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Yuhan Zhang Date

**A Co-Twin Control Study of Fine Particulate Matter and the Prevalence of Metabolic Syndrome Risk Factors**

By

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Master of Public Health

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# A Co-Twin Control Study of Fine Particulate Matter and the Prevalence of Metabolic Syndrome Risk Factors

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2019

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An abstract of
A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
in partial fulfillment of the requirements for the degree of
Master of Public Health
in Epidemiology
2021

## Abstract

### A Co-Twin Control Study of Fine Particulate Matter and the Prevalence of Metabolic Syndrome Risk Factors

By Yuhan Zhang

**Background:** The relationship between ambient fine particulate matter ($PM_{2.5}$) and metabolic syndrome (MetS) is understudied. It also remains unknown whether familial factors play a role in this relationship.

**Methods:** In a study of 566 middle-aged twins, we examined the association of $PM_{2.5}$ with MetS risk factors, measured by a MetS score as a summation of individual risk factors (range, 0 to 5). High-resolution $PM_{2.5}$ estimates were obtained through previously validated models that incorporated monitor and satellite derived data. We estimated two-year average $PM_{2.5}$ concentrations based on the ZIP code of each twin's residence. We used ordinal response models adapted for twin studies.

**Results:** When treating twins as individuals, the odds ratio of having 1-point higher MetS score was 1.86 for each 10 μg/m3-increase in exposure to PM2.5 (confidence interval [CI]: 1.05, 3.29), after adjusting for potential confounders. This association was mainly between pairs; the odds ratio was 2.06 (CI: 1.06, 3.99) for each 10 μg/m3-increase in the average pairwise exposure level. We found no significant difference in MetS scores within pairs who were discordant for $PM_{2.5}$ exposure.

**Conclusion:** In conclusion, higher $PM_{2.5}$ in residence area is associated with more MetS risk factors. This association, however, is confounded by shared familial factors.

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**Acknowledgements**

Completion of this thesis would not have been possible without the help of many people who had provided me essential guidance on the research methodologies and scientific writing.

I am very grateful to my thesis advisor, Dr. Viola Vaccarino, for her thoughtful assistance with identifying and framing the aims of this thesis, for her deep methodological expertise that enabled me to conduct statistically rigorous work, and for her patience in answering my confusions so that I could better understand and explain the results.

I am also sincerely grateful to my field advisor, Dr. Liuhua Shi, who provided much-appreciated direct assistance with data management and careful guidance on thesis writing.

I would like to acknowledge Dr. Joel Schwartz' lab for access to their air pollution data. And I really appreciate the support provided by The United States Department of Veterans Affairs.

Cheers!

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## INTRODUCTION

The metabolic syndrome (MetS) is one of the leading global public-health challenges [1,2]. Formally defined in the late 1970's [3,4], MetS has attracted growing attention, partially due to its increasing prevalence throughout the world [5]. MetS is composed of interrelated risk factors, including abdominal obesity, dyslipidemia, elevated blood pressure, and high glucose concentration [6]; and is related to approximately a 2-fold higher risk for cardiovascular disease (CVD) and a 5-fold higher risk for diabetes mellitus [1]. An estimated 25% of the global population is affected by MetS [7]; the prevalence in United States is even higher, reaching 33% [8]. While genetic factors and lifestyle choices may contribute to the rapid increase in MetS, environmental factors such as ambient air pollution are also thought to play a role [9].

Both short- and long-term exposure to ambient air pollution have been associated with increased morbidity and total mortality [10-13]. The Global Burden of Disease study [14] estimated that disease related to air pollution is responsible for more than four million deaths per year globally. Specifically, air pollution that falls under the category of fine particle pollution (particles with a diameter of 2.5 μm or less) has been extensively studied for its negative effects [15,16]. Especially concerning is the link of $PM_{2.5}$ exposure with CVD [17,18]. Elevated $PM_{2.5}$ exposure has been associated with increased incidence and prevalence of CVD, as well as CVD mortality and CVD-related hospital admissions [19-21].

Part of the association of $PM_{2.5}$ exposure and CVD could occur through influencing CVD risk factors. While less is known about the relationship of $PM_{2.5}$ with specific risk factors [12]. recent epidemiological studies have pointed to a relationship between long-term exposure to $PM_{2.5}$ and MetS risk factors [9,22-24]. For instance, air pollutants, such as $PM_{2.5}$, $PM_{10}$, and $NO_2$, have been associated with blood lipid abnormalities including increased total cholesterol and low-density lipoprotein cholesterol levels, and decreased high-density lipoprotein (HDL) cholesterol levels [25-28]. Long-term exposure to $PM_{2.5}$ has also been linked to hypertension and type 2 diabetes mellitus [23,29]. Several biological mechanisms have been proposed to explain these associations, including increased oxidative stress and inflammation [21]. autonomic nervous system activation with its effects on blood pressure and metabolism [30], adverse effects on endothelial function and insulin resistance [31,32]. and epigenetic modifications [33,34].

It is also possible that familial and genetic factors could contribute to the relationship between particulate matter pollution and MetS risk factors. The latter are likely influenced by familial factors affecting lifestyle choices that begin early in life, such as dietary habits and activity behaviors, as well as early life stressful exposures and social conditions. While these early exposures can affect the risk of future CVD [35-38], they can also influence the place where people live as adults, and therefore, their future exposure to air pollution. For example, results from the Netherlands Kinship Panel Study showed that the residential environment during childhood is strongly associated with the current residential environment [39]. Genetic factors may also play a

role [40]. However, no previous study has considered familial and genetic confounding in the association between air pollution and MetS.

This study aims to clarify the association between long-term exposure to $PM_{2.5}$ and MetS risk factors using a cross-sectional co-twin study design. We specifically sought to assess the influence of familial and genetic factors on the association between $PM_{2.5}$ and MetS risk factors.

## METHODS

### *Study population*

This study is based on twin participants in the Emory Twins Study, which recruited twin pairs from the Vietnam Era Twin Registry. The Vietnam Era Twin Registry is a national sample of male monozygotic and dizygotic twins from all military branches who served on active duty during the Vietnam era (1964-1975). The methods for the construction of the registry have been described in detail [41]. The Emory Twin Study included 283 twin pairs (566 individuals) born between 1946 and 1956, for the study of the effect of psychological and behavioral factors in the development of subclinical CVD. Twin pairs where at least one member reported a previous history of CVD based on a 1990 survey were excluded, and pairs who were discordant for depression or posttraumatic stress disorder were oversampled. Details on the inclusion criteria and study protocol have been described [42,43]. For this study, 11 participants with missing

addresses were excluded, yielding a final sample of 555 twins in the analysis, 273 pairs and 9 individual twins. Zygosity was obtained through DNA typing.

All twins were examined, in pairs, during an in-person clinical visit between 2002 and 2010. Medical history, anthropometric measurements, and blood samples were obtained for the measurement of CVD risk factors. Standardized questionnaires for the assessment of sociodemographic and behavioral factors were also administered. The protocol was approved by the Institutional Review Board of Emory University and informed consent was obtained from all participants.

*Measurement of metabolic syndrome score*

MetS risk factors were defined based on the 2005 AHA-NHLBI criteria [44], and include waistline circumference, blood pressure, triglycerides, HDL cholesterol and fasting glucose. We first assigned each of the five MetS risk factors a score of 0 or 1 to represent absence or presence of the risk factor, respectively (Table 1). The 5 components were then summed, yielding an overall MetS score, ranging from 0 to 5, as an overall measure of the MetS profile on an ordinal scale. Waist circumference and blood pressure were measured by a research nurse following standard procedures. For systolic and diastolic blood pressure, the average of two measurements taken 5 minutes apart was used in the analyses. HDL cholesterol, total triglycerides, and plasma fasting glucose were measured from venous blood samples after an overnight fast. Total triglycerides

were determined by enzymatic methods (Beckman Coulter Diagnostics, Fullerton, CA). Direct HDL cholesterol was measured with homogeneous assays (Equal Diagnostics, Exton, PA). Glucose levels were measured on the Beckman CX7 chemistry autoanalyzer.

*Measurement of air pollution*

Ambient $PM_{2.5}$ levels across contiguous United States were estimated using well-validated prediction methods [45]. Briefly, we used an ensemble model that integrated three machine learning algorithms and multiple predictor variables to estimate daily concentrations of $PM_{2.5}$ at a spatial resolution of 1 km × 1 km. The ensemble model was based on a generalized additive model that combined different estimates of $PM_{2.5}$ from neural network, random forest and gradient boosting with each learner being geographically weighted. We fit the three baseline algorithms with monitoring data from Environmental Protection Agency Air Quality System and incorporated satellite derived aerosol optical depth measurements, meteorological variables, chemical transport model outputs, and land-use terms as predictor variables to estimate $PM_{2.5}$ levels in unmonitored areas. Details of the data sources have been well documented [45]. The cross-validated $R^2$ was 0.86 for daily $PM_{2.5}$ predictions and 0.89 for annual estimates, which indicate excellent model performance. In the present study, two-year average $PM_{2.5}$ concentrations (the previous year and current year of Emory visit) at ZIP code-level were calculated and assigned to each of our participants based on the year of clinic visit and their ZIP code of residence at that time.

*Other measurements*

We collected information on potential confounders including individual-level demographic characteristics (age, education, and employment), behavioral factors (physical activity, smoking, and alcohol drinking habits), medical history, and ZIP code-level socioeconomic status and population density. Educational level was recorded as years of education and employment status was classified as being currently employed or unemployed. We used standard questionnaires to assess smoking status and alcohol consumption [46,47]. Participants were classified as current smokers or non-current smokers (never or past smokers), and the number of alcoholic beverages they consumed in a typical week was calculated. Current physical activity status was measured using the Baecke questionnaire, which assesses occupational, sport and non-sport related leisure physical activity, and provides a continuous score of physical activity level [48]. We also assessed whether twins developed coronary heart disease after the initial 1990 survey. Coronary heart disease was defined as a previous diagnosis of myocardial infarction or angina pectoris, or previous hospitalizations for acute coronary syndromes or coronary revascularization procedures. ZIP code-level socioeconomic data (percentage of poverty) and population density were retrieved from the 2000 U.S. Census, the 2010 U.S. Census, and the American Community Survey for each year of study visits, from 2002 to 2010.

*Statistical methods*

The exposure variable was analyzed as a continuous variable and the main outcome variable (the MetS score) was analyzed as an ordinal variable with 5 possible levels. We used mixed models to fit ordinal response data for twin studies, with a random effects term to account for correlations between the two brothers [49,50]. Initially, original exposure levels of each individual were used in the mixed model, which is described as follows:

$$\ln\left[\frac{P(Y_{ij} \geq k)}{1 - P(Y_{ij} \geq k)}\right] = \beta_0 + \beta_c X_{ij} + \alpha_i + \varepsilon_{ij}, \quad (1)$$

where $\alpha_i$ captures the random intercept applying to the twin pair *i* and $\varepsilon_{ij}$ is the usual random error for individuals. We use *Y* to denote the ordinal outcome with *k* used to represent the MetS score ranging from 0 to 5. *X* denotes the exposure level; *i* is the index of twin pairs and *j* =1, 2 indexes the individual twins within pairs. The coefficient $\beta_c$ measures the change in the logit of the probability of response for each unit change in *X.*

Next, exposure data were partitioned into between-pair and within-pair terms. The model is presented below:

$$\ln\left[\frac{P(Y_{ij} \geq k)}{1 - P(Y_{ij} \geq k)}\right] = \beta_0 + \beta_B \overline{X}_\iota + \beta_W (X_{ij} - \overline{X}_\iota) + \alpha_i + \varepsilon_{ij}. \quad (2)$$

In this notation, the between-pair coefficient $\beta_B$ measures the difference in logits based on the change of average pairwise $PM_{2.5}$ exposure levels; the within-pair coefficient $\beta_W$ gives the expected change in logits based on change of the difference between an individual's *X* and their twin-pair average, and therefore inherently controlled for familial factors and early

environmental influences. In addition, daily activities and other environmental influences during the examination day are controlled by design in within-pair comparisons, since twin pairs were examined together. We conducted a series of models that sequentially adjusted for potential confounders to examine the association between $PM_{2.5}$ concentration and MetS score. Adding sets of potential confounders at a time, sequential regression models adjusted for the following factors: ZIP code-level population density and poverty; demographic factors (age, education, and employment); and history of coronary heart disease. Individual health behaviors (physical activity, smoking, and alcohol consumption) were not considered as confounding factors, but given their known relationship with MetS, were adjusted for in a separate sensitivity analysis.

Waistline circumference, blood pressure, triglycerides, HDL cholesterol and fasting glucose were all analyzed as continuous variables using mixed models for twin studies, where the within and between terms were constructed in a similar way as above [49].

Familial confounding factors would be indicated if the estimate for within-pair effects is smaller, and the estimate for between pair effects is larger, respectively, than the estimate in the analysis of twins analyzed as individuals [51]. Lastly, we stratified the analysis for monozygotic and dizygotic twin pairs. Monozygotic twins share 100% of their genetic material in addition to early environment, thus any association within monozygotic pairs cannot be ascribed to genes or early shared environmental factors. Dizygotic twins share familial factors, but on average only share 50% of their genes. Therefore, comparison of the within-pair effect size of monozygotic twins

with dizygotic twins provides information on whether genetic confounding is present. All analyses were completed in SAS, version 9.4 (SAS Institute, Inc., Cary, North Carolina), and statistical significance was defined at a two-sided $\alpha = 0.05$.

## RESULTS

The 555 twins in the analysis included 273 pairs (167 monozygotic pairs and 106 dizygotic pairs), and 9 unpaired twins with a mean age of 55.5 years. The average MetS score was 2.7, with a range of 0 to 5 and a standard deviation (SD) of 1.4. The mean of two-year average $PM_{2.5}$ concentration in the overall sample was 11.1 $\mu g/m^3$ (range: 2.3-21.1; SD: 3.0). Overall, 88.3% of twins within a pair lived in different ZIP codes, and 84.9% of the overall sample lived in different ZIP codes. Among 241 (88.3%) twin pairs who were discordant for $PM_{2.5}$ exposure levels, the mean difference between brothers was 0.8 $\mu g/m^3$, with a range from 0 $\mu g/m^3$ to 7.0 $\mu g/m^3$. Descriptive statistics for metabolic indicators and other study variables are shown in Table 2.

### *$PM_{2.5}$ and metabolic syndrome score*

In the analyses of twins as individuals (Table 3), there was an association between $PM_{2.5}$ concentration and MetS score that slightly strengthened after sequentially adjusting for ZIP code-level population density and socioeconomic factors, as well as individual demographic variables,

and CVD history. In the model adjusted for all these factors, the odds ratio of having a 1-point higher MetS score was 1.86 for each 10 μg/$m^3$-increase in exposure to $PM_{2.5}$ concentration (CI: 1.05, 3.29).

When the effect of $PM_{2.5}$ was separated into between-pair and within-pair components, significant associations were found between-pairs but not within-pairs (Table 3). In the fully adjusted model, the odds ratio of having a 1-point higher MetS score was 2.06 (CI: 1.06, 3.99) for each 10 μg/$m^3$-increase in exposure level across twin pairs. In contrast, none of the models showed significant associations within pairs, indicating that $PM_{2.5}$ exposure had little effect on metabolic health after controlling for shared factors for twins within pairs. There was no statistical interaction between zygosity and the within-pair differences in exposure ($P = 0.85$). The analysis of $PM_{2.5}$ concentration and individual metabolic components yielded weaker and not significant associations (Tables 4).

*Sensitivity analysis*

The effect estimate for the analysis of twins as individuals was attenuated but remained marginally significant after additionally adjusting for health behaviors (odds ratio = 1.78; 95% CI: 1.00, 3.17; $P = 0.05$), while the effect estimates for between-pairs analysis remained similar (odds ratio = 2.03; 95% CI: 1.03, 3.99; $P = 0.04$).

## DISCUSSION

In this study of middle-aged Vietnam-era twins, long-term exposure to higher $PM_{2.5}$ concentration was found to be associated with the higher MetS score among twins as individuals and comparing twin pairs. However, no significant associations were found in within-pair analyses by comparing twins discordant for $PM_{2.5}$ exposure levels, who are naturally matched for familial factors. Given that there is no significant interaction between zygosity and within-pair effects, shared genetic factors do not appear to play a role in this association. These results suggest that the relationship between fine particulate matter and MetS score is confounded by shared non-genetic familial factors. When we examined the associations between $PM_{2.5}$ concentrations and each MetS component separately, no single MetS risk factor seemed to be driving the association.

To our knowledge, our study is the first to investigate the association between ambient $PM_{2.5}$ concentrations and MetS score in a twin study. Our results among twins analyzed as individuals are consistent with previous investigations that have observed a positive association between $PM_{2.5}$ and MetS in different geographical areas and populations. A study conducted among 3769 Swiss adults reported that each 10 $\mu g/m^3$ increase in 10-year mean $PM_{10}$ in ambient air (where $PM_{2.5}$ contributed 70-80% to the $PM_{10}$ fraction) accounted for 31% increase in the odds of MetS defined by the International Diabetes Federation criteria [22]. More recent studies reported similar associations [9,23,24,27]. Our results showing that the individual level association is driven by

differences across pairs rather than within pairs, indicate that these associations reported in the literature may be explained by unmeasured confounding familial factors.

Although previous studies have been fairly consistent in reporting an association between $PM_{2.5}$ and MetS, studies examining individual MetS risk factors including hypertension, type 2 diabetes mellitus, body weight, glucose metabolism and lipid profile, others have reported inconsistent results [23,28,29,52-54]. The lack of association between $PM_{2.5}$ and individual MetS risk factors in several previous studies is in agreement with our findings, and suggests that the aggregation of metabolic risk factors in the MetS definition provides more information than the individual risk factors alone.

While the pathophysiological mechanisms of MetS are complex, the results of our study suggest that familial factors play an important role in MetS and may also contribute to the likelihood of individual exposure to ambient pollution in adulthood. Indeed, the link between the residential environment during childhood and adulthood are well established [39], and familial aggregation and the role of genetic factors in MetS and its components are well known [55-59]. Evidence of the association between social or economic disadvantage and metabolic syndrome are also well documented [60-62]. Factors that are shared early in life within families, like socioeconomic condition, could lead to increased risk of MetS and at the same time increased likelihood of air pollution exposure. For example, substantial disparities exist in burden of $PM_{2.5}$ exposure based on social disadvantage [63,64], and it has been suggested that the heterogeneous geographic

exposure to air pollutants with increased vulnerability for specific population subgroups has environmental justice implications [65]. Thus, the same social conditions that explain population disparities in exposure to environmental pollutants may also explain propensity towards developing MetS risk factors. Our study is unique in being able to consider these early-life factors as confounders in the relationship of air pollution with adverse health consequences.

The co-twin study design is an ideal approach to study causal factors related to complex conditions like MetS, as it provides a useful analog to the counterfactual design [51]. Twin pairs allow natural matching for many unmeasured confounding factors likely to influence complex traits, such as genes, early environment exposures, and parental factors. The analysis of twins as individuals, as well as the decomposition of the exposure into between and within pair effects, allows to examine the potential influence of familial confounding factors on the association. However, there are several limitations in our study. First, the sample size for within-pair analyses was relatively small and there was limited variance in $PM_{2.5}$ concentrations within pair. This could have contributed to the null within-pair findings. Second, due to the cross-sectional design, we were unable to assess the temporal relation between fine particulate matter and metabolic disorders. Moreover, our participants were middle-aged male veterans, and therefore the results may not be generalizable to other populations. Finally, although we considered important confounders at the individual level and at the ZIP code level, unmeasured confounders are also possible. On the other hand, our study was strengthened by the large, homogeneous sample of twins from across the entire US, and the large proportion of twin brothers living in different

geographical areas.

## CONCLUSIONS

Among Vietnam-era veterans, $PM_{2.5}$ exposure is associated with a higher prevalence of MetS, but this relationship is primarily the result of familial factors that influence both the likelihood of MetS and the likelihood to be exposed to air pollution in adult life. Future research should explore the specific early-life behavioral or environmental exposures that are involved in the association of exposure to $PM_{2.5}$ with MetS in adulthood. Our results indicate that prevention of early life exposures is key in reducing the risk of developing MetS in adult life.

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**TABLES**

Table 1. Metabolic Syndrome Score Definition

| Health metrics | Levels | Score | Definition |
|---|---|---|---|
| Waist | poor | 1 | > 102 cm |
| | ideal | 0 | ≤ 102 cm |
| Blood Pressure | poor | 1 | SBP≥ 130 or DBP ≥ 80 mmHg |
| | ideal | 0 | SBP < 130 and DBP < 80 mmHg |
| Total Triglycerides | poor | 1 | ≥ 250 mg/dL |
| | ideal | 0 | < 250 mg/dL |
| HDL Cholesterol | poor | 1 | < 40 mg/dL |
| | ideal | 0 | ≥ 40 mg/dL |
| Fasting Glucose | poor | 1 | ≥ 100 mg/dL |
| | ideal | 0 | < 100 mg/dL |
| Total Score | | Range = 0-5 | |

DBP, diastolic blood pressure; HDL, high-density lipoprotein; SBP, systolic blood pressure.

Table 2. Demographic, Behavioral, Cardiovascular, and Air Pollution Characteristics of twins, Emory Twins Study, 2002–2010

| Characteristic and Variable | Total Number | Mean (SD) or % |
|---|---|---|
| **Demographic Factors** | | |
| Age (years) | 555 | 55.5 (3.1) |
| Education (no. of years) | 554 | 14.1 (2.2) |
| Currently Employed (%) | 554 | 73.1 |
| Monozygotic Twins (%) | 555 | 61.1 |
| **Behavioral Factors** | | |
| Baecke Score [a] | 550 | 7.2 (1.8) |
| Current Smoker (%) | 555 | 25.2 |
| Alcohol Consumption Per Week | 552 | 5.1 (9.7) |
| **Cardiovascular Factors** | | |
| History of Cardiovascular Disease (%) | 555 | 12.3 |
| Systolic Blood Pressure (mmHg) | 555 | 130.3 (16.1) |
| Diastolic Blood Pressure (mmHg) | 555 | 81.1 (10.4) |
| Blood Pressure ≥ 130/85 mmHg (%) | 555 | 68.7 |
| HDL Cholesterol (mg/dL) | 555 | 39.7 (19.8) |
| HDL Cholesterol < 40 mg/dL (%) | 555 | 60.2 |
| Triglycerides (mg/dL) | 555 | 179.4 (95.2) |
| Triglycerides ≥ 150 mg/dL (%) | 555 | 55.7 |
| Plasma Glucose (mg/dL) | 555 | 103.0 (21.9) |
| Plasma Glucose ≥ 100 mg/dL (%) | 555 | 51.5 |
| Waist Circumstance (cm) | 553 | 99.9 (12.4) |
| Waist > 102 cm (%) | 553 | 36.7 |
| Metabolic Syndrome Score | 555 | 2.7 (1.4) |
| Metabolic Syndrome (%) | 555 | 57.8 |
| **Area-Level Environmental Factors** | | |
| Percentage Below poverty Level | 554 | 8.0 (4.7) |
| Population Density (1,000 person/mile$^2$) | 554 | 1.7 (2.8) |
| Air $PM_{2.5}$ Concentration (μg/m$^3$) | 555 | 11.1 (3.0) |
| Between-Pair $PM_{2.5}$ Concentration [b] | 555 | 11.1 (2.7) |
| Within-Pair Difference in $PM_{2.5}$ Concentration [c] | 555 | 0.81 (1.1) |

Values presented are means (SD) unless otherwise specified.

HDL, high-density lipoprotein; $PM_{2.5}$, fine particulate matter. [a] The Baecke Physical Activity Scale was used to assess physical activity; [b] Average pairwise $PM_{2.5}$ concentration; [c] Difference between individual $PM_{2.5}$ exposure and twin-average exposure level.

Table 3. Adjusted and Unadjusted Associations Between Metabolic Syndrome Score and $PM_{2.5}$ Concentrations*, Emory Twins Study, 2002–2010

| Model | Total Number | Individuals [a] | | Between Pairs [b] | | Within Pairs [c] | |
|---|---|---|---|---|---|---|---|
| | | Odds Ratio (95% CI) | *P* value | Odds Ratio (95% CI) | *P* value | Odds Ratio (95% CI) | *P* value |
| Model 1 (Unadjusted) | 555 | 1.60 (0.91, 2.82) | 0.10 | 1.84 (0.95, 3.58) | 0.07 | 0.90 (0.42, 1.93) | 0.79 |
| Model 2 (+Population Density, Poverty) [#] | 554 | 1.77 (1.00, 3.13) | 0.05 | 2.01 (1.03, 3.93) | 0.04 | 1.02 (0.47, 2.20) | 0.96 |
| Model 3 (+ Individual Demographic Variables: age, education, employment) | 552 | 1.87 (1.05, 3.33) | 0.03 | 2.11 (1.07, 4.14) | 0.03 | 1.15 (0.49, 2.68) | 0.75 |
| Model 4 (+ CVD History) | 552 | 1.86 (1.05, 3.29) | 0.03 | 2.06 (1.06, 3.99) | 0.03 | 1.22 (0.50, 2.98) | 0.66 |

CVD, cardiovascular disease; $PM_{2.5}$, fine particulate matter. * Results are presented as the odds ratio for a 1-point larger metabolic syndrome score for each 10 $\mu g/m^3$-increase in the concentrations of $PM_{2.5}$ exposure. The metabolic syndrome score is the ordinal outcome variable. Odds ratios in these models reflect: [a] Exposure value for each individual; [b] Average exposure value for each pair; [c] Difference between individual exposure and twin-average exposure level. [#] Population density and poverty are at ZIP code level, and all other potential confounders adjusted are at individual level.

Table 4. Adjusted Association (Using Model 4) Between Continuous Metabolic Biomarkers and $PM_{2.5}$ Concentration*, Emory Twins Study, 2002–2010

| Variable Name | Total Number | Individuals [a] Effect Estimate (95% CI) | *P* value | Between Pairs [b] Effect Estimate (95% CI) | *P* value | Within Pairs [c] Effect Estimate (95% CI) | *P* value |
|---|---|---|---|---|---|---|---|
| Waist Circumstance (cm) | 550 | 0.83 (-2.77, 4.43) | 0.65 | 0.48 (-4.12, 5.08) | 0.84 | 1.38 (-4.27, 7.03) | 0.63 |
| Systolic Blood Pressure (mmHg) | 552 | -0.08 (-4.77, 4.61) | 0.97 | 1.11 (-4.58, 6.79) | 0.70 | -2.66 (-10.79, 5.47) | 0.52 |
| Diastolic Blood Pressure (mmHg) | 552 | 2.47 (-0.60, 5.55) | 0.12 | 3.38 (-0.39, 7.14) | 0.08 | 0.65 (-4.58, 5.87) | 0.81 |
| HDL Cholesterol (mg/dL) | 552 | -1.28 (-5.46, 2.91) | 0.55 | -4.43 (-9.75, 0.89) | 0.10 | 3.69 (-2.94, 10.32) | 0.28 |
| Triglycerides (mg/dL) | 552 | 4.05 (-24.41, 32.51) | 0.78 | 6.06 (-28.87, 40.98) | 0.73 | 0.24 (-47.74, 48.23) | 0.99 |
| Plasma Glucose (mg/dL) | 552 | 2.52 (-3.77, 8.82) | 0.43 | 1.73 (-5.86, 9.33) | 0.65 | 4.18 (-6.83, 15.18) | 0.46 |

HDL, high-density lipoprotein; $PM_{2.5}$, fine particulate matter. * The individual metabolic syndrome risk factors are the outcome variables. Coefficients in these models reflect: [a] Exposure value for each individual; [b] Average exposure value for each pair; [c] Difference between individual exposure and twin-average exposure level.