Association of Cardiopulmonary Health Effects with Source Appointed Ambient Fine Particulate in Beijing, China: A Combined Analysis from the HVNR Study.

ARTICLE *in* ENVIRONMENTAL SCIENCE & TECHNOLOGY · FEBRUARY 2014

Impact Factor: 5.33 · DOI: 10.1021/es404778w · Source: PubMed

11 AUTHORS, INCLUDING:

Shaowei Wu
Harvard T.H. Chan School of Public Health
52 PUBLICATIONS **318** CITATIONS
SEE PROFILE

Jing Huang
Peking University Health Science Center
14 PUBLICATIONS **123** CITATIONS
SEE PROFILE

Masayuki Shima
Hyogo College of Medicine
80 PUBLICATIONS **543** CITATIONS
SEE PROFILE

Xinbiao Guo
Peking University
57 PUBLICATIONS **1,237** CITATIONS
SEE PROFILE

Environmental Science & Technology

Article

pubs.acs.org/est

Association of Cardiopulmonary Health Effects with Source-Appointed Ambient Fine Particulate in Beijing, China: A Combined Analysis from the Healthy Volunteer Natural Relocation (HVNR) Study

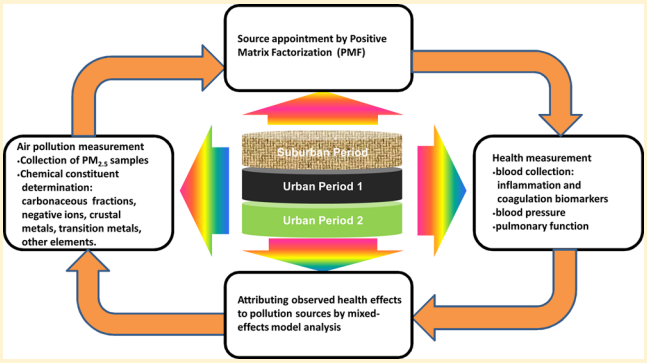
Shaowei Wu,[†] Furong Deng,[†] Hongying Wei,[†] Jing Huang,[†] Xin Wang,[†] Yu Hao,[†] Chanjuan Zheng,[†] Yu Qin,[†] Haibo Lv,[†] Masayuki Shima,[‡] and Xinbiao Guo*[,†]

[†]Department of Occupational and Environmental Health Sciences, Peking University School of Public Health, Beijing, China

[‡]Department of Public Health, Hyogo College of Medicine, Hyogo, Japan

Supporting Information

ABSTRACT: Previous studies have associated ambient particulate chemical constituents with adverse cardiopulmonary health effects. However, specific pollution sources behind the cardiopulmonary health effects of ambient particles are uncertain. We examined the cardiopulmonary health effects of fine particles ($PM_{2.5}$) from different pollution sources in Beijing, China, among a panel of 40 healthy university students. Study subjects were repeatedly examined for a series of cardiopulmonary health indicators during three 2-month-long study periods (suburban period, urban period 1, and urban period 2) in 2010−2011 before and after relocating from a suburban campus to an urban campus with changing air pollution levels and contents. Daily ambient $PM_{2.5}$ mass samples were collected over the study and measured for 29 chemical constituents in the laboratory. Source appointment for ambient $PM_{2.5}$ was performed using Positive Matrix Factorization, and mixed-effects models were used to estimate the cardiopulmonary effects associated with source-specific $PM_{2.5}$ concentrations. Seven $PM_{2.5}$ sources were identified as traffic emissions (12.0%), coal combustion (22.0%), secondary sulfate/nitrate (30.2%), metallurgical emission (0.4%), dust/soil (12.4%), industry (6.9%), and secondary organic aerosol (9.9%). Ambient $PM_{2.5}$ in the suburban campus had larger contributions from secondary sulfate/nitrate (41.8% vs. 22.9%−26.0%) and metallurgical emission (0.7% vs. 0.3%) as compared to that in the urban campus), whereas $PM_{2.5}$ in the urban campus had larger contributions from traffic emissions (13.0%−16.3% vs. 5.1%), coal combustion (21.0%−30.7% vs. 10.7%), and secondary organic aerosol (9.7%−12.0% vs. 8.7%) as compared to that in the suburban campus. Potential key sources were identified for $PM_{2.5}$ effects on inflammatory biomarkers (secondary sulfate/nitrate and dust/soil), blood pressure (coal combustion and metallurgical emission), and pulmonary function (dust/soil and industry). Analyses using another source appointment tool Unmix yielded a similar pattern of source contributions and associated health effects. In conclusion, ambient $PM_{2.5}$ in Beijing suburban and urban areas has two distinct patterns of source contributions, and $PM_{2.5}$ from different sources may play important roles on different aspects of $PM_{2.5}$-related cardiopulmonary health effects.



INTRODUCTION

Ambient particulate air pollution is a known risk factor for adverse cardiopulmonary health effects,[1] and particulate matter (PM) with aerodynamic diameter less than 2.5 μm ($PM_{2.5}$) has received great attention in recent years due to its high potential to induce adverse health responses.[2] Ambient air pollution is a major environmental problem in China[3] and ranks fourth among the risk factors that constitute the largest number of attributable disability-adjusted life-years in China.[4] Air pollution levels in Chinese megacities are high, and related pollution sources are complicated.[5−8] However, data on the adverse health effects associated with different PM air pollution sources are still rare in China. Only a few epidemiologic studies have provided evidence for the association between various PM chemical constituents and adverse health outcomes in China.[9,10]

Various chemical constituents originating from different pollution sources constitute the ambient PM.[8,11−13] A better understanding of the PM chemical constituents and related pollution sources responsible for the adverse health effects may potentially lead to more targeted and effective regulations and

Received: October 28, 2013
Revised: January 21, 2014
Accepted: February 12, 2014
Published: February 12, 2014

subsequently favor the public health.[1] As an attempt to provide evidence for the cardiopulmonary health effects associated with different pollution sources in the context of Chinese suburban and urban air pollution, we utilized data from a panel study, the Healthy Volunteer Natural Relocation (HVNR) study, which followed a panel of 40 young, healthy university students before and after their natural relocation from a suburban campus to an urban campus with different air pollution levels and contents in Beijing, China, and repeatedly measured a series of cardiopulmonary health indicators among them. A major strength of the HVNR study is that local air pollution sources differed between the suburban and urban areas involved in the study and resulted in significant differences in the chemical contents of ambient $PM_{2.5}$, and therefore, the short-term health effects of specific $PM_{2.5}$ chemical constituents and pollution sources could be well-investigated among the study subjects who served as their own controls.

MATERIALS AND METHODS

Study Protocols. The HVNR study is a panel study designed to assess the short-term health effects of ambient particulate air pollution in Beijing, China.[14] Beijing covers an area of 16 410 km^2, has about 20 million inhabitants, and is 160 km from the nearest coastline. Study subjects included 41 male, healthy university students who were free of smoking and lived in the school dormitories of a local university (Beijing Institute of Technology, BIT). BIT has two campuses (BIT Liangxiang campus and BIT main campus) about 30 km apart.[14] The BIT Liangxiang campus is located in Beijing's suburban area and the BIT main campus is located in Beijing's downtown area. Local air pollution sources around these two campuses are quite different. The BIT Liangxiang campus is about 2000 m from the nearest freeway and is surrounded by a number of active construction sites and industrial facilities. The BIT main campus is located in the downtown area along the northwest inner side of the third ring road that circles the city, and there are no active construction sites or industrial facilities around this campus. All the students underwent their first 2 years of undergraduate training at the BIT Liangxiang campus from September 2008 to July 2010 and then relocated to the BIT main campus for the next 2 years of study from August 2010 to July 2012. They completed biweekly study visits 12 times before and after their relocation between these two campuses. Four study visits were scheduled within each the following three periods: suburban period from April 22 to June 20, 2010, at the BIT Liangxiang campus before the relocation and urban period 1 from September 3 to November 8, 2010, and urban period 2 from April 10 to June 12, 2011, at the BIT main campus after the relocation. During each study visit, each subject had a blood sample drawn and resting blood pressure (BP) was measured. One subject dropped out during the study, leaving 40 subjects with 464 study visits over the study. A subgroup of 21 subjects also provided daily morning and evening pulmonary function measurements over the three 2-month-long study periods. The study was approved by the Institutional Review Board of Peking University Health Science Center, and informed consent was obtained from each subject before the study began.

Ambient Air Pollution Measurements. Daily levels of ambient $PM_{2.5}$ were measured in a central air-monitoring station located within 300 m of school dormitories in each campus. We collected $PM_{2.5}$ mass samples and determined the following 29 chemical constituents in the laboratory using professional techniques: carbonaceous fractions including organic carbon (OC) and elemental carbon (EC); ions including sulfate (SO_4^{2-}), nitrate (NO_3^-), chloride (Cl^-) and fluoride (F^-); crustal metals including aluminum (Al), calcium (Ca), potassium (K), sodium (Na), magnesium (Mg), strontium (Sr) and barium (Ba); transition metals including iron (Fe), zinc (Zn), copper (Cu), titanium (Ti), cobalt (Co), molybdenum (Mo), cadmium (Cd), vanadium(V), chromium (Cr), manganese (Mn), and nickel (Ni); and several other metals/metalloid elements, including arsenic (As), stannum (Sn), antimony (Sb), selenium (Se), and lead (Pb). We estimated levels of primary OC (POC) and secondary OC (SOC) based on OC/EC data. A detailed description for the air pollution measurement and analysis, estimation of OC fractions, and estimation of measurement uncertainty is available in the Supporting Information.

Health Measurements. Detailed information on health measurements could be found in our previous publications.[14−16] Briefly, all subjects underwent biweekly blood collection (on 1200 h) and resting BP measurements (between 1300 and 1500 h) 12 times over three study periods. Blood samples were measured for an informative set of circulatory biomarkers using enzyme-linked immunosorbent assays (CUSABIO BioTech Co., Ltd., Wuhan, China). Specifically, we measured two inflammatory markers of tumor necrosis factor alpha (TNF-α) and fibrinogen, two fibrinolytic factors of plasminogen activator inhibitor type 1 (PAI-1) and tissue-type plasminogen activator (t-PA), a platelet adhesion and aggregation marker of von Willebrand factor (vWF), and a platelet activation marker of soluble platelet selectin (sP-selectin). BP were measured with an Omron 705IT automated oscillometric monitor (HEM-759-E, Omron Healthcare Co., Ltd. Kyoto, Japan) at least three times, and the second and third sets of readings were averaged to calculate systolic BP (SBP) and diastolic BP (DBP). Pulse pressure (PP) was calculated as the difference between the average SBP and DBP values. A subgroup of the study subjects (n = 21) performed daily morning (0600−1100 h) and evening (2100−0100 h) pulmonary function measurements using an electronic peak expiratory flow (PEF) and forced expiratory volume within 1 s (FEV_1) diary meter (model 2110; Vitalograph Ltd., Buckingham, UK). They also used a symptom diary to record respiratory symptoms throughout the study. Weight and height were measured during the first study visit in each time period, and body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared.

Statistical Analysis. We used USEPA Positive Matrix Factorization (PMF) v3.0 to perform source appointment analysis for ambient $PM_{2.5}$.[17] The PMF model was developed by Paatero and Tapper[18,19] and has been used as a popular tool to assess the ambient PM source contributions in previous air pollution studies.[11−13,20] We excluded chemical species that were frequently present at concentrations below the detection limit or with a low signal-to-noise ratio. The remaining 28 species were used in the PMF analysis: POC, SOC, EC, SO_4^{2-}, NO_3^-, Cl^-, Al, Ca, K, Na, Mg, Sr, Ba, Fe, Zn, Cu, Ti, Co, Mo, Cd, V, Cr, Mn, As, Sn, Sb, Se, and Pb. Measurement uncertainties were developed using method detection limit and root median squared percent error based on collocated measurements (Supporting Information, Table S1). Constituent data on 5 days out of the overall 188 days were excluded from the PMF analysis due to extreme events that would not be modeled well by PMF (4 days due to significant Asian sand

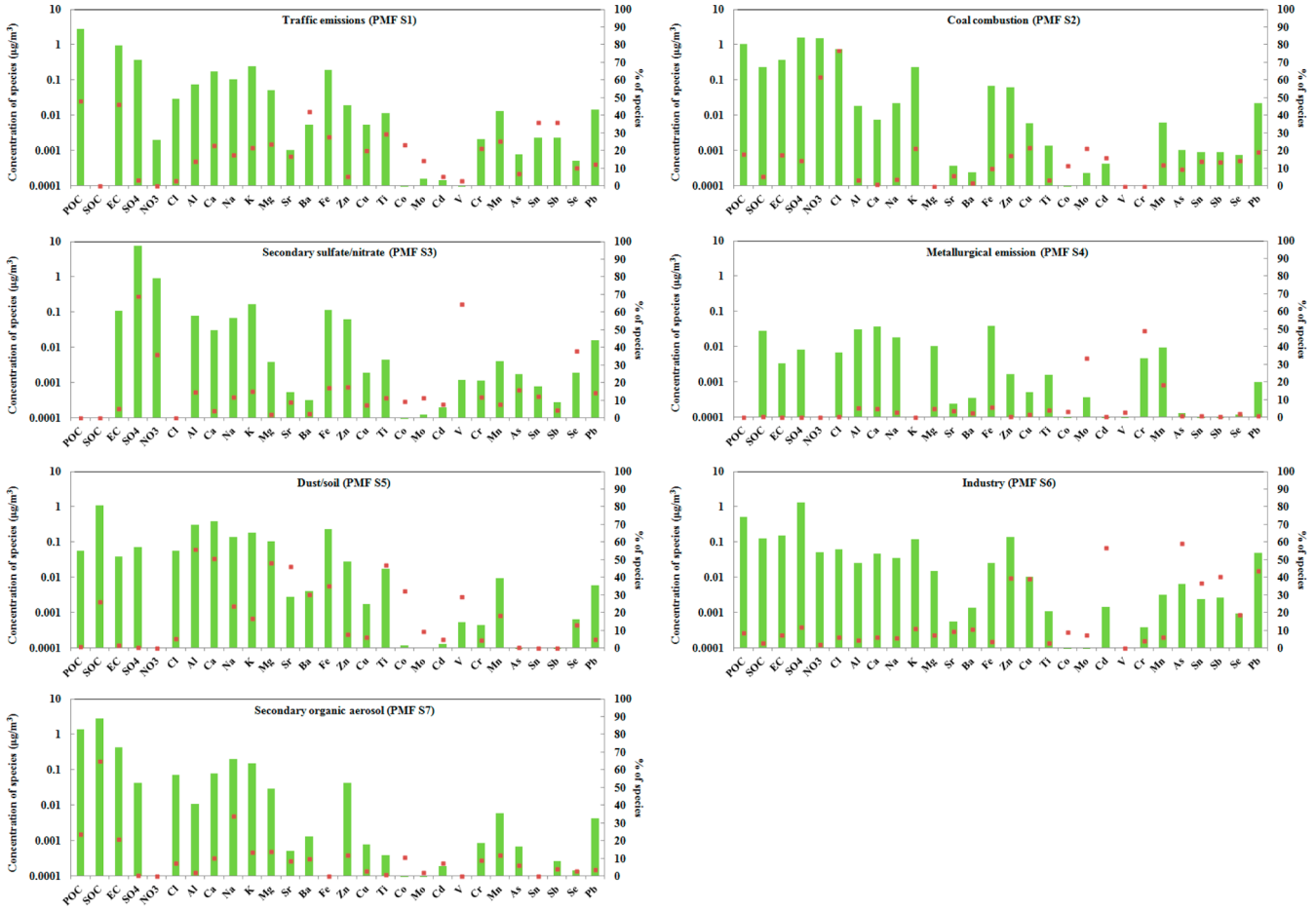


Figure 1. Source profiles (expressed in both mass concentrations in $\mu g/m^3$ and percentages of chemical species) resolved from the PMF analysis for ambient $PM_{2.5}$ in Beijing, China, during three study periods in 2010−2011. Primary *Y*-axis (left side, for green columns), concentrations of species ($\mu g/m^3$); secondary *Y*-axis (right side, for red squares), percentages of species (%).

dust storms and 1 day due to an extremely high SOC concentration).[17] After numerous base and bootstrap runs, an optimal solution with a 10% model uncertainty identified seven $PM_{2.5}$ sources that were stratified with the input data and physically interpretable. An additional factor rotation was performed by assigning a value of −1.3 to the *FPEAK* parameter in order to alleviate the rotational ambiguity and to yield a more physically realistic solution.[19] Finally, we sought to examine the stability of resolved source profiles and contributions and associated health effects over different source appointment methodologies by using another frequently used source appointment tool, Unmix.[21,22]

Mixed-effects models with a random intercept for each subject were then used to estimate the health effects associated with source-specific $PM_{2.5}$ concentrations. To improve data normality, data of circulating biomarkers were log-transformed[15] and data of pulmonary function were transformed into percentage deviation variables before analysis.[16] BP data were normally distributed and therefore were used in the analysis without transformation. Three statistical models were used to assess the consistency of estimated source effects based on our previous analyses: single-source model, source-$PM_{2.5}$ joint model, and two-pollutant (source) model.[14−16] To evaluate the cumulative effects of exposure, we used average source-specific $PM_{2.5}$ concentrations during the previous 1−7 days before health measurements as the exposure metrics. We adjusted the following covariates in the final models: age, BMI, study period, day of week, long-term time trend, respiratory symptom, temperature, and relative humidity. Long-term time trend was adjusted for by including a day-of-study variable and a squared day-of-study variable in the models, and we also adjusted for timing of measurements by including an hour-of-day variable for BP and pulmonary function analyses.[14,16] Final results are reported as changes with 95% confidence intervals (CIs) in health variables associated with interquartile range (IQR) increases in source-specific $PM_{2.5}$ concentrations at key exposure metrics. Specifically, exposure metrics of 1−3 d averages were used for circulating biomarkers and BP variables and exposure metrics of 1, 3, 5, and 7 d averages were used for pulmonary function as demonstrated to best capture the air pollution effects in our previous studies.[14−16] All analyses were performed using SAS 9.2 (SAS Institute, Cary, NC), and the significance level is set at $p < 0.05$ (two-tailed).

RESULTS

Exposure and Health Data. Baseline characteristics of subjects who provided daily pulmonary function measurements were similar to those of all eligible subjects (Supporting Information, Table S2). Ambient $PM_{2.5}$ concentrations showed a decreasing trend over the study, whereas different $PM_{2.5}$ chemical constituents showed heterogeneous changes over the three study periods (Supporting Information, Table S3). Among the health variables, inflammatory biomarkers TNF-α

dx.doi.org/10.1021/es404778w | Environ. Sci. Technol. 2014, 48, 3438−3448

Table 1. $PM_{2.5}$ Source Contributions in Mean Daily Mass Concentrations ($\mu g/m^3$) and Percentages (%) by Study Period According to Positive Matrix Factorization

	suburban period (04/22/2010 to 06/20/2010)		urban period 1 (09/03/2010 to 11/08/2010)		urban period 2 (04/10/2010 to 06/12/2010)		
	mass	% of $PM_{2.5}$	mass	% of $PM_{2.5}$	mass	% of $PM_{2.5}$	interquartile range
total $PM_{2.5}$	82.0		78.1		59.9		63.4
PMF S1: traffic emissions	5.1	6.3	12.7	16.3	7.8	13.0	10.2
PMF S2: coal combustion	10.7	13.0	24.0	30.7	12.6	21.0	18.7
PMF S3: secondary sulfate/nitrate	34.2	41.8	17.9	22.9	15.6	26.0	31.3
PMF S4: metallurgical emission	0.6	0.7	0.2	0.3	0.2	0.3	0.3
PMF S5: dust/soil	12.4	15.1	5.9	7.6	9.5	15.8	11.2
PMF S6: industry	4.9	5.9	5.4	6.9	4.9	8.1	6.6
PMF S7: secondary organic aerosol	7.1	8.7	7.6	9.7	7.2	12.0	6.5
unknown	7.0	8.5	4.4	5.7	2.2	3.7	--

and fibrinogen, SBP and PP, and pulmonary function measures generally showed higher levels in the urban periods than in the suburban period, whereas four hemostatic biomarkers, PAI-1, t-PA, vWF, and sP-selectin, showed decreasing trends over the three study periods (Supporting Information, Table S4).

$PM_{2.5}$ Source Profiles. The PMF analysis resolved seven possible $PM_{2.5}$ sources as traffic emissions (12.0%), coal combustion (22.0%), secondary sulfate/nitrate (30.2%), metallurgical emission (0.4%), dust/soil (12.4%), industry (6.9%), and secondary organic aerosol (9.9%) over the study (Figure 1 and Table 1). Results from PMF bootstrap runs suggested that the model with a 10% uncertainty yielded the most optimal solution, as indicated by an average mapping correction rate of 93.6% when the minimum correlation *R*-value was set to 0.60 (Supporting Information, Table S5).

The first source (PMF S1) was traffic emissions, as reflected by the high loadings of POC and EC and a moderate loading of Mn (Figure 1). Fossil fuels including gasoline and diesel are known to emit a lot of POC and EC. Traffic emissions may contain high Mn, a component of methylcyclopentadienyl manganese tricarbonyl, which is widely used as an antiknock agent in gasoline.[23] Contributions of this source to $PM_{2.5}$ mass were much higher in the urban periods (13.0%−16.3%) than in the suburban period (6.3%) (Table 1). This is in line with the increased traffic emissions after relocating from the suburban campus to the urban campus.

The second source (PMF S2) was coal consumption, as identified by high loadings of POC, EC, Cl^-, and NO_3^-. Both chemical analysis of ambient $PM_{2.5}$ samples[24] and source profiles measured in the laboratory[25] have suggested that Cl^- can be used as a tracer species for coal combustion in Beijing. Although combustion sources emit few nitrates, they can emit large quantities of nitrogen oxides (NO_X) which could be rapidly transformed to nitric acid, regardless of the meteorological conditions.[26] Heating boilers using coal as the primary energy source can emit a lot of NO_X in Beijing,[27] and a previous study also found a high NO_3^- loading in the coal combustion source in Beijing.[22] Contribution of this source to $PM_{2.5}$ mass was much higher in the urban period 1 (30.7%) than in the other two periods (13.0%−21.0%), which is consistent with the fact that coal consumption level is much higher in the heating season (mid-October to mid-March) than in the nonheating season (mid-March to mid-October) in Beijing.

The third source (PMF S3) was a mixture of secondary sulfate and secondary nitrate. Both sulfate and nitrate may originate from chemical transformation of precursor pollutants (e.g., sulfur dioxide and NO_X) and long-range transported aerosols.[8] Contribution of this source to $PM_{2.5}$ mass was higher in the suburban period (41.8%) than in the urban periods (22.9%−26.0%), which is consistent with the decreasing trend of its dominant species (i.e., SO_4^{2-}) over the study periods (Supporting Information, Table S3). The major source for sulfur dioxide is coal burning in Beijing,[12] whereas the major sources for NO_X may include automobile exhaust and fuel consumption of heating boilers in Beijing.[27] Industrial facilities using coal as the major energy source may have contributed to the larger productions of sulfur dioxide and related secondary sulfate in the suburban period. Similar to several previous studies in Beijing[8,20,22] and other areas,[26,28] we were not able to differentiate secondary sulfate and secondary nitrate in the present analysis. This partly may be due to the high correlation between these two species because of similar formation and transportation processes.

The fourth source (PMF S4) was interpreted as metallurgical emission, as indicated by high loadings of Mo, Cr, and Mn and a moderate loading of Fe. These metals could be emitted from industrial metallurgical processes.[8,29] Contribution of this source to $PM_{2.5}$ mass was small but much higher in the suburban period (0.7%) than in the urban periods (0.3%). This finding suggests that some industrial metal smelting facilities near the suburban campus may be the major contributor to this source over the study.

The fifth source (PMF S5) was dust and soil, as highlighted by high loadings of several crustal metals: Al, Ca, Mg, Sr, Ba, Fe, Ti, Co, and V.[11,12] Contributions of this source to $PM_{2.5}$ mass were much higher in the suburban period and urban period 2 (15.1%−15.8%, spring season) than in urban period 1 (7.6%, autumn season). Beijing is the pathway for long-range transportation of Asian dust, which could reach the north Pacific, especially during the spring dust storm period.[8,30] Additionally, construction activities around the suburban campus may also have contributed to the highest mass concentration of this source in the suburban period (12.4 vs 5.9−9.5 $\mu g/m^3$ in the urban periods). This source also has a moderate loading of SOC, which is consistent with a previous study reporting dust as one of the major sources for OC in Beijing.[25] Our results further suggest that the organic contents in the dust source may be predominantly in the form of SOC rather than POC.

The sixth source (PMF S6) was interpreted as industry, as reflected by high loadings of Zn, Cu, Cd, As, and Pb. A previous study in Beijing also identified a similar industrial $PM_{2.5}$ source

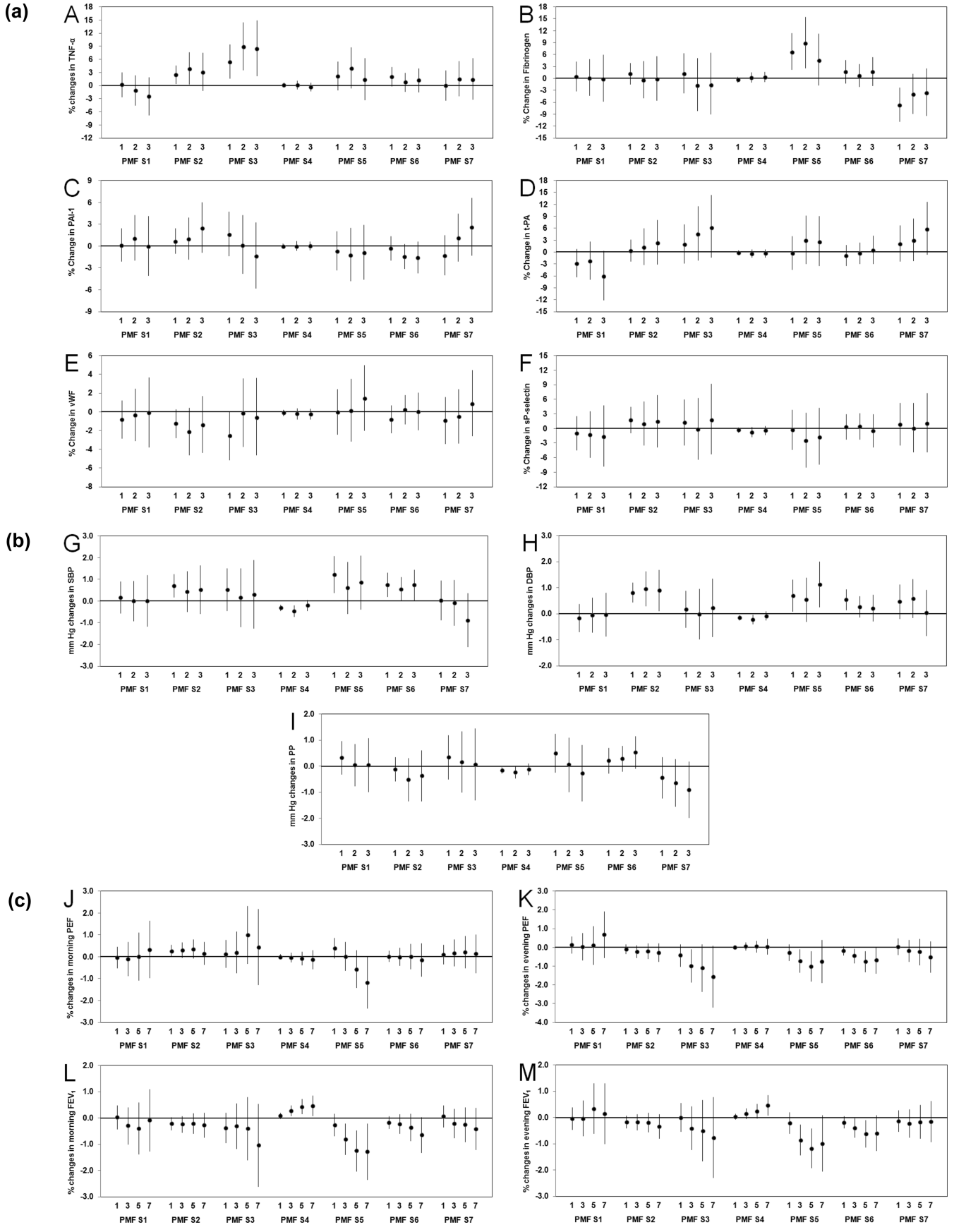


Figure 2. Estimated changes with 95% confidence intervals in health variables associated with interquartile range increases in PMF-resolved source-specific $PM_{2.5}$ concentrations at key exposure metrics in single-source models. *X*-axis (upper), exposure metrics (moving average concentrations of 1, 2, 3, 5, 7 days before the health measurement); *X*-axis (lower), pollution sources (PMF S1, traffic emissions; PMF S2, coal combustion; PMF S3,

dx.doi.org/10.1021/es404778w | *Environ. Sci. Technol.* 2014, 48, 3438−3448

Figure 2. continued

secondary sulfate/nitrate; PMF S4, metallurgical emission; PMF S5, dust/soil; PMF S6, industry; and PMF S7, secondary organic aerosol). (a) Circulating biomarker series: (A) TNF-α, (B) fibrinogen, (C) PAI-1, (D) t-PA, (E) vWF, and (F) sP-selectin. (b) BP series: (G) SBP, (H) DBP, and (I) PP. (c) Pulmonary function series: (J) morning PEF, (K) evening PEF, (L) morning FEV_1, and (M) evening FEV_1.

high in these elements and attributed it mostly to emissions from nonferrous metal smelters.[8] In addition, that study also identified a separate metallurgical emission source high in Fe and Mn (Cr and Mo were not used in their source appointment). Contributions of this source to $PM_{2.5}$ mass were higher in the urban periods (6.9%-8.1%) than in the suburban period (5.9%). However, this difference in source contributions between periods was not obvious in terms of average mass concentrations (ranging from 4.9 to 5.4 $\mu g/m^3$ over the three study periods). There are also a number of industrial facilities (e.g., nonferrous metal smelters) located in the other suburban areas that surround the Beijing urban area, and these industrial facilities may have contributed to this source in the urban area over the study and thereby attenuated the source contribution difference between the suburban campus and urban campus.

The seventh source (PMF S7) was interpreted as secondary organic aerosol, as characterized by a high loading of SOC. SOC is formed through an atmospheric chemical conversion processes of the organic precursors, and its formation is strengthened when the photochemical activity is intensive under favorable meteorological conditions.[31] Contribution of this source to $PM_{2.5}$ mass showed a modest increasing trend over the three study periods (8.7%−12.0%). Our study was conducted in spring and autumn seasons with modest meteorological conditions, and thus, the major factor that would have influenced the formation of SOC was the emission of organic precursors (i.e., POC). Accordingly, POC levels also showed an increasing trend over the three study periods (Supporting Information, Table S3), which is consistent with the changes in the secondary organic aerosol source.

$PM_{2.5}$ sources resolved by PMF showed good correlations with their key chemical constituents (Supporting Information, Table S6). Unmix analysis resolved six $PM_{2.5}$ sources that are similar to the first six sources resolved by PMF (Supporting Information, Tables S7 and S8). Although the specific source contributions in mass concentrations and percentages varied between these two source appointment methods, the trends of source contributions over different study periods were essentially consistent between these two methods. However, Unmix could not resolve a separate source of secondary organic aerosol as the PMF. A majority of SOC was incorporated into traffic emissions (Unmix S1) and dust/soil (Unmix S5) by Unmix. Specifically, the "metallurgical emission" source (Unmix S4) has a much higher Fe loading as compared to the "industry" source (Unmix S6), further suggesting two possible patterns of industrial emissions as previously identified by Sun et al.[8] Correlations between total $PM_{2.5}$ and PMF-resolved sources are similar to those between total $PM_{2.5}$ and Unmix-resolved sources (Supporting Information, Table S9).

Estimated Health Effects of $PM_{2.5}$ from Different Sources. Figure 2 shows the estimated short-term cardiopulmonary health effects associated with PMF-resolved source-specific $PM_{2.5}$ concentrations at key exposure metrics. We found significant increases in TNF-α associated with 1−2 d average $PM_{2.5}$ from coal combustion and with 1−3 d average $PM_{2.5}$ from secondary sulfate/nitrate (Figure 2a). There were also significant increases in fibrinogen associated with 1−2 d average $PM_{2.5}$ from dust/soil. Among the associations between source-specific $PM_{2.5}$ and circulating biomarkers, only the increase in TNF-α associated with $PM_{2.5}$ from secondary sulfate/nitrate at 2-d moving average was consistent in two-source and source-$PM_{2.5}$ joint models (Figure 3A). Additionally, the increase in fibrinogen associated with $PM_{2.5}$ from dust/soil during the previous day was also generally consistent over various models, except in the model adjusting for $PM_{2.5}$ from secondary organic aerosol (Figure 3B).

There were significant increases in both SBP and DBP associated with $PM_{2.5}$ from coal combustion, dust/soil, and industry at different exposure metrics, among which the associations between DBP and $PM_{2.5}$ from coal combustion were most consistent (Figure 2b). We also found significant declines in all three BP variables associated with 1−2 d average $PM_{2.5}$ from metallurgical emission. Among these associations, the increase in DBP associated with 1 d average $PM_{2.5}$ from coal combustion and declines in SBP and DBP associated with 1 d average $PM_{2.5}$ from metallurgical emission were consistent over different models (Figure 3).

$PM_{2.5}$ from dust/soil and industry were significantly associated with declines in evening PEF and morning and evening FEV_1 at different exposure metrics (Figure 2c). The significant declines in evening PEF and morning and evening FEV_1 associated with 5 d average $PM_{2.5}$ from dust/soil were consistent over different models, and the declines in evening PEF and evening FEV_1 associated with $PM_{2.5}$ from industry were also consistent over various models, except in the source-$PM_{2.5}$ joint models (Figure 3). In particular, there were significant increases in morning and evening FEV_1 associated with $PM_{2.5}$ from metallurgical emission. However, these positive associations were not consistent in two-source or source-$PM_{2.5}$ joint models.

Analyses using Unmix-resolved source-specific $PM_{2.5}$ data showed similar results as compared to those using PMF-resolved data (Supporting Information, Figures S1 and S2).

DISCUSSION

Only a handful of previous studies have assessed the associations between source-specific $PM_{2.5}$ and clinically significant health outcomes, i.e., hospitalizations and mortality due to cardiovascular and respiratory diseases.[13,32−37] However, few studies have ever investigated the potential roles of different pollution sources on the subclinical effects (e.g., biological changes in specific health-related variables) of mechanistic and pathophysiological relevance through which PM air pollution may promote the development of adverse health outcomes. In the present study, we are able to perform a comprehensive analysis for the potential subclinical cardiopulmonary effects in healthy adults associated with ambient $PM_{2.5}$ from different pollution sources in Beijing, China. To our best knowledge, this is the first study that investigated the associations of $PM_{2.5}$ from different pollution sources with a series of subclinical cardiopulmonary health variables in the context of suburban and urban air pollution simultaneously. With comprehensive data on daily levels of various $PM_{2.5}$

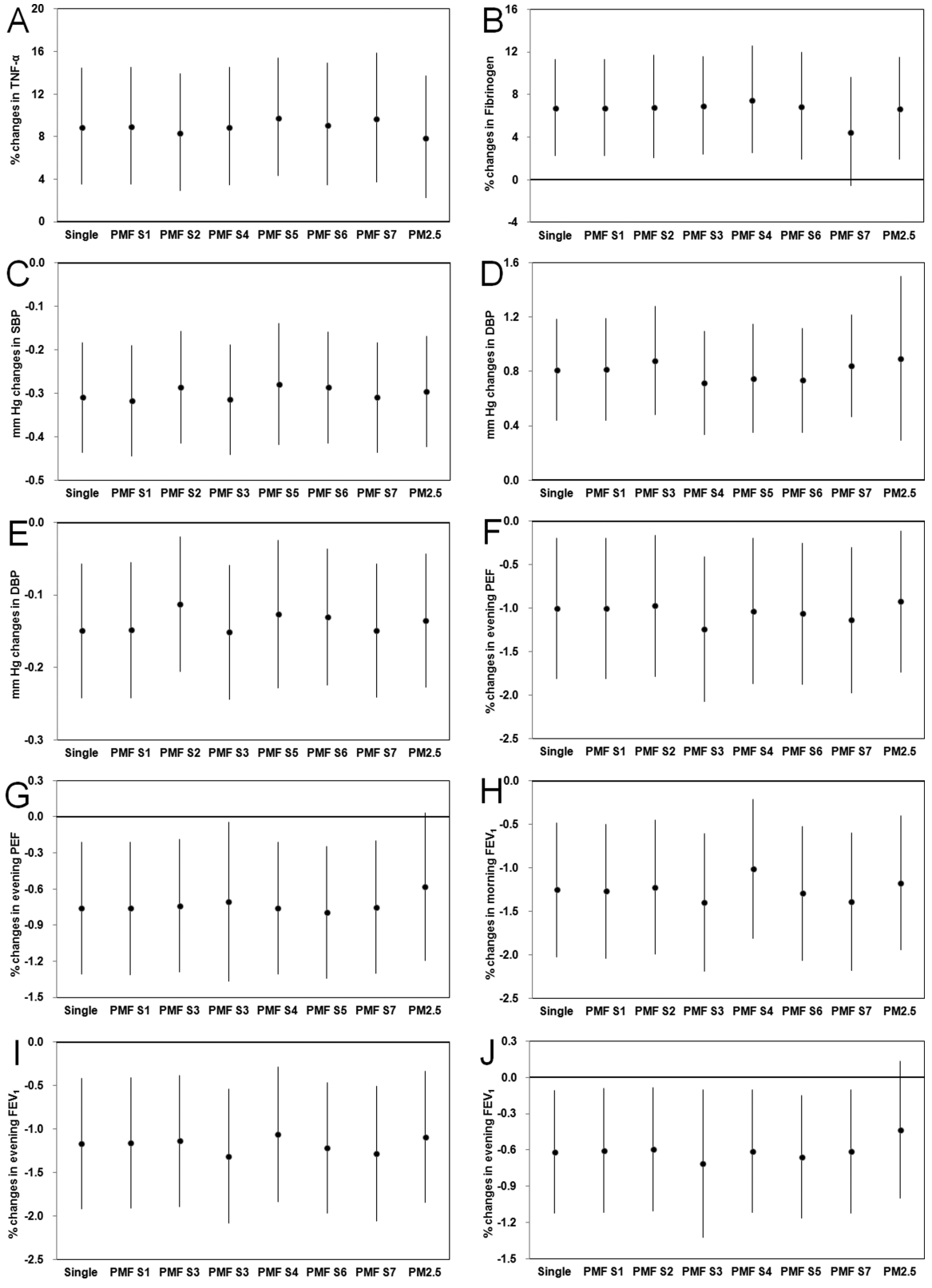


Figure 3. Estimated changes with 95% confidence intervals in health variables associated with interquartile range increases in PMF-resolved source-specific $PM_{2.5}$ concentrations at key exposure metrics in single-source models, two-source models, and source-$PM_{2.5}$ joint models. *X*-axis: "single" indicates effect estimate of a source from the single-source model; "PMF S1" through "PMF S7" indicate effect estimates of the source from two-source models with adjustment for each of the other PMF-resolved sources (PMF S1, traffic emissions; PMF S2, coal combustion; PMF S3, secondary sulfate/nitrate; PMF S4, metallurgical emission; PMF S5, dust/soil; PMF S6, industry; and PMF S7, secondary organic aerosol); and "$PM_{2.5}$" indicates the effect estimate of the source from the source-$PM_{2.5}$ joint model. (A) TNF-α and secondary sulfate/nitrate (PMF S3) at 2 d moving average, (B) fibrinogen and dust/soil (PMF S5) at 1 d average, (C) SBP and metallurgical emission (PMF S4) at 1 d average, (D) DBP and coal combustion (PMF S2) at 1 d average, (E) DBP and metallurgical emission (PMF S4) at 1 d average, (F) evening PEF and dust/soil (PMF S5)

dx.doi.org/10.1021/es404778w | *Environ. Sci. Technol.* 2014, 48, 3438−3448

Figure 3. continued

at 5 d moving average, (G) evening PEF and industry (PMF S6) at 5 d moving average, (H) morning FEV_1 and dust/soil (PMF S5) at 5 d moving average, (I) evening FEV_1 and dust/soil (PMF S5) at 5 d moving average, and (J) evening FEV_1 and industry (PMF S6) at 5 d moving average.

chemical constituents over 6 months, we were able to identify a group of pollution sources for ambient $PM_{2.5}$ in Beijing during the study. These resolved sources fitted the input data well and were physically interpretable according to previous studies in Beijing.[8,11,12,20,22,24,25]

On the basis of the revolved source profiles, we were able to estimate $PM_{2.5}$ source contributions over different study periods and short-term health effects of source-specific $PM_{2.5}$. Few studies have compared so many chemical constituents and associated pollution sources of ambient $PM_{2.5}$ between suburban and urban areas in Chinese cities, and our results suggest two distinct source contribution patterns in the suburban area and urban area of a Chinese megacity, Beijing. Specifically, $PM_{2.5}$ in Beijing's suburban area has larger contributions from secondary sulfate/nitrate (41.8%), metallurgical emission (0.7%), and dust/soil (15.1%), whereas $PM_{2.5}$ in Beijing's urban area has larger contributions from traffic emissions (13.0%−16.3%), coal combustion (21.0%−30.7%), and secondary organic aerosol (9.7%−12.0%). It is clear that ambient air pollution in Beijing's urban area is highly dominated by combustion-related sources (i.e., fossil fuels). Traffic emissions have been increasing rapidly in Beijing due to the rapid increase in the number of motor vehicles, whereas coal combustion still maintains at a high level due to enormous energy demand during recent years.[3,6] In contrast, the major sources for $PM_{2.5}$ in the suburban area are consistent with the fact that the suburban campus is surrounded by active construction sites and industrial facilities.

Results from model analysis provide evidence for the key potential pollution sources behind the short-term health effects of specific PM chemical constituents. Specifically, we found significant increases in TNF-α and fibrinogen associated with $PM_{2.5}$ from secondary sulfate/nitrate and dust/soil, respectively; significant increases in DBP associated with $PM_{2.5}$ from coal combustion; and significant declines in pulmonary function measures (i.e., evening PEF, morning and evening FEV_1) associated with $PM_{2.5}$ from dust/soil and industry. These associations are generally consistent over different statistical models and are also consistent with our previous analyses on specific $PM_{2.5}$ chemical constituents.[14−16] For example, we found consistent increases in fibrinogen associated with several crustal metals (i.e., Mg, Fe, Ti, and Co)[15] which were enriched in the dust/soil source (Figure 1). The increases in DBP associated with $PM_{2.5}$ from coal combustion are consistent with our previous findings that carbonaceous fractions and Cl^- were strongly associated with increases in DBP.[14] The declines in pulmonary function measures associated with $PM_{2.5}$ from industry are also consistent with the inverse associations between these pulmonary function measures and several metals (i.e., Cu, Cd, As, and Sn)[16] which were enriched in the industry source (Figure 1). The above findings are consistent using either PMF- or Unmix-resolved source-specific $PM_{2.5}$ data. These results suggest that the resolved source profiles are generally representative of the key chemical constituents, and data on both trace constituents and source contributions may be useful when assess the health effects associated with PM air pollution.

However, there are also some inconsistencies. For example, we found strong associations between several carbonaceous fractions (i.e., OC, EC, and POC) and DBP in our previous analysis,[14] whereas DBP was not associated with $PM_{2.5}$ from traffic emissions in the present analysis (Figure 2b); TNF-α was strongly associated with SOC in our previous analysis[15] but not secondary organic aerosol source in the present analysis (Figure 2a); $PM_{2.5}$ from dust/soil was associated with significant declines in pulmonary function measures, whereas the major tracers (i.e., Al, Ca, Mg, Sr, Ba, Fe, Ti, Co, and V) of this source were not consistently associated with these pulmonary function measures in our previous analysis.[16] However, it should be noted that the source appointment analysis will decompose each chemical constituent into several different sources, and it is likely that the potential health effect of a constituent may also be decomposed into several different sources during the process. For example, POC and EC were decomposed into three major sources (i.e., traffic emissions, coal combustion, and secondary organic aerosol) in the present analysis. Although $PM_{2.5}$ from traffic emissions was not associated with DBP, $PM_{2.5}$ from coal combustion was significantly associated with increased DBP, and $PM_{2.5}$ from secondary organic aerosol was also positively (although insignificantly) associated with DBP (Figure 2b). Similarly, SOC was also decomposed into three major sources (i.e., secondary organic aerosol, dust/soil, and coal combustion) in the present analysis. Although $PM_{2.5}$ from secondary organic aerosol was not significantly associated with TNF-α, $PM_{2.5}$ from coal combustion was significantly associated with increased TNF-α, and $PM_{2.5}$ from dust/soil also showed positive associations (although did not reach statistical significance) with TNF-α (Figure 2a). On the other hand, each source contains multiple constituents and its potential health effect may be a combination of the effects of these constituents. Although several constituents (e.g., Al, Ca, Mg, Sr, Ba, Fe, Ti, Co, and V) only have a weak effect on pulmonary function when looked at separately, they were able to elicit a significant effect when combined together (e.g., dust/soil) (Figure 2c). Therefore, the source appointment gives us an opportunity to look at the relationship between ambient PM air pollution and health from a different view.

Coal combustion and secondary sulfate/nitrate were two major sources associated with increased TNF-α and BP levels in the present study. Both sources are related to fossil fuel combustion.[11,12,27] Our results are consistent with previous findings that combustion-related PM exposures are associated with increased levels of systematic inflammatory biomarkers and BP[38−40] and therefore are potentially in line with previous epidemiological studies that reported combustion-related PM as the critical pollutant that is responsible for the increased cardiovascular morbidity and mortality.[13,32−37] Furthermore, a previous study found increased respiratory hospital admissions associated with steel metal-works-related $PM_{2.5}$,[32] whereas our study also found consistent inverse associations between pulmonary function and $PM_{2.5}$ from industry. Another animal study found that the lung dose of bioavailable transition metal, but not instilled PM mass, was the primary determinant of acute lung inflammatory response in rats.[41] Therefore, it is possible that trace metals and related source(s) may play a

more important role in the pulmonary effects of ambient PM. We also found a significant increase in fibrinogen and significant declines in pulmonary function measures associated with $PM_{2.5}$ from dust/soil. PM collected from roadside, which is typically rich in crustal material, has been shown to have a great potency to induce cellular defenses in vitro and thus may possess the ability to induce toxic effects in the cardiopulmonary system.[42]

We also found significant inverse associations of BP variables with $PM_{2.5}$ from metallurgical emission, which may be due to the high loading of Mn in this source. Environmental Mn is generally considered to reduce hypertension risk,[43] and animal experiments have demonstrated that infusing Mn into conscious, restrained rats will result in decreased BP.[44] However, it should be noted that the levels of $PM_{2.5}$ from metallurgical emission showed a decreasing trend over the three study periods, which was opposite to the increasing trends of levels of $PM_{2.5}$ from several other major sources. Therefore, it is possible that the observed associations between $PM_{2.5}$ from metallurgical emission and health variables may be related to the reverse trends in pollution levels. Further research is needed to examine whether these opposite associations suggest a different action pattern of $PM_{2.5}$ from metallurgical emission as compared to $PM_{2.5}$ from the other sources.

The strengths of this study include the novel prospective study design, multiple repeated measurements on the same group of subjects, the use of two different source appointment methods, and the use of various statistical analytic approaches to identify the potential health effects of $PM_{2.5}$ from different pollution sources. Study limitations include the use of air pollution data from central air monitoring stations rather than exposure data at individual level; the inability to account for indoor air pollution, which may also have contributed to the observed health effects;[45,46] and the potentially limited generalizability of the study findings to other population subgroups (e.g., susceptible subjects including elders and children).

In summary, we demonstrated a comprehensive analysis on the short-term cardiopulmonary effects associated with $PM_{2.5}$ from different pollution sources in Beijing, China. We identified a group of $PM_{2.5}$ sources during the study using two different source appointment methods. Our study and previous studies in Beijing[8,11,12,20,22,24,25] all suggest a mixed pollution pattern of ambient PM in Beijing, as evidenced by the major $PM_{2.5}$ sources of fossil fuel combustion, industrial emissions, secondary aerosols, and dust/soil. Specifically, ambient $PM_{2.5}$ in Beijing suburban area and urban area has two distinct patterns of source contributions. Potential key sources were identified for $PM_{2.5}$ effects on inflammatory biomarkers (secondary sulfate/nitrate and dust/soil), BP (coal combustion and metallurgical emission), and pulmonary function (dust/soil and industry). These findings suggest that $PM_{2.5}$ from different sources may play important roles in different aspects of $PM_{2.5}$-related cardiopulmonary health effects. Interestingly, we did not find significant associations between traffic emissions and health variables. However, these results do not mean that traffic emissions play no role in the $PM_{2.5}$-related health effects. Traffic is one of the major sources for the precursor pollutants (i.e., NO_X) of secondary nitrate,[27] which was found to be strongly associated with increased TNF-α (Figure 2a). Several major species of traffic-related emissions (e.g., POC, EC, NO_X) are actually components of fossil fuel combustion. Furthermore, over 70% of the PMF resolved $PM_{2.5}$, including $PM_{2.5}$ from traffic emissions, coal combustion, secondary sulfate/nitrate and secondary organic aerosol, was predominantly related to combustion of fossil fuels, which may be the major source behind the observed health effects. It has been reported that China's demand for fossil fuels (e.g., coal, oil, and natural gas) has been continuously increasing during recent years along with the rapid economic expansion,[47] and Beijing is frequently ranked among the top cities with the highest air pollution levels in the world due to high consumption of these fossil fuels.[3] Therefore, our findings not only provide clues for the specific pollution sources associated with short-term cardiopulmonary effects of ambient $PM_{2.5}$ but may also have potential implications for the developments of relevant air pollution control strategies and policies with the aim to protect the public health.

■ ASSOCIATED CONTENT

Supporting Information

Details of ambient air pollution measurement and analysis, subject characteristics, $PM_{2.5}$ chemical constituent data, cardiopulmonary health data, and supplementary results. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*Phone: 86-10-82801176; fax: 86-10-62375580; e-mail: guoxb@bjmu.edu.cn.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

The authors thank the affiliated hospital of Beijing Institute of Technology for providing necessary assistance with the study. This work was supported by Grants from the National Natural Science Foundation of China (No. 81072267), the National Key Technologies R&D Program of China (No. 2006BAI19B06), and the Academic Award for Excellent Doctoral Candidates of the Ministry of Education of the People's Republic of China (S.W.)

■ REFERENCES

(1) Brook, R. D.; Rajagopalan, S.; Pope, C. A., 3rd.; Brook, J. R.; Bhatnagar, A.; Diez-Roux, A. V.; Holguin, F.; Hong, Y.; Luepker, R. V.; Mittleman, M. A.; Peters, A.; Siscovick, D.; Smith, S. C., Jr.; Whitsel, L.; Kaufman, J. D. Particulate matter air pollution and cardiovascular disease: An update to the scientific statement from the American Heart Association. *Circulation* **2010**, *121*, 2331−2378.

(2) Valavanidis, A.; Fiotakis, K.; Vlachogianni, T. Airborne particulate matter and human health: Toxicological assessment and importance of size and composition of particles for oxidative damage and carcinogenic mechanisms. *J. Environ. Sci. Health C. Environ. Carcinog. Ecotoxicol. Rev.* **2008**, *26*, 339−362.

(3) Watts, J. China: The air pollution capital of the world. *Lancet* **2009**, *366*, 1761−1762.

(4) Yang, G.; Wang, Y.; Zeng, Y.; Gao, G. F.; Liang, X.; Zhou, M.; Wan, X.; Yu, S.; Jiang, Y.; Naghavi, M.; Vos, T.; Wang, H.; Lopez, A. D.; Murray, C. J. Rapid health transition in China, 1990−2010: Findings from the Global Burden of Disease Study 2010. *Lancet* **2013**, *381* (9882), 1987−2015.

(5) Chan, C. K.; Yao, X. Air pollution in mega cities in China. *Atmos. Environ.* **2008**, *42*, 1−42.

(6) Stone, R. Beijing's marathon run to clean foul air nears finish line. *Science* **2008**, *321*, 636−637.

(7) Wang, S.; Zhao, M.; Xing, J.; Wu, Y.; Zhou, Y.; Lei, Y.; He, K.; Fu, L.; Hao, J. Quantifying the air pollutants emission reduction during the 2008 Olympic games in Beijing. *Environ. Sci. Technol.* **2010**, *44* (8), 2490−2496.
(8) Sun, Y.; Zhuang, G.; Wang, Y.; Han, L.; Guo, J.; Dan, M.; Zhang, W.; Wang, Z.; Hao, Z. The air-borne particulate pollution in Beijing—Concentration, composition, distribution and sources. *Atmos. Environ.* **2004**, *38*, 5991−6004.
(9) Cao, J.; Xu, H.; Xu, Q.; Chen, B.; Kan, H. Fine particulate matter constituents and cardiopulmonary mortality in a heavily polluted Chinese city. *Environ. Health Perspect.* **2012**, *120*, 373−378.
(10) Huang, W.; Cao, J.; Tao, Y.; Dai, L.; Lu, S. E.; Hou, B.; Wang, Z.; Zhu, T. Seasonal variation of chemical species associated with short-term mortality effects of $PM_{2.5}$ in Xi'an, a central city in China. *Am. J. Epidemiol.* **2012**, *175* (6), 556−566.
(11) Song, Y.; Zhang, Y.; Xie, S.; Zeng, L.; Zheng, M.; Salmon, L. G.; Shao, M.; Slanina, S. Source apportionment of $PM_{2.5}$ in Beijing by positive matrix factorization. *Atmos. Environ.* **2006**, *40* (8), 1526−1537.
(12) Song, Y.; Tang, X.; Xie, S.; Zhang, Y.; Wei, Y.; Zhang, M.; Zeng, L.; Lu, S. Source apportionment of $PM_{2.5}$ in Beijing in 2004. *J. Hazard. Mater.* **2007**, *146* (1−2), 124−130.
(13) Thurston, G. D.; Ito, K.; Mar, T.; Christensen, W. F.; Eatough, D. J.; Henry, R. C.; Kim, E.; Laden, F.; Lall, R.; Larson, T. V.; Liu, H.; Neas, L.; Pinto, J.; Stölzel, M.; Suh, H.; Hopke, P. K. Workgroup report: Workshop on source apportionment of particulate matter health effects—Intercomparison of results and implications. *Environ. Health Perspect.* **2005**, *13* (12), 1768−1774.
(14) Wu, S.; Deng, F.; Huang, J.; Wang, H.; Shima, M.; Wang, X.; Qin, Y.; Zheng, C.; Wei, H.; Hao, Y.; Lv, H.; Lu, X.; Guo, X. Blood pressure changes and chemical constituents of particulate air pollution: Results from the healthy volunteer natural relocation (HVNR) study. *Environ. Health Perspect.* **2013**, *121* (1), 66−72.
(15) Wu, S.; Deng, F.; Wei, H.; Huang, J.; Wang, H.; Shima, M.; Wang, X.; Qin, Y.; Zheng, C.; Hao, Y.; Guo, X. Chemical constituents of ambient particulate air pollution and biomarkers of inflammation, coagulation and homocysteine in healthy adults: A prospective panel study. *Part. Fibre Toxicol.* **2012**, *9*, 49.
(16) Wu, S.; Deng, F.; Hao, Y.; Shima, M.; Wang, X.; Zheng, C.; Wei, H.; Lv, H.; Lu, X.; Huang, J.; Qin, Y.; Guo, X. Chemical constituents of fine particulate air pollution and pulmonary function in healthy adults, the Healthy Volunteer Natural Relocation study. *J. Hazard. Mater.* **2013**, *260*, 183−191.
(17) Norris, G.; Vedantham, R.; Wade, K.; Brown, S.; Prouty, J.; Foley, C.; Martin, L. *EPA Positive Matrix Factorization (PMF) 3.0 Fundamentals & User Guide*; EPA 600/R-08/108; U.S. Environmental Protection Agency, Office of Research and Development: Washington, DC, July 2008.
(18) Paatero, P.; Tapper, U. Positive matrix factorization: A non-negative factor model with optimal utilization of error estimates of data values. *Envirometrics* **1994**, *5*, 111−126.
(19) Paatero, P. *User's Guide for Positive Matrix Factorization Programs PMF2 and PMF3, Part1, Tutorial*; University of Helsinki: Helsinki, Finland, 2004.
(20) Zhang, R.; Jing, J.; Tao, J.; Hsu, S. C.; Wang, G.; Cao, J.; Lee, C. S. L.; Zhu, L.; Chen, Z.; Zhao, Y.; Shen, Z. Chemical characterization and source apportionment of $PM_{2.5}$ in Beijing: Seasonal perspective. *Atmos. Chem. Phys.* **2013**, *13*, 7053−7074.
(21) Norris, G.; Vedantham, R.; Duvall, R. *EPA Unmix 6.0 Fundamentals & User Guide*; EPA/600/R-07/089; U.S. Environmental Protection Agency, Office of Research and Development: Washington, DC, July 2007.
(22) Song, Y.; Xie, S.; Zhang, Y.; Zeng, L.; Salmon, L. G.; Zheng, M. Source apportionment of PM2.5 in Beijing using principal component analysis/absolute principal component scores and UNMIX. *Sci. Total Environ.* **2006**, *372*, 278−286.
(23) Loranger, S.; Zayed, J. Contribution of methylcyclopentadienyl manganese tricarbonyl (MMT) to atmospheric Mn concentration near expressway: Dispersion modeling estimations. *Atmos. Environ.* **1995**, *29*, 591−599.
(24) Duan, F. K.; He, K. B.; Yang, F. M.; Yu, X. C.; Cadle, S. H.; Chan, T.; Mulawa, P. A. Concentrations and chemical characteristics of $PM_{2.5}$ in Beijing, China: 2001−2002. *Sci. Total Environ.* **2006**, *355*, 264−275.
(25) Zheng, M.; Salmon, L. G.; Schauer, J. J.; Zeng, L.; Kiang, C. S.; Zhang, Y.; Cass, G. R. Seasonal trends in $PM_{2.5}$ source contributions in Beijing, China. *Atmos. Environ.* **2005**, *39*, 3967−76.
(26) Harrison, R. M.; Smith, D. J. T.; Pio, C. A.; Castro, L. M. Comparative receptor modeling study of airborne particulate pollutants in Birmingham (United Kingdom), Coimbra (Portugal) and Lahore (Pakistan). *Atmos. Environ.* **1997**, *31*, 3309−3321.
(27) Chen, J.; Wang, W.; Zhang, J.; Liu, H.; Ren, L.; Liu, X.; Zhang, W.; Wang, X. Characteristics of gaseous pollutants near a main traffic line in Beijing and its influencing factors. *Atmos. Res.* **2009**, *94*, 470−480.
(28) Almeida, S. M.; Pio, C. A.; Freitas, M. C.; Reis, M. A.; Trancoso, M. A. Source apportionment of fine and coarse particulate matter in a sub-urban area at the Western European Coast. *Atmos. Environ.* **2005**, *39*, 3127−3138.
(29) Ott, H. C.; Prior, C.; Herold, M.; Riha, M.; Laufer, G.; Ott, G. Respiratory symptoms and bronchoalveolar lavage abnormalities in molybdenum exposed workers. *Wien. Klin. Wochenschr.* **2004**, *116* (Suppl 1), 25−30.
(30) Zhuang, G.; Guo, J.; Yuan, H.; Zhao, C. The compositions, sources, and size distribution of the dust storm from China in spring of 2000 and its impact on the global environment. *China Sci. Bull.* **2001**, *46* (12), 895−901.
(31) Duan, F. K.; He, K. B.; Ma, Y. L.; Jia, Y. T.; Yang, F. M.; Lei, Y.; Tanaka, S.; Okuta, T. Characteristics of carbonaceous aerosols in Beijing, China. *Chemosphere* **2005**, *60*, 355−364.
(32) Lall, R.; Ito, K.; Thurston, G. Distributed lag analyses of daily hospital admissions and source-apportioned fine particle air pollution. *Environ. Health Perspect.* **2011**, *119*, 455−460.
(33) Ostro, B.; Tobias, A.; Querol, X.; Alastuey, A.; Amato, F.; Pey, J.; Pérez, N.; Sunyer, J. The effects of particulate matter sources on daily mortality: A case-crossover study of Barcelona, Spain. *Environ. Health Perspect.* **2011**, *119* (12), 1781−1787.
(34) Ito, K.; Christensen, W. F.; Eatough, D. J.; Henry, R. C.; Kim, E.; Laden, F.; Lall, R.; Larson, T. V.; Neas, L.; Hopke, P. K.; Thurston, G. D. PM source apportionment and health effects: 2. An investigation of intermethod variability in associations between source-apportioned fine particle mass and daily mortality in Washington, DC. *J. Exposure Sci. Environ. Epidemiol.* **2006**, *16* (4), 300−310.
(35) Sarnat, J. A.; Marmur, A.; Klein, M.; Kim, E.; Russell, A. G.; Sarnat, S. E.; Mulholland, J. A.; Hopke, P. K.; Tolbert, P. E. Fine particle sources and cardiorespiratory morbidity, an application of chemical mass balance and factor analytical source-apportionment methods. *Environ. Health Perspect.* **2008**, *116*, 459−466.
(36) Ozkaynak, H.; Thurston, G. D. Associations between 1980 U.S. mortality rates and alternative measures of airborne particle concentration. *Risk Anal.* **1987**, *7* (4), 449−461.
(37) Laden, F.; Neas, L. M.; Dockery, D. W.; Schwartz, J. Association of fine particulate matter from different sources with daily mortality in six U.S. cities. *Environ. Health Perspect.* **2000**, *108* (10), 941−947.
(38) Chuang, K. J.; Chan, C. C.; Su, T. C.; Lee, C. T.; Tang, C. S. The effect of urban air pollution on inflammation, oxidative stress, coagulation, and autonomic dysfunction in young adults. *Am. J. Respir. Crit. Care Med.* **2007**, *176*, 370−376.
(39) Delfino, R. J.; Staimer, N.; Tjoa, T.; Gillen, D. L.; Polidori, A.; Arhami, M.; Kleinman, M. T.; Vaziri, N. D.; Longhurst, J.; Sioutas, C. Air pollution exposures and circulating biomarkers of effect in a susceptible population: Clues to potential causal component mixtures and mechanisms. *Environ. Health Perspect.* **2009**, *117*, 1232−1238.
(40) Delfino, R. J.; Tjoa, T.; Gillen, D. L.; Staimer, N.; Polidori, A.; Arhami, M.; Jamner, L.; Sioutas, C.; Longhurst, J. Traffic-related air pollution and blood pressure in elderly subjects with coronary artery disease. *Epidemiology* **2010**, *21*, 396−404.
(41) Costa, D. L.; Dreher, K. L. Bioavailable transition metals in particulate matter mediate cardiopulmonary injury in healthy and

compromised animal models. *Environ. Health Perspect.* **1997**, *105* (5), 1053−1060.
(42) Hetland, R. B.; Cassee, F. R.; Refsnes, M.; Schwarze, P. E.; Lag, M.; Boere, A. J.; Dybing, E. Release of inflammatory cytokines, cell toxicity and apoptosis in epithelial lung cells after exposure to ambient air particles of different size fractions. *Toxicol. In Vitro* **2004**, *18*, 203−212.
(43) Houtman, J. P. Trace elements and cardiovascular diseases. *J. Cardiovasc. Risk* **1996**, *3* (1), 18−25.
(44) Kasten, T. P.; Settle, S. L.; Misko, T. P.; Currie, M. G.; Nickolsa, G. A. Manganese potentiation of nitric oxide-mediated vascular relaxation. *Eur. J. Pharmacol.* **1994**, *253*, 35−43.
(45) Lin, L. Y.; Chen, H. W.; Su, T. L.; Hong, G. B.; Huang, L. C.; Chuang, K. J. The effects of indoor particle exposure on blood pressure and heart rate among young adults: An air filtration-based intervention study. *Atmos. Environ.* **2011**, *45*, 5540−5544.
(46) Lin, L. Y.; Chuang, H. C.; Liu, I. J.; Chen, H. W.; Chuang, K. J. Reducing indoor air pollution by air conditioning is associated with improvements in cardiovascular health among the general population. *Sci. Total Environ.* **2013**, *463*−*464*, 176−181.
(47) Wang, S.; Dai, J.; Su, M. Material flow analysis of fossil fuels in China during 2000−2010. *Sci. World J.* **2012**, 625828 DOI: 10.1100/2012/625828.