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Supplemental Material

Leukocyte Traits and Exposure to Ambient Particulate Matter Air Pollution in the Women's Health Initiative and Atherosclerosis Risk in Communities Study

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Table S1. Additional details for populations with estimated leukocyte composition data, Women's Health Initiative (1993-2002) and Atherosclerosis Risk in Communities study (1990-1995)

Study name	Alternative name	Abbreviation	Study PIs	Website
Ancillary Study 315	Epigenetic Mechanisms of PM-Mediated Cardiovascular Disease	EMPC	Eric Whitsel Andrea Baccarelli Lifang Hou	https://projectreporter.nih.gov/project_info_description.cfm?aid=9054857&icde=40216248&ddparam=&ddvalue=&ddsueb=&cr=1&csb=default&cs=ASC&pball=
Broad Agency Award 23	Integrative Genomics and Risk of CHD and Related Phenotypes in the Women's Health Initiative	BAA23	Themistocles Assimes Phil Tsao Devin Absher Steve Horvath	https://www.whi.org/researchers/data/WHIStudies/StudySites/BA23/pages/home.aspx
Ancillary Study 311	Bladder Cancer and Leukocyte Methylation study	AS311	Parveen Bhatti	https://www.whi.org/researchers/data/WHIStudies/StudySites/AS311/Pages/home.aspx
ARIC-African Americans	NA	ARIC-AA	Eric Boerwinkle	NA
ARIC-European Americans	NA	ARIC-EA	Myriam Fornage Eric Boerwinkle	NA

Table S2. Characteristics of n=8,457 participants with estimated leukocyte composition data before imputation, Women's Health Initiative (1993-2002) and Atherosclerosis Risk in Communities study (1990-1995)

Characteristic	WHI & ARIC n = 8,457	WHI-EMPC n = 2,160	WHI-AS311 n = 822	WHI-BAA23 n = 1,910	ARIC-AA ^a n = 2,534	ARIC-EA ^b n = 1,031
Male, n (%)	1,380 (16.3)	0 (0.0)	0 (0.0)	0 (0.0)	943 (37.2)	437 (42.4)
Age (years), mean (SD)	61.5 (7.4)	63.7 (7.0)	65.4 (7.1)	64.8 (7.1)	56.6 (5.9)	59.9 (5.5)
Race / ethnicity, n (%)						
American Indian or Alaskan Native	51 (0.6)	50 (2.3)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
Asian or Pacific islander	147 (1.7)	132 (6.1)	15 (1.8)	0 (0.0)	0.0 (0.0)	0 (0.0)
Black or African American	3,737 (44.2)	544 (25.2)	58 (7.1)	601 (31.5)	2534 (100.0)	0 (0.0)
Hispanic/Latino	717 (8.5)	314 (14.5)	24 (2.9)	379 (19.8)	-- ^c	-- ^c
Other	42 (0.5)	33 (1.5)	9 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)
White (not of Hispanic origin) or European American	3763 (44.5)	1,087 (50.3)	715 (86.9)	930 (48.7)	0 (0.0)	1,031 (100.0)
Education, n (%)						
High school education or lower	4,030 (47.9)	591 (28.6)	177 (21.7)	609 (32.2)	1,562 (61.8)	479 (46.5)
More than high school	4,378 (52.1)	1,551 (71.4)	640 (78.3)	1,283 (67.8)	964 (38.2)	552 (53.5)
Smoking status, n (%)						
Never	4,044 (48.5)	1,126 (53.3)	367 (45.5)	1,007 (53.6)	1,113 (44.9)	431 (41.8)
Former	3,042 (36.5)	828 (39.2)	371 (46.0)	685 (36.4)	756 (30.1)	402 (39.0)
Current	1,255 (15.0)	158 (7.5)	69 (8.6)	188 (10.0)	642 (25.6)	198 (19.2)
Alcohol use, n (%)						
Never	1,883 (22.4)	289 (13.6)	90 (11.0)	307 (16.1)	876 (34.9)	321 (31.1)
Former	2,156 (25.7)	610 (28.7)	155 (18.9)	450 (23.6)	795 (31.6)	146 (14.2)
Current	4,351 (51.9)	1,225 (57.7)	575 (70.1)	1,146 (60.2)	841 (33.5)	564 (54.7)
Body mass index (kg/m ²), mean (SD)	29.2 (6.1)	29.5 (5.9)	28.0 (6.2)	29.9 (6.1)	30.1 (6.3)	26.2 (4.4)
Physical activity (MET-hours/week), mean (SD)	12.3 (12.9)	10.3 (12.5)	11.6 (12.6)	10.0 (12.6)	12.8 (11.3)	20.6 (14.2)
Neighborhood SES (z-score sum)	-2.4 (5.9)	-1.6 (5.7)	0.2 (5.2)	-2.6 (5.8)	-5.9 (4.3)	2.8 (4.8)
Leukocyte count (cell/uL), mean (SD)	5,846 (1,607)	5,864 (1,507)	5,924 (1,481)	6,074 (1,610)	5,609 (1,675)	5,972 (1,611)
CD8+ T cells (%)	9 (6)	10 (7)	9 (4)	5 (5)	12 (5)	10 (4)
CD4 +T cells (%)	18 (7)	20 (7)	17 (7)	21 (7)	16 (7)	16 (6)
Nature killer cells (%)	7 (5)	2 (2)	9 (5)	9 (5)	7 (5)	7 (4)
B cells (%)	7 (4)	5 (4)	6 (3)	9 (4)	8 (3)	6 (3)
Monocytes (%)	10 (3)	12 (3)	11 (3)	8 (3)	9 (3)	8 (3)
Granulocytes (%)	49 (12)	50 (12)	49 (12)	48 (12)	48 (13)	54 (12)

^aParticipants were from Jackson (90%) or Forsyth County (10%)

^bParticipants were from Forsyth County (90%), Minneapolis (8%) or Washington County (2%)

^cARIC recruitment and data collection occurred before the National Institute of Health required collection of information about Hispanic/Latino ethnicity

Table S3. Mean (SD) particulate matter concentrations among n=8,457 with estimated leukocyte composition data before imputation, Women's Health Initiative (1993-2002) and Atherosclerosis Risk in Communities study (1990-1995)

PM ($\mu\text{g}/\text{m}^3$)	WHI & ARIC n = 8,457	WHI-EMPC n = 2,160	WHI-AS311 n = 822	WHI-BAA23 n = 1,910	ARIC-AA ^a n = 2,534	ARIC-EA ^b n = 1,031
PM ₁₀						
2-day	31.7 (12.1)	28.5 (11.1)	28.2 (10.8)	28.4 (10.9)	36.1 (12.4)	35.9 (11.5)
7-day	30.8 (9.3)	27.6 (7.9)	27.2 (8.2)	27.8 (8.3)	35.2 (9.3)	34.9 (8.2)
1-month	21.90 (5.9)	20.8 (6.6)	20.1 (6.1)	20.9 (6.5)	20.5 (4.6)	23.1 (5.2)
12-month	21.0 (4.2)	21.1 (5.3)	20.4 (4.8)	21.1 (4.8)	19.9 (1.7)	23.7 (2.4)
PM _{2.5}						
1-month	13.3 (4.5)	13.8 (5.7)	12.1 (3.9)	12.2 (4.1)	13.1 (3.1)	15.4 (4.3)
12-month	13.2 (3.2)	13.8 (4.4)	12.1 (2.8)	12.2 (2.9)	12.7 (1.3)	15.9 (2.1)
PM _{2.5-10}						
1-month	7.7 (4.0)	7.0 (5.2)	8.0 (4.3)	8.8 (4.8)	7.3 (2.1)	7.7 (2.5)
12-month	7.8 (3.2)	7.3 (4.2)	8.3 (3.8)	8.9 (4.0)	7.2 (0.8)	7.8 (1.4)

Abbreviations: AA, African Americans; ARIC, Atherosclerosis Risk in Communities; AS311, Ancillary Study 311; BAA23, Broad Agency Award 23; CI, confidence intervals; EA, European Americans; EMPC, Epigenetic Mechanisms of Particulate Matter-Mediated Cardiovascular Disease; PM, particulate matter; PM₁₀, PM < 10 μm in diameter; PM_{2.5}, PM < 2.5 μm in diameter; PM_{2.5-10}, PM > 2.5 and < 10 μm in diameter; SD, standard deviation; WHI, Women's Health Initiative

^aParticipants were from Jackson (90%) or Forsyth County (10%)

^bParticipants were from Forsyth County (90%), Minneapolis (8%) or Washington County (2%)

Table S4. Pooled difference in leukocyte count (Δ , cell/ μL) per 10 $\mu\text{g}/\text{m}^3$ increase in 28- and 365-day mean PM_{10} concentrations among $n=165,675$ participants, Women's Health Initiative (1993-2002) and Atherosclerosis Risk in Communities study (1986-1998)

	Model 1 ^a		Model 2 ^b		Model 3 ^c	
	Δ (95% CI) cell/ μL	$P_{\text{Cochran's } Q^d}$	Δ (95% CI) cell/ μL	$P_{\text{Cochran's } Q^d}$	Δ (95% CI) cell/ μL	$P_{\text{Cochran's } Q^d}$
PM_{10} ($\mu\text{g}/\text{m}^3$)						
28-day mean	-7 (-23, 9)	0.38	-8 (-25, 8)	0.37	-11 (-26, 5)	0.41
365-day mean	-32 (-95, 30)	0.95	-38 (-101, 24)	0.98	-26 (-84, 34)	0.99

Abbreviations: ARIC, Atherosclerosis Risk in Communities; CI, confidence intervals; PM, particulate matter; PM_{10} , $\text{PM} < 10 \mu\text{m}$ in diameter; WHI, Women's Health Initiative

^aModel 1 adjusted for race/ethnicity, age, gender (in ARIC), randomly assigned treatment group (in WHI), mean temperature, mean dew point, mean barometric pressure, season, and a restricted cubic natural spline function of calendar time with one knot per calendar year

^bModel 2 adjusted for all covariates in Model 1 and additionally for individual-level education and neighborhood socioeconomic status

^cModel 3 adjusted for all covariates in Model 2 and additionally for smoking status, alcohol use, body mass index, and physical activity

^dHomogeneity of associations among strata was tested using Cochran's Q test statistic, where a $P_{\text{Cochran's } Q} < 0.10$ suggests there is evidence to reject the null hypothesis of homogeneity

Table S5. Pooled difference in estimated leukocyte proportion (Δ , %) per 10 $\mu\text{g}/\text{m}^3$ increase in PM concentrations among n=8,457 participants, Women's Health Initiative (1993-2002) and Atherosclerosis Risk in Communities study (1990-1995)

	CD8+ T cells		CD4+ T cells		Natural Killer cells		B cells		Monocytes		Granulocytes	
	Δ % (95% CI) ^a	$P_{\text{Cochran's } Q^b}$	Δ % (95% CI) ^a	$P_{\text{Cochran's } Q^b}$	Δ % (95% CI) ^a	$P_{\text{Cochran's } Q^b}$	Δ % (95% CI) ^a	$P_{\text{Cochran's } Q^d}$	Δ % (95% CI) ^a	$P_{\text{Cochran's } Q^b}$	Δ % (95% CI) ^a	$P_{\text{Cochran's } Q^b}$
PM₁₀ ($\mu\text{g}/\text{m}^3$)												
2-day mean	0.1 (-0.4, 0.6)	0.14	-0.1 (-0.4, 0.3)	0.04	0.0 (-0.3, 0.3)	0.97	-0.2 (-0.4, 0.0)	0.36	0.0 (-0.1, 0.2)	0.56	0.1 (-0.2, 0.3)	0.64
7-day mean	0.3 (-0.2, 0.8)	0.36	-0.2 (-0.5, 0.1)	0.39	-0.1 (-0.5, 0.3)	0.33	-0.4 (-0.7, -0.1)	0.85	-0.1 (-0.3, 0.2)	0.55	-0.2 (-0.5, 0.1)	0.37
1-month mean	-0.4 (-1.2, 0.4)	0.22	-0.1 (-0.6, 0.5)	0.19	-0.3 (-0.9, 0.4)	0.23	-0.2 (-0.6, 0.3)	0.62	0.2 (-0.4, 0.7)	0.07	0.4 (-0.1, 0.8)	0.34
12-month mean	-0.3 (-1.2, 0.5)	0.75	0.0 (-0.5, 0.6)	0.45	-0.4 (-1.5, 0.8)	0.11	-0.3 (-1.0, 0.3)	0.61	-0.3 (-0.7, 0.1)	0.43	-0.1 (-0.9, 0.8)	0.16
PM_{2.5} ($\mu\text{g}/\text{m}^3$)												
1-month mean	-1.1 (-1.8, -0.3)	0.55	-0.3 (-1.1, 0.6)	0.15	-0.5 (-2.0, 1.1)	0.00	-0.5 (-1.1, 0.1)	0.71	-0.1 (-0.5, 0.3)	0.40	1.2 (0.6, 1.7)	0.81
12-month mean	-1.2 (-2.3, -0.1)	0.84	0.3 (-0.5, 1.1)	0.39	-1.5 (-3.8, 0.8)	0.02	-0.8 (-1.8, 0.2)	0.42	-0.4 (-0.9, 0.1)	0.66	1.0 (-0.3, 2.3)	0.25
PM_{2.5-10} ($\mu\text{g}/\text{m}^3$)												
1-month mean	0.5 (-1.0, 1.9)	0.16	0.0 (-0.6, 0.5)	0.59	-0.1 (-0.9, 0.7)	0.93	-0.1 (-0.8, 0.6)	0.83	0.1 (-0.7, 0.8)	0.16	-0.6 (-1.2, 0.0)	0.40
12-month mean	0.3 (-1.6, 2.3)	0.21	-0.2 (-1.1, 0.7)	0.34	0.1 (-1.0, 1.2)	0.79	-0.1 (-1.1, 0.9)	0.64	-0.2 (-0.9, 0.4)	0.62	-1.2 (-2.3, 0.0)	0.19

Abbreviations: ARIC, Atherosclerosis Risk in Communities; CI, confidence intervals; PM, particulate matter; PM₁₀, PM < 10 μm in diameter; PM_{2.5}, PM < 2.5 μm in diameter; PM_{2.5-10}, PM > 2.5 and < 10 μm in diameter; WHI, Women's Health Initiative

^aModel adjusted for race/ethnicity, age, gender (in ARIC), randomly assigned treatment group (in WHI), mean temperature, mean dew point, mean barometric pressure, and season

^bHomogeneity of associations among strata was tested using Cochran's Q test statistic, where a $P_{\text{Cochran's } Q} < 0.10$ suggests there is evidence to reject the null hypothesis of homogeneity

Table S6. Pooled difference in estimated leukocyte proportion (Δ , %) per 10 $\mu\text{g}/\text{m}^3$ increase in PM concentrations among n=8,457 participants, Women's Health Initiative (1993-2002) and Atherosclerosis Risk in Communities study (1990-1995)

	CD8+ T cells		CD4+ T cells		Natural Killer cells		B cells		Monocytes		Granulocytes	
	Δ % (95% CI) ^a	<i>P</i> _{Cochran's Q} ^b	Δ % (95% CI) ^a	<i>P</i> _{Cochran's Q} ^b	Δ % (95% CI) ^a	<i>P</i> _{Cochran's Q} ^b	Δ % (95% CI) ^a	<i>P</i> _{Cochran's Q} ^b	Δ % (95% CI) ^a	<i>P</i> _{Cochran's Q} ^b	Δ % (95% CI) ^a	<i>P</i> _{Cochran's Q} ^b
PM₁₀ ($\mu\text{g}/\text{m}^3$)												
2-day mean	0.1 (-0.3, 0.6)	0.14	-0.1 (-0.4, 0.3)	0.04	0.0 (-0.3, 0.3)	0.98	-0.2 (-0.4, 0.0)	0.39	0.0 (-0.1, 0.2)	0.45	0.1 (-0.2, 0.3)	0.65
7-day mean	0.3 (-0.2, 0.8)	0.36	-0.2 (-0.5, 0.1)	0.40	-0.1 (-0.5, 0.3)	0.36	-0.4 (-0.7, -0.1)	0.93	-0.1 (-0.3, 0.2)	0.51	-0.2 (-0.5, 0.1)	0.39
1-month mean	-0.4 (-1.2, 0.4)	0.21	-0.1 (-0.7, 0.5)	0.13	-0.3 (-0.9, 0.4)	0.26	-0.2 (-0.7, 0.3)	0.63	0.2 (-0.4, 0.8)	0.06	0.4 (-0.1, 0.9)	0.32
12-month mean	-0.4 (-1.3, 0.4)	0.68	0.1 (-0.5, 0.7)	0.38	-0.4 (-1.6, 0.8)	0.10	-0.4 (-1.1, 0.3)	0.62	-0.3 (-0.7, 0.2)	0.38	0.0 (-0.9, 0.9)	0.16
PM_{2.5} ($\mu\text{g}/\text{m}^3$)												
1-month mean	-1.1 (-1.8, -0.3)	0.55	-0.3 (-1.2, 0.6)	0.12	-0.5 (-2.0, 1.0)	0.01	-0.5 (-1.1, 0.1)	0.73	0.0 (-0.5, 0.4)	0.39	1.2 (0.6, 1.8)	0.76
12-month mean	-1.2 (-2.3, 0.0)	0.86	0.3 (-0.5, 1.1)	0.40	-1.6 (-3.9, 0.7)	0.03	-0.9 (-1.9, 0.1)	0.41	-0.4 (-0.9, 0.2)	0.63	1.1 (-0.1, 2.4)	0.29
PM_{2.5-10} ($\mu\text{g}/\text{m}^3$)												
1-month mean	0.4 (-0.9, 1.8)	0.19	0.1 (-0.5, 0.6)	0.66	-0.1 (-0.9, 0.7)	0.85	-0.1 (-0.8, 0.6)	0.78	0.1 (-0.7, 0.8)	0.15	-0.6 (-1.2, -0.1)	0.41
12-month mean	0.1 (-2.0, 2.2)	0.20	-0.1 (-0.9, 0.7)	0.42	0.1 (-1.0, 1.2)	0.79	-0.3 (-1.3, 0.8)	0.71	-0.2 (-0.9, 0.4)	0.57	-1.2 (-2.4, 0.0)	0.18

Abbreviations: ARIC, Atherosclerosis Risk in Communities; CI, confidence intervals; PM, particulate matter; PM₁₀, PM < 10 μm in diameter; PM_{2.5}, PM < 2.5 μm in diameter; PM_{2.5-10}, PM > 2.5 and < 10 μm in diameter; WHI, Women's Health Initiative

^aModel adjusted for race/ethnicity, age, gender (in ARIC), randomly assigned treatment group (in WHI), mean temperature, mean dew point, mean barometric pressure, season, individual-level education and neighborhood socioeconomic status

^bHomogeneity of associations among strata was tested using Cochran's Q test statistic, where a *P*_{Cochran's Q} < 0.10 suggests there is evidence to reject the null hypothesis of homogeneity

Table S7. Pooled difference in measured leukocyte proportion (Δ , %) per 10 $\mu\text{g}/\text{m}^3$ increase in $\text{PM}_{2.5}$ concentrations among n=8,646 participants, Atherosclerosis Risk in Communities study (1986-1992)

	Lymphocytes	Monocytes	Granulocytes
	Δ %	Δ %	Δ %
	(95% CI) ^a	(95% CI) ^a	(95% CI) ^a
$\text{PM}_{2.5}$ ($\mu\text{g}/\text{m}^3$)			
1-month mean	0.8 (-0.0, 1.6)	-1.7 (-2.5, -0.8)	0.9 (0.1, 1.6)
12-month mean	-3.5 (-5.4, -1.6)	3.1 (0.9, 5.3)	0.4 (-1.3, 2.2)

Abbreviations: ARIC, Atherosclerosis Risk in Communities; CI, confidence intervals; PM, particulate matter; PM_{10} , $\text{PM} < 10 \mu\text{m}$ in diameter

^aModel adjusted for race/ethnicity, age, gender (in ARIC), randomly assigned treatment group (in WHI), mean temperature, mean dew point, mean barometric pressure, season, individual-level education, neighborhood socioeconomic status, smoking status, alcohol use, body mass index, and physical activity

Table S8. Pooled difference in CD4:CD8 ratio (Δ , %) per 10 $\mu\text{g}/\text{m}^3$ increase in PM concentrations among $n=8,457$ participants, Women's Health Initiative (1993-2002) and Atherosclerosis Risk in Communities study (1990-1995)

	CD4:CD8 ratio	
	Δ % (95% CI) ^a	$P_{\text{Cochran's } Q}$ ^b
PM₁₀ ($\mu\text{g}/\text{m}^3$)		
2-day mean	-0.3 (-0.7, 0.1)	0.03
7-day mean	-0.5 (-1.0, 0.0)	0.43
1-month mean	0.2 (-0.5, 1.0)	0.80
12-month mean	0.3 (-0.8, 1.3)	0.66
PM_{2.5} ($\mu\text{g}/\text{m}^3$)		
1-month mean	0.9 (-0.1, 2.0)	0.15
12-month mean	1.3 (-0.2, 2.8)	0.72
PM_{2.5-10} ($\mu\text{g}/\text{m}^3$)		
1-month mean	-0.6 (-1.8, -0.6)	0.69
12-month mean	-0.9 (-2.5, 0.8)	0.13

Abbreviations: ARIC, Atherosclerosis Risk in Communities; CI, confidence intervals; PM, particulate matter; PM₁₀, PM < 10 μm in diameter; PM_{2.5}, PM < 2.5 μm in diameter; PM_{2.5-10}, PM > 2.5 and < 10 μm in diameter; WHI, Women's Health Initiative

^aModel adjusted for race/ethnicity, age, gender (in ARIC), randomly assigned treatment group (in WHI), mean temperature, mean dew point, mean barometric pressure, season, individual-level education, neighborhood socioeconomic status, smoking status, alcohol use, body mass index, and physical activity

^bHomogeneity of associations among strata was tested using Cochran's Q test statistic, where a $P_{\text{Cochran's } Q} < 0.10$ suggests there is evidence to reject the null hypothesis of homogeneity

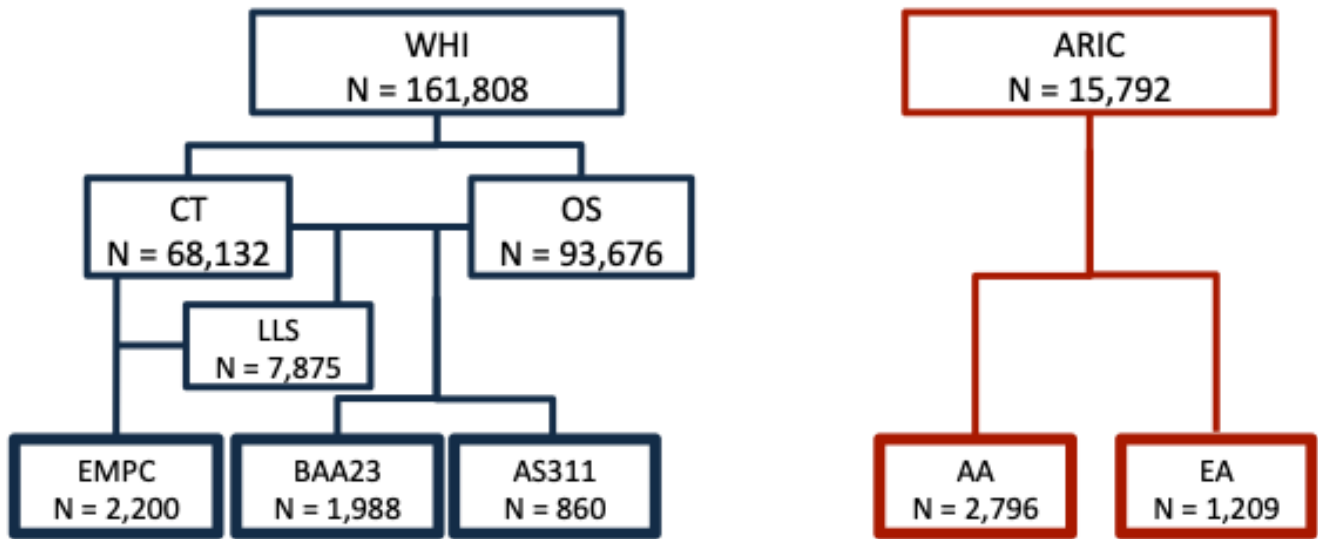


Figure S1. Diagram of Women's Health Initiative (1993-2002) and Atherosclerosis Risk in Communities study (1986-1998) populations and subpopulations with leukocyte composition data.

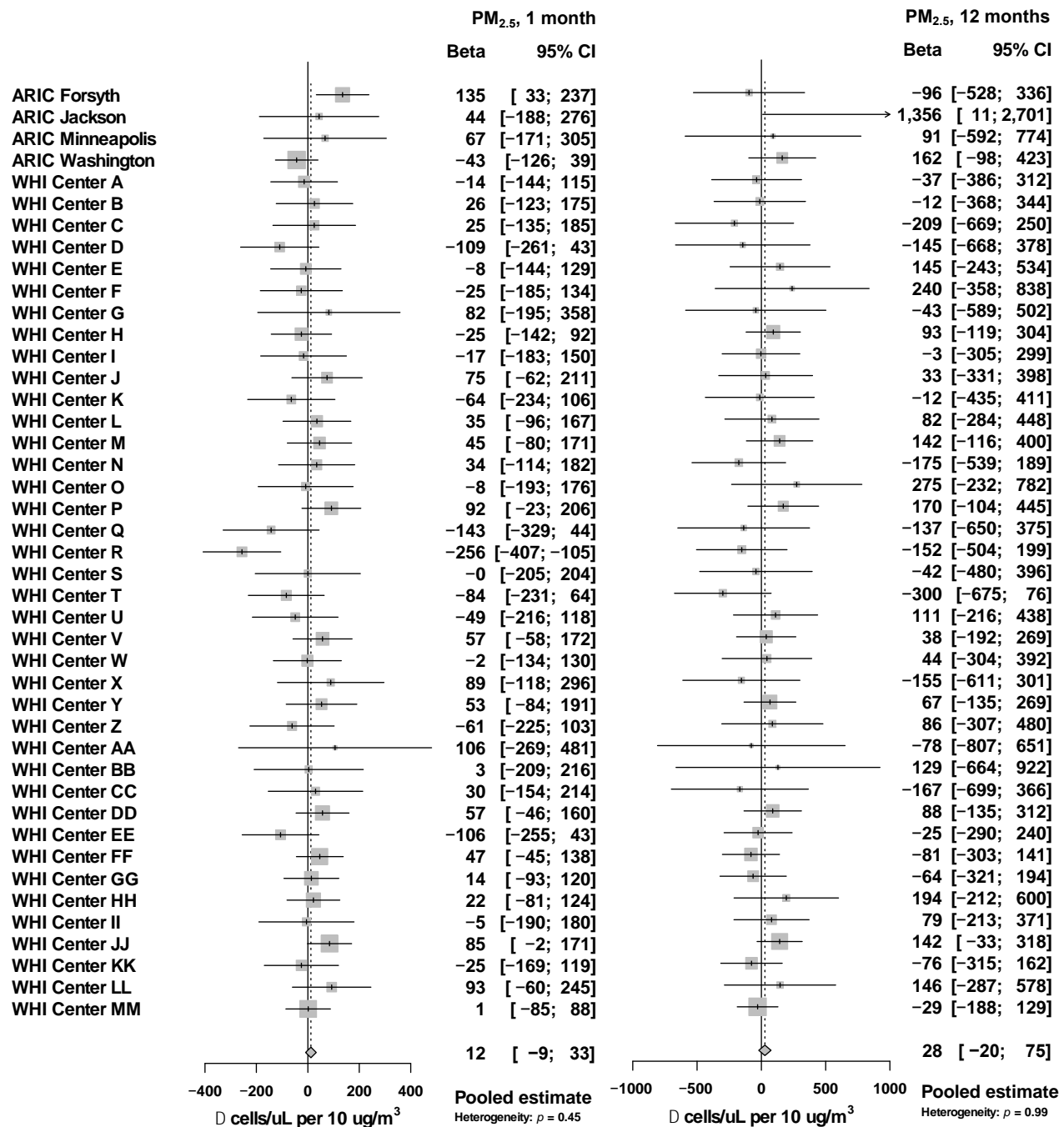


Figure S2. Study/center-specific and pooled differences in leukocyte count (Δ , cell/ μ L) per 10 μ g/ m^3 increase in 1- and 12-month mean concentrations of PM_{2.5} among n=165,675 participants, Women's Health Initiative (1993-2002) and Atherosclerosis Risk in Communities study (1986-1998). The models adjusted for race/ethnicity, age, sex (in ARIC), randomly assigned treatment group (in WHI), mean temperature, mean dew point, mean barometric pressure, season, and a restricted cubic natural spline function of calendar date with one knot per year, individual-level education, neighborhood socioeconomic status, smoking status, alcohol use, body mass index, and physical activity.

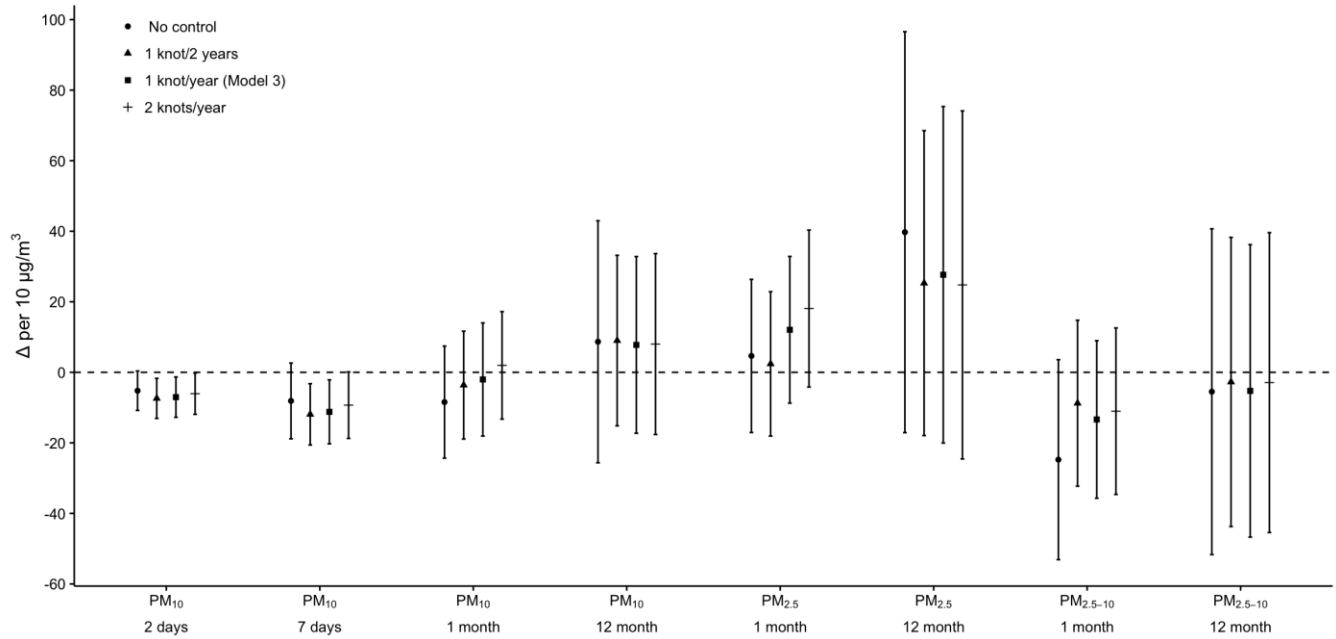


Figure S3. Pooled difference in leukocyte count (Δ , cell/ μL) per $10 \mu\text{g}/\text{m}^3$ increase in PM among $n=165,675$ participants, Women's Health Initiative (1993-2002) and Atherosclerosis Risk in Communities study (1986-1998). The models adjusted for race/ethnicity, age, sex (in ARIC), randomly assigned treatment group (in WHI), mean temperature, mean dew point, mean barometric pressure, season, individual-level education, neighborhood socioeconomic status, smoking status, alcohol use, body mass index, and physical activity (\bullet), with additional adjustment for a restricted cubic natural spline function of calendar date with 1 knot for every 2 years (\blacktriangledown), 1 knot per year (\blacksquare), and 2 knots per year (+).

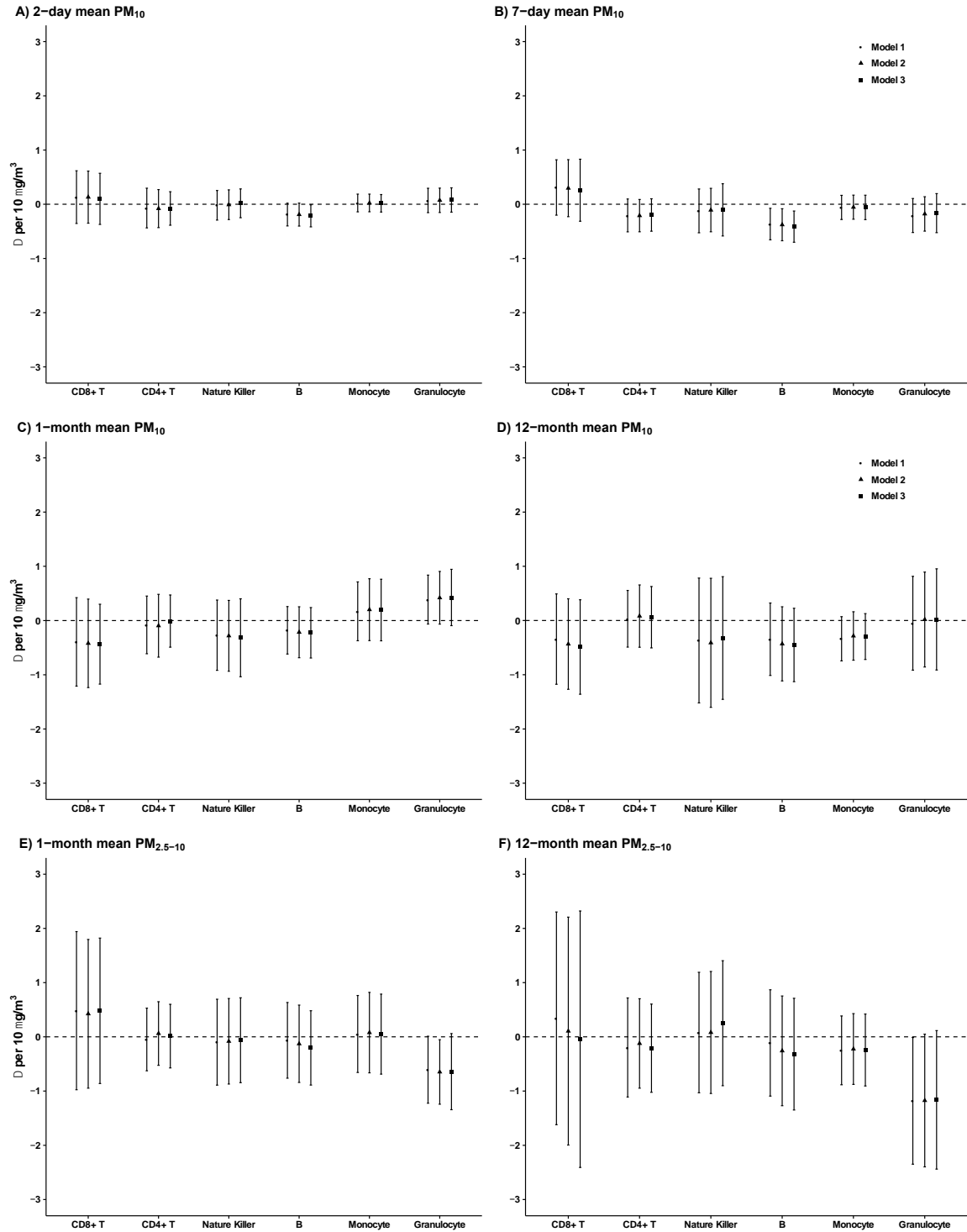


Figure S4. Pooled difference in leukocyte composition (Δ , % point) per $10 \mu\text{g}/\text{m}^3$ increase in A) 2- and B) 7-day mean PM_{10} ; C) 1- and D) 12-month mean PM_{10} ; and E) 1- and F) 12-month mean $\text{PM}_{2.5-10}$ concentrations among $n=8,457$ participants, Women's Health Initiative (1993-2002) and Atherosclerosis Risk in Communities study (1990-1995). Model 1 adjusted for race/ethnicity, age, sex (in ARIC), randomly assigned treatment group (in WHI), mean temperature, mean dew point, mean barometric pressure, season, and subpopulation-specific covariates. Model 2 also adjusted for individual-level education and neighborhood socioeconomic status. Model 3 additionally adjusted for smoking status, alcohol use, body mass index, and physical activity.