Personal Black Carbon Exposure Influences Ambulatory Blood Pressure
Air Pollution and Cardiometabolic Disease (AIRCMD-China) Study

Xiaoyi Zhao,* Zhichao Sun,* Yanping Ruan, Jianhua Yan, Bhramar Mukherjee, Fumo Yang, Fengkui Duan, Lixian Sun, Ruijuan Liang, Hui Lian, Shuyang Zhang, Quan Fang, Dongfeng Gu, Jeffrey R. Brook, Qinghua Sun, Robert D. Brook, Sanjay Rajagopalan, Zhongjie Fan

Abstract—Few prospective studies have assessed the blood pressure effect of extremely high air pollution encountered in Asia’s megacities. The objective of this study was to evaluate the association between combustion-related air pollution with ambulatory blood pressure and autonomic function. During February to July 2012, personal black carbon was determined for 5 consecutive days using microaethalometers in patients with metabolic syndrome in Beijing, China. Simultaneous ambient fine particulate matter concentration was obtained from the Beijing Municipal Environmental Monitoring Center and the US Embassy. Twenty-four–hour ambulatory blood pressure and heart rate variability were measured from day 4. Arterial stiffness and endothelial function were obtained at the end of day 5. For statistical analysis, we used generalized additive mixed models for repeated outcomes and generalized linear models for single/summary outcomes. Mean (SD) of personal black carbon and fine particulate matter during 24 hours was 4.66 (2.89) and 64.2 (36.9) μg/m³. Exposure to high levels of black carbon in the preceding hours was associated significantly with adverse cardiovascular responses. A unit increase in personal black carbon during the previous 10 hours was associated with an increase in systolic blood pressure of 0.53 mmHg and diastolic blood pressure of 0.37 mmHg (95% confidence interval, 0.17–0.89 and 0.10–0.65 mmHg, respectively), a percentage change in low frequency to high frequency ratio of 5.11 and mean interbeat interval of −0.06 (95% confidence interval, 0.62–9.60 and −0.11 to −0.01, respectively). These findings highlight the public health effect of air pollution and the importance of reducing air pollution. (Hypertension. 2014;63:871-877.) • Online Data Supplement

Key Words: air pollution ■ blood pressure ■ carbon black ■ particulate matter

The updated global burden of disease report has once again highlighted the importance of air pollution as an important risk factor contributing to global mortality.1 Approximately 90% of the world lives in regions exceeding the World Health Organization Air Quality annual standards for fine particulate matter <2.5 μm (PM2.5).2 In East Asia, PM2.5 ranks as the fourth leading risk factor for premature death because its megacities face some of the highest concentrations in the world.3–5 We and others have provided evidence that ambient air pollution exposure is associated with increases in blood pressure (BP), likely via acute autonomic imbalance, which together may represent a plausible mechanism of air pollution–mediated acute cardiovascular events.6,6 These associations have been reported typically at relatively low ambient levels of PM2.5 in North America and Europe. Whether these adverse hemodynamic and autonomic responses persist in relation to the >10-fold higher PM2.5 concentrations encountered in East Asia is unknown.7 This is important in the light of analyses demonstrating that the dose–response relationship for mortality because of PM2.5 is attenuated at higher concentrations.8 In this prospective study, we investigated the association between personal level exposure to black carbon (BC) as well as ambient PM2.5 with 24-hour ambulatory BP (ABP) and 24-hour heart rate variability (HRV) in a cohort of individuals with the metabolic syndrome living in Beijing, China, and who are chronically exposed to high pollution levels.
Methods

Study Population and Design

Subjects with metabolic syndrome (n=65) were recruited from clinics affiliated with the Peking Union Medical College (PUMC) Hospital. The main motivation to conduct our experiments in metabolic syndrome was to study a patient group at high risk for transitioning to overt type 2 diabetes mellitus. The Institutional Review Board at PUMC Hospital approved the protocol, and every subject signed a written informed consent (NCT01548300). Eligibility criteria included nonsmoking adults between 35 and 75 years living in a nonsmoking home in Beijing. Metabolic syndrome was defined by International Diabetes Federation criteria specific for Asians as waist circumference >90 cm in men and >80 cm in women plus any 2 of the following: triglyceride level >150 mg/dL, high-density lipoprotein protein <40 mg/dL in men and <50 mg/dL in women, systolic BP (SBP) >130 mm Hg, fasting plasma glucose >100 mg/dL, or previously diagnosed type 2 diabetes mellitus. Exclusion criteria included smoking within past 1 year, severe occupational exposure to pollutants, intake of drugs that may alter baseline insulin sensitivity or endothelial function (eg, antioxidants, multivitamins, folic acid, fish oil supplementation, and l-arginine), and use of nonsteroidal anti-inflammatory drugs. The study protocol has been detailed previously. Briefly, during day 0, subjects arrived at the clinic and underwent baseline measurements, including body mass index, waist circumference, and waist-to-hip ratio, and were fit with the BC monitor and a global positioning device (USGlobalSat DG-100 Datalogger). The participants were advised to continue their usual daily activities and maintain a diary during the 5-day period, during which they wore personal exposure monitors. On day 4, they wore the ABP and Holter monitor for 24 hours and completed a diary defining their activities and locations for each half-hour period. On day 5, the subjects received tests that include (1) endothelial function assessment, (2) pulse wave velocity and central aortic BP measurement, and (3) blood draws. All patients were enrolled between February 14, 2012, and July 14, 2012.

Exposure Measurements and Meteorologic Variables

Personal BC was measured every 5 minutes during a 5-day period using a microaethalometer (AethLabs MicroAeth AE51). As a quality check, time series of 5-minute ambient BC concentrations was collected continuously from a dual wavelength aethalometer (a model AE-20 Aethalometer; Magee Scientific, CA) at a fixed site in PUMC Hospital since May 28, 2012. In addition, ambient PM$_{2.5}$ concentrations were determined continuously using a tapered element oscillating microbalance sampler (TEOM, operated hourly at 50°C) at a fixed monitoring site at Tsinghua University (northwest Beijing, between the Fourth and Fifth Ring Roads) since June 15, 2012; official Beijing Municipal Environmental Monitoring Center (BMEMC) network data of hourly PM$_{2.5}$ was obtained for the Cheongzhuan site situated in the North Second Ring Road; postings of hourly PM$_{2.5}$ readings on a Twitter feed by US Embassy in Beijing located at Northeast Third Ring Road were also collected. Meteorologic measurements of ambient temperature and relative humidity were obtained from the China Meteorologic Administration for the whole study period.

24-Hour ABP Monitoring

ABP assessment was performed by a portable, lightweight, noninvasive monitor with a self-inflating cuff (Spacelabs Healthcare ABP Monitors; 90207, WA). SBP, diastolic BP (DBP), and heart rate (HR) were measured repeatedly every 20 minutes during daytime (0600–2200 hours) and every 30 minutes at night-time (2200–0600 hours) during a 24-hour period starting from 9:00 AM on day 4. Averages of ABP measurements (ie, SBP, DBP, and HR) during daytime, night-time, and 24 hours were also calculated for further analysis.

24-Hour Ambulatory ECG (Holter ECG)

HRV assessment was performed during a 24-hour period on day 4 for each subject using the 3-lead SpaceLabs recorder and the Impresario Holter system (Spacelabs Healthcare, WA). Frequency and time domain parameters were analyzed every 20 minutes during daytime and every 30 minutes at night-time to match with ABP measurements. Frequency domain analysis provided estimates of the spectrum density of R-R intervals within specific frequency bandwidths, including total power (0.01–1.00 Hz), low frequency (LF; 0.04–0.15 Hz), high frequency (HF; 0.15–0.40 Hz), and the ratio of LF to HF (LF/HF). Time domain analysis included the following: SD of all N-N intervals obtained during the 5 minutes; proportion of the N-N intervals >5 ms; square root of the mean squared differences of successive N-N intervals; and mean of the R–R intervals. All HRV indices were transformed logarithmically to meet the normality assumption.

Endothelial Function, Pulse Wave Velocity, and Central Aortic BP Measurement

With the patient in supine position and after 30 minutes of resting quietly, the pulse wave velocity of the carotid and femoral arteries was measured, estimating the delay with respect to the ECG wave. Endothelial function was measured by the reactive hyperemia peripheral arterial tonometry index (EndoPat2000, Itamar Medical, Israel). Pulse wave velocity and central aortic BP were estimated with the SphygmoCor CP noninvasive device (AtCor Medical, Australia).

Blood Tests

Fasting blood samples were drawn from subjects on day 5 and routine laboratory evaluations were conducted (lipid profile, creatinine, and glycohemoglobin).

Statistical Analysis

Construction of Different Exposure Measures From the Raw Data

Daily means of PM$_{2.5}$ at 3 monitoring sites across Beijing (Tsinghua University, BMEMC, US Embassy) were calculated. The average of the daily means from 3 monitoring sites was used as a representation of integrated daily mean of ambient PM$_{2.5}$. Because there were no data on PM$_{2.5}$ at Tsinghua University before June 15th, the integrated daily mean of ambient PM$_{2.5}$ in the BMEMC and US Embassy sites before that date was used. Previous studies have suggested a subacute effect (2- to 5-day averages) of PM$_{2.5}$ on BP; hence, we calculated the averages for preceding 24 hours (1-day lag) and 48 to 72 hours (3-day lag) and averages of cumulative exposure to 3 and 5 days (3- and 5-day averages) as illustrated in Figure S1 in the online-only Data Supplement, for each subject, before their clinical visit on day 5. Similarly, personal-level BC concentrations were averaged at multiple lags (1- and 3-day lags) and time intervals (3- and 5-day averages) from 5-minute repeated recordings for each subject.

Descriptive Statistics

Summary level descriptive statistics were computed for demographic parameters, exposure characteristics, meteorologic variables, and functional end points including 24-hour ABP, 24-hour HRV analysis, endothelial function, pulse wave velocity, and blood test assessments. Pearson correlation coefficients were calculated to evaluate the relationships among daily means of exposure end points, including ambient BC at PUMC, personal-level BC, and regional PM$_{2.5}$ from 3 monitoring sites.

Analysis of Single/Summary Outcome Measures

For outcomes that comprised 1 value per subject, we used standard multiple linear regression models to examine their associations with air pollutants. In our models, we regressed averages of 24-hour HRV indices, averages of 24-hour ABP (daytime, night-time, or 24-hour average), endothelial function index, or pulse wave velocity on...
personal BC or ambient PM$_{2.5}$ using different lagging (1- and 3-day lags) or averaging intervals (3- and 5-day averages), with age, sex, and body mass index adjusted. To capture potential nonlinear effects of mean temperature and relative humidity (averaged during the 24 hours before the measurement of the outcome), we included 2 smoothing terms corresponding to these predictors under a generalized additive model. The significance of the smoothing term was then tested, and the model was simplified to a linear model when appropriate based on the decision of this test. Changes in ABP and percentage changes in HRV associated with 1-$\mu$g/m$^3$ increase in personal BC or a 10-$\mu$g/m$^3$ increase in ambient PM$_{2.5}$ at different lagging or averaging time periods were estimated along with corresponding Wald-type confidence intervals (CIs). All models were evaluated for outliers and influential observations by residual diagnostics.

### Analysis of Outcome Data With Repeated Measures

Because linear regression model does not account for within-subject correlation of repeated outcome measures, we also investigated the effect of personal-level BC on the repeated measures of ABP or HRV indices using the generalized additive mixed model. The temporal structure of the exposure–response relationship was assessed using 1- to 10-hour moving averages of BC concentrations before each ABP measurements. All models controlled for age, sex, body mass index, hypertension (yes/no), and diabetes mellitus (yes/no). Linear terms of mean temperature and relative humidity during the 24-hour period were found to be adequate and adjusted in the model. Resting HR was also included as a likely confounder for outcomes representing HRV indices. A penalized cubic spline function of time with 8 degrees of freedom was used to capture nonlinear fixed effects of time, and an autoregressive covariance structure among residual errors within subjects was used. This model choice was governed by the Akaike information criterion. Effects associated with 1-$\mu$g/m$^3$ increase in personal BC at each averaging time period were estimated. To assess the potential effect of HR on ABP, sensitivity analyses were conducted, adjusting for the time-varying variable HR in the generalized additive mixed models with ABP as outcome. We also conducted sensitivity analyses including a factor representing micro-aethalometer assignment as a random effect because of the concern of differences in BC measurement among devices.

All analyses were performed with statistical package R version 2.15.2 (www.r-project.org). Statistical significance was assessed using a 2-sided Wald test at the significance level of 0.05.

### Results

#### Baseline Characteristics

Table 1 provides baseline patient characteristics, which included patients who met International Diabetes Federation criteria for metabolic syndrome with a mean HbA1c of 6.16%. Figure 1 depicts the personal-level BC, ambient BC, and ambient PM$_{2.5}$ concentrations from the 3 sites during the study period. Strong correlations were found for daily means of PM$_{2.5}$ from 3 fixed sites located in different parts of the city ($r=0.85–0.95, P<0.0001$) and daily means of BC at personal and ambient levels ($r=0.84, P<0.0001$; Table S1). Personal BC also correlated well with regional PM$_{2.5}$ measurements with Pearson correlation coefficients of 0.73 to 0.78 ($P<0.0001$) as illustrated in Table S1, although the mean concentration of personal BC (5.08 $\mu$g/m$^3$) was $>10\%$ of ambient PM$_{2.5}$ (74 $\mu$g/m$^3$) during the same period. Table 2 provides the summary of exposure concentrations, temperature, and relative humidity for the subjects. The mean of 5-day average of ambient PM$_{2.5}$ (68.9 $\mu$g/m$^3$; SD, 25.2 $\mu$g/m$^3$) was $>3$-fold higher than the US National Air Quality Standard ($<15$ $\mu$g/m$^3$). The mean of the 5-day average of personal BC (4.77 $\mu$g/m$^3$; SD, 1.76 $\mu$g/m$^3$) was substantially higher than the average urban BC concentrations in North America (0.2–1.9 $\mu$g/m$^3$).

#### Effect of PM$_{2.5}$ and BC on ABP

Figure 2 displays the temporal variation of ABP and personal BC during a 24-hour period. ABP measures displayed normal diurnal variation during the 24-hour study period, with a decrease during sleep and a surge in the early morning hours. Daily BC concentration displayed a bimodal pattern, with peaks between 7:00 and 8:00 am and between 7:00 and 11:00 pm, and with the lowest levels generally appearing around noon.

In generalized additive mixed model analysis, we observed positive association between personal BC and BP for averaging periods ranging from 6 to 10 hours (Figure 3). Effects of BC on changes for ambulatory SBP were slightly greater in magnitude than for DBP across all the time periods examined, with an increase of 0.53 mm Hg (95% CI, 0.17–0.89 mm Hg) in SBP and an increase of 0.37 mm Hg (95% CI, 0.10–0.65 mm Hg) in DBP for 1-$\mu$g/m$^3$ increase in BC during
the previous 10 hours. We observed that the 10-hour moving average resulted in the greatest changes of ambulatory SBP, whereas 9-hour moving average resulted in the greatest change of DBP (0.39 mmHg; 95% CI, 0.12–0.66 mmHg) and HR (0.31 bpm; 95% CI, 0.07–0.55 bpm). Inclusion of microaethalometer assignment as a random effect or adjusting for HR as a time-varying covariate for outcomes SBP and DBP did not appreciably change the results.

Personal levels of BC averaged over the lagging and averaging intervals on the scale of days depicted in Table S2, however, did not show any significant association with aggregate summary measures of ABP (daytime average, night-time average, or 24-hour average). Similarly, no significant association between cumulative averages or single-day lags for PM$_{2.5}$ exposure and summary measures of ABP was observed (Table S3).

**Effect of PM$_{2.5}$ and BC on HRV Indices**

Multivariable-adjusted associations of HRV indices with 1- to 10-hour moving averages of personal-level BC concentration using generalized additive mixed model are presented in Figure 4. The 7-hour moving average of personal BC was found to be marginally associated with LF/HF and mean R-R interval. Longer averaging times showed stronger magnitudes of association in LF/HF and mean R-R interval, with the largest associations exhibited for the 10-hour moving average that a 1-μg/m$^3$ increment in personal BC was associated with 5.11% (95% CI, 0.62–9.60) increase of LF/HF and 0.06% (95% CI, 0.01–0.11) reduction of mean R-R interval, respectively. No evidence of statistically significant association between personal BC concentration and any other HRV indices was observed. Consistent results were found when adding the microaethalometer assignment as a random effect in the models.

Associations of PM$_{2.5}$ and BC over multiple lagging and averaging intervals on the scale of days with summary measures of HRV indices were assessed. However, no significant change in 24-hour average of HRV indices was seen with exposure to day lags or averages of personal-level BC (Table S4). Similarly, no change in HRV summary measures was associated with day lags or averages of PM$_{2.5}$ exposure (Table S5).

**Effects of BC and PM$_{2.5}$ on Endothelial Function and Arterial Stiffness**

There was no significant association between different lags or moving averages of BC or PM$_{2.5}$ with either endothelial function or arterial stiffness measures.

**Discussion**

BC has gained attention as a product and marker of combustion-related anthropogenic air pollution, often showing independent health associations distinct from those induced by background ambient PM$_{2.5}$. Our results demonstrate an effect of anthropogenic combustion-related air pollution (BC) on ABP and HRV in patients with metabolic syndrome in Beijing, a city continually facing extreme levels of air pollutants.

Although previous associations between exposures to ambient air pollutants and BP have been reported, these generally have been observed to occur in response to concentrations that are several folds lower. It is not clear whether adverse cardiovascular actions of air pollutants persist at the markedly higher levels encountered in Asia. Furthermore, few studies have evaluated the effects of air pollutants in patients with metabolic syndrome, a population at risk for development of type II diabetes mellitus, and hypertension. Previous findings suggest that obese individuals and those with the metabolic syndrome may be at a greater risk. The rise in the prevalence of the metabolic syndrome as well as the marked levels of air pollutants in Beijing offered a unique opportunity to investigate this relationship. Exposure to BC measured at the personal-level during the previous 10 hours was associated with elevations in both SBP and DBP, which are consistent to the effect on ABP in studies performed in North America (Table S6). In the study by Delfino et al., in patients with coronary artery disease, outdoor BC showed small but significant associations with SBP and DBP especially under longer exposures, with each μg/m$^3$ increase in BC during 8 hours resulting in an increase of 0.36 mmHg in SBP. Our findings demonstrate similar degrees of BP elevation per 1-μg/m$^3$
change in BC, despite the levels of exposure being ≈3-fold higher. Other studies that have examined the associations with BC and BP involved sitting clinic BP and lacked the ability to resolve BP and BC measurements hourly. Differences in study design and the use of sphygmomanometric measurement of sitting BP rather than ABP make direct comparison difficult. Two previous studies in Beijing have shown the effect of traffic-related air pollution on BP and a beneficial effect of facemasks in reducing BP.21,22 In the first study conducted in healthy volunteers, a 2-hour walk with a facemask was associated with a 7-mmHg lower SBP and improved 24-hour HRV measures.21 A subsequent study among subjects with stable coronary artery disease demonstrated a favorable effect of facemask intervention in reducing ABP (3 mmHg reduction) during the walk along with improvement in HRV indices.22 In controlled exposure studies, we and others have demonstrated an increase in BP of a similar magnitude within hours of exposure to PM 2.5.23,24 The doses used in these studies were accomplished with concentrators that, although unrealistic in North America, simulate concentrations routinely encountered in China.8 Thus, the consistency of our observations across a range of doses, study designs, and importantly in a susceptible population renders our findings that are much more relevant.

Several mechanisms for the acute effects of inhaled particulates and BP have been proposed. Activation of the sympathetic nervous system via reflex arcs originating from the lung altered vascular tone secondary to rapid endothelial dysfunction or reduced arterial stiffness and impaired baroreceptor sensitivity.3,4 Our data seem to suggest small effects of BC and autonomic tone within the same time frame as the effects on BP. The 7-hour moving average of personal BC was associated marginally with LF/HF and mean R-R interval. The largest association was seen with the 10-hour moving average, with increments in personal BC associated with increase in LF/HF and reduction of mean R-R intervals. No association was found between indices of endothelial function or arterial stiffness and exposure to BC, suggesting that at least at this level of exposure, changes in these pathways are unlikely to influence BP.

In contrary to consistent significant findings with personal BC, our analyses with ambient levels of PM 2.5 did not exhibit any association with cardiovascular outcomes. There could be several reasons responsible for the lack of significance with PM 2.5. First, ambient level PM 2.5 was used as a proxy for personal PM 2.5 exposure in the assessment of the exposure–response relationship in our study. There is evidence for a large gradation and even discordance in exposure doses between ambient measures of PM 2.5 and personal PM 2.5.25 Previous studies have suggested that personal-level exposure to PM 2.5 may elicit different responses than background ambient levels because of the varying sources and chemical composition of PM 2.5.26,27 A second reason may have to do with the temporal resolution of our measures. Growing evidences have shown that the time course of the PM 2.5 effect
on HRV occurred acutely within 24 hours. However, we assessed associations with lagged and cumulative PM$_{2.5}$ on the scale of days rather than hours, precluding further investigation of exposure–response relationship at a higher temporal resolution. Third, it has been observed that the dose–response relationship for mortality because of PM$_{2.5}$ is not a linear function, with lower slopes at higher concentrations. Therefore, we explored the possibility of nonlinear exposure effect on cardiovascular outcomes by including a smoothing term corresponding to 5-day average of ambient PM$_{2.5}$ concentration under a generalized additive model, with little statistical evidence of nonlinearity (Figure S2). Finally, our study was conducted with a relatively small sample size, and the PM$_{2.5}$ exposure measurements among patients examined in the same week at their first study visit may have contributed to limited variability because of the use of integrated daily mean of ambient PM$_{2.5}$, thereby reducing the power for detecting a significant exposure effect.

There were several strengths of the current study, including measurement of exposure and outcomes in metabolic syndrome patients who represent an at-risk patient population, the use of personal-level BC monitoring, and multiple functional outcomes to provide readouts on putative mechanistic pathways. We acknowledge that although we used BC as a surrogate for anthropogenic sources of air pollution, the precise components of traffic-related pollutants that contribute to BP remain elusive. One additional limitation is the lack of information on personal-level PM$_{2.5}$ or other copollutants. Thus, we cannot rule out the possibility that personal-level PM$_{2.5}$ or other fractions of PM$_{1.0}$ may have demonstrated an association with BP. In general, previous studies have demonstrated that the correlation between outdoor level of traffic-related pollutants such as BC and nitrogen-dioxide with PM$_{2.5}$ are strong. Indeed, there was a high degree of correlation between personal BC and PM$_{2.5}$, whereas ambient BC closely mirrored personal BC. A final limitation may be that our findings may not be generalizable to all patients.

**Perspectives**

Our study demonstrates an important linkage between elevated BP and altered HRV and exposure to combustion-related pollutants. These findings highlight the public health effect of air pollution and the importance of reducing anthropogenic air pollution.

**Acknowledgments**

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**Disclosures**

None.

**References**


What Is New?

- Few prospective studies have evaluated the association between personal exposures of traffic-related air pollution and blood pressure in susceptible populations in environments associated with extremely high levels of air pollutants.

What Is Relevant?

- In this study, we describe an association between personal black carbon exposure (a measure of traffic-related air pollution) and ambulatory systolic blood pressure and diastolic blood pressure. Changes in black carbon were also associated with alterations in heart rate variability indices.

Summary

Our findings suggest that the relationship between urbanization and hypertension may have complex underpinnings, with factors such as air pollution contributing to increases in blood pressure via autonomic alterations.
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EXPANDED METHODS and DATA SUPPLEMENT

Personal Black Carbon Exposure Influences Ambulatory Blood Pressure: Air Pollution and Cardio-metabolic Disease (AIRCMD-China) Study
Running Title: Personal BC Exposure Influences ABP

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Expanded Methods

Statistical Analysis

Analysis of outcome data with repeated measures. We used generalized additive mixed models (GAMMs) to examine the association between personal level BC and repeated measures of ABP or HRV indices every 20 or 30 minutes. We treated BC as time-varying covariate corresponding to each 20-minute (daytime) or 30-minute (night time) interval over a 24-hour period, therefore subjects with complete observations contributed 64 data points for both exposure and outcome variables, while subjects with more than half of the repeated measurements missing were excluded from our analysis (2 subjects excluded). The temporal structure of associations was assessed using 1 to 10-hour moving average of BC concentrations before each ABP measurements, and this time window was used because longer duration would cause a significant proportion of moving averages being calculated based on the same set of data points considering the total length of ABP/HRV monitoring. The fitted GAMMs with random intercepts were of the form:

\[ Y_{ij} = \beta_0 + \beta_1 BC_{ij} + \beta_2 Confounders_i + Spline(Time_{ij}) + b_i + e_{ij} \]

where \( Y_{ij} \) refers to the ABP or HRV outcomes (e.g. SBP, HR, or LF) for subject \( i \) at \( j^{th} \) 20 or 30-minute time interval, \( BC_{ij} \) is the average of BC concentration monitored on subject \( i \), 1 to 10 hours prior to the ABP measurement during the \( j^{th} \) time interval, and \( Time_{ij} \) is the time (with 9am on 4\(^{th}\) day as time 0 and the following 24 hours recorded as 0.33, 0.66,\ldots, 24) corresponding to the start of the \( j^{th} \) time interval on subject \( i \). \( \beta_0 \) is the overall intercept, \( \beta_1 \) is the estimated BC effect, \( \beta_2 \) is a vector of estimated effects for adjusted confounders, \( b_i \) is the random intercept for subject \( i \), and \( e_{ij} \) is the
independently distributed residual error for subject i at j^{th} time interval. Confounders adjusted in the model include binary variables gender, hypertension, and diabetes, and continuous variables age, BMI, mean temperature and relative humidity during the 24-hour period of ABP monitoring, where hypertension and diabetes were selected based on the inclusion criteria that adding the covariate leads to a change in estimated BC effect greater than 10%, and the linear form of temperature and relative humidity was determined by the test of significance for a non-linear term. A natural spline function denoted by $Spline(.)$ with 8 degrees of freedom and an autoregressive covariance structure among residual errors within subject were used. This model choice was governed by the Akaike information criterion (AIC). Effects associated with 1 $\mu$g/m$^3$ increase in personal BC at each averaging time period were estimated.
## Supplemental Tables

**Table S1.** Pearson correlations for the daily means of exposure end-points

<table>
<thead>
<tr>
<th>Pollutant and monitoring sites</th>
<th>BC</th>
<th>PM$_{2.5}$</th>
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<tr>
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<td>PUMC</td>
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<tr>
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<tr>
<td>PUMC</td>
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<td>US embassy</td>
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Associations between paired pollutants were tested using Pearson’s correlation coefficients, p-values < 0.0001.
Table S2. Estimated effects of multiple lagging and averaging intervals of BC (1-day, 3-day lags, and 3-day, 5-day averages) per µg/m³ change on averages of 24-hour ABP measures using multiple linear regression (N=62)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>1-day lag</th>
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<th>5-day average</th>
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<td>β (SE)</td>
<td>p-value</td>
<td>β (SE)</td>
<td>p-value</td>
<td>β (SE)</td>
<td>p-value</td>
<td>β (SE)</td>
<td>p-value</td>
</tr>
<tr>
<td>SBP (24-hour)</td>
<td>-0.20 (0.57)</td>
<td>0.72</td>
<td>0.09 (0.93)</td>
<td>0.92</td>
<td>0.41 (0.94)</td>
<td>0.67</td>
<td>0.23 (1.02)</td>
<td>0.82</td>
</tr>
<tr>
<td>SBP (daytime)</td>
<td>-0.01 (0.59)</td>
<td>0.99</td>
<td>0.19 (0.95)</td>
<td>0.84</td>
<td>0.62 (0.96)</td>
<td>0.53</td>
<td>0.44 (1.04)</td>
<td>0.67</td>
</tr>
<tr>
<td>SBP (night time)</td>
<td>-0.80 (0.58)</td>
<td>0.17</td>
<td>-0.26 (0.94)</td>
<td>0.78</td>
<td>-0.26 (0.96)</td>
<td>0.79</td>
<td>-0.42 (1.04)</td>
<td>0.69</td>
</tr>
<tr>
<td>DBP (24-hour)</td>
<td>0.39 (0.35)</td>
<td>0.27</td>
<td>0.04 (0.56)</td>
<td>0.94</td>
<td>0.77 (0.57)</td>
<td>0.18</td>
<td>0.49 (0.62)</td>
<td>0.43</td>
</tr>
<tr>
<td>DBP (daytime)</td>
<td>0.51 (0.36)</td>
<td>0.16</td>
<td>0.06 (0.58)</td>
<td>0.92</td>
<td>0.82 (0.59)</td>
<td>0.17</td>
<td>0.52 (0.64)</td>
<td>0.42</td>
</tr>
<tr>
<td>DBP (night time)</td>
<td>0.04 (0.38)</td>
<td>0.91</td>
<td>-0.11 (0.60)</td>
<td>0.86</td>
<td>0.56 (0.62)</td>
<td>0.37</td>
<td>0.35 (0.67)</td>
<td>0.61</td>
</tr>
<tr>
<td>Heart rate (24-hour)</td>
<td>0.43 (0.46)</td>
<td>0.35</td>
<td>-0.48 (0.74)</td>
<td>0.52</td>
<td>0.43 (0.76)</td>
<td>0.58</td>
<td>-0.01 (0.82)</td>
<td>0.99</td>
</tr>
<tr>
<td>Heart rate (daytime)</td>
<td>0.50 (0.49)</td>
<td>0.31</td>
<td>-0.44 (0.80)</td>
<td>0.58</td>
<td>0.55 (0.81)</td>
<td>0.50</td>
<td>0.15 (0.88)</td>
<td>0.87</td>
</tr>
<tr>
<td>Heart rate (night time)</td>
<td>0.21 (0.41)</td>
<td>0.61</td>
<td>-0.67 (0.65)</td>
<td>0.31</td>
<td>-0.01 (0.67)</td>
<td>0.99</td>
<td>-0.53 (0.72)</td>
<td>0.46</td>
</tr>
</tbody>
</table>

All models controlled for age, gender, BMI, temperature and relative humidity. SE, standard error.
**Table S3.** Estimated effects of multiple lagging and averaging intervals of PM$_{2.5}$ (1-day, 3-day lags, and 3-day, 5-day averages) per 10 µg/m$^3$ change on averages of 24-hour ABP measures using multiple linear regression (N=63)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>1-day lag</th>
<th></th>
<th>3-day lag</th>
<th></th>
<th>3-day average</th>
<th></th>
<th>5-day average</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$\beta$ (SE)</td>
<td>$p$-value</td>
<td>$\beta$ (SE)</td>
<td>$p$-value</td>
<td>$\beta$ (SE)</td>
<td>$p$-value</td>
<td>$\beta$ (SE)</td>
<td>$p$-value</td>
</tr>
<tr>
<td>SBP (24-hour)</td>
<td>-0.02 (0.44)</td>
<td>0.97</td>
<td>0.58 (0.45)</td>
<td>0.20</td>
<td>0.39 (0.60)</td>
<td>0.52</td>
<td>0.10 (0.65)</td>
<td>0.88</td>
</tr>
<tr>
<td>SBP (daytime)</td>
<td>0.12 (0.45)</td>
<td>0.78</td>
<td>0.63 (0.46)</td>
<td>0.18</td>
<td>0.57 (0.61)</td>
<td>0.36</td>
<td>0.31 (0.67)</td>
<td>0.65</td>
</tr>
<tr>
<td>SBP (night time)</td>
<td>-0.47 (0.44)</td>
<td>0.30</td>
<td>0.40 (0.46)</td>
<td>0.39</td>
<td>-0.17 (0.62)</td>
<td>0.78</td>
<td>-0.52 (0.67)</td>
<td>0.44</td>
</tr>
<tr>
<td>DBP (24-hour)</td>
<td>0 (0.27)</td>
<td>0.99</td>
<td>0.23 (0.28)</td>
<td>0.40</td>
<td>0.29 (0.37)</td>
<td>0.44</td>
<td>0.23 (0.40)</td>
<td>0.57</td>
</tr>
<tr>
<td>DBP (daytime)</td>
<td>0.07 (0.28)</td>
<td>0.80</td>
<td>0.21 (0.28)</td>
<td>0.46</td>
<td>0.35 (0.38)</td>
<td>0.36</td>
<td>0.28 (0.41)</td>
<td>0.49</td>
</tr>
<tr>
<td>DBP (night time)</td>
<td>-0.22 (0.29)</td>
<td>0.44</td>
<td>0.26 (0.29)</td>
<td>0.38</td>
<td>0.06 (0.40)</td>
<td>0.87</td>
<td>0.03 (0.43)</td>
<td>0.95</td>
</tr>
<tr>
<td>Heart rate (24-hour)</td>
<td>0.08 (0.35)</td>
<td>0.82</td>
<td>0.34 (0.36)</td>
<td>0.35</td>
<td>0.46 (0.48)</td>
<td>0.34</td>
<td>0.30 (0.53)</td>
<td>0.57</td>
</tr>
<tr>
<td>Heart rate (daytime)</td>
<td>0.14 (0.38)</td>
<td>0.72</td>
<td>0.37 (0.39)</td>
<td>0.34</td>
<td>0.56 (0.51)</td>
<td>0.28</td>
<td>0.42 (0.56)</td>
<td>0.45</td>
</tr>
<tr>
<td>Heart rate (night time)</td>
<td>-0.10 (0.31)</td>
<td>0.74</td>
<td>0.21 (0.32)</td>
<td>0.51</td>
<td>0.14 (0.43)</td>
<td>0.75</td>
<td>-0.09 (0.46)</td>
<td>0.85</td>
</tr>
</tbody>
</table>

All models controlled for age, gender, BMI, temperature and relative humidity. SE, standard error.
Table S4. Estimated effects of multiple lagging and averaging intervals of BC (1-day, 3-day lags, and 3-day, 5-day averages) per µg/m³ change on averages of 24-hour HRV indices using multiple linear regression (N=64)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>1-day lag</th>
<th></th>
<th></th>
<th>3-day lag</th>
<th></th>
<th></th>
<th>3-day average</th>
<th></th>
<th></th>
<th>5-day average</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>β (SE)</td>
<td>p-value</td>
<td>β (SE)</td>
<td>p-value</td>
<td>β (SE)</td>
<td>p-value</td>
<td>β (SE)</td>
<td>p-value</td>
<td>β (SE)</td>
<td>p-value</td>
<td>β (SE)</td>
<td>p-value</td>
</tr>
<tr>
<td>LF</td>
<td>0.046 (0.027)</td>
<td>0.09</td>
<td>0.075 (0.043)</td>
<td>0.09</td>
<td>0.047 (0.045)</td>
<td>0.30</td>
<td>0.091 (0.048)</td>
<td>0.06</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HF</td>
<td>0.021 (0.034)</td>
<td>0.54</td>
<td>0.084 (0.054)</td>
<td>0.12</td>
<td>-0.013 (0.056)</td>
<td>0.82</td>
<td>0.043 (0.061)</td>
<td>0.48</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TP</td>
<td>0.031 (0.026)</td>
<td>0.23</td>
<td>0.076 (0.041)</td>
<td>0.07</td>
<td>0.026 (0.043)</td>
<td>0.55</td>
<td>0.068 (0.046)</td>
<td>0.14</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LF/HF</td>
<td>0.026 (0.022)</td>
<td>0.25</td>
<td>-0.008 (0.036)</td>
<td>0.82</td>
<td>0.060 (0.036)</td>
<td>0.10</td>
<td>0.049 (0.040)</td>
<td>0.23</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SDNN</td>
<td>0.013 (0.012)</td>
<td>0.27</td>
<td>0.033 (0.019)</td>
<td>0.08</td>
<td>0.020 (0.020)</td>
<td>0.31</td>
<td>0.032 (0.021)</td>
<td>0.13</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>rMSSD</td>
<td>0.010 (0.015)</td>
<td>0.51</td>
<td>0.054 (0.028)</td>
<td>0.06</td>
<td>0.001 (0.025)</td>
<td>0.98</td>
<td>0.031 (0.027)</td>
<td>0.25</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>pNN50</td>
<td>0.028 (0.041)</td>
<td>0.49</td>
<td>0.123 (0.064)</td>
<td>0.06</td>
<td>0.015 (0.066)</td>
<td>0.82</td>
<td>0.078 (0.072)</td>
<td>0.28</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>meanRR</td>
<td>-0.004 (0.007)</td>
<td>0.55</td>
<td>0.011 (0.010)</td>
<td>0.31</td>
<td>-0.005 (0.011)</td>
<td>0.67</td>
<td>0.001 (0.012)</td>
<td>0.90</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

All models controlled for age, gender, BMI, resting heart rate, temperature and relative humidity. SE, standard error.
Table S5. Estimated effects of multiple lagging and averaging intervals of PM$_{2.5}$ (1-day, 3-day lags, and 3-day, 5-day averages) per 10 µg/m$^3$ change on averages of 24-hour HRV indices using multiple linear regression (N=64)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>1-day lag</th>
<th></th>
<th>3-day lag</th>
<th></th>
<th>3-day average</th>
<th></th>
<th>5-day average</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>β (SE)</td>
<td>$p$-value</td>
<td>β (SE)</td>
<td>$p$-value</td>
<td>β (SE)</td>
<td>$p$-value</td>
<td>β (SE)</td>
<td>$p$-value</td>
</tr>
<tr>
<td>LF</td>
<td>0.24 (0.21)</td>
<td>0.26</td>
<td>0.27 (0.20)</td>
<td>0.19</td>
<td>0.39 (0.28)</td>
<td>0.17</td>
<td>0.49 (0.31)</td>
<td>0.12</td>
</tr>
<tr>
<td>HF</td>
<td>0.14 (0.26)</td>
<td>0.60</td>
<td>0.06 (0.25)</td>
<td>0.81</td>
<td>-0.08 (0.35)</td>
<td>0.82</td>
<td>0.11 (0.39)</td>
<td>0.78</td>
</tr>
<tr>
<td>TP</td>
<td>0.16 (0.20)</td>
<td>0.44</td>
<td>0.17 (0.19)</td>
<td>0.37</td>
<td>0.16 (0.27)</td>
<td>0.55</td>
<td>0.25 (0.29)</td>
<td>0.40</td>
</tr>
<tr>
<td>LF/HF</td>
<td>0.10 (0.17)</td>
<td>0.55</td>
<td>0.21 (0.16)</td>
<td>0.21</td>
<td>0.47 (0.25)</td>
<td>0.07</td>
<td>0.38 (0.25)</td>
<td>0.14</td>
</tr>
<tr>
<td>SDNN</td>
<td>0.08 (0.09)</td>
<td>0.41</td>
<td>0.10 (0.09)</td>
<td>0.28</td>
<td>0.13 (0.12)</td>
<td>0.29</td>
<td>0.12 (0.14)</td>
<td>0.38</td>
</tr>
<tr>
<td>rMSSD</td>
<td>0.03 (0.12)</td>
<td>0.77</td>
<td>0.08 (0.11)</td>
<td>0.49</td>
<td>-0.07 (0.16)</td>
<td>0.64</td>
<td>0.03 (0.17)</td>
<td>0.89</td>
</tr>
<tr>
<td>pNN50</td>
<td>0.12 (0.31)</td>
<td>0.71</td>
<td>0.12 (0.30)</td>
<td>0.69</td>
<td>-0.17 (0.42)</td>
<td>0.68</td>
<td>0.03 (0.46)</td>
<td>0.94</td>
</tr>
<tr>
<td>meanRR</td>
<td>0.002 (0.050)</td>
<td>0.96</td>
<td>-0.044 (0.048)</td>
<td>0.37</td>
<td>-0.063 (0.067)</td>
<td>0.35</td>
<td>-0.041 (0.073)</td>
<td>0.57</td>
</tr>
</tbody>
</table>

All models controlled for age, gender, BMI, resting blood pressure, temperature and relative humidity. SE. standard error.
Table S6. Summary of reported black carbon effects on blood pressure from multiple publications

<table>
<thead>
<tr>
<th>Reference</th>
<th>Location</th>
<th>Exposure method</th>
<th>BC Mean (SD), unit: μg/m³</th>
<th>BP measurement method</th>
<th>SBP change per μg/m³ BC (95% CI), unit: mmHg</th>
<th>DBP change per μg/m³ BC (95% CI), unit: mmHg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mordukhovich et al., 2009&lt;sup&gt;18&lt;/sup&gt;</td>
<td>Boston, Massachusetts, USA</td>
<td>Ambient BC at fixed site</td>
<td>1.10 (0.43)</td>
<td>Standard mercury sphygmomanometer</td>
<td>3.40 (0.23, 6.56)</td>
<td>2.02 (0.35, 3.70)</td>
</tr>
<tr>
<td>Wilker et al., 2010&lt;sup&gt;19&lt;/sup&gt;</td>
<td>Boston, Massachusetts, USA</td>
<td>Ambient BC at fixed site</td>
<td>0.98 (0.42)&lt;sup&gt;†&lt;/sup&gt;</td>
<td>Standard mercury sphygmomanometer</td>
<td>8.48 (6.67, 10.27)&lt;sup&gt;†&lt;/sup&gt;</td>
<td>6.55 (5.57, 7.52)&lt;sup&gt;†&lt;/sup&gt;</td>
</tr>
<tr>
<td>Hoffmann et al., 2012&lt;sup&gt;20&lt;/sup&gt;</td>
<td>Boston, Massachusetts, USA</td>
<td>Ambient BC at fixed site</td>
<td>0.53 (0.39)</td>
<td>Automated oscillometric sphygmomanometer</td>
<td>8.98 (1.58, 16.37)&lt;sup&gt;‡&lt;/sup&gt;</td>
<td>4.50 (0.90, 7.80)&lt;sup&gt;‡&lt;/sup&gt;</td>
</tr>
<tr>
<td>Delfino et al., 2010&lt;sup&gt;5&lt;/sup&gt;</td>
<td>Los Angeles, California, USA</td>
<td>Outdoor and home BC</td>
<td>1.67 (0.79)</td>
<td>Ambulatory BP monitoring</td>
<td>1h: 0.12 (-0.29, 0.52)&lt;sup&gt;§&lt;/sup&gt;</td>
<td>4h: 0.09 (-0.44, 0.62)&lt;sup&gt;§&lt;/sup&gt;</td>
</tr>
<tr>
<td>AIRCMD</td>
<td>Beijing, China</td>
<td>Personal BC</td>
<td>4.77 (1.76)</td>
<td>Ambulatory BP monitoring</td>
<td>1h: 0.06 (-0.15, 0.27)&lt;sup&gt;§&lt;/sup&gt;</td>
<td>4h: 0.15 (-0.14, 0.44)&lt;sup&gt;§&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>8h: 0.36 (-0.28, 1.00)</td>
<td>8h: 0.45 (0.11, 0.79)&lt;sup&gt;§&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3d: 2.02 (0.59, 3.45)</td>
<td>10h: 0.53 (0.17, 0.89)&lt;sup&gt;§&lt;/sup&gt;</td>
</tr>
<tr>
<td>AIRCMD</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>4h: 0.19 (-0.11, 0.47)</td>
<td>4h: 0.15 (-0.07, 0.38)&lt;sup&gt;§&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>8h: 0.28 (-0.06, 0.64)</td>
<td>8h: 0.36 (0.10, 0.62)&lt;sup&gt;§&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3d: 1.25 (0.48, 2.02)</td>
<td>10h: 0.37 (0.10, 0.65)&lt;sup&gt;§&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

* Linear mixed effect model adjusted for age, cigarette smoking, pack-years of smoking, season of clinical visit, weekday of clinical visit, BMI, diabetes status, statin use, fasting glucose level, 7-day average of temperature (linear and quadratic), 7-day average of relative humidity (linear and quadratic), hour of clinical visit, year of clinical visit, years of education, race/ethnicity, antihypertensive medication use, and daily alcohol intake.

† Linear mixed effect model adjusted for age, BMI, smoking status, season, 7-day average of BC, and 7-day average of temperature. Daily average of BC from September 2006 to July 2010 was presented as median (interquartile range).

‡ Linear mixed effect model adjusted for season, age, sex, BMI, and years of diabetes, with 5-day average of BC before the BP measurement as the exposure metrics.
§ Linear mixed effect model adjusted for temperature, hour of day, posture, and actigraph activity.

ǁ Generalized additive mixed model adjusted for subjects, age, gender, BMI, temperature, relative humidity, hypertension, diabetes, and smooth function of the time.
Supplemental Figures

Figure S1

Constructed exposure measures for multiple lags and averaging intervals during a 5-day period for each subject.
Figure S2

Estimated spline terms and 95% confidence bands of 5-day average of ambient PM$_{2.5}$ concentration under generalized additive models relating summary measures of ABP and HRV, and single measures of endothelial function and arterial compliance. Degree of freedom (DF) was estimated by generalized cross validation. P-value was assessed by the test for non-linear term of PM$_{2.5}$ concentration.