SUPPLEMENTAL MATERIAL

EXPANDED STATISITCAL METHODS

Associations with $PM_{2.5}$ exposures and microparticles and markers of inflammation were evaluated by estimating two similar regression models. The first model used a fixed effects regression approach that controls for subject-specific differences by estimating a fixed effects model as follows:

$$Y_{it} = \alpha_1 + \alpha_2 + \ldots + \alpha_{72} + \beta(P_t) + \varepsilon_{it}$$

where Y_{it} is the outcome variable for individual i on day t; $\alpha_1 + \alpha_2 + \ldots + \alpha_{72}$ are the fixed effects coefficients that adjust for subject-specific differences; β is the coefficient that measures the association between $PM_{2.5}$ and the outcome variable, P_t is $PM_{2.5}$ averaged over the 24 h period prior to the blood draw on day *t*; and ε_{it} is the model error. The second model uses a subject-mean adjusted approach that accounts for subject-specific differences by subtracting out subject-level means as follows:

$$\Delta Y_{it} = (Y_{it} - \bar{Y}_i)_{it} = \alpha + \beta(P_t) + \varepsilon_{it}$$

where $\bar{Y}_i$ is the mean value for individual *i*. The difference between the two models is that the fixed effects model controls for subject-level differences by estimating subject-specific fixed effects as part of the model. The subject-mean adjusted model controls for subject-level differences by first subtracting out the subject-level means, and regressing deviations from these means (ΔY_{it}) on $PM_{2.5}$.

To illustrate associations, plots of the subject-specific differences over pollution concentrations along with regression plots were generated. To explore the sensitivity of the results, models were estimated that excluded observations from any participant who reported any acute illness at time of the blood draw, models that controlled for time exercised on the day of the draw and the day before the draw, models that controlled for whether or not female subjects were menstruating, and models that excluded observations for days with $PM_{2.5}$ concentrations greater than 100 $\mu g/m^3$. Additionally, rather than using $PM_{2.5}$ concentrations 24 h prior to the blood draws, models that used $PM_{2.5}$ concentrations 12 h and 48 h, respectively, were estimated. Finally, using data for the final two winter/spring time periods, models that included interaction terms for gender and $PM_{2.5}$, and fish oil (versus placebo) and $PM_{2.5}$ were estimated to test for effect modification by gender and by fish oil supplement use.

For the 42 analyzed human cytokines and the 2 adhesion proteins, we also estimated the fixed effects and subject-means adjusted models as described above. The percent change (and 95% Cis) for each analyte per 10 $\mu g/m^3$ increase in $PM_{2.5}$ relative to the mean value of the analyte were calculated and plotted. The results are ordered based on t-values—resulting in the most statistically significant positive associations being on the left. This approach was used in order comprehensively evaluate all of the measures analytes, allow for direct comparisons and evaluation of the strength of the statistical associations with key markers of systemic inflammation, and to mitigate concerns regarding multiple testing and selective reporting.

All of the statistical analyses were conducted using SAS, version 9.4 (SAS Institute, Inc., Cary, North Carolina).

Supplemental Table I. Regression coefficients for $PM_{2.5}$ from fixed effect and subject-mean adjusted modeling approaches

	Fixed Effect		Subject-mean adjusted		
Outcome variables	**Coefficient (x 10) (Std. Error)**	**P-value**	**Coefficient (x 10) (Std. Error)**	**P-value**	**R^2**
Microparticles					
MP, EPC	-0.12 (0.45)	0.787	-0.09 (0.34)	0.796	0.00
MP, Platelet	-1.85 (0.73)	0.012	-1.33 (0.55)	0.017	0.02
MP, Endothelial	1.39 (0.20)	<0.001	1.00 (0.16)	<0.001	0.11
MP, Lung Endothelial	0.58 (0.09)	<0.001	0.42 (0.07)	<0.001	0.10
MP, Non-lung Endothelial	0.79 (0.13)	<0.001	0.56 (0.10)	<0.001	0.09
MP, Venous Endothelial	0.67 (0.11)	<0.001	0.48 (0.09)	<0.001	0.09
MP, Lung Venous Endothelial	0.54 (0.09)	<0.001	0.39 (0.07)	<0.001	0.08
MP, Arterial Endothelial	0.51 (0.1)	<0.001	0.37 (0.07)	<0.001	0.07
MP, Lung Arterial Endothelial	0.43 (0.09)	<0.001	0.31 (0.07)	<0.001	0.06
MP, Activated Endothelial	-0.88 (0.34)	0.010	-0.63 (0.26)	0.014	0.02
MP, Lung Activated Endothelial	0.006 (0.09)	0.940	0.005 (0.06)	0.943	0.00
MP, Venous Activated Endothelial	-0.02 (0.14)	0.871	-0.02 (0.10)	0.876	0.00
MP, Lung Venous Activated Endothelial	-0.002 (0.08)	0.979	-0.002 (0.06)	0.980	0.00
MP, Arterial Activated Endothelial	0.04 (0.11)	0.690	0.03 (0.08)	0.702	0.00
MP, Lung Arterial Activated Endothelial	0.07 (0.10)	0.501	0.05 (0.07)	0.518	0.00
Immune cells					
Monocytes	1063.78 (228.46)	<0.001	863.99 (185.95)	<0.001	0.06
Natural killer cells	812.89 (224.51)	<0.001	660.22 (182.24)	<0.001	0.03
Helper T cells	2649.31 (620.36)	<0.001	2151.75 (504.36)	<0.001	0.05
Killer T cells	1278.28 (398.93)	0.002	1038.21 (323.52)	0.001	0.03
B cells	-382.57 (376.38)	0.310	-310.72 (304.33)	0.308	0.00
Platelet-monocyte aggregates	0.25 (0.11)	0.019	0.20 (0.09)	0.020	0.01

Supplemental Table II. Summary statistics and regression coefficients (and standard errors) for $PM_{2.5}$ from subject-mean adjusted regression results for all measured cytokines and adhesion molecules with out-of-range observations imputed using the florescent intensity and the relevant minimum or maximum values of the standard curve as recommended.

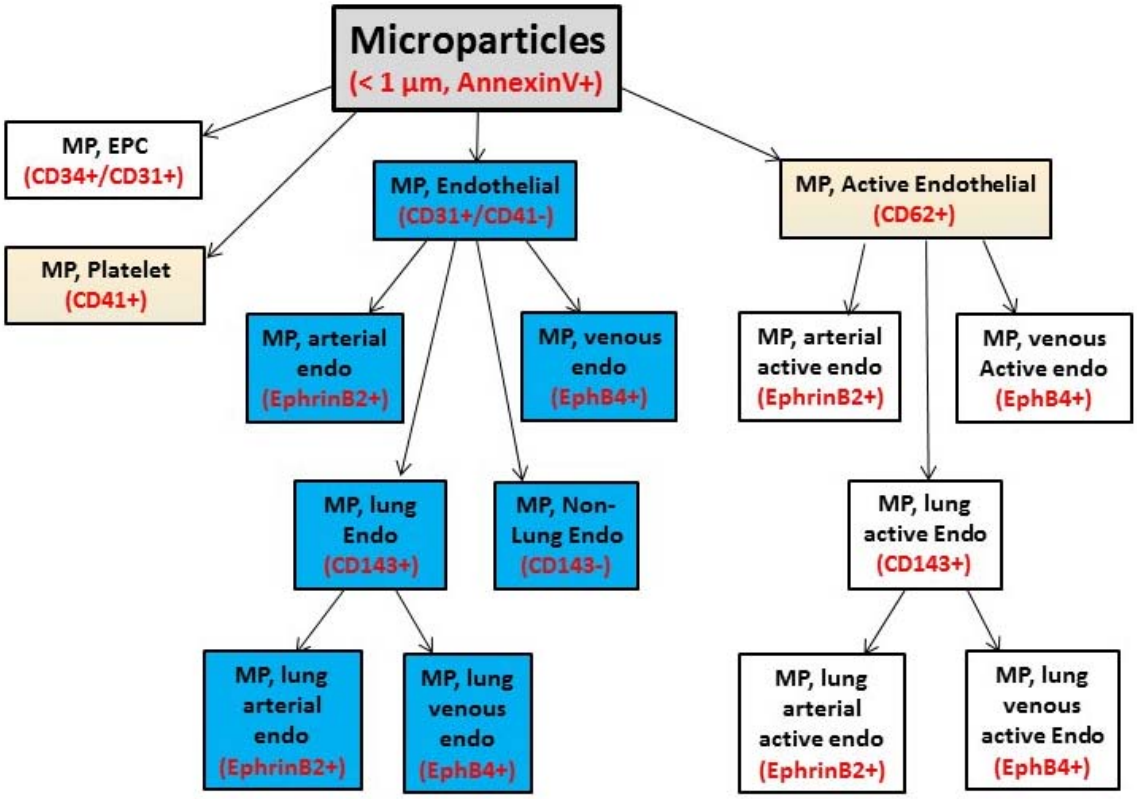
Analyte	N of Obs.	Mean	SD	Fixed Effects Estimate	P-value	Subject Mean Estimate	P-value	R square
TNFα	370	20.79	18.91	1.54 (0.23)	<0.0001	1.25 (0.19)	<0.0001	0.1063
sICAM-1	370	37723.12	11579.62	771.58 (153.2)	<0.0001	628.43 (125.19)	<0.0001	0.0641
MCP-1	370	255.7	105.67	6.41 (1.34)	<0.0001	5.22 (1.09)	<0.0001	0.0583
IL-8	370	42.42	68.69	3.63 (0.86)	<0.0001	2.96 (0.7)	<0.0001	0.0464
MIP-1α	370	24.35	30.61	1.06 (0.26)	<0.0001	0.86 (0.21)	<0.0001	0.0442
MIP-1β	370	68.95	116.06	2.02 (0.64)	0.0017	1.65 (0.52)	0.0016	0.0266
IP-10	370	135.17	92.6	4.97 (1.65)	0.0028	4.05 (1.34)	0.0027	0.0242
sVCAM-1	370	389023.08	89651.48	2809.7 (1268.56)	0.0275	2288.44 (1030.08)	0.0269	0.0132
IL-6	370	2.45	4.92	0.11 (0.06)	0.0494	0.09 (0.05)	0.0484	0.0105
IL-10	370	5.05	9.17	0.14 (0.07)	0.0532	0.11 (0.06)	0.0523	0.0102
IL-1β	370	5.7	16.12	0.35 (0.19)	0.0639	0.29 (0.15)	0.0628	0.0094
IL-9	370	2.39	4.47	0.03 (0.02)	0.1209	0.02 (0.01)	0.1193	0.0066
IL-15	370	5.38	12.96	0.08 (0.07)	0.2678	0.06 (0.06)	0.2657	0.0034
IL-1RA	370	109.75	248.43	1.12 (1.05)	0.2837	0.92 (0.85)	0.2815	0.0032
IL-13	370	33.31	67.58	0.29 (0.28)	0.2876	0.24 (0.22)	0.2855	0.0031
IL-12P70	370	16.23	38.92	0.22 (0.22)	0.3169	0.18 (0.18)	0.3147	0.0027
G-CSF	370	29.22	84.05	0.34 (0.38)	0.3806	0.27 (0.31)	0.3784	0.0021
Eotaxin-1	370	101.6	44.54	0.31 (0.41)	0.4538	0.25 (0.33)	0.4517	0.0015
IL-5	370	3.19	6.6	0.01 (0.02)	0.5475	0.01 (0.02)	0.5456	0.001
IL-1α	370	32.2	94.66	0.43 (0.85)	0.6106	0.35 (0.69)	0.609	0.0007
TNFβ	370	224.79	500.19	0.95 (2.16)	0.6592	0.78 (1.75)	0.6577	0.0005
MCp-3	368	124.65	225.41	0.41 (0.99)	0.6759	0.34 (0.8)	0.6743	0.0005
IL-12P40	370	70.62	190.82	0.32 (0.8)	0.69	0.26 (0.65)	0.6886	0.0004
FGF-2	370	124.34	137.68	0.36 (1.16)	0.7545	0.29 (0.94)	0.7534	0.0003
TGF-α	370	8.23	23.9	0.04 (0.15)	0.8154	0.03 (0.12)	0.8146	0.0001
GM-CSF	370	25.73	55.6	0.05 (0.24)	0.8507	0.04 (0.2)	0.85	<0.0001
IL-17A	370	8.46	13.86	0.02 (0.09)	0.8507	0.01 (0.08)	0.85	<0.0001
Fractalkine	370	82.53	217.07	0.14 (1.36)	0.9167	0.12 (1.11)	0.9163	<0.0001
IL-2	370	4.76	14.34	0.01 (0.16)	0.9562	0.01 (0.13)	0.956	<0.0001
IL-7	370	1.86	3.01	0 (0.02)	0.957	0 (0.02)	0.9568	<0.0001
IFNy	370	29.22	77.66	0 (0.59)	0.9994	0 (0.48)	0.9994	<0.0001
IL-4	370	2.36	10.74	-0.01 (0.06)	0.9336	0 (0.05)	0.9333	<0.0001
PDGF-BB	370	18537.05	27508.78	-140.45 (549.09)	0.7983	-114.39 (445.19)	0.7974	0.0002
Flt-3L	370	3.58	21.98	-0.15 (0.26)	0.5736	-0.12 (0.21)	0.5718	0.0009
IL-18	370	94.8	81.4	-0.47 (0.79)	0.554	-0.38 (0.64)	0.5522	0.001
MDC	370	547.14	243.61	-1.97 (2.66)	0.4593	-1.61 (2.16)	0.4572	0.0015
IFNa2	370	74.23	181.96	-1.09 (1.47)	0.4585	-0.89 (1.19)	0.4564	0.0015
IL-3	370	1.97	6.7	-0.03 (0.04)	0.4532	-0.03 (0.03)	0.4511	0.0015
VEGF-A	355	95.53	118.99	-1.34 (0.93)	0.1511	-1.09 (0.75)	0.1478	0.0059
GROα	370	2830.76	1317.08	-31.78 (14.59)	0.0302	-25.89 (11.85)	0.0296	0.0128

RANTES	370	2513.11	2784.59	-143.17 (43.13)	0.001	-116.61 (35.09)	0.001	0.0291
PDGF-AA	370	1438.19	466.94	-19.39 (4.96)	0.0001	-15.79 (4.04)	0.0001	0.0399
sCD40L	370	1521.46	713.2	-47.38 (8.63)	<0.0001	-38.59 (7.07)	<0.0001	0.075
EGF	370	197.96	137.85	-15.34 (1.93)	<0.0001	-12.5 (1.6)	<0.0001	0.1429

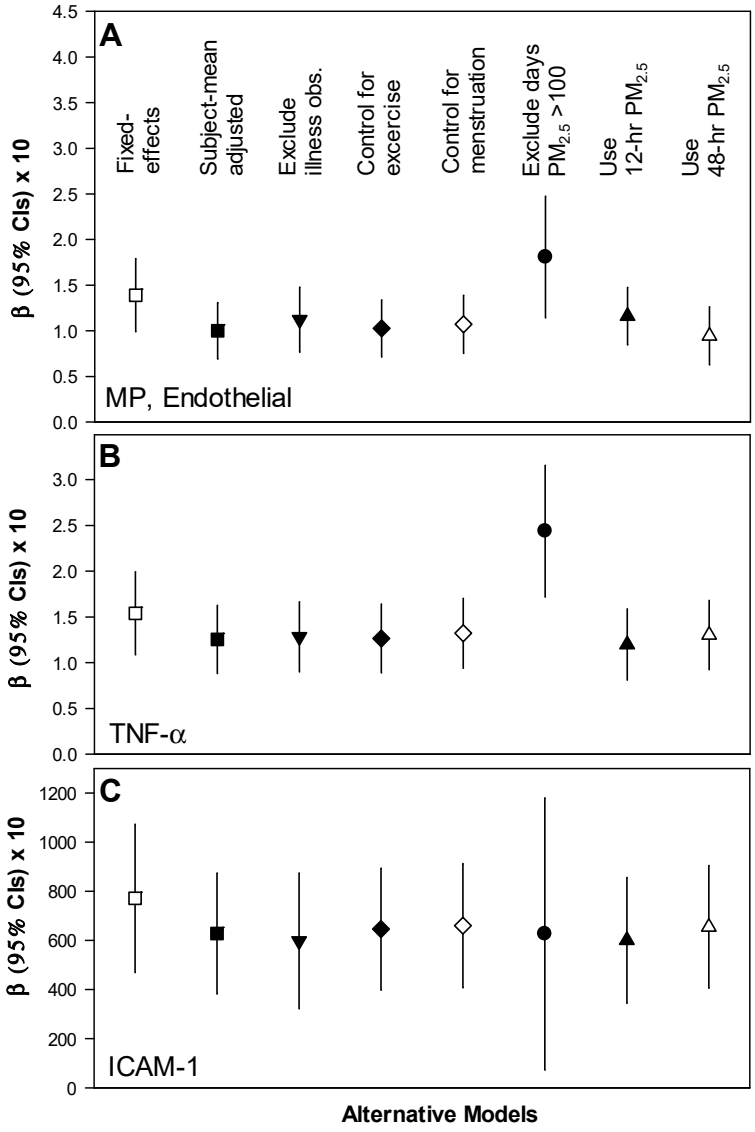
Supplemental Table III. Summary statistics and regression coefficients (and standard errors) for $PM_{2.5}$ from all of the measured cytokines and adhesion molecules with out-of-range observations treated as missing observations.

Analyte	N of Obs.	Mean	SD	Fixed Effects Estimate	P-value	Subject Mean Estimate	P-value	R^2
TNFα	366	21.01	18.89	1.55 (0.23)	<0.0001	1.26 (0.19)	<0.0001	0.1066
sICAM-1	370	37723.12	11579.62	771.58 (153.2)	<0.0001	628.43 (125.19)	<0.0001	0.0641
MCP-1	370	255.7	105.67	6.41 (1.34)	<0.0001	5.22 (1.09)	<0.0001	0.0583
MIP-1a	222	40.16	30.61	1.1 (0.29)	0.0002	0.81 (0.21)	0.0002	0.0601
IL-8	266	58.75	74.95	3.74 (1.19)	0.0019	2.64 (0.87)	0.0028	0.0334
IP-10	370	135.17	92.6	4.97 (1.65)	0.0028	4.05 (1.34)	0.0027	0.0242
MIP-1β	287	88.7	125.03	2.06 (0.72)	0.0048	1.59 (0.56)	0.0049	0.0274
sVCAM-1	370	389023.08	89651.48	2809.7 (1268.56)	0.0275	2288.44 (1030.08)	0.0269	0.0132
IL-9	370	2.39	4.47	0.03 (0.02)	0.1209	0.02 (0.01)	0.1193	0.0066
IL-10	179	9.76	11.45	0.21 (0.14)	0.13	0.16 (0.11)	0.122	0.0135
IL-6	155	4.96	6.86	0.16 (0.12)	0.1764	0.1 (0.08)	0.1982	0.0108
IL-1β	232	8.72	19.77	0.39 (0.32)	0.2343	0.26 (0.22)	0.2512	0.0057
IL-13	150	81.22	86.17	0.57 (0.53)	0.2842	0.46 (0.42)	0.2776	0.0080
IL-1RA	161	251.39	326.49	2 (2.21)	0.3679	1.58 (1.73)	0.3636	0.0052
IL-15	198	9.5	16.67	0.11 (0.14)	0.432	0.08 (0.1)	0.433	0.0031
Eotaxin-1	370	101.6	44.54	0.31 (0.41)	0.4538	0.25 (0.33)	0.4517	0.0015
IL-12P70	274	21.69	43.96	0.24 (0.32)	0.4478	0.17 (0.23)	0.454	0.0021
G-CSF	225	47.63	103.77	0.46 (0.68)	0.4929	0.33 (0.49)	0.4921	0.0021
IL-5	175	6.04	8.76	0.03 (0.05)	0.5587	0.02 (0.04)	0.5476	0.0021
MCp-3	139	328.95	259.93	0.91 (1.88)	0.6284	0.73 (1.49)	0.6236	0.0018
TNFβ	153	542.69	658.72	1.92 (4.15)	0.645	1.5 (3.24)	0.6452	0.0014
IL-1α	258	45.9	110.65	0.51 (1.17)	0.6624	0.4 (0.89)	0.6525	0.0008
IL-12P40	182	142.9	252.77	0.38 (1.62)	0.8132	0.29 (1.23)	0.8125	0.0003
GM-CSF	277	34.16	62.04	0.04 (0.31)	0.8982	0.03 (0.24)	0.8956	<0.0001
FGF-2	306	149.68	138.6	0.1 (1.15)	0.9336	0.08 (0.89)	0.9328	<0.0001
IL-7	140	3.85	4.19	0 (0.05)	0.9789	0 (0.04)	0.9782	<0.0001
Fractalkine	220	138.37	267.7	-0.02 (2.5)	0.9924	-0.02 (1.79)	0.9923	<0.0001
TGF-α	168	17.35	33.3	0 (0.34)	0.9907	0 (0.25)	0.9906	<0.0001
IL-2	202	8.19	18.74	-0.03 (0.31)	0.9282	-0.02 (0.22)	0.9262	<0.0001
IFNy	193	55.43	100.74	-0.19 (1.23)	0.8792	-0.13 (0.88)	0.8783	0.0001
IL-4	54	12.45	26.11	-0.08 (0.55)	0.8797	-0.06 (0.36)	0.874	0.0005
IL-17A	271	11.31	15.23	-0.05 (0.12)	0.6486	-0.04 (0.09)	0.6499	0.0008
PDGF-BB	332	19514.18	28883.97	-258.72 (566.73)	0.6484	-204.19 (446.09)	0.6474	0.0006
IL-18	350	100.03	80.6	-0.49 (0.84)	0.5601	-0.39 (0.67)	0.5594	0.0010
MDC	370	547.14	243.61	-1.97 (2.66)	0.4593	-1.61 (2.16)	0.4572	0.0015
IL-3	370	1.97	6.7	-0.03 (0.04)	0.4532	-0.03 (0.03)	0.4511	0.0015

IFNa2	301	91.1	197.97	-1.54 (1.89)	0.418	-1.2 (1.47)	0.4134	0.0022
Flt-3L	8	136.71	69.01	-51.81 (48.5)	0.3343	-47.57 (42.82)	0.3091	0.1706
VEGF-A	218	155.17	117.64	-1.55 (1.19)	0.1953	-1.19 (0.89)	0.1804	0.0083
GROα	370	2830.76	1317.08	-31.78 (14.59)	0.0302	-25.89 (11.85)	0.0296	0.0128
RANTES	350	2085.29	2191.45	-92.64 (36.08)	0.0108	-73.68 (28.78)	0.0109	0.0185
PDGF-AA	370	1438.19	466.94	-19.39 (4.96)	0.0001	-15.79 (4.04)	0.0001	0.0399
sCD40L	370	1521.46	713.2	-47.38 (8.63)	<0.0001	-38.59 (7.07)	<0.0001	0.0750
EGF	370	197.96	137.85	-15.34 (1.93)	<0.0001	-12.5 (1.6)	<0.0001	0.1429



Supplemental Figure I. Stylized summary of findings regarding $PM_{2.5}$ associations with circulating microparticles. The color shading indicates the following: white, not significantly associated with $PM_{2.5}$; blue, positively associated with $PM_{2.5}$; tan, negatively associated with $PM_{2.5}$.



Supplemental Figure II. Selected sensitivity analysis. Forrest plot of point estimates and 95% CIs of the coefficient of $PM_{2.5}$ (x 10) for endothelial microparticles (Panel A), TNFα (Panel B), and sICAM-1 (Panel C) using various regression models. These models include: fixed-effects and subject-mean adjusted models with all observations; subject-mean adjusted models excluding draws from participants who reported illness; models controlling for concurrent and previous days' time exercising; models controlling for menstruation; models that exclude days with $PM_{2.5}$ concentrations greater than 100 $\mu g/m^3$; and models that used $PM_{2.5}$ concentrations 12 h and 48 h prior to blood draws (rather than 24 h).