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Association of Air Pollution Exposures with High Density Lipoprotein Cholesterol and Particle Number: The Multi-Ethnic Study of Atherosclerosis

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Abstract

OBJECTIVE—The relationship between air pollution and cardiovascular disease may be explained by changes in high-density lipoprotein (HDL).

APPROACH AND RESULTS—We examined the cross-sectional relationship between air pollution and both HDL cholesterol (HDL-C) and HDL particle number (HDL-P) in the Multi-Ethnic Study of Atherosclerosis Air Pollution study (MESA Air). Study participants were 6,654 white, African-American, Hispanic, and Chinese men and women, 45–84 years of age. We estimated individual residential ambient fine particulate pollution exposure ($PM_{2.5}$) and black carbon (BC) concentrations using a fine-scale likelihood-based spatiotemporal model and cohort-specific monitoring. Exposure periods were averaged to 12 months, 3 months, and two weeks prior to exam. HDL-C and HDL-P were measured in the year 2000 using the cholesterol oxidase method and nuclear magnetic resonance spectroscopy, respectively. We used multivariable linear regression to examine the relationship between air pollution exposure and HDL measures. A 0.7 $10^{-6}m^{-1}$ higher exposure to black carbon (a marker of traffic-related pollution) averaged over a one year period was significantly associated with a lower HDL-C (−1.68 mg/dL (95% CI: −2.86, −0.50), and approached significance with HDL-P (−0.55 mg/dL (95% CI: −1.13, 0.03). In the three month averaging time period, a 5 μg/m3 higher $PM_{2.5}$ was associated with lower HDL-P (−0.64 μmol/L (95% CI: −1.01, −0.26), but not HDL-C (−0.05 mg/dL (95% CI: −0.82, 0.71).

CONCLUSIONS—These data are consistent with the hypothesis that exposure to air pollution is adversely associated with measures of HDL.

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Introduction

High density lipoprotein (HDL) particles possess numerous potentially cardioprotective qualities[1]. HDL particles transport cholesterol from lipid-carrying macrophages and are vital in the maintenance of net cholesterol balance in the arterial wall[1]. Despite strong epidemiologic evidence that HDL cholesterol (HDL-C) is inversely associated with cardiovascular events, recent clinical trials that raised HDL-C have failed to show benefit [2–5]. Recent studies suggest measurement of HDL particle number (HDL-P) may better reflect the cardioprotective qualities of HDL than HDL-C[6–8].

Ambient air pollution is associated with atherosclerosis, heart failure, and cardiovascular death[9–15]. Air pollution may affect HDL through inflammation and oxidative stress, promoting changes in HDL structure and function that results in proatherogenic or dysfunctional HDL[16,17]. Exposures to both fine and ultrafine particulate matter (PM) have been associated with development of dysfunctional HDL and reduced HDL anti-inflammatory capacity in some (but not all) experimental studies[18–21]. The association between ambient air pollution and HDL-C, HDL-P and HDL particle size, has not been well-studied.

We examined the relation between long and short-term concentration of air pollutants – $PM_{2.5}$ and black carbon (BC) – and measures of HDL structure in a multiethnic cohort of adults without clinical cardiovascular disease. We hypothesized that exposure to higher levels of air pollution would be associated not only with lower HDL-C, but also with lower HDL-P, which may better reflect HDL function. In a secondary analysis, we examined associations between short-term $PM_{2.5}$ concentrations and HDL. The Multi-Ethnic Study of Atherosclerosis (MESA) - an on-going study of risk factors that predict progression to clinically overt cardiovascular disease or progression of the subclinical disease in a racially diverse population - provides a unique opportunity to combine highly refined measures of air pollution exposure with multiple measures of HDL, including particle number, size, and concentration, in a multi-ethnic population.

Materials and Methods

Materials and Methods are available in the online-only Data Supplement.

Results

Of the 6,814 MESA participants, 160 participants had missing data on HDL, covariates and exposure, leaving 6,654 for analysis. Individually-weighted exposure estimates were available for 5,330 participants and black carbon exposure estimates were available for 6,557 participants. The current study population was comprised of 53% female and 18% with less than a high school education. Participants were 28% African American, 12% Chinese American, 22% Hispanic and 39% White. Sixteen percent of the study population used lipid-lowering drugs, and 45% had hypertension. Predicted individually-weighted $PM_{2.5}$ concentrations in the year 2000 ranged from 4.8 to 21.6 $\mu g/m^3$, with an interquartile range (IQR) of 4.1 $\mu g/m^3$. BC concentrations ranged from 0.28 to 4.77 $10^{-6}m^{-1}$, with an IQR of 0.7 $10^{-6}m^{-1}$. Mean (standard deviation [SD]) HDL-P in our study population was

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34.0 (6.6) μmol/L. Mean (SD) HDL-C in our study population was 50.8 (15.5) mg/dL (Table 1).

HDL Cholesterol

We found a non-significant association between higher $PM_{2.5}$ concentrations and lower HDL-C concentrations (Table 2). In the 2-week averaging period, adjusting for age, sex, race/ethnicity and site only, we observed a significant −0.86 mg/dL (95% CI: −1.38, −0.34) difference in HDL-C for a 5-μg/m^3 higher $PM_{2.5}$, however this association attenuated (and became non–significant) after adjustment for other covariates. We found no significant association between short-term (0 to 5 days prior) $PM_{2.5}$ exposure or outdoor $PM_{2.5}$ exposure and HDL-C (Table 3).

We found a significant association between higher concentrations of black carbon and lower HDL-C levels. A 0.7 $10^{-6}m^{-1}$ higher BC at the one year averaged time period was associated with a −1.68 mg/dL (95% CI: −2.86 to −0.50; p = 0.001) lower HDL-C when adjusted for covariates in our final model (Table 2). Sensitivity analyses additionally adjusting for HDL-P, pack-years smoked, income, niacin use, short-term pollutant concentrations, both annual averaged PM2.5 and BC simultaneously, and models with random slopes and intercepts for site did not meaningfully change the results.

HDL Particle Number

We found a significant inverse association between medium-term (3-month and 2-week) $PM_{2.5}$ concentrations and HDL-P, but not in the one-year period, although the association in that period was of similar magnitude and direction (Table 2). A 5-μg/m^3 higher 3-month average $PM_{2.5}$ concentration was associated with a −0.64 μmol/L (95% CI: −1.02 to −0.26) lower HDL-P, and a 5-μg/m^3 higher 2-week average $PM_{2.5}$ was associated with a −0.29 μmol/L (95% CI: −0.57, −0.01) lower HDL-P in multivariate-adjusted models (Table 2). In the short-term $PM_{2.5}$ analysis, we found a significant inverse association between higher $PM_{2.5}$ in the 5 days before blood draw and HDL-P (−0.21 μmol/L per 5 μg/m^3 (95% CI: −0.38, −0.04) (Table 3). Averaging periods that included fewer days before the blood draw had no association with HDL-P.

Adjustment for HDL-C did not significantly change the association between $PM_{2.5}$ and HDL-P in the 3-month averaging time period, although the association in the 2-week time was attenuated and not significant (Supplementary Table 1). We found no significant associations between outdoor $PM_{2.5}$ and HDL-P in fully-adjusted models. Sensitivity analyses additionally adjusting for HDL-C, pack-years smoked, income, niacin use, short-term pollutant concentrations, models adjusting for both pollutants simultaneously, and models with random slopes and intercepts for site did not meaningfully change the results. The findings related to the 3-month exposure period were not affected, in direction or significance, by adjusting for the 3-day average $PM_{2.5}$ concentration. Adjusted for 3-day average $PM_{2.5}$, a 5μg/m3 higher $PM_{2.5}$ over the 3-month time period was associated with a −0.50 (95% CI: −0.92, −0.09) change in HDL-P.

We did not find a significant association between BC and HDL-P in the one-year averaging period, although it borderline and in the same direction as previous associations. A 0.7

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$10^{-6}m^{-1}$ higher BC exposure was associated with −0.55 μmol/L (95% CI: −1.13, 0.03) lower HDL-P. This association did not change with adjustment for mean HDL particle size, HDL-C, pack-years smoked, income, and niacin use. Models using random intercepts and slopes to control for site also showed no change.

We found a significant interaction between sex and the association between black carbon and HDL-C (p for interaction<0.001), with the association stronger in women for black carbon and HDL-C (−2.63 mg/dL; 95% CI: −4.46, −0.81) than men (−0.65 mg/dL; 95% CI: −2.14, 0.84). We observed a stronger relationship in women for 3-month exposure to $PM_{2.5}$ and HDL-P (−0.71 μmol/L; [95% CI: −1.33, −0.09] for women, compared to −0.48 μmol/L; [95% CI: −0.93, −0.02] for men (p for interaction=0.02)). The same phenomenon was observed for 2-week exposure to $PM_{2.5}$ and HDL-P (−0.42 μmol/L; [95% CI: −0.89, 0.05] for women, compared to −0.15 μmol/L; [95% CI: −0.49, 0.18] for men (p for interaction=0.03).) While the interaction was not significant, we observed that among those taking lipid lowering medications, one year averaged BC was associated with a −2.60 mg/dL (95% CI −5.18, −0.02) change in HDL-C, compared to a −1.38 mg/dL (95% CI −2.70, −0.05) change in HDL-C among those not taking lipid lowering medication. Among those with hypertension, one year averaged BC was associated with a −1.94 mg/dL (95% CI −3.76, −0.13) change in HDL-C, compared to a −1.48 mg/dL (95% CI −3.04, 0.09) change in HDL-C among those without hypertension. Among those taking lipid lowering medications, three-month averaged $PM_{2.5}$ was associated with a −1.36 mg/dL (95% CI −2.26, −0.46) change in HDL-P, compared to a −0.47 mg/dL (95% CI −0.89, −0.06) change in HDL-P among those not taking lipid lowering medication. Among those with hypertension, three-month averaged $PM_{2.5}$ was associated with a −0.75 mg/dL (95% CI −1.35, −0.15) change in HDL-P, compared to a −0.56 mg/dL (95% CI −1.04, −0.07) change in HDL-P among those without hypertension. We found no other significant interactions.

Discussion

In a large, multiethnic cohort study of men and women free of prevalent clinical cardiovascular disease, we found higher concentrations of $PM_{2.5}$ over a 3 month time period was associated with lower HDL-P, and higher annual concentrations of BC were associated with lower HDL-C. . Lower HDL particle numbers have been associated with increasing cIMT and cardiovascular events in previous studies, and lower HDL-C is a traditional risk factor for CVD[1,6,8,22].

In MESA participants, a 5 μg/m3 higher concentration of $PM_{2.5}$ over a 3 month time period was associated with a −0.64 μmol/L lower HDL-P. This observed lower HDL-P is comparable to other traditional risk factors such as those observed in smoking cessation studies (1.0 μmol/L change).[23]. Lower HDL-P levels in MESA participants have been independently associated with carotid atherosclerosis and coronary heart disease. A 0.7 $10^{-6}m^{-1}$ higher exposure to black carbon over a one year period was also associated with a −1.68 mg/dL lower concentration of HDL-C. This lower HDL-C can be compared to the effect of quitting smoking (2.4 mg/dL change) on HDL-C in smoking cessation programs[23]. These associations persisted after control for smoking and other risk factors for HDL. Effect sizes for $PM_{2.5}$ and HDL-P increased from day of blood draw to 5-day, 2-week and finally to

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3-month averaged time periods, which may indicate a potential cumulative exposure effect. However we did not see an association between one-year averaged $PM_{2.5}$ and HDL-P, suggesting that potential effects of air pollution on HDL may be more short or medium-term.

This is the first large observational study to suggest an association between air pollution exposure and HDL particle number. Our results build on previous work suggesting an association between air pollution and HDL through the use of additional properties of HDL which may be potentially more clinically relevant, and examining them in a multiethnic cohort with excellent measurement of covariates and cutting edge assessment of air pollution exposure. This study contributes to the hypothesis that air pollution may act through HDL to contribute to cardiovascular disease at comparably low levels found in developed countries. In examining different pollutant averaging times, our study also adds information suggesting that air pollution may be associated with changes in HDL in both the short and the medium term, and that both time periods may be relevant for examining the effect of air pollution on CVD risk factors.

Two cohort studies, conducted by Chuang et al, in Taiwan have previously investigated the relationship between air pollution and HDL in humans. In a population-based survey, they reported a decrease in HDL-C per IQR increase in PM_{10} over a 1-day averaging period before blood draw[24]. In a separate cross-sectional analysis, they found no association between a one IQR increase in one-year averaged air pollution exposure before blood draw and HDL-C in a cohort of 1023 subjects aged 54 to 90 living in Taiwan[25]. These studies relied on central-site monitoring data and had limited data on likely confounding variables such as SES, smoking, physical activity, and use of lipid-lowering medications, which are associated with both air pollution and HDL, and may explain why our study found differing results. Our results are consistent with a prior occupational study of $PM_{2.5}$ and HDL-C in a repeated measures panel study of welders[26]. Those exposed to high $PM_{2.5}$ during welding experienced an acute decrease of −2.6 mg/dL (95% CI −5.3, −0.0) in circulating HDL-C levels 18 hours following exposure compared to their baseline levels[26]. These magnitude of effect sizes werehigher than those observed in our study, however welders were exposed to much higher concentrations of pollutants.

Characteristics of HDL beyond total concentration are likely important in the protective effects of the lipoprotein. In our study we focused on particle number as an alternate characteristic, though there is reason to believe that functional characteristics—not assessed here—are also important, and may be affected by air pollutant or other exposures such as tobacco smoke[18–20,27–31]. For example, in Yin et al, samples of HDL from mice exposed to fine and ultrafine PM were found to have significantly reduced HDL anti-inflammatory properties compared unexposed mice, suggesting that PM exposure may reduce the ability of HDL to protect against atherosclerosis[19]. Experimental study of HDL function and structure is needed to confirm and further characterize the effect of air pollution on HDL.

As a whole, these studies are consistent with the hypothesis that exposure to air pollution increases risk of CVD. Our findings support hypotheses that HDL may play a role in the biological pathway explaining the association between air pollution and CVD[17]. PM has

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been shown to induce creation of dysfunction HDL, which is associated with reduced protection against atherosclerosis through inability to participate in reverse cholesterol transport and antioxidation[17,19,32].

Both the relationship between $PM_{2.5}$ and HDL-P, as well the relationship between BC and HDL-C were modified by sex. In both cases, the association between air pollution and HDL was stronger in women, although the association in men was still negative. Women typically have higher levels of both HDL-P and HDL-C than men, which has been attributed to higher estrogen production in women[33]. Some research has suggested that air pollutants may induce estrogen-disrupting effects, acting as a potential xenoestrogen involved in generation reactive oxygen species and induction of oxidative stress[34,35]. While many of the women in our study were post-menopausal, air pollution-related disruption of the HDL-raising effects of estrogen may explain the stronger results observed in women. Our study found no significant evidence of effect modification by age, race/ethnicity, diabetes, smoking, obesity, or site. Our sensitivity analyses examining adjustment for other aspects of HDL did not strongly change the conclusions of our study. The positive association between 3-month average of $PM_{2.5}$ and HDL-C when controlling for HDL-P is difficult to interpret, however it may be explained by a reduction in the number of small, cholesterol-depleted HDL particles, leaving the average amount of cholesterol in HDL particles higher on a per-particle basis. Smaller HDL particles may play a more important role in cholesterol efflux than larger particles, so a reduction in the number of smaller HDL particles supports the hypothesis that the relationship between air pollution and cardiovascular disease could be mediated through change in cholesterol efflux.[36] We also observed associations between HDL and individually-weighted $PM_{2.5}$ - which takes into account participant's time spent indoors – but not outdoor $PM_{2.5}$, which simply estimates PM2.5 outside a participant's home. Since many study subjects spend the majority of their time indoors, this estimate will contain some error, as only a fraction of outdoor air pollution penetrates into homes. Subjects also spend time away from their homes, and may also spend time in traffic on roadways, which can be significant source of air pollution exposure itself, further exposing them to air pollution that is generally not taken into account by outdoor air pollution exposure estimates.

This study has a number of strengths as a large, population-based, multiethnic cohort able to examine the relationship between air pollution and advanced measures of HDL. The MESA study features measurement of numerous covariates, with multiple levels of quality control[37]. Great care was taken in producing high-quality air pollution estimates, with cohort-specific monitoring and modeling, and with special attention paid to minimizing measurement error in the estimates[38,39]. This is the first study to examine air pollution and measures of HDL particle number and size in a large cohort setting. However, while our exposure models are more accurate and less susceptible to measurement error than distance to monitor or nearest roadway analyses, we cannot rule out the limitation of measurement error in our models. The measurement error in air pollution estimates is likely to be independent of HDL measurements, so we would generally expect this error to be non-differential and bias estimates towards the null, representing an underestimation of the true measure of effect. Air pollution is a complex mixture of particles and gases, and it is possible that our estimates may be driven by a different, highly correlated pollutant that is

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unmeasured, or an interaction between the pollutants, rather than $PM_{2.5}$ or BC per se. Further study of multipollutant models and mixtures will be needed to confirm these results. Another limitation of our study is its cross-sectional design. HDL-P was only been measured at one point in time, and a snapshot analysis of air pollution and HDL cannot provide valid inference on the effect of air pollution on HDL over time. Although estimates of air pollution represent participants' exposure in the time period before HDL was measured, associations from this study should be interpreted with caution. Finally, while covariates were measured carefully during exams, we cannot rule out the possibility that residual confounding exists due to potentially important covariates being unmeasured or measured with error.

In summary, we found evidence that exposure to $PM_{2.5}$ and BC were associated with changes in several measures of HDL, and short-term exposure was associated with lower HDL-P in our study of a multi-ethnic population free of cardiovascular disease.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

PM	particulate matter
BC	black carbon
MESA	Multi-Ethnic Study of Atherosclerosis

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Table 1

Characteristics of MESA Participants in Study

	All Participants (N = 6814)	Participants with complete data (N=6654)	Participants with complete individually-weighted estimates (N=5330)
Age, mean ± SD, y	62.2 ± 10.2	62.2 ± 10.2	61.4 ± 10.0
Male, No. (%)	3213 (47.2)	3134 (47.1)	2527 (47.4)
Race/ethnicity, No. (%)			
non-Hispanic White	2622 (38.5)	2567 (38.6)	2118 (39.7)
Black	1893 (27.8)	1831 (27.5)	1427 (26.8)
Hispanic	1496 (21.9)	1466 (22.0)	1132 (21.2)
Chinese	803 (11.8)	790 (11.9)	653 (12.2)
Smoker, No. (%)			
Never	3417 (50.3)	3344 (50.3)	2716 (51.1)
Former	2487 (36.6)	2448 (36.8)	1957 (36.8)
Current	887 (13.1)	862 (13.0)	644 (12.1)
Current alcohol users, No. (%)	3749 (68.5)	3677 (68.6)	3044 (70.6)
Physical Activity, mean ± SD, hrs/day	12.6 ± 5.9	12.6 ± 5.9	12.8 ± 5.8
Body mass index, mean ± SD, kg/m^2	28.3 ± 5.5	28.3 ± 5.5	28.3 ± 5.4
Diabetes Mellitus, No. (%)			
Normal	4992 (73.5)	4895 (73.6)	3993 (75.1)
Impaired fasting glucose	939 (13.8)	922 (13.9)	725 (13.6)
Nontreated DM	179 (2.6)	177 (2.7)	120 (2.3)
Treated DM	680 (10.0)	660 (9.9)	478 (9.0)
Hypertension, No. (%)	3058 (44.9)	2984 (44.9)	2289 (43.0)
Any lipid-lowering medication, No. (%)	1100 (16.1)	1080 (16.2)	873 (16.4)
Post-menopausal, No. (%)	2949 (82.0)	2884 (82.0)	2259 (80.7)
Systolic blood pressure, mean ± SD, mm Hg	126.6 ± 21.5	126.6 ± 21.5	125.4 ± 20.7
Diastolic blood pressure, mean ± SD, mm Hg	72.0 ± 10.3	72.0 ± 10.3	71.8 ± 10.2
Homeostatic model assessment of insulin resistance (HOMA-IR), mean (SD), mg/dL	2.7 ± 6.4	2.7 ± 6.5	2.6 ± 6.5
C-reactive protein, mean ± SD, (mg/L)	3.8 ± 5.9	3.8 ± 5.8	3.6 ± 5.4
Triglycerides, mean ± SD, mg/dL	131.6 ± 88.8	132.0 ± 89.4	131.0 ± 87.4
Low-density lipoprotein, mean ± SD, mg/dL	117.2 ± 31.5	117.2 ± 31.4	117.1 ± 31.1
Total cholesterol, mean ± SD, mg/dL	194.2 ± 35.7	194.3 ± 35.7	194.1 ± 35.4
HDL Cholesterol, mean ± SD, mg/dL	51.0 ± 14.8	51.0 ± 14.8	51.1 ± 14.8
HDL Particle number, mean ± SD, μmol/L	34.0 ± 6.6	34.1 ± 6.6	34.2 ± 6.7
$PM_{2.5}$ individual year 2000, mean ± SD, $\mu g/m^3$	10.9 ± 3.3	10.9 ± 3.3	10.9 ± 3.3
$PM_{2.5}$ outdoor year 2000, mean ± SD, $\mu g/m^3$	16.7 ± 2.9	16.7 ± 2.9	16.6 ± 2.8
Black carbon year 2000, mean ± SD, $10^{-6}/m^{-1}$	0.9 ± 0.5	0.9 ± 0.5	0.9 ± 0.5

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Table 2

Associations between long and medium-term air pollutants and HDL - MESA Air

	Individually-weighted $PM_{2.5}$ (5μg/m3)	**Outdoor $PM_{2.5}$ (5μg/m^3)**	**Black carbon (0.7 10^{-6}/m^{-1})**
Year 2000 average	βeta, (95% CI)		
HDL-C (mg/dL)			
Minimally adjusted Model	−0.13 (−1.24, 0.98)	0.85 (−0.69, 2.40)	−1.40 (−2.58, −0.22)
Final Model	−0.50 (−1.61, 0.61)	0.86 (−0.67, 2.38)	−1.68 (−2.86, −0.50)
HDL-P (μmol/L)			
Minimally adjusted Model	−0.15 (−0.65, 0.34)	0.33 (−0.35, 1.02)	−0.47 (−1.00, 0.05)
Final Model	−0.21 (−0.75, 0.33)	0.42 (−0.32, 1.17)	−0.55 (−1.13, 0.03)
Three Month Average	Individually-weighted $PM_{2.5}$ (5μg/m^3)	Outdoor $PM_{2.5}$ (5μg/m^3)	*Black carbon not available at this level
HDL-C (mg/dL)			
Minimally adjusted Model	−0.002 (−0.75, 0.74)	0.88 (0.27, 1.48)	
Final Model	−0.05 (−0.82, 0.71)	0.47 (−0.17, 1.10)	
HDL-P (μmol/L)			
Minimally adjusted Model	−0.64 (−0.97, −0.31)	−0.28 (−0.55, −0.01)	
Final Model	−0.64 (−1.02, −0.26)	−0.27 (−0.58, 0.04)	
Two week Average	Individually-weighted $PM_{2.5}$ (5μg/m^3)	Outdoor $PM_{2.5}$ (5μg/m^3)	*Black carbon not available at this level
HDL-C (mg/dL)			
Minimally adjusted Model	−0.86 (−1.38, −0.34)	−0.01 (−0.38, 0.37)	
Final Model	−0.39 (−0.97, 0.18)	0.14 (−0.26, 0.55)	
HDL-P (μmol/L)			
Minimally adjusted Model	−0.35 (−0.58, −0.12)	−0.13 (−0.29, 0.04)	
Final Model	−0.29 (−0.57, −0.01)	−0.07 (−0.27, 0.12)	

Abbreviations: HDL = high-density lipoproteins, PM = particulate matter

Minimally adjusted model is adjusted only for age, site, sex, and race/ethnicity

Final adjusted model is adjusted for the factors in the minimally adjusted model plus BMI, education, physical activity (MET min-wk), smoking (never/former/current), current alcohol use (y/n), diabetes (normal/IFG/Untreated/Treated), hypertension (y/n), use of lipid-lowering drugs (y/n), outdoor temperature, relative humidity, HOMA-IR, log CRP, LDL-C, and triglycerides

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Table 3

Associations between measures of HDL and short-term exposure to fine particulate air pollution on the day of blood collection and the days prior

Model	Change in HDL per 5 μg/m^3 higher average $PM_{2.5}$ prior to blood draw			
	Day of blood draw	1 day prior	3 days prior	5 days prior
HDL-C (mg/dL)				
Minimally adjusted Model	−0.14 (−0.37, 0.10)	−0.06 (−0.28, 0.16)	−0.06 (−0.34, 0.23)	−0.20 (−0.54, 0.14)
Final model	0.02 (−0.21, 0.26)	0.05 (−0.17, 0.28)	0.01 (−0.28, 0.30)	−0.06 (−0.42, 0.29)
HDL-P (μmol/L)				
Minimally adjusted Model	−0.04 (−0.15, 0.06)	−0.06 (−0.15, 0.04)	−0.11 (−0.23, 0.02)	−0.17 (−0.32, −0.02)
Final model	−0.06 (−0.17, 0.06)	−0.06 (−0.17, 0.04)	−0.13 (−0.27, 0.01)	−0.21 (−0.38, −0.04)

Abbreviations: HDL = high-density lipoproteins, PM = particulate matter

Minimally adjusted model is adjusted only for age, site, sex, and race/ethnicity

Final adjusted model is adjusted for the factors in the minimally adjusted model plus BMI, education, physical activity (MET min-wk), smoking (never/former/current), current alcohol use (y/n) diabetes (normal/IFG/Untreated/Treated), hypertension (y/n), use of lipid-lowering drugs (y/n), HOMA-IR, log CRP, LDL-C, and triglycerides