



Research Report 192, Pt 1

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

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Appendix B.3. Analyses of Prothrombotic Vascular State 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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Primary Endpoints

1. Descriptive Statistics

Table B.3.1. Descriptive Statistics

	0 ppb			70 ppb			120 ppb		
	<i>N</i>	Mean	SD	<i>N</i>	Mean	SD	<i>N</i>	Mean	SD
MP-TFA (pg/mL)									
Pre-exposure	84	0.15	0.17	84	0.13	0.18	86	0.15	0.20
4 hr post-exposure	84	0.15	0.19	84	0.14	0.15	86	0.18	0.20
22 hr post-exposure	80	0.14	0.15	84	0.12	0.14	84	0.15	0.16
Monocyte-platelet conjugate count									
Pre-exposure	78	50.1	47.7	73	47.4	42.0	76	52.9	49.7
4 hr post-exposure	78	51.2	42.6	73	44.8	31.2	76	51.0	42.2
22 hr post-exposure	74	45.1	40.1	73	42.7	27.8	74	49.7	41.9

2. MP-TFA (pg/mL)

The following figure shows the change in microparticle-associated tissue factor activity (MP-TFA) from pre- to post-exposure over time. The data come from Table B.3.1.

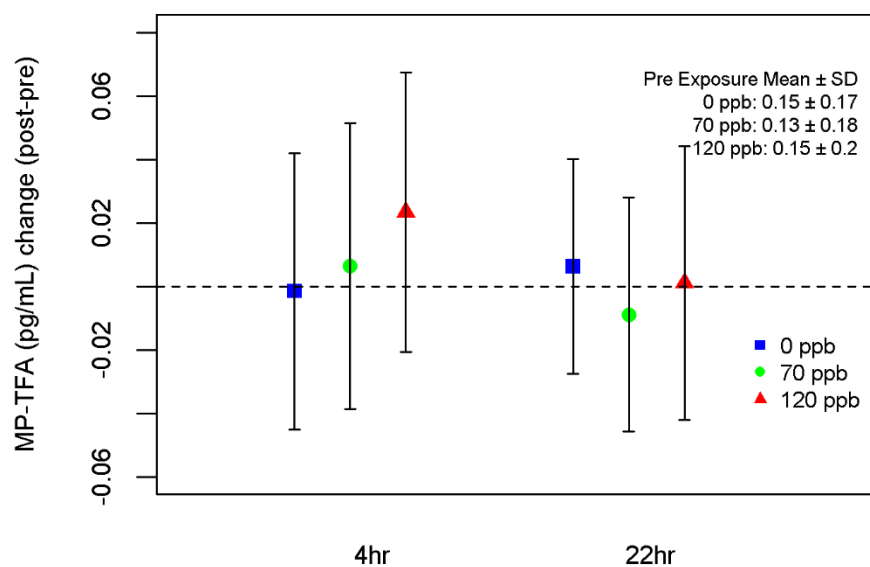


Figure B.3.2. Change in MP-TFA at different post-exposure times and at each ozone exposure.

Main Analysis of Ozone Effect

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

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

Table B.3.2a. Type III Sum of Squares for Change in MP-TFA (pg/mL)

Effect	P Value
4-hr vs. 22-hr change	0.5059
Ozone exposure	0.7719
Site	0.3531

Table B.3.2b. Mixed Model for Change from in MP-TFA (pg/mL)

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	0.01835	-0.03016	0.06687	0.4540
Change between pre- and post-exposure				
4-hr change	0.01077	-0.02129	0.04284	0.5059
22-hr change	0			
Ozone exposure				
120 ppb	0.009139	-0.02997	0.04825	0.6451
70 ppb	-0.00480	-0.04401	0.03441	0.8091
0 ppb	0			
Site				
URMC	-0.02251	-0.07562	0.03060	0.4017
UNC	-0.04004	-0.09496	0.01489	0.1509
UCSF	0			

Analyses of Interactions

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

Table B.3.2c. Type III Sum of Squares for Change in MP-TFA (pg/mL), Including Ozone Exposure, by Age Interaction

Effect	<i>P</i> Value
Ozone exposure	0.8289
4-hr vs. 22-hr change	0.5092
Site	0.3463
Age	0.0939
Ozone exposure by age	0.1326

Table B.3.2d. Mixed Model for Change in MP-TFA (pg/mL), Including Ozone Exposure, by Age Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	<i>P</i> Value
Intercept	0.01892	-0.02920	0.06703	0.4365
4-hr change	0.01067	-0.02132	0.04265	0.5092
22-hr change	0			
Ozone exposure				
120 ppb	0.008102	-0.03095	0.04715	0.6826
70 ppb	-0.00367	-0.04283	0.03549	0.8534
0 ppb	0			
Site				
URMC	-0.02719	-0.07999	0.02560	0.3086
UNC	-0.03907	-0.09337	0.01524	0.1562
UCSF	0			
Age	0.005159	-0.00180	0.01212	0.1441
Ozone exposure by age				
120 ppb by age	0.002623	-0.00592	0.01117	0.5466
70 ppb by age	-0.00587	-0.01441	0.002671	0.1774
0 ppb by age	0			

As we can see from the tables below,

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

Table B.3.2e. Type III Sum of Squares for Change in MP-TFA (pg/mL), Including Ozone Exposure, by Sex Interaction

Effect	<i>P</i> Value
Ozone exposure	0.8791
4-hr vs. 22-hr change	0.5015
Site	0.5611
Sex	0.0233
Ozone exposure by sex	0.1426

Table B.3.2f. Mixed Model for Change in MP-TFA (pg/mL), Including Ozone Exposure, by Sex Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	<i>P</i> Value
Intercept	0.02891	-0.02900	0.08682	0.3237
4-hr change	0.01086	-0.02112	0.04283	0.5015
22-hr change	0			
Ozone exposure				
120 ppb	0.008068	-0.05201	0.06814	0.7912
70 ppb	0.03465	-0.02543	0.09472	0.2565
0 ppb	0			
Site				
URMC	-0.01409	-0.06645	0.03826	0.5938
UNC	-0.02950	-0.08397	0.02497	0.2845
UCSF	0			
Sex				
Female	-0.02920	-0.09309	0.03470	0.3661
Male	0			
Ozone exposure by sex				
120 ppb by female	0.002236	-0.07675	0.08123	0.9555
70 ppb by female	-0.06748	-0.1466	0.01166	0.0941
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 MP-TFA by GSTM1 status – MP-TFA increased after 120 ppb, but not 70 ppb, ozone exposure in GSTM1-sufficient subjects relative to GSTM1-null subjects.

Table B.3.2g. Type III Sum of Squares for Change in MP-TFA (pg/mL), Including Ozone Exposure, by GSTM1 Status Interaction

Effect	P Value
Ozone exposure	0.5484
4-hr vs. 22-hr change	0.5040
Site	0.3016
GSTM1 status	0.3088
Ozone exposure by GSTM1 status	0.0300

Table B.3.2h. Mixed Model for Change in MP-TFA (pg/mL), Including Ozone Exposure, by GSTM1 Status Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	0.02795	-0.02591	0.08180	0.3050
4-hr change	0.01075	-0.02111	0.04262	0.5040
22-hr change	0			
Ozone exposure				
120 ppb	-0.03365	-0.08433	0.01704	0.1917
70 ppb	-0.01529	-0.06567	0.03509	0.5498
0 ppb	0			
Site				
URMC	-0.02478	-0.07822	0.02867	0.3591
UNC	-0.04309	-0.09818	0.01199	0.1235
UCSF	0			
GSTM1 status				
Sufficient	-0.02004	-0.08466	0.04459	0.5391
Null	0			
Ozone exposure by GSTM1 status				
120 ppb by sufficient	0.1026	0.02361	0.1816	0.0112
70 ppb by sufficient	0.02610	-0.05337	0.1056	0.5176
0 ppb by sufficient	0			
120 ppb by null	0			
70 ppb by null	0			
0 ppb by null	0			

3. Monocyte–Platelet Conjugate Count

The following figure shows the descriptive analysis of the change in monocyte–platelet conjugate count between pre- and post-exposure at 4 hours and 22 hours. The data come from Table B.3.1.

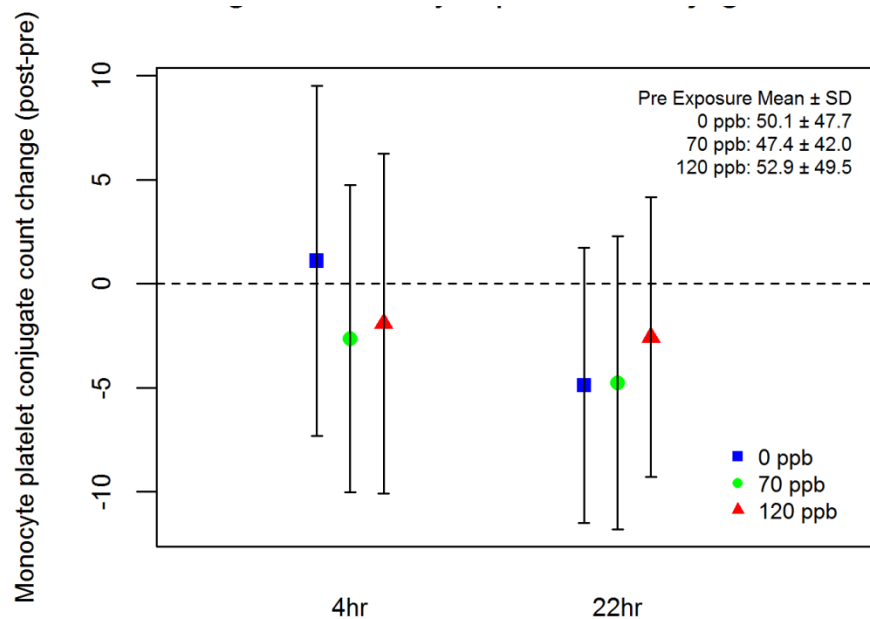


Figure B.3.3. Change in monocyte–platelet conjugate count at different post-exposure times and at each ozone exposure.

Main Analysis of Ozone Effect

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

- there were no differences between the 4-hour post-exposure and 22-hour post-exposure monocyte–platelet conjugate count;
- there were no differences in monocyte–platelet conjugate count across the ozone exposures; and
- there were no differences in monocyte–platelet conjugate count across the 3 sites.

Table B.3.3a. Type III Sum of Squares for Change in Monocyte–Platelet Conjugate Count

Effect	<i>P</i> Value
4-hr vs. 22-hr change	0.2618
Ozone exposure	0.8733
Site	0.0864

Table B.3.3b. Mixed Model for Change in Monocyte–Platelet Conjugate Count

Effect	Estimate	Lower 95% CI	Upper 95% CI	<i>P</i> Value
Intercept	-5.0605	-14.0625	3.9414	0.2666
Change between pre- and post-exposure				
4-hr change	3.0654	-2.3325	8.4634	0.2618
22-hr change	0			
Ozone exposure				
120 ppb	-0.2215	-6.8144	6.3715	0.9472
70 ppb	-1.6197	-8.2637	5.0242	0.6306
0 ppb	0			
Site				
URMC	6.7733	-3.5427	17.0894	0.1950
UNC	-5.3061	-16.7076	6.0955	0.3571
UCSF	0			

Analyses of Interactions

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

Table B.3.3c. Type III Sum of Squares for Change in Monocyte–Platelet Conjugate Count, Including Ozone Exposure, by Age Interaction

Effect	P Value
Ozone exposure	0.9081
4-hr vs. 22-hr change	0.2569
Site	0.0792
Age	0.5372
Ozone exposure by age	0.0129

Table B.3.3d. Mixed Model for Change in Monocyte–Platelet Conjugate Count, Including Ozone Exposure, by Age Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	-5.5101	-14.5331	3.5130	0.2277
4-hr change	3.0678	-2.2788	8.4144	0.2569
22-hr change	0			
Ozone exposure				
120 ppb	-0.01842	-6.5524	6.5156	0.9956
70 ppb	-1.2811	-7.8672	5.3050	0.7012
0 ppb	0			
Site				
URMC	7.4358	-3.0101	17.8817	0.1604
UNC	-5.0148	-16.5025	6.4728	0.3875
UCSF	0			
Age	0.9097	-0.4044	2.2237	0.1721
Ozone exposure by age				
120 ppb by age	-1.5055	-2.9512	-0.05978	0.0413
70 ppb by age	-2.1514	-3.6146	-0.6881	0.0041
0 ppb by age	0			

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

Table B.3.3e. Type III Sum of Squares for Change in Monocyte–Platelet Conjugate Count, Including Ozone Exposure, by Sex Interaction

Effect	<i>P</i> Value
Ozone exposure	0.7431
4-hr vs. 22-hr change	0.2610
Site	0.0932
Sex	0.2788
Ozone exposure by sex	0.0565

Table B.3.3f. Mixed Model for Change in Monocyte–Platelet Conjugate Count, Including Ozone Exposure, by Sex Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	<i>P</i> Value
Intercept	-1.8003	-12.6622	9.0616	0.7423
4-hr change	3.0573	-2.3178	8.4324	0.2610
22-hr change	0			
Ozone exposure				
120 ppb	-8.5897	-18.6945	1.5151	0.0951
70 ppb	-9.4668	-19.5729	0.6393	0.0661
0 ppb	0			
Site				
URMC	5.8391	-4.5235	16.2016	0.2654
UNC	-6.1262	-17.5921	5.3398	0.2907
UCSF	0			
Sex				
Female	-4.5065	-16.2816	7.2685	0.4484
Male	0			
Ozone exposure by sex				
120 ppb by female	14.4962	1.2034	27.7889	0.0328
70 ppb by female	13.7163	0.3521	27.0805	0.0443
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 monocyte–platelet conjugate count by GSTM1 status — monocyte–platelet conjugate count increased after 70 ppb, but not 120 ppb, ozone exposure in GSTM1-sufficient subjects relative to GSTM1-null subjects.

Table B.3.3g. Type III Sum of Squares for Change in Monocyte–Platelet Conjugate Count, Including Ozone Exposure, by GSTM1 Status Interaction

Effect	P Value
Ozone exposure	0.9390
4-hr vs. 22-hr change	0.2556
Site	0.0928
GSTM1 status	0.5940
Ozone exposure by GSTM1 status	0.0488

Table B.3.3h. Mixed Model for Change in Monocyte–Platelet Conjugate Count, Including Ozone Exposure, by GSTM1 Status Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	-2.1503	-12.1337	7.8330	0.6692
4-hr change	3.0918	-2.2811	8.4646	0.2556
22-hr change	0			
Ozone exposure				
120 ppb	-5.0290	-13.5514	3.4935	0.2454
70 ppb	-8.4437	-17.1319	0.2446	0.0567
0 ppb	0			
Site				
URMC	6.6473	-3.7384	17.0329	0.2064
UNC	-5.2867	-16.7125	6.1391	0.3598
UCSF	0			
GSTM1 status				
Sufficient	-6.9313	-18.6975	4.8350	0.2445
Null	0			
Ozone exposure by GSTM1 status				
120 ppb by sufficient	11.7578	-1.6029	25.1185	0.0841
70 ppb by sufficient	16.2552	2.8723	29.6380	0.0176
0 ppb by sufficient	0			
120 ppb by null	0			
70 ppb by null	0			
0 ppb by null	0			

Secondary Endpoints

4. Descriptive Statistics

Table B.3.4. Descriptive Statistics

	0 ppb			70 ppb			120 ppb		
	<i>N</i>	Mean	SD	<i>N</i>	Mean	SD	<i>N</i>	Mean	SD
vWf (ng/mL)									
Pre-exposure	85	23774.0	24127.0	85	22101.0	26088.1	84	22450.3	21076.3
4 hr post-exposure	85	23606.5	26519.2	85	23198.3	26646.7	84	21234.9	19271.9
22 hr post-exposure	82	24703.3	25631.4	85	22359.2	36850.5	82	21645.4	24122.8
Fibrinogen (µg/mL)									
Pre-exposure	85	1649.4	2270.0	85	1790.0	2118.4	84	1319.0	1304.7
4 hr post-exposure	85	1459.2	1836.7	85	1520.8	1625.4	84	1346.0	1321.3
22 hr post-exposure	82	1657.1	2069.0	85	1544.9	1795.9	82	1749.0	1864.5
Activated platelet count									
Pre-exposure	82	20927.7	21222.8	80	18031.1	18312.0	82	19654.0	16465.4
4 hr post-exposure	81	17532.7	12192.9	79	16117.8	14006.0	82	16152.5	13679.8
22 hr post-exposure	78	20587.0	37302.4	79	15922.9	14867.4	80	16487.2	13555.2
Platelet MP count									
Pre-exposure	81	5205.2	4028.4	80	5101.1	2940.9	81	5397.6	4112.5
4 hr post-exposure	80	4677.8	3207.6	79	5025.9	3619.3	81	5038.3	3314.0
22 hr post-exposure	77	4236.3	2237.8	79	4557.0	2554.8	79	4948.2	3251.6

	0 ppb			70 ppb			120 ppb		
	<i>N</i>	Mean	SD	<i>N</i>	Mean	SD	<i>N</i>	Mean	SD
Activated platelet MP count									
Pre-exposure	81	832.3	1076.6	80	723.0	752.1	81	763.0	561.3
4 hr post-exposure	80	686.8	620.1	79	706.8	679.5	81	685.6	448.8
22 hr post-exposure	77	590.8	415.8	79	603.3	427.4	79	668.1	422.4
CD142+MP count									
Pre-exposure	80	25033.5	40847.4	80	22555.8	32787.7	80	29834.9	56386.7
4 hr post-exposure	79	22881.8	50998.0	79	15907.7	20139.5	80	20071.2	31808.0
22 hr post-exposure	76	15082.1	23611.4	79	17851.5	31657.5	78	19492.0	28543.7
CD40 Ligand MP count									
Pre-exposure	80	33283.4	57668.5	80	32007.5	48664.5	80	37502.8	66018.2
4 hr post-exposure	79	30629.2	60380.1	79	23561.1	31098.3	80	24390.1	31387.4
22 hr post-exposure	76	21909.8	30699.2	79	20977.3	23635.2	78	26681.8	36682.2
Platelet count (1000/uL)									
Pre-exposure	84	236.8	51.8	85	237.2	59.3	85	233.9	51.3
4 hr post-exposure	83	231.4	48.5	85	230.7	61.2	84	228.8	52.3
22 hr post-exposure	80	230.3	54.9	85	226.7	61.5	81	225.9	52.7

5. vWF (ng/mL)

The following figure shows the change in von Willebrand factor levels from pre- to -post-exposure over time. The data come from Table B.3.4.

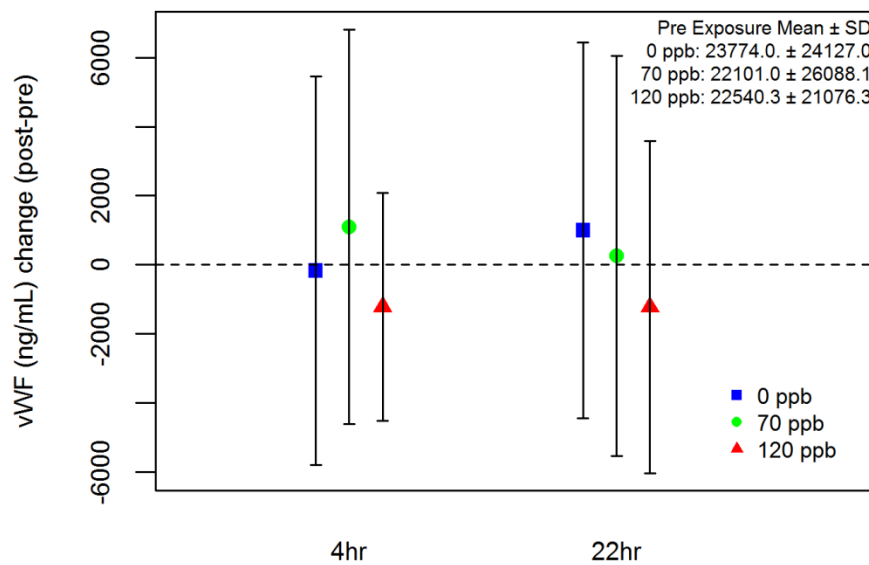


Figure B.3.5. Change in vWF at different post-exposure times and at each ozone exposure.

Main Analysis of Ozone Effect

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

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

Table B.3.5a. Type III Sum of Squares for Change in vWF (ng/mL)

Effect	P Value
4-hr vs. 22-hr change	0.9547
Ozone exposure	0.7652
Site	0.3647

Table B.3.5b. Mixed Model for Change in vWF (ng/mL)

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	-105.06	-5602.69	5392.58	0.9698
Change between pre- and post-exposure				
4-hr change	-121.71	-4373.15	4129.73	0.9547
22-hr change	0			
Ozone exposure				
120 ppb	-1527.57	-6719.36	3664.22	0.5621
70 ppb	246.31	-4913.39	5406.00	0.9250
0 ppb	0			
Site				
URMC	-945.13	-6460.51	4570.26	0.7341
UNC	2869.86	-2834.81	8574.53	0.3200
UCSF	0			

Analyses of Interactions

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

Table B.3.5c. Type III Sum of Squares for Change in vWF (ng/mL), Including Ozone Exposure, by Age Interaction

Effect	<i>P</i> Value
Ozone exposure	0.8486
4-hr vs. 22-hr change	0.9652
Site	0.3598
Age	0.8370
Ozone exposure by age	0.0184

Table B.3.5d. Mixed Model for Change in vWF (ng/mL), Including Ozone Exposure, by Age Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	<i>P</i> Value
Intercept	-166.65	-5671.01	5337.71	0.9521
4-hr change	-93.0021	-4313.12	4127.12	0.9652
22-hr change	0			
Ozone exposure				
120 ppb	-1235.92	-6394.67	3922.84	0.6368
70 ppb	113.39	-5018.77	5245.56	0.9653
0 ppb	0			
Site				
URMC	-1026.61	-6614.20	4560.98	0.7157
UNC	2879.61	-2865.84	8625.05	0.3217
UCSF	0			
Age	495.05	-340.77	1330.88	0.2421
Ozone exposure by age				
120 ppb by age	-1381.68	-2511.52	-251.84	0.0167
70 ppb by age	54.6178	-1072.74	1181.97	0.9242
0 ppb by age	0			

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

Table B.3.5e. Type III Sum of Squares for Change in vWF (ng/mL), Including Ozone Exposure, by Sex Interaction

Effect	P Value
Ozone exposure	0.7904
4-hr vs. 22-hr change	0.9476
Site	0.4014
Sex	0.3958
Ozone exposure by sex	0.8219

Table B.3.5f. Mixed Model for Change in vWF (ng/mL), Including Ozone Exposure, by Sex Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	-2137.09	-9030.42	4756.24	0.5392
4-hr change	-141.28	-4400.70	4118.14	0.9476
22-hr change	0			
Ozone exposure				
120 ppb	127.59	-7888.64	8143.83	0.9750
70 ppb	1934.97	-6142.89	10013	0.6368
0 ppb	0			
Site				
URMC	-1253.23	-6834.28	4327.82	0.6563
UNC	2456.79	-3341.50	8255.09	0.4018
UCSF	0			
Sex				
Female	3936.79	-3765.98	11640	0.3123
Male	0			
Ozone exposure by sex				
120 ppb by female	-2851.28	-13387	7684.37	0.5938
70 ppb by female	-2932.25	-13447	7582.36	0.5826
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.3.5g. Type III Sum of Squares for Change in vWF (ng/mL), Including Ozone Exposure, by GSTM1 Status Interaction

Effect	P Value
Ozone exposure	0.7844
4-hr vs. 22-hr change	0.9485
Site	0.3684
GSTM1 status	0.8161
Ozone exposure by GSTM1 status	0.5072

Table B.3.5h. Mixed Model for Change in vWF (ng/mL), Including Ozone Exposure, by GSTM1 Status Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	-1073.07	-7345.27	5199.13	0.7345
4-hr change	-138.69	-4393.06	4115.68	0.9485
22-hr change	0			
Ozone exposure				
120 ppb	-595.78	-7384.71	6193.14	0.8626
70 ppb	2810.22	-3959.62	9580.05	0.4136
0 ppb	0			
Site				
URMC	-862.68	-6446.73	4721.37	0.7594
UNC	2937.35	-2817.18	8691.88	0.3129
UCSF	0			
GSTM1 status				
Sufficient	2242.38	-5455.40	9940.16	0.5639
Null	0			
Ozone exposure by GSTM1 status				
120 ppb by sufficient	-2249.77	-12798	8298.07	0.6742
70 ppb by sufficient	-6112.99	-16582	4355.63	0.2506
0 ppb by sufficient	0			
120 ppb by null	0			
70 ppb by null	0			
0 ppb by null	0			

6. Fibrinogen (µg/mL)

The following figure shows the change in fibrinogen levels from pre- to post-exposure over time. The data come from Table B.3.4.

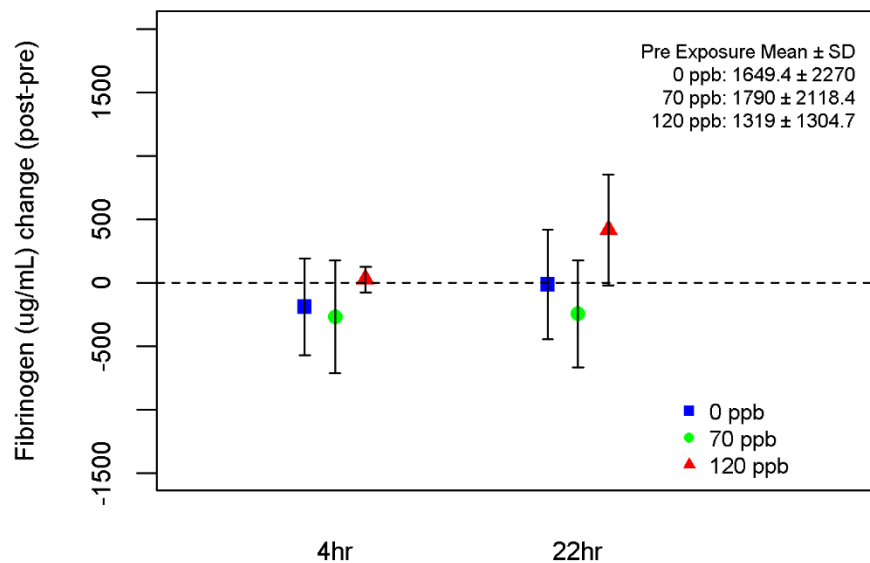


Figure B.3.6. Change in fibrinogen at different post-exposure times and at each ozone exposure.

Main Analysis of Ozone Effect

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

- there were no differences between the 4-hour and 22-hour post-exposure changes in fibrinogen;
- there were marginally significant ozone effects on fibrinogen; and
- there were no differences in fibrinogen across the 3 sites.

Table B.3.6a. Type III Sum of Squares for Change in Fibrinogen (µg/mL)

Effect	P Value
4-hr vs. 22-hr change	0.2172
Ozone exposure	0.0480
Site	0.5459

Table B.3.6b. Mixed Model for Change in Fibrinogen (µg/mL)

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	-145.31	-564.21	273.59	0.4922
Change between pre- and post-exposure				
4-hr change	-197.11	-512.34	118.12	0.2172
22-hr change	0			
Ozone exposure				
120 ppb	317.29	-67.8233	702.40	0.1057
70 ppb	-157.25	-539.93	225.42	0.4183
0 ppb	0			
Site				
URMC	182.48	-246.59	611.56	0.4001
UNC	234.06	-209.54	677.67	0.2971
UCSF	0			

Analyses of Interactions

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

Table B.3.6c. Type III Sum of Squares for Change in Fibrinogen ($\mu\text{g}/\text{mL}$), Including Ozone Exposure, by Age Interaction

Effect	P Value
Ozone exposure	0.0391
4-hr vs. 22-hr change	0.2172
Site	0.5518
Age	0.1877
Ozone exposure by age	0.3022

Table B.3.6d. Mixed Model for Change in Fibrinogen ($\mu\text{g}/\text{mL}$), Including Ozone Exposure, by Age Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	-144.51	-562.35	273.32	0.4934
4-hr post change	-197.04	-512.17	118.09	0.2172
22-hr change	0			
Ozone exposure				
120 ppb	328.73	-56.5776	714.04	0.0940
70 ppb	-162.78	-546.08	220.51	0.4029
0 ppb	0			
Site				
URMC	151.47	-277.99	580.93	0.4850
UNC	240.29	-201.18	681.76	0.2821
UCSF	0			
Age	51.8549	-11.2448	114.95	0.1059
Ozone exposure by age				
120 ppb by age	-63.2502	-147.63	21.1327	0.1414
70 ppb by age	-14.1422	-98.3379	70.0534	0.7414
0 ppb by age	0			

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

Table B.3.6e. Type III Sum of Squares for Change in Fibrinogen ($\mu\text{g}/\text{mL}$), Including Ozone Exposure, by Sex Interaction

Effect	<i>P</i> Value
Ozone exposure	0.0537
4-hr vs. 22-hr change	0.2182
Site	0.5717
Sex	0.9156
Ozone exposure by sex	0.9927

Table B.3.6f. Mixed Model for Change in Fibrinogen ($\mu\text{g}/\text{mL}$), Including Ozone Exposure, by Sex Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	<i>P</i> Value
Intercept	-138.08	-661.81	385.66	0.6014
4-hr post change	-197.14	-513.14	118.86	0.2182
22-hr change	0			
Ozone exposure				
120 ppb	292.50	-302.16	887.16	0.3329
70 ppb	-181.16	-780.53	418.22	0.5515
0 ppb	0			
Site				
URMC	179.06	-256.84	614.95	0.4163
UNC	229.91	-222.82	682.64	0.3154
UCSF	0			
Sex				
Female	-8.0632	-590.85	574.73	0.9781
Male	0			
Ozone exposure by sex				
120 ppb by female	42.5216	-739.33	824.37	0.9146
70 ppb by female	40.2589	-739.99	820.50	0.9190
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 significant difference in fibrinogen by GSTM1 status, with fibrinogen decreasing from pre- to post-exposure in GSTM1-sufficient subjects relative to GSTM1-null subjects independent of ozone exposure; and
- the ozone effect did not differ by GSTM1 status.

Table B.3.6g. Type III Sum of Squares for Change in Fibrinogen (µg/mL), Including Ozone Exposure, by GSTM1 Status Interaction

Effect	P Value
Ozone exposure	0.0217
4-hr vs. 22-hr change	0.2246
Site	0.3715
GSTM1 status	0.0061
Ozone exposure by GSTM1 status	0.1102

Table B.3.6h. Mixed Model for Change in Fibrinogen (µg/mL), Including Ozone Exposure, by GSTM1 Status Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	54.6307	-408.90	518.17	0.8152
4-hr change	-193.56	-508.12	121.01	0.2246
22-hr change	0			
Ozone exposure				
120 ppb	95.1419	-406.82	597.11	0.7087
70 ppb	-35.7679	-536.32	464.78	0.8880
0 ppb	0			
Site				
URMC	247.37	-165.11	659.85	0.2363
UNC	273.16	-151.91	698.24	0.2048
UCSF	0			
GSTM1 status				
Sufficient	-575.26	-1144.23	-6.2970	0.0476
Null	0			
Ozone exposure by GSTM1 status				
120 ppb by sufficient	542.43	-237.46	1322.32	0.1715
70 ppb by sufficient	-274.07	-1048.10	499.97	0.4854
0 ppb by sufficient	0			
120 ppb by null	0			
70 ppb by null	0			
0 ppb by null	0			

7. Activated Platelet Count

The following figure shows the change in activated platelet count from pre- to post-exposure over time. The data come from Table B.3.4.

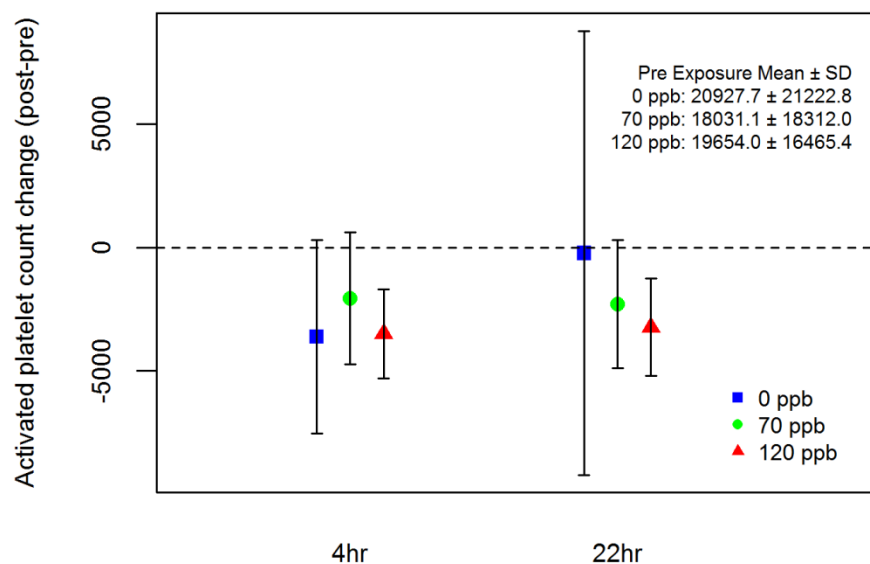


Figure B.3.7. Change in activated platelet count at different post-exposure times and at each ozone exposure.

Main Analysis of Ozone Effect

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

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

Table B.3.7a. Type III Sum of Squares for Change in Activated Platelet Count

Effect	<i>P</i> Value
4-hr vs. 22-hr change	0.5038
Ozone exposure	0.7813
Site	0.0608

Table B.3.7b. Mixed Model for Change from in Activated Platelet Count

Effect	Estimate	Lower 95% CI	Upper 95% CI	<i>P</i> Value
Intercept	-4874.08	-9565.46	-182.70	0.0419
Change between pre- and post-exposure				
4-hr change	-1179.50	-4673.01	2314.00	0.5038
22-hr change	0			
Ozone exposure				
120 ppb	-1437.33	-5686.64	2811.97	0.5050
70 ppb	-314.26	-4590.61	3962.09	0.8848
0 ppb	0			
Site				
URMC	5508.75	662.04	10355	0.0264
UNC	4878.29	-266.37	10023	0.0628
UCSF	0			

Analyses of Interactions

As we can see from the tables below, there was a marginally significant effect of ozone on activated platelet count by age — an increase in age was associated with an increase in activated platelet counts after exposure to 70 ppb, but not to 120 ppb, ozone.

Table B.3.7c. Type III Sum of Squares for Change in Activated Platelet Count, Including Ozone Exposure, by Age Interaction

Effect	P Value
Ozone exposure	0.7647
4-hr vs. 22-hr change	0.5134
Site	0.0614
Age	0.4694
Ozone exposure by age	0.0457

Table B.3.7d. Mixed Model for Change in Activated Platelet Count, Including Ozone Exposure, by Age Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	-4995.47	-9693.93	-297.01	0.0375
4-hr change	-1146.62	-4620.59	2327.36	0.5134
22-hr change	0			
Ozone exposure				
120 ppb	-1395.71	-5625.17	2833.76	0.5155
70 ppb	-75.6735	-4337.70	4186.36	0.9721
0 ppb	0			
Site				
URMC	5372.61	469.92	10275	0.0321
UNC	5185.01	12.0058	10358	0.0495
UCSF	0			
Age	799.50	85.8827	1513.11	0.0286
Ozone exposure by age				
120 ppb by age	-715.70	-1645.10	213.70	0.1308
70 ppb by age	-1186.80	-2129.37	-244.24	0.0137
0 ppb by age	0			

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

Table B.3.7e. Type III Sum of Squares for Change in Activated Platelet Count, Including Ozone Exposure, by Sex Interaction

Effect	P Value
Ozone exposure	0.7095
4-hr vs. 22-hr change	0.5018
Site	0.0784
Sex	0.7670
Ozone exposure by sex	0.7642

Table B.3.7f. Mixed Model for Change in Activated Platelet Count, Including Ozone Exposure, by Sex Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	-4672.21	-10584	1239.87	0.1198
4-hr change	-1186.55	-4684.49	2311.40	0.5018
22-hr change	0			
Ozone exposure				
120 ppb	-3047.69	-9756.48	3661.10	0.3709
70 ppb	-193.27	-6902.21	6515.66	0.9547
0 ppb	0			
Site				
URMC	5415.60	474.01	10357	0.0321
UNC	4709.47	-597.72	10017	0.0812
UCSF	0			
Sex				
Female	-194.84	-6782.24	6392.56	0.9532
Male	0			
Ozone exposure by sex				
120 ppb by female	2686.86	-5989.96	11364	0.5416
70 ppb by female	-202.06	-8916.52	8512.41	0.9635
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.3.7g. Type III Sum of Squares for Change in Activated Platelet Count, Including Ozone Exposure, by GSTM1 Status Interaction

Effect	P Value
Ozone exposure	0.8851
4-hr vs. 22-hr change	0.5060
Site	0.0566
GSTM1 status	0.6518
Ozone exposure by GSTM1 status	0.0732

Table B.3.7h. Mixed Model for Change in Activated Platelet Count, Including Ozone Exposure, by GSTM1 Status Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	-2142.47	-7468.70	3183.76	0.4259
4-hr change	-1169.03	-4649.46	2311.40	0.5060
22-hr change	0			
Ozone exposure				
120 ppb	-5018.08	-10535	499.01	0.0743
70 ppb	-3996.71	-9614.20	1620.78	0.1619
0 ppb	0			
Site				
URMC	5667.08	777.37	10557	0.0237
UNC	4904.30	-265.82	10074	0.0627
UCSF	0			
GSTM1 status				
Sufficient	-6745.84	-13243	-248.26	0.0421
Null	0			
Ozone exposure by GSTM1 status				
120 ppb by sufficient	8672.73	69.9997	17275	0.0482
70 ppb by sufficient	8752.80	131.34	17374	0.0467
0 ppb by sufficient	0			
120 ppb by null	0			
70 ppb by null	0			
0 ppb by null	0			

8. Platelet MP Count

The following figure shows the change in platelet microparticle (MP) count from pre- to post-exposure over time. The data come from Table B.3.4.

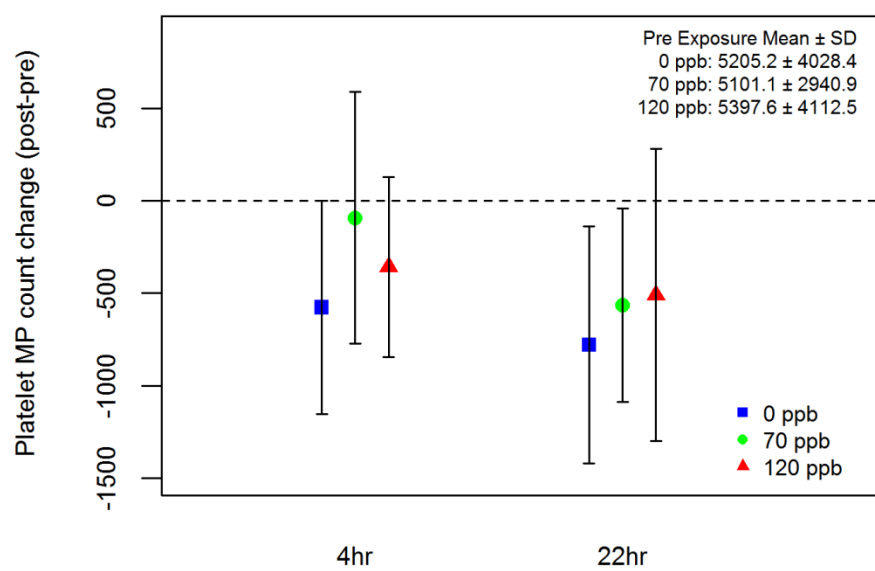


Figure B.3.8. Change in platelet MP count at different post-exposure times and at each ozone exposure.

Main Analysis of Ozone Effect

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

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

Table B.3.8a. Type III Sum of Squares for Change in Platelet MP Count

Effect	P Value
4-hr vs. 22-hr change	0.2777
Ozone exposure	0.5238
Site	0.3410

Table B.3.8b. Mixed Model for Change from Platelet MP Count

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	-1128.61	-1836.31	-420.92	0.0021
Change between pre- and post-exposure				
4-hr change	268.34	-220.07	756.75	0.2777
22-hr change	0			
Ozone exposure				
120 ppb	213.69	-382.57	809.95	0.4800
70 ppb	341.73	-256.87	940.33	0.2612
0 ppb	0			
Site				
URMC	559.05	-200.39	1318.49	0.1469
UNC	378.10	-424.11	1180.30	0.3513
UCSF	0			

Analyses of Interactions

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

Table B.3.8c. Type III Sum of Squares for Change in Platelet MP, Including Ozone Exposure, by Age Interaction

Effect	P Value
Ozone exposure	0.5122
4-hr vs. 22-hr change	0.2762
Site	0.4120
Age	0.2189
Ozone exposure by age	0.2217

Table B.3.8d. Mixed Model for Change in Platelet MP, Including Ozone Exposure, by Age Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	-1113.10	-1820.19	-406.01	0.0024
4-hr change	268.78	-218.85	756.41	0.2762
22-hr change	0			
Ozone exposure				
120 ppb	196.17	-399.33	791.67	0.5162
70 ppb	350.47	-248.29	949.23	0.2493
0 ppb	0			
Site				
URMC	500.14	-263.71	1263.99	0.1964
UNC	382.08	-419.06	1183.22	0.3455
UCSF	0			
Age	26.4104	-78.6162	131.44	0.6182
Ozone exposure by age				
120 ppb by age	81.7402	-49.3692	212.85	0.2210
70 ppb by age	-29.8205	-162.40	102.76	0.6586
0 ppb by age	0			

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

Table B.3.8e. Type III Sum of Squares for Change in Platelet MP, Including Ozone Exposure, by Sex Interaction

Effect	P Value
Ozone exposure	0.4374
4-hr vs. 22-hr change	0.2759
Site	0.3231
Sex	0.6830
Ozone exposure by sex	0.4511

Table B.3.8f. Mixed Model for Change in Platelet MP, Including Ozone Exposure, by Sex Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	-1298.97	-2184.57	-413.37	0.0045
4-hr change	269.50	-219.12	758.13	0.2759
22-hr change	0			
Ozone exposure				
120 ppb	686.98	-262.40	1636.37	0.1549
70 ppb	571.08	-372.27	1514.44	0.2335
0 ppb	0			
Site				
URMC	579.68	-191.26	1350.61	0.1385
UNC	415.73	-407.74	1239.19	0.3182
UCSF	0			
Sex				
Female	252.90	-715.80	1221.60	0.6049
Male	0			
Ozone exposure by sex				
120 ppb by female	-781.39	-2001.73	438.94	0.2078
70 ppb by female	-384.29	-1605.34	836.75	0.5350
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.3.8g. Type III Sum of Squares for Change in Platelet MP, Including Ozone Exposure, by GSTM1 Status Interaction

Effect	P Value
Ozone exposure	0.6542
4-hr vs. 22-hr change	0.2768
Site	0.3157
GSTM1 status	0.4819
Ozone exposure by GSTM1 status	0.4145

Table B.3.8h. Mixed Model for Change in Platelet MP, Including Ozone Exposure, by GSTM1 Status Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	-1242.36	-2035.68	-449.03	0.0025
4-hr change	268.99	-219.65	757.62	0.2768
22-hr change	0			
Ozone exposure				
120 ppb	472.70	-299.71	1245.12	0.2285
70 ppb	663.64	-123.66	1450.95	0.0979
0 ppb	0			
Site				
URMC	583.76	-183.00	1350.52	0.1337
UNC	400.25	-406.18	1206.68	0.3264
UCSF	0			
GSTM1 status				
Sufficient	239.31	-720.58	1199.20	0.6212
Null	0			
Ozone exposure by GSTM1 status				
120 ppb by sufficient	-642.34	-1858.05	573.38	0.2982
70 ppb by sufficient	-761.08	-1974.54	452.39	0.2172
0 ppb by sufficient	0			
120 ppb by null	0			
70 ppb by null	0			
0 ppb by null	0			

9. Activated Platelet MP Count

The following figure shows the change in activated platelet microparticle (MP) count from pre- to post-exposure over time. The data come from Table B.3.4.

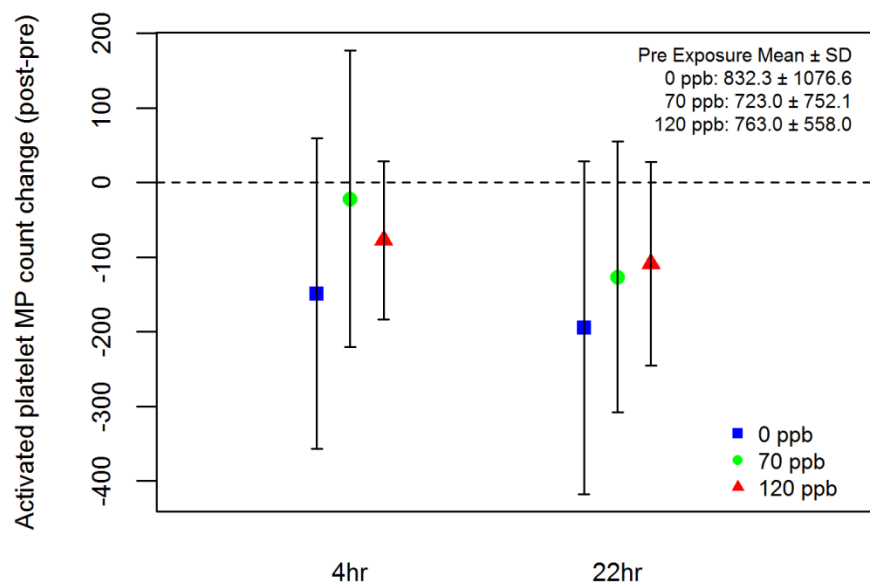


Figure B.3.9. Change in activated platelet MP count at different post-exposure times and at each ozone exposure.

Main Analysis of Ozone Effect

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

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

Table B.3.9a. Type III Sum of Squares for Change in Activated Platelet MP Count

Effect	P Value
4-hr vs. 22-hr change	0.3992
Ozone exposure	0.5135
Site	0.1787

Table B.3.9b. Mixed Model for Change in Activated Platelet MP Count

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	-285.98	-495.03	-76.9391	0.0079
Change between pre- and post-exposure				
4-hr change	58.5538	-78.8628	195.97	0.3992
22-hr change	0			
Ozone exposure				
120 ppb	75.3203	-92.5845	243.22	0.3769
70 ppb	92.8930	-75.7148	261.50	0.2781
0 ppb	0			
Site				
URMC	202.15	-27.8999	432.20	0.0842
UNC	42.8466	-199.53	285.23	0.7260
UCSF	0			

Analyses of Interactions

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

Table B.3.9c. Type III Sum of Squares for Change in Activated Platelet MP, Including Ozone Exposure, by Age Interaction

Effect	P Value
Ozone exposure	0.5189
4-hr vs. 22-hr change	0.3948
Site	0.2621
Age	0.1497
Ozone exposure by age	0.4373

Table B.3.9d. Mixed Model for Change in Activated Platelet MP, Including Ozone Exposure, by Age Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	-281.58	-490.28	-72.8888	0.0088
4-hr change	59.1040	-78.2985	196.51	0.3948
22-hr change	0			
Ozone exposure				
120 ppb	74.1150	-93.8176	242.05	0.3846
70 ppb	92.5690	-76.3193	261.46	0.2806
0 ppb	0			
Site				
URMC	181.88	-49.0618	412.82	0.1210
UNC	46.8823	-194.76	288.52	0.7005
UCSF	0			
Age	29.4452	-1.1366	60.0271	0.0589
Ozone exposure by age				
120 ppb by age	-19.0599	-56.0321	17.9124	0.3114
70 ppb by age	-22.7901	-60.1905	14.6103	0.2316
0 ppb by age	0			

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

Table B.3.9e. Type III Sum of Squares for Change in Activated Platelet MP, Including Ozone Exposure, by Sex Interaction

Effect	P Value
Ozone exposure	0.4616
4-hr vs. 22-hr change	0.3987
Site	0.1574
Sex	0.3650
Ozone exposure by sex	0.8387

Table B.3.9f. Mixed Model for Change in Activated Platelet MP, Including Ozone Exposure, by Sex Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	-278.45	-537.45	-19.4523	0.0354
4-hr change	58.7535	-78.9812	196.49	0.3987
22-hr change	0			
Ozone exposure				
120 ppb	116.41	-151.38	384.20	0.3918
70 ppb	153.34	-112.86	419.53	0.2569
0 ppb	0			
Site				
URMC	217.32	-14.9294	449.57	0.0663
UNC	66.6214	-180.88	314.12	0.5938
UCSF	0			
Sex				
Female	-34.2804	-316.15	247.58	0.8094
Male	0			
Ozone exposure by sex				
120 ppb by female	-67.8170	-412.06	276.43	0.6977
70 ppb by female	-101.61	-446.15	242.94	0.5610
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.3.9g. Type III Sum of Squares for Change in Activated Platelet MP, Including Ozone Exposure, by GSTM1 Status Interaction

Effect	P Value
Ozone exposure	0.5229
4-hr vs. 22-hr change	0.3992
Site	0.1594
GSTM1 status	0.3897
Ozone exposure by GSTM1 status	0.6417

Table B.3.9h. Mixed Model for Change in Activated Platelet MP, Including Ozone Exposure, by GSTM1 Status Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	-258.31	-491.67	-24.9605	0.0305
4-hr change	58.6451	-78.9763	196.27	0.3992
22-hr change	0			
Ozone exposure				
120 ppb	43.8246	-173.89	261.54	0.6914
70 ppb	130.86	-91.1949	352.92	0.2461
0 ppb	0			
Site				
URMC	212.22	-19.7789	444.22	0.0725
UNC	49.8932	-193.52	293.31	0.6845
UCSF	0			
GSTM1 status				
Sufficient	-82.1523	-361.68	197.37	0.5604
Null	0			
Ozone exposure by GSTM1 status				
120 ppb by sufficient	77.9148	-264.79	420.62	0.6539
70 ppb by sufficient	-84.9452	-427.03	257.14	0.6244
0 ppb by sufficient	0			
120 ppb by null	0			
70 ppb by null	0			
0 ppb by null	0			

10. CD142+ MP Count

The following figure shows the change in CD142+ MP count from pre- to post-exposure over time. The data come from Table B.3.4.

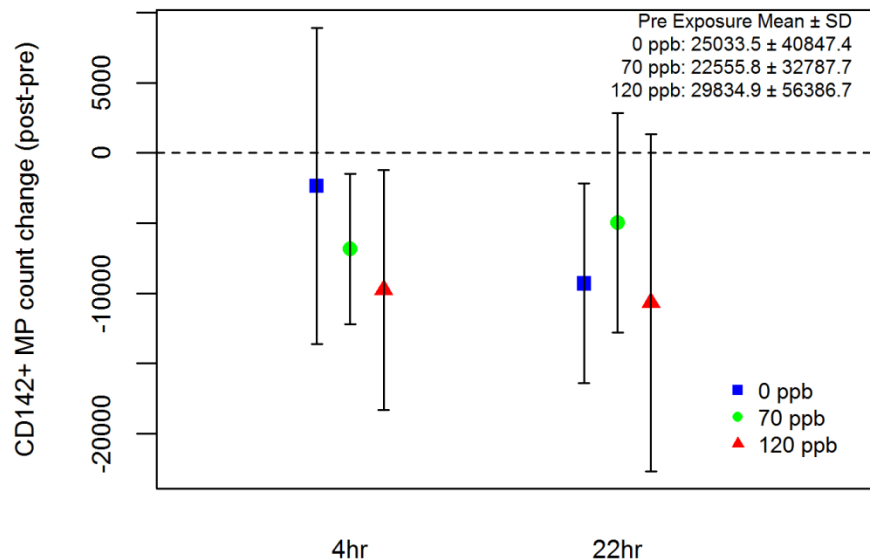


Figure B.3.10a. Change in CD142+ MP count at different post-exposure times and at each ozone exposure.

Main Analysis of Ozone Effect

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

- there were no differences between the 4-hr and 22-hr post-exposure CD142+ MP count;
- there were no differences in CD142+ MP count across the ozone exposures; and
- there were no differences in CD142+ MP count across the 3 sites.

Table B.3.10a. Type III Sum of Squares for Change in CD142+ MP Count

Effect	P Value
4-hr vs. 22-hr change	0.5938
Ozone exposure	0.5513
Site	0.1252

Table B.3.10b. Mixed Model for Change in CD142+ MP Count

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	-2215.64	-12543	8111.25	0.6707
Change between pre- and post-exposure				
4-hr change	1864.21	-5060.27	8788.70	0.5938
22-hr change	0			
Ozone exposure				
120 ppb	-4444.20	-12932	4043.56	0.3026
70 ppb	-927.12	-9418.57	7564.32	0.8295
0 ppb	0			
Site				
URMC	-1880.87	-13160	9398.14	0.7410
UNC	-11357	-23216	501.43	0.0603
UCSF	0			

Analyses of Interactions

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

Table B.3.10c. Type III Sum Of Squares For Change In CD142+ MP Count, Including Ozone Exposure, by Age Interaction

Effect	P Value
Ozone exposure	0.5787
4-hr vs. 22-hr change	0.5985
Site	0.1251
Age	0.7937
Ozone exposure by age	0.3956

Table B.3.10d. Mixed Model for Change in CD142+ MP Count, Including Ozone Exposure, by Age Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	-2095.61	-12465	8273.86	0.6887
4-hr change	1841.76	-5086.52	8770.04	0.5985
22-hr change	0			
Ozone exposure				
120 ppb	-4369.04	-12864	4125.68	0.3112
70 ppb	-1250.43	-9762.10	7261.24	0.7720
0 ppb	0			
Site				
URMC	-2092.06	-13504	9320.11	0.7163
UNC	-11510	-23427	408.04	0.0582
UCSF	0			
Age	95.9370	-1433.00	1624.88	0.9010
Ozone exposure by age				
120 ppb by age	-580.18	-2445.79	1285.43	0.5413
70 ppb by age	706.24	-1177.34	2589.82	0.4614
0 ppb by age	0			

The following figure shows the change in CD142+ MP count from pre- to post-exposure over time by sex.

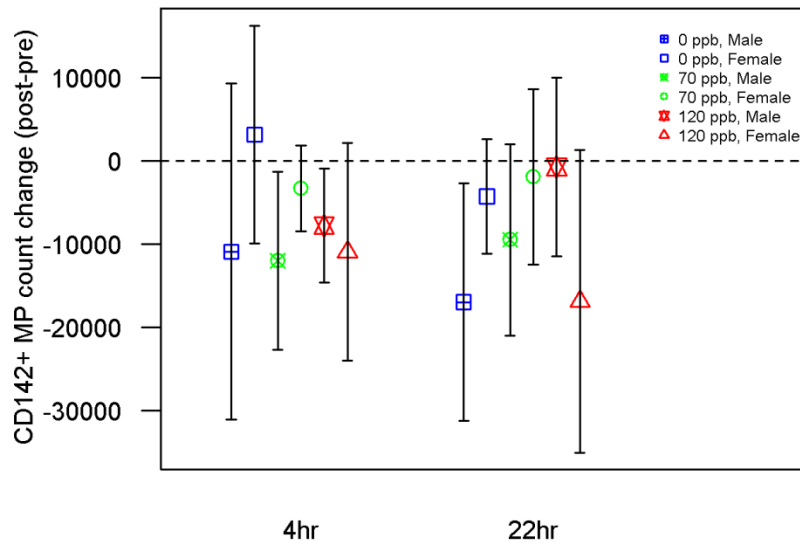


Figure B.3.10b. Change in CD142+ MP count at different post-exposure times for males and females at each ozone exposure.

As we can see from the tables below, there was a marginally significant difference in the ozone effects on CD142+ MP count by sex — CD142+ MP count in women decreased from pre-exposure to post-exposure relative to men at 120 ppb, but not 70 ppb, ozone exposure.

Table B.3.10e. Type III Sum of Squares for Change in CD142+ MP Count, Including Ozone Exposure, by Sex Interaction

Effect	P Value
Ozone exposure	0.9085
4-hr vs. 22-hr change	0.5869
Site	0.0887
Sex	0.2403
Ozone exposure by sex	0.0231

Table B.3.10f. Mixed Model for Change in CD142+ MP Count, Including Ozone Exposure, by Sex Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	-10472	-23309	2365.41	0.1085
4-hr change	1885.13	-4987.93	8758.20	0.5869
22-hr change	0			
Ozone exposure				
120 ppb	9699.89	-3868.29	23268	0.1599
70 ppb	1989.91	-11365	15345	0.7689
0 ppb	0			
Site				
URMC	-2924.97	-14296	8445.82	0.6102
UNC	-12787	-24867	-707.51	0.0383
UCSF	0			
Sex				
Female	15002	994.39	29009	0.0361
Male	0			
Ozone exposure by sex				
120 ppb by Female	-23011	-40320	-5702.32	0.0095
70 ppb by Female	-4668.80	-21886	12548	0.5929
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.3.10g. Type III Sum of Squares for Change in CD142+ MP Count, Including Ozone Exposure, by GSTM1 Status Interaction

Effect	P Value
Ozone exposure	0.3831
4-hr vs. 22-hr change	0.5965
Site	0.1155
GSTM1 status	0.2242
Ozone exposure by GSTM1 status	0.2470

Table B.3.10h. Mixed Model for Change in CD142+ MP Count, Including Ozone Exposure, by GSTM1 Status Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	-6579.71	-18079	4919.62	0.2583
4-hr change	1848.05	-5066.61	8762.71	0.5965
22-hr change	0			
Ozone exposure				
120 ppb	1257.64	-9701.01	12216	0.8209
70 ppb	457.45	-10648	11563	0.9352
0 ppb	0			
Site				
URMC	-2581.36	-13927	8763.98	0.6520
UNC	-11835	-23714	44.2694	0.0508
UCSF	0			
GSTM1 status				
Sufficient	11894	-2032.88	25821	0.0931
Null	0			
Ozone exposure by GSTM1 status				
120 ppb by sufficient	-14198	-31481	3085.74	0.1067
70 ppb by sufficient	-3922.20	-21128	13284	0.6531
0 ppb by sufficient	0			
120 ppb by null	0			
70 ppb by null	0			
0 ppb by null	0			

11. CD40 Ligand MP Count

The following figure shows the change in CD40 ligand MP count from pre- to post-exposure over time. The data come from Table B.3.4.

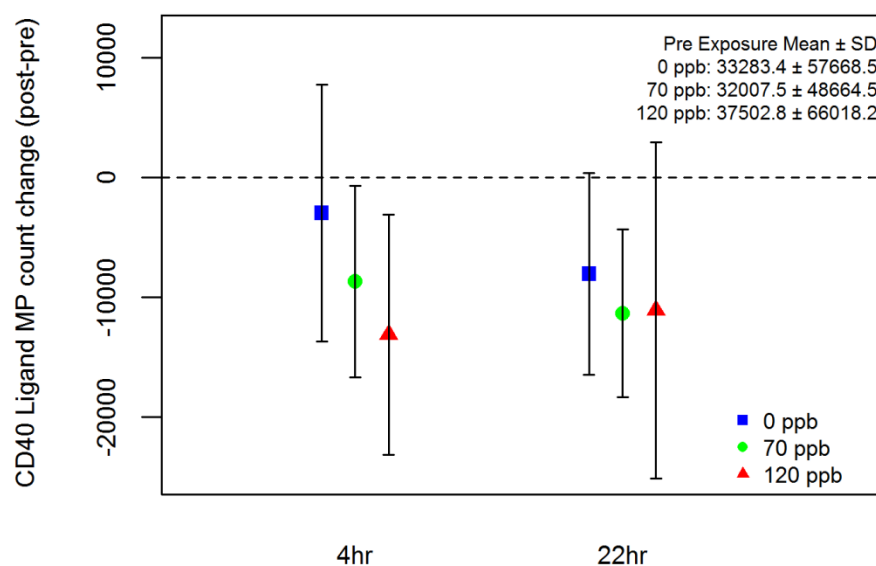


Figure B.3.11a. Change in CD40 ligand MP count at different post-exposure times and at each ozone exposure.

Main Analysis of Ozone Effect

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

- there were no differences between the 4-hour and 22-hour post-exposure CD40 ligand MP count;
- there were no differences in CD40 ligand MP count across the ozone exposures; and
- there were no differences in CD40 ligand MP count across the 3 sites.

Table B.3.11a. Type III Sum of Squares for Change in CD40 Ligand MP Count

Effect	P Value
4-hr vs. 22-hr change	0.6343
Ozone exposure	0.3056
Site	0.1226

Table B.3.11b. Mixed Model for Change in CD40 Ligand MP Count

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	-130.99	-12427	12165	0.9831
Change between pre- and post-exposure				
4-hr change	1717.04	-5435.42	8869.50	0.6343
22-hr change	0			
Ozone exposure				
120 ppb	-6516.86	-15307	2273.62	0.1451
70 ppb	-5186.68	-13984	3610.69	0.2459
0 ppb	0			
Site				
URMC	-3397.94	-17644	10848	0.6365
UNC	-14710	-29610	189.74	0.0529
UCSF	0			

Analyses of Interactions

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

Table B.3.11c. Type III Sum of Squares for Change in CD40 Ligand MP Count, Including Ozone Exposure, by Age Interaction

Effect	P Value
Ozone exposure	0.2953
4-hr vs. 22-hr change	0.6412
Site	0.1209
Age	0.6063
Ozone exposure by age	0.3330

Table B.3.11d. Mixed Model for Change in CD40 Ligand MP Count, Including Ozone Exposure, by Age Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	45.4507	-12286	12377	0.9942
4-hr change	1682.41	-5471.14	8835.96	0.6412
22-hr change	0			
Ozone exposure				
120 ppb	-6442.19	-15236	2351.58	0.1499
70 ppb	-5573.79	-14387	3239.25	0.2134
0 ppb	0			
Site				
URMC	-3884.16	-18272	10504	0.5927
UNC	-14973	-29922	-24.3381	0.0496
UCSF	0			
Age	14.5513	-1736.86	1765.96	0.9869
Ozone exposure by age				
120 ppb by age	-181.56	-2112.36	1749.24	0.8534
70 ppb by age	1164.59	-786.42	3115.60	0.2413
0 ppb by age	0			

The following figure shows the change in CD40 ligand MP count from pre- to post-exposure over time by sex.

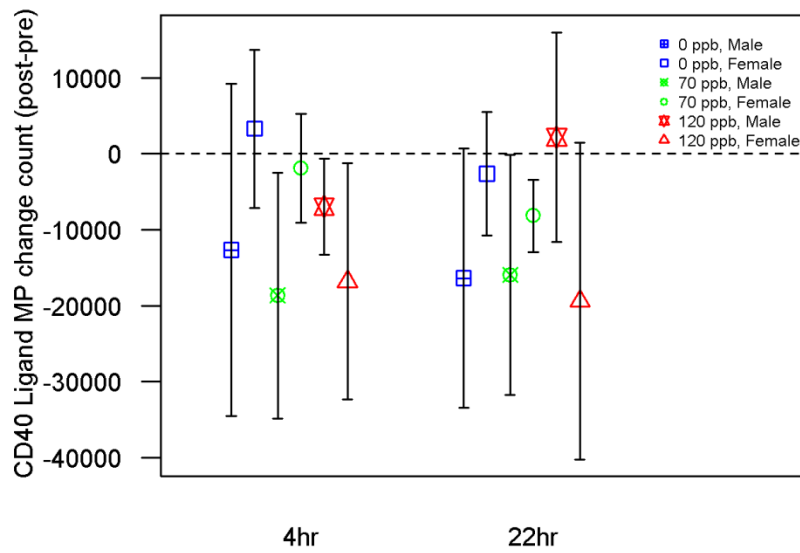


Figure B.3.11b. Change in CD40 ligand MP count at different post-exposure times for males and females at each ozone exposure.

As we can see from the tables below, there was a significant difference in the ozone effect on CD40 ligand MP count by sex — CD40 ligand MP count in women decreased from pre-exposure to post-exposure relative to males at 120 ppb, but not at 70 ppb, ozone exposure.

Table B.3.11e. Type III Sum of Squares for Change in CD40 Ligand MP Count, Including Ozone Exposure, by Sex Interaction

Effect	P Value
Ozone exposure	0.5599
4-hr vs. 22-hr change	0.6218
Site	0.0919
Sex	0.3167
Ozone exposure by sex	0.0008

Table B.3.11f. Mixed Model for Change in CD40 Ligand MP Count, Including Ozone Exposure, by Sex Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	-9788.86	-24744	5166.21	0.1965
4-hr change	1750.82	-5280.68	8782.33	0.6218
22-hr change	0			
Ozone exposure				
120 ppb	12844	-1086.37	26774	0.0705
70 ppb	-3515.62	-17232	10201	0.6133
0 ppb	0			
Site				
URMC	-4601.15	-19011	9808.89	0.5271
UNC	-16293	-31521	-1065.50	0.0363
UCSF	0			
Sex				
Female	17539	1478.89	33600	0.0327
Male	0			
Ozone exposure by sex				
120 ppb by female	-31405	-49167	-13642	0.0006
70 ppb by female	-2572.14	-20246	15102	0.7741
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.3.11g. Type III Sum of Squares for Change in CD40 Ligand MP Count, Including Ozone Exposure, by GSTM1 Status Interaction

Effect	P Value
Ozone exposure	0.2140
4-hr vs. 22-hr change	0.6398
Site	0.1069
GSTM1 status	0.1435
Ozone exposure by GSTM1 status	0.4134

Table B.3.11h. Mixed Model for Change in CD40 Ligand MP Count, Including Ozone Exposure, by GSTM1 Status Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	P Value
Intercept	-5249.28	-18770	8271.12	0.4421
4-hr change	1689.24	-5463.20	8841.67	0.6398
22-hr change	0			
Ozone exposure				
120 ppb	-1729.46	-13092	9632.90	0.7640
70 ppb	-3604.35	-15131	7922.10	0.5376
0 ppb	0			
Site				
URMC	-4506.37	-18767	9754.47	0.5313
UNC	-15450	-30309	-591.26	0.0417
UCSF	0			
GSTM1 status				
Sufficient	14277	-1645.86	30200	0.0782
Null	0			
Ozone exposure by GSTM1 status				
120 ppb by sufficient	-11938	-29865	5989.97	0.1903
70 ppb by sufficient	-4357.74	-22204	13489	0.6302
0 ppb by sufficient	0			
120 ppb by null	0			
70 ppb by null	0			
0 ppb by null	0			

12. Platelet Count (1000/ μ L)

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

- there were marginally significant differences between the 4-hour and 22-hour post-exposure platelet counts;
- there were no ozone effects on platelet count; and
- there were significant changes in platelet count across the 3 sites.

Table B.3.12a. Type III Sum of Squares for Change in Platelet Count (1000/ μ L)

Effect	<i>P</i> Value
4-hr vs. 22-hr change	0.0399
Ozone exposure	0.1901
Site	<0.0001

Table B.3.12b. Mixed Model for Change in Platelet Count (1000/ μ L)

Effect	Estimate	Lower 95% CI	Upper 95% CI	<i>P</i> Value
Intercept	-14.5587	-18.9606	-10.1568	<0.0001
Change between pre- and post-exposure				
4-hr change	2.6133	0.1231	5.1036	0.0399
22-hr change	0			
Ozone exposure				
120 ppb	1.3232	-1.7301	4.3765	0.3934
70 ppb	-1.4710	-4.4976	1.5557	0.3387
0 ppb	0			
Site				
URMC	5.0305	-0.1373	10.1982	0.0563
UNC	13.4758	8.1100	18.8417	<0.0001
UCSF	0			

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

Table B.3.12c. Type III Sum of Squares for Change in Platelet Count (1000/ μ L), Including Ozone Exposure, by Age Interaction

Effect	<i>P</i> Value
Ozone exposure	0.1487
4-hr vs. 22-hr change	0.0398
Site	<0.0001
Age	0.1343
Ozone exposure by age	0.1644

Table B.3.12d. Mixed Model for Change in Platelet Count (1000/ μ L), Including Ozone Exposure, by Age Interaction

Intercept	-14.6051	-18.9761	-10.2341	<0.0001
4-hr change	2.6114	0.1250	5.0977	0.0398
22-hr change	0			
Ozone exposure				
120 ppb	1.4399	-1.6139	4.4937	0.3533
70 ppb	-1.5621	-4.5927	1.4685	0.3103
0 ppb	0			
Site				
URMC	5.4537	0.3030	10.6044	0.0382
UNC	13.4814	8.1646	18.7983	<0.0001
UCSF	0			
Age	-0.3055	-0.9231	0.3121	0.3279
Ozone exposure by age				
120 ppb by age	-0.4049	-1.0807	0.2709	0.2395
70 ppb by age	0.2388	-0.4315	0.9091	0.4841
0 ppb by age	0			

As we can see from the tables below, there was a marginally significant difference in the ozone effect on platelet count in women relative to men.

Table B.3.12e. Type III Sum of Squares for Change in Platelet Count (1000/ μ L), Including Ozone Exposure, by Sex Interaction

Effect	<i>P</i> Value
Ozone exposure	0.3896
4-hr vs. 22-hr change	0.0398
Site	<0.0001
Sex	0.5119
Ozone exposure by sex	0.0259

Table B.3.12f. Mixed Model for Change in Platelet Count (1000/ μ L), Including Ozone Exposure, by Sex Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	<i>P</i> Value
Intercept	-14.1037	-19.3646	-8.8428	<0.0001
4-hr change	2.5974	0.1244	5.0705	0.0398
22-hr change	0			
Ozone exposure				
120 ppb	-0.7714	-5.3933	3.8504	0.7421
70 ppb	1.3000	-3.3219	5.9219	0.5794
0 ppb	0			
Site				
URMC	5.2752	0.03163	10.5188	0.0487
UNC	13.8190	8.3491	19.2889	<0.0001
UCSF	0			
Sex				
Female	-1.1075	-6.7815	4.5666	0.6988
Male	0			
Ozone exposure by sex				
120 ppb by female	3.6625	-2.4619	9.7869	0.2394
70 ppb by female	-4.7114	-10.7963	1.3736	0.1282
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.3.12g. Type III Sum of Squares for Change in Platelet Count (1000/ μ L), Including Ozone Exposure, by GSTM1 Status Interaction

Effect	<i>P</i> Value
Ozone exposure	0.1515
4-hr vs. 22-hr change	0.0391
Site	<0.0001
GSTM1 status	0.2151
Ozone exposure by GSTM1 status	0.5995

Table B.3.12h. Mixed Model for Change in Platelet Count (1000/ μ L), Including Ozone Exposure, by GSTM1 Status Interaction

Effect	Estimate	Lower 95% CI	Upper 95% CI	<i>P</i> Value
Intercept	-13.3776	-18.2621	-8.4932	<0.0001
4-hr change	2.6282	0.1347	5.1218	0.0391
22-hr change	0			
Ozone exposure				
120 ppb	0.3098	-3.7451	4.3646	0.8803
70 ppb	-1.2169	-5.2210	2.7871	0.5493
0 ppb	0			
Site				
URMC	5.3737	0.1948	10.5527	0.0422
UNC	13.7593	8.3876	19.1309	<0.0001
UCSF	0			
GSTM1 status				
Sufficient	-3.2703	-8.8937	2.3530	0.2507
Null	0			
Ozone exposure by GSTM1 status				
120 ppb by sufficient	2.3442	-3.8283	8.5168	0.4544
70 ppb by sufficient	-0.6397	-6.7663	5.4869	0.8369
0 ppb by sufficient	0			
120 ppb by null	0			
70 ppb by null	0			
0 ppb by null	0			

Abbreviations and Other Terms

CD142+	tissue factor expressing microparticle
GSTM1	glutathione S-transferase Mu 1
HR	heart rate
MOSES	Multicenter Ozone Study in oldEr Subjects
MP	microparticle
MP-TFA	microparticle-associated tissue factor activity
ppb	part per billion
SD	standard deviation
UCSF	University of California at San Francisco
UNC	University of North Carolina at Chapel Hill
URMC	University of Rochester Medical Center
vWF	von Willebrand factor