ppb by null	0			
0 ppb by null	0			

As we can see from the tables below, there is no interaction between ozone and time, suggesting that the ozone effect is not different at 15 minutes and 22 hours.

Table B.4.9.i. Type III Sum of Squares for change in FEV₁, Including Ozone Exposure, by Time Interaction

Effect	P Value	
15-min vs. 22-hr change	<0.0001	
Ozone exposure	0.0028	
Site	0.3837	
Ozone exposure by time	0.5886	

Table B.4.9j. Mixed Model* for Change in FEV₁, Including Ozone Exposure, by Time Interaction

		Lower	Upper	
Effect	Estimate	95% CI	95% CI	<i>P</i> Value
Intercept	0.09721	0.06994	0.1245	<0.0001
Change between post- and pre-exposure				
15-min change	0			
22-hr change	-0.04023	-0.06644	-0.01402	0.0030
Ozone exposure				
120 ppb	-0.02369	-0.04980	0.002409	0.0749
70 ppb	-0.00701	-0.03303	0.01901	0.5955
0 ppb	0			
Site				
URMC	-0.01963	-0.04845	0.009177	0.1790
UNC	-0.01479	-0.04425	0.01466	0.3208
UCSF	0			
Ozone exposure by time (change at 15 min				
vs. 22 hr)				
120 ppb	-0.01768	-0.05454	0.01917	0.3449
70 ppb	-0.01540	-0.05220	0.02140	0.4098
0 ppb	0			
* Time, ozone exposure, and site treated as fi	xed effects, and	subject treate	d as a randon	n effect.

* Time, ozone exposure, and site treated as fixed effects, and subject treated as a random effect Pre-exposure measurement taken 10 minutes prior to exposure.

10. FVC (L)

The following figure shows the change from pre- to post-exposure in FVC (L) at 15 minutes and 22 hours. The data come from Table B.4.1a.



Figure B.4.10. Change in FVC at 15 minutes and 22 hours post-exposure at each ozone exposure.

Main Analysis of Ozone Effect

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

- there were differences between the 15-min post-exposure and 22-hour postexposure FVC;
- there were marginally significant differences in FVC across the ozone exposures; and
- there was no difference in FVC across the 3 sites.

Table B.4.10a. Type III Sum of Squares for Change in FVC (L)		
Effect	P Value	
15-min vs. 22-hr change	<0.0001	
Ozone exposure	0.0106	
Site	0.0580	

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Table B.4.10b. Mixed Model for Change in FVC (L)

		Lower	Upper	
Effect	Estimate	95% CI	95% CI	P Value
Intercept	0.03287	0.000637	0.06510	0.0457
Change between pre- and post-exposure				
15-min change	0.06138	0.04163	0.08113	<0.0001
22-hr change	0			
Ozone exposure				
120 ppb	-0.03718	-0.06121	-0.01316	0.0026
70 ppb	-0.01925	-0.04324	0.004738	0.1150
0 ppb	0			
Site				
URMC	-0.00271	-0.03950	0.03407	0.8837
UNC	-0.04009	-0.07770	-0.00248	0.0370
UCSF	0			

Analyses of Interactions

As we can see from the tables below,

- there was a marginally significant age effect on the pre- to post-exposure change in FVC, independent of ozone; and
- the ozone effect did not differ by age.

Table B.4.10c. Type III Sum of S	Squares for	Change in	FVC (L), I	Including	Ozone
Exposure, by Age Interaction					

Effect	<i>P</i> Value
Ozone exposure	0.0115
15-min vs. 22-hr change	<0.0001
Site	0.0357
Age	0.0434
Ozone exposure by age	0.6591

		Lower	Upper	
Effect	Estimate	95% CI	95% CI	P Value
Intercept	0.03220	0.000359	0.06404	0.0475
15-min change	0.06140	0.04162	0.08117	<0.0001
22-hr change	0			
Ozone exposure				
120 ppb	-0.03699	-0.06110	-0.01287	0.0028
70 ppb	-0.01856	-0.04263	0.005511	0.1299
0 ppb	0			
Site				
URMC	0.001420	-0.03492	0.03776	0.9382
UNC	-0.04056	-0.07749	-0.00364	0.0317
UCSF	0			
Age	-0.00240	-0.00691	0.002114	0.2934
Ozone exposure by age				
120 ppb by age	-0.00059	-0.00590	0.004720	0.8269
70 ppb by age	-0.00237	-0.00767	0.002936	0.3806
0 ppb by age	0			

Table B.4.10d. Mixed Model for Change in FVC (L), Including Ozone Exposure, by Age Interaction

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

Table B.4.10e. Type III Sum of Squares for Change in FVC (L), Including OzoneExposure, by Sex Interaction

Effect	<i>P</i> Value
Ozone exposure	0.0057
15-min vs. 22-hr change	<0.0001
Site	0.0755
Sex	0.5393
Ozone exposure by sex	0.3790

		Lower	Upper	
Effect	Estimate	95% CI	95% CI	P Value
Intercept	0.04605	0.006806	0.08529	0.0220
15-min change	0.06134	0.04159	0.08109	<0.0001
22-hr change	0			
Ozone exposure				
120 ppb	-0.05742	-0.09541	-0.01944	0.0033
70 ppb	-0.02514	-0.06297	0.01269	0.1913
0 ppb	0			
Site				
URMC	-0.00119	-0.03846	0.03608	0.9497
UNC	-0.03789	-0.07629	0.000515	0.0531
UCSF	0			
Sex				
Female	-0.02419	-0.06636	0.01798	0.2572
Male	0			
Ozone exposure by sex				
120 ppb by female	0.03377	-0.01528	0.08282	0.1759
70 ppb by female	0.009854	-0.03908	0.05879	0.6915
0 ppb by female	0			
120 ppb by male	0			
70 ppb by male	0			
0 ppb by male	0			

Table B.4.10f. Mixed Model for Change in FVC (L), Including Ozone Exposure, by Sex Interaction

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

Table B.4.10g. Type III Sum of Squares for Change in FVC (L), IncludingOzone Exposure, by GSTM1 Status Interaction

Effect	<i>P</i> Value	
Ozone exposure	0.0167	
15-min vs. 22-hr change	<0.0001	
Site	0.0437	
GSTM1 status	0.0524	
Ozone exposure by GSTM1 status	0.5974	

		Lower	Upper	
Effect	Estimate	95% CI	95% CI	P Value
Intercept	0.02863	-0.00696	0.06422	0.1134
15-min change	0.06141	0.04164	0.08118	<0.0001
22-hr change	0			
Ozone exposure				
120 ppb	-0.04520	-0.07688	-0.01352	0.0054
70 ppb	-0.02930	-0.06098	0.002381	0.0697
0 ppb	0			
Site				
URMC	-0.00629	-0.04267	0.03008	0.7316
UNC	-0.04311	-0.08024	-0.00598	0.0234
UCSF	0			
GSTM1 status				
Sufficient	0.01539	-0.02574	0.05652	0.4588
Null	0			
Ozone exposure by GSTM1 status				
120 ppb by sufficient	0.01897	-0.02972	0.06765	0.4429
70 ppb by sufficient	0.02362	-0.02496	0.07220	0.3384
0 ppb by sufficient	0			
120 ppb by null	0			
70 ppb by null	0			
0 ppb by null	0			

Table B.4.10h. Mixed Model for Change in FVC (L), Including Ozone Exposure, by GSTM1 Status Interaction

As we can see from the tables below, there is no interaction between ozone and time, suggesting that the ozone effect is not different at 15 minutes and 22 hours.

Table B.4.10i. Type III Sum of Squares for Change in FVC (L), Including Ozone Exposure, by Time Interaction

Effect	P Value
15-min vs. 22-hr change	<0.0001
Ozone exposure	0.0108
Site	0.0580
Ozone exposure by time	0.6277

		Lower	Upper	
Effect	Estimate	95% CI	95% CI	P Value
Intercept	0.08746	0.05233	0.1226	<0.0001
Change between post- and pre-exposure				
15-min change	0			
22-hr change	-0.04782	-0.08203	-0.01361	0.0067
Ozone exposure				
120 ppb	-0.02720	-0.06128	0.006873	0.1169
70 ppb	-0.00885	-0.04282	0.02512	0.6077
0 ppb	0			
Site				
URMC	-0.00270	-0.03949	0.03410	0.8845
UNC	-0.04009	-0.07770	-0.00247	0.0370
UCSF	0			
Ozone exposure by time (change at 15 min vs. 22 hr)				
120 ppb	-0.01992	-0.06804	0.02820	0.4149
70 ppb	-0.02080	-0.06885	0.02724	0.3938
0 ppb	0			

Table B.4.10j. Mixed Model* for Change in FVC (L), Including Ozone Exposure, by Time Interaction

* Time, ozone exposure, and site treated as fixed effects, and subject treated as a random effect. Pre-exposure measurement taken 10 minutes prior to exposure.

11. FEV₁/FVC

The following figure shows the change from pre- to post-exposure in FEV_1/FVC at 15 minutes and 22 hours. The data come from Table B.4.1a.



Figure B.4.11. Change in FEV₁/FVC at 15 minutes and 22 hours post-exposure at each ozone exposure.

Main Analysis of Ozone Effect

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

- there were no differences between the 15-min post-exposure and 22-hour postexposure in FEV₁/FVC;
- there were no differences in FEV₁/FVC across the ozone exposures; and
- there were marginally significant differences in FEV₁/FVC across the 3 sites.

Table B.4.11a. Type III Sum of Squares for Change in FEV ₁ /FVC				
Effect	P Value			
15-min vs. 22-hr change	0.3099			
Ozone exposure	0.6949			
Site	0.0127			

J		Lower	Upper	
Effect	Estimate	95% CI	95% CI	P Value
Intercept	0.6157	0.1261	1.1053	0.0143
Change between pre- and post-exposure				
15-min change	0.1401	-0.1325	0.4127	0.3099
22-hr change	0			
Ozone exposure				
120 ppb	-0.1344	-0.4661	0.1973	0.4251
70 ppb	-0.02332	-0.3545	0.3078	0.8896
0 ppb	0			
Site				
URMC	-0.3701	-0.9477	0.2075	0.2061
UNC	0.4843	-0.1063	1.0748	0.1067
UCSF	0			

Table B.4.11b. Mixed Model for Change in FEV₁/FVC

Analyses of Interactions

Ozone exposure by age

Age

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

Exposure, by Age Interaction		
Effect	P Value	
Ozone exposure	0.6933	
15-min vs. 22-hr change	0.3115	
Site	0.0123	

Table B.4.11c. Type III Sum of Squares for Change in FEV ₁ /FVC, Including Oz	one
Exposure, by Age Interaction	

Table B.4.11d. Mixed Model for Change in FE	V₁/FVC, Including Ozone Exposure, by
Age Interaction	

0.6775

0.9962

		Lower	Upper	
Effect	Estimate	95% CI	95% CI	P Value
Intercept	0.6174	0.1254	1.1094	0.0146
15-min change	0.1399	-0.1333	0.4132	0.3115
22-hr change	0			
Ozone exposure				
120 ppb	-0.1355	-0.4687	0.1978	0.4234
70 ppb	-0.02362	-0.3562	0.3090	0.8887
0 ppb	0			
Site				
URMC	-0.3837	-0.9679	0.2005	0.1950
UNC	0.4858	-0.1079	1.0795	0.1074
UCSF	0			
Age	0.009670	-0.05828	0.07762	0.7778
Ozone exposure by age				
120 ppb by age	0.003197	-0.07020	0.07659	0.9318
70 ppb by age	0.001026	-0.07227	0.07432	0.9781
0 ppb by age	0			

As we can see from the tables below, there was a marginally significant difference in the ozone effect on FEV_1/FVC by sex — FEV_1/FVC in women decreased from preexposure to post-exposure relative to men at 120 ppb ozone, but not 70 ppb ozone exposure.

 Table B.4.11e. Type III Sum of Squares for Change in FEV₁/FVC, Including Ozone

 Exposure, by Sex Interaction

Effect	P Value	
Ozone exposure	0.8909	
15-min vs. 22-hr change	0.3027	
Site	0.0100	
Sex	0.2047	
Ozone exposure by sex	0.0291	

Table B.4.11f. Mixed Model for Change in FEV₁/FVC, Including Ozone Exposure, by Sex Interaction

		Lower	Upper	
Effect	Estimate	95% CI	95% CI	P Value
Intercept	0.4574	-0.1276	1.0425	0.1237
15-min change	0.1414	-0.1296	0.4124	0.3027
22-hr change	0			
Ozone exposure				
120 ppb	0.4023	-0.1189	0.9235	0.1294
70 ppb	0.3447	-0.1743	0.8638	0.1916
0 ppb	0			
Site				
URMC	-0.3173	-0.8982	0.2636	0.2804
UNC	0.5554	-0.04322	1.1541	0.0686
UCSF	0			
Sex				
Female	0.1915	-0.4312	0.8142	0.5424
Male	0			
Ozone exposure by sex				
120 ppb by female	-0.8946	-1.5676	-0.2216	0.0095
70 ppb by female	-0.6158	-1.2872	0.05559	0.0720
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.4.11g. Type III Sum of Squares for Change in FEV₁/FVC, Including Ozone Exposure, by GSTM1 Status Interaction

Effect	<i>P</i> Value
Ozone exposure	0.5615
15-min vs. 22-hr change	0.3122
Site	0.0114
GSTM1 status	0.0479
Ozone exposure by GSTM1 status	0.1676

Table B.4.11h. Mixed Model for Change in FEV₁/FVC, Including Ozone Exposure, by GSTM1 Status Interaction

		Lower	Upper	
Effect	Estimate	95% CI	95% CI	P Value
Intercept	0.6233	0.08767	1.1589	0.0231
15-min change	0.1392	-0.1329	0.4113	0.3122
22-hr change	0			
Ozone exposure				
120 ppb	0.1155	-0.3205	0.5516	0.6016
70 ppb	0.1969	-0.2391	0.6329	0.3740
0 ppb	0			
Site				
URMC	-0.3133	-0.8838	0.2572	0.2779
UNC	0.5326	-0.04977	1.1150	0.0725
UCSF	0			
GSTM1 status				
Sufficient	-0.1039	-0.7129	0.5052	0.7354
Null	0			
Ozone exposure by GSTM1 status				
120 ppb by sufficient	-0.5908	-1.2609	0.07928	0.0836
70 ppb by sufficient	-0.5178	-1.1865	0.1508	0.1282
0 ppb by sufficient	0			
120 ppb by null	0			
70 ppb by null	0			
0 ppb by null	0			

12. FEF₂₅₋₇₅ (L/sec)

The following figure shows the change from pre- to post-exposure in FEF_{25-75} (L/sec) at 15 minutes and 22 hours. The data come from Table B.4.1a.



Figure B.4.12. Change in FEF_{25-75} at 15 minutes and 22 hours post-exposure at each ozone exposure.

Main Analysis of Ozone Effect

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

- there were differences between the 15-min post-exposure and 22-hour post-exposure FEF₂₅₋₇₅;
- there were no differences in FEF₂₅₋₇₅ across the ozone exposures; and
- there were no differences in FEF_{25-75} across the 3 sites.

Effect	P Value	
15-min vs. 22-hr change	0.0006	
Ozone exposure	0.2861	
Site	0.1219	

Table B.4.12b. Mixed Model for Change in FEF₂₅₋₇₅ (L/sec)

		Lower	Upper	
Effect	Estimate	95% CI	95% CI	P Value
Intercept	0.1230	0.04970	0.1963	0.0013
Change between pre- and post-exposure				
15-min change	0.07558	0.03325	0.1179	0.0006
22-hr change	0			
Ozone exposure				
120 ppb	-0.04135	-0.09285	0.01015	0.1149
70 ppb	-0.01833	-0.06975	0.03309	0.4825
0 ppb	0			
Site				
URMC	-0.06717	-0.1526	0.01830	0.1219
UNC	0.01364	-0.07375	0.1010	0.7570
UCSF	0			

Analyses of Interactions

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

Table B.4.12c. Type III Sum of Squares for Change in FEF₂₅₋₇₅ (L/sec), Including Ozone Exposure, by Age Interaction

Effect	<i>P</i> Value
Ozone exposure	0.3155
15-min vs. 22-hr change	0.0006
Site	0.1531
Age	0.5223
Ozone exposure by age	0.6592

Table B.4.12d. Mixed Model for Change in FEF₂₅₋₇₅ (L/sec), Including Ozone Exposure, by Age Interaction

		Lower	Upper	
Effect	Estimate	95% CI	95% CI	P Value
Intercept	0.1218	0.04825	0.1954	0.0015
15-min change	0.07563	0.03324	0.1180	0.0006
22-hr change	0			
Ozone exposure				
120 ppb	-0.03980	-0.09149	0.01190	0.1305
70 ppb	-0.01719	-0.06879	0.03441	0.5117
0 ppb	0			
Site				
URMC	-0.06404	-0.1504	0.02228	0.1438
UNC	0.01329	-0.07443	0.1010	0.7639
UCSF	0			
Age	0.000464	-0.00978	0.01071	0.9283
Ozone exposure by age				
120 ppb by age	-0.00504	-0.01642	0.006349	0.3851
70 ppb by age	-0.00392	-0.01529	0.007454	0.4988
0 ppb by age	0			

As we can see from the tables below, there was a marginally significant difference in the ozone effect on FEF_{25-75} by sex — FEF_{25-75} in women decreased from pre-exposure to post-exposure relative to men at both 70 and 120 ppb ozone exposure.

Table B.4.12e. Type III Sum of Squares for Change in FEF₂₅₋₇₅ (L/sec), Including Ozone Exposure, by Sex Interaction

Effect	P Value	
Ozone exposure	0.4824	
15-min vs. 22-hr change	0.0006	
Site	0.1236	
Sex	0.2769	
Ozone exposure by sex	0.0181	

Table B.4.12f. Mixed Model for Change in FEF₂₅₋₇₅ (L/sec), Including Ozone Exposure, by Sex Interaction

		Lower	Upper	
Effect	Estimate	95% CI	95% CI	P Value
Intercept	0.08965	0.001556	0.1777	0.0462
15-min change	0.07569	0.03366	0.1177	0.0006
22-hr change	0			
Ozone exposure				
120 ppb	0.02895	-0.05188	0.1098	0.4806
70 ppb	0.06614	-0.01436	0.1466	0.1067
0 ppb	0			
Site				
URMC	-0.06053	-0.1467	0.02566	0.1662
UNC	0.02268	-0.06614	0.1115	0.6128
UCSF	0			
Sex				
Female	0.04658	-0.04748	0.1406	0.3275
Male	0			
Ozone exposure by sex				
120 ppb by female	-0.1173	-0.2217	-0.01293	0.0278
70 ppb by female	-0.1413	-0.2455	-0.03721	0.0081
0 ppb by female	0			
120 ppb by male	0			
70 ppb by male	0			
0 ppb by male	0			

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

Table B.4.12g. Type III Sum of Squares for Change in FEF₂₅₋₇₅ (L/sec), Including Ozone Exposure, by GSTM1 Status Interaction

Effect	P Value	
Ozone exposure	0.2556	
15-min vs. 22-hr change	0.0006	
Site	0.1352	
GSTM1 status	0.3313	
Ozone exposure by GSTM1 status	0.5997	

Table B.4.12h. Mixed Model for Change in FEF₂₅₋₇₅ (L/sec), Including Ozone Exposure, by GSTM1 Status Interaction

		Lower	Upper	
Effect	Estimate	95% CI	95% CI	P Value
Intercept	0.1229	0.04145	0.2044	0.0036
15-min change	0.07554	0.03316	0.1179	0.0006
22-hr change	0			
Ozone exposure				
120 ppb	-0.02760	-0.09551	0.04031	0.4235
70 ppb	0.004200	-0.06371	0.07211	0.9030
0 ppb	0			
Site				
URMC	-0.06297	-0.1489	0.02298	0.1488
UNC	0.01719	-0.07055	0.1049	0.6978
UCSF	0			
GSTM1 status				
Sufficient	-0.00622	-0.09925	0.08681	0.8945
Null	0			
Ozone exposure by GSTM1 status				
120 ppb by sufficient	-0.03247	-0.1368	0.07190	0.5400
70 ppb by sufficient	-0.05298	-0.1571	0.05115	0.3166
0 ppb by sufficient	0			
120 ppb by null	0			
70 ppb by null	0			
0 ppb by null	0			

Abbreviations and Other Terms

CC16	club cell protein 16
FEF ₂₅₋₇₅	forced expiratory flow between 25 and 75% of FEV
FEV ₁	forced expiratory volume in 1 second
FVC	forced vital capacity
GSTM1	glutathione S-transferase Mu 1
IL-6	interleukin 6
IL-8	interleukin 8
Ln	natural logarithm
MOSES	multicenter ozone study in elderly subjects
NERI	New England Research Institute
PMN	polymorphonuclear neutrophils
ppb	part per billion
SD	standard deviation
TNF-α	tumor necrosis factor alpha
UCSF	University of California at San Francisco
UNC	University of North Carolina at Chapel Hill
URMC	University of Rochester Medical Center