



The Association between Short-term Exposure to Fine Particulate Matter and Outpatient Visit in Beijing, China

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(Received 19 Oct 2016; accepted 21 Mar 2017)

Abstract

Background: We tried to investigate the effect of PM_{2.5} on daily counts of outpatient visits in the Guang'anmen Hospital to determine if short-term PM_{2.5} exposure with extremely high concentration affects cardiopulmonary function of Beijing residents.

Methods: Outpatient visits and PM_{2.5} data from 01/11/2011 to 03/31/2013 were extracted from the Guang'anmen Hospital and the American Embassy in Beijing, respectively. Followed by using a semi-parametric generalized additive model (GAM) with time dependent covariates, we analyzed the association between PM_{2.5} concentrations and daily count of outpatient visits on Day 0, 1, 2, 3, 4 and 5 of PM_{2.5} exposure.

Results: Overall, 284354 subjects were collected. There were significant associations of short-term PM_{2.5} exposures with outpatient visits for cardiopulmonary diseases ($P < 0.05$). Specifically, a 10 $\mu\text{g}/\text{m}^3$ increase in PM_{2.5} was positively associated with a 0.74% of increase in angina visit on the first day and 0.50% increased visit on the second day ($P < 0.05$). With an increase in PM_{2.5}, the cough and respiratory visits significantly decreased by 0.17% and 0.30% on the first day, respectively ($P < 0.05$). However, there were significant positive associations of PM_{2.5} with increased cough and respiratory visits (increased by 0.17% and 0.10%, respectively) on the fifth day ($P < 0.05$).

Conclusion: Our association studies showed an instant effect of PM_{2.5} level on cardiovascular outpatient visit in the Guang'anmen Hospital in Beijing while a lag effect on respiratory outpatient visits.

Keywords: Air pollution, Fine particulate matter (PM_{2.5}), Association study, Short-term outpatient visits, Cardiopulmonary disease

Introduction

Particulate matter plays an important role in air pollution, defined as the matter of aerodynamic equivalent diameter less than 10 μm (PM₁₀). PM_{2.5}, named as fine particulate matter no more than 2.5 μm in diameter, is major component of PM₁₀ at 83%, drawn more attention recently in

China (1). Carbonaceous materials, secondary inorganic aerosols (SIA), and mineral dust (Al, Ca, Fe, and Mg) are the three essential components of airborne PM in Beijing, as being main contributors to wintertime haze and adverse effects on people healthy (2). They are generated

initially from natural and anthropogenic sources including biomass burning, vehicle exhaust, and industry, or secondary pollutants through heterogeneous chemical reactions (3). Air pollution in such circumstances in Beijing has turned more and more severe since 2000, due to rapid developments in Chinese economics, technology, and automotive industry, as well as population explosion in Beijing (4). Increased exposure to ambient particulate matter has a variety of adverse health effects including increased mortality, morbidity, hospital admission and outpatient visits (5-8). Researchers focused more on the adverse health effect of $PM_{2.5}$ instead of PM_{10} because $PM_{2.5}$ is a critical component in ambient particulate matter, and has been proved to be more significantly associated with acute health outcomes, as compared to PM_{10} (9). $PM_{2.5}$ can remain suspended for longer time, easily go into indoor environment, and be transported over much longer distance (10). Several studies in toxicological and physiological fields had suggested that $PM_{2.5}$ apparently affected human health, especially when sulfates, nitrates, acids, metals, and chemicals were adsorbed onto their surfaces (11-13). Those fine particles can go deeply and quickly into lower respiratory tract and even into alveolar region (14). Due to 'spill-over effect' of pulmonary inflammation or translocation into the circulation, $PM_{2.5}$ might have adverse effect on respiratory and cardiovascular systems. There have been many scientific pieces of evidence showing the long-term effect of air pollution on respiratory and cardiovascular diseases (15-18). Less is known about the short-term influence of air quality on respiratory and cardiovascular diseases.

A few studies had discussed the relationship between $PM_{2.5}$ short-term exposure and outpatient visit for respiratory and cardiovascular diseases. One study in Shanghai found that short-term $PM_{2.5}$ exposure was associated with the increase of outpatient and emergency room visits (19). A survey in Beijing reported that the increase of $PM_{2.5}$ results in elevation of respiratory mortality and morbidity. The growth rate of respiratory morbidity was highest even when $PM_{2.5}$ was 40–60 $\mu\text{g}/\text{m}^3$ (20). Although $PM_{2.5}$ concentration was

associated with respiratory and cardiovascular diseases, few of them showed the adverse health effect with such high $PM_{2.5}$ levels in Beijing. In our study, the maximal concentration of $PM_{2.5}$ was up to 491 $\mu\text{g}/\text{m}^3$ with the average of 96.99 $\mu\text{g}/\text{m}^3$. It is necessary to investigate the transient effect of $PM_{2.5}$ with such extremely high concentration on human cardiopulmonary system in Beijing. It would help to detect adverse effect of extremely high level of $PM_{2.5}$ after short-term exposure, as well as to understand further its pathophysiological mechanisms of action of $PM_{2.5}$.

The composition and sources of $PM_{2.5}$ particles vary dramatically by location, leading to different effects on public health. Beijing, as one of cities with the nation's highest levels of $PM_{2.5}$ concentration, traffic density, and residential population, is facing more and more severe problems that need public health studies to solve in this region. Fig. 1 showed Beijing's monthly average $PM_{2.5}$ levels from the data set containing nearly 50000 hourly readings from Apr 8, 2008, to Mar 31, 2014, according to the US Embassy monitor.

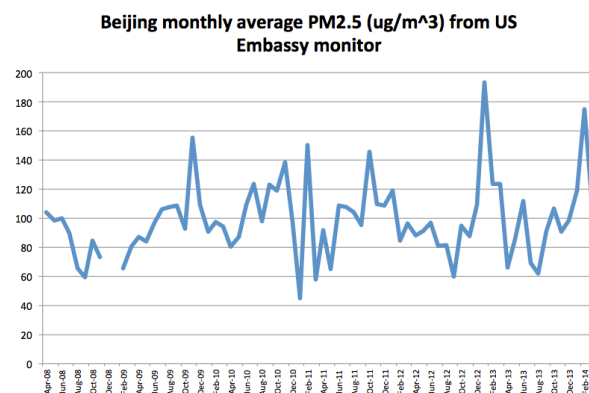


Fig. 1: $PM_{2.5}$ concentration trends

Especially in the recent decade in Beijing, air pollution mainly due to $PM_{2.5}$ has gradually become one of the largest risk factors for both cardiovascular and respiratory diseases. As the outpatient medical treatment processes of Chinese medical care system are quite different from other countries, our patients usually, do not need to schedule appointments before they see their doctors in China. They could walk into hospitals di-

rectly and check in time to see available doctors once they feel uncomfortable. Moreover, the Guang'anmen Hospital is one of the largest academic hospitals in downtown of Beijing, in China and Guang'anmen Hospital in Beijing as shown in Fig. 2A and Fig. 2B.

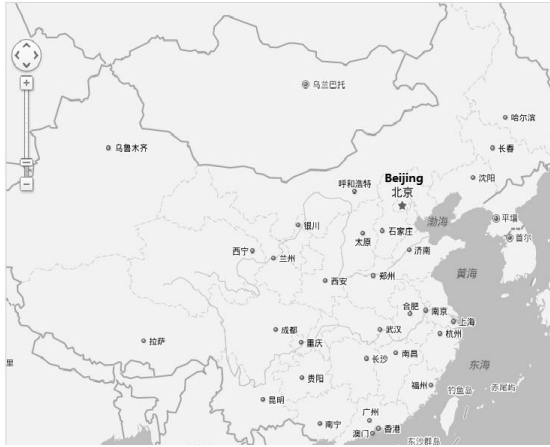


Fig. 2: A: China map and the location of Beijing From Baidu Map V8.9.0



Fig. 2: B: Beijing map and the location of Guang'anmen hospital* From Baidu Map V8.9.0

Therefore, an outpatient visit for cardiopulmonary disease in the hospital would be a great indicator to reflect the short-term effect of air pollution in Beijing, differing from the $PM_{2.5}$ long-term effect on hospitalization for cardiopulmonary disease.

In present study, we tried to investigate the effect of $PM_{2.5}$ on daily counts of outpatient visits in the

Guang'anmen Hospital to determine if short-term $PM_{2.5}$ exposure with extremely high concentration based on time-series data from 2011 to 2013 in Beijing transiently affects cardiopulmonary function of Beijing residents.

Methods

Ethics statement

The study design has been approved by the IRB of the Guang'anmen Hospital. This was a retrospective study and no written informed consent was needed from the participants. Patients' records/information was de-identified prior to analysis.

Data collection

Beijing is located in the north of China with the world's worst smog and about 21.7 millions of residential population in total. The daily $PM_{2.5}$ concentrations from Nov 1st in 2011 until Mar 31st in 2013 were obtained from the American Embassy in Beijing. The data, including average daily temperature, dew point, relative humidity, air pressure, visibility and wind speed in Beijing, were collected from daily weather report by the Chinese Meteorological Administration.

The data of daily outpatient visits with 284354 patients were extracted from the electronic medical database of the Guang'anmen Hospital. The number of daily outpatient visits varied from 6500 to 11000, excluding the days when the outpatient clinic was closed. Only the visits for pulmonary and cardiovascular divisions were included in the study. In addition, the major complaints about outpatient visits were also extracted from the electronic medical records: a cough (ICD-10 R05xx01) and angina visits (ICD-10 I20.902).

Statistical analysis

All the statistical analysis were performed using the software -Statistical Analysis System (SAS) for evaluating mean, minimum, median, maximum, standard deviation (SD) and interquartile range (IQR) values. Spearman correlation analysis was used to identify the association of temperature, dew point, relative humidity, air pressure, visibility, and wind speed, respectively. Since the

generalized additive model (GAM) had been widely used for pollution studies (21,22), we also utilized time course of semi-parametric GAM to estimate the association of PM_{2.5} level with daily outpatient visit for either cardiovascular or respiratory disease, as well as other confounding factors including seasonality, long-term trend, meteorological factors and day of the week, respectively. We analyzed outpatient visits on Day 0, 1, 2, 3, 4 and 5 of PM_{2.5} exposure to display the daily effect of PM_{2.5} on risks in cardiovascular and pulmonary diseases. The relative risks (RRs) were

calculated to determine the change of outpatient visit with a 10 µg/m³ increase in PM_{2.5}.

Results

Overall, 284354 patients had been collected during about one and half years in our study. The basic characteristics and daily meteorological factors, and PM_{2.5} concentrations during the same period were shown in details (Table 1).

Table 1: A descriptive statistics of meteorological factors, air pollutants and outpatient visits; Numbers shown are mean±SD or proportion

Meteorological factors			
Temperature (°C)			8.35±11.84
Dew point (°C)			-1.35±13.78
Relative humidity (%)			55.5±20.22
Pressure (mpa)			1018.99±10.24
Visibility (km)			9.74±7.7
Wind speed (km/h)			9.95±5.53
Atmospheric pollutants			
PM _{2.5} (µg/m ³)			96.99±88.96
Outpatient visits			
Respiratory division		Cardiovascular division	
Visits per day	210±104	Visits per day	340±159
Age (year)	51± 11	Age (year)	61± 9
Male (%)	47	Male (%)	52
Cough visits*	169±78	Angina visits&	10±9

* Cough visits: the visits whose major complaint was cough

&Angina visits: the visits whose major complaint was angina

The Spearman correlation analysis showed that the PM_{2.5} level in Beijing was significantly and positively correlated with dew point, humidity, while negatively associated with visibility and wind speed ($P<0.05$) (Table 2). PM_{2.5} exposure significantly affected the outpatient visit for angina as a chief complaint (RR=1.007, 95% confidence interval, CI: 1.003-1.012, $P=0.003$), while

no statistically significant relationship between the PM_{2.5} level and daily cardiovascular division visit was found (RR=1.000, 95% CI: 0.999-1.001, $P=0.742$). PM_{2.5} level also affected the outpatient visits for both cough (RR=0.998, 95% CI: 0.997-0.999, $P<0.001$) and total respiratory outpatient visits (RR = 1.001, 95% CI: 1.000-1.002, $P=0.013$) (Table 3).

Table 2: The correlation coefficient of air pollutants PM_{2.5} and meteorological factors

	Temperature (°C)	Dew point (°C)	Humidity (%)	Pressure (mpa)	Visibility (km)	Wind speed (km/h)
PM _{2.5} (µg/m ³)	0.095	0.323*	0.568*	-0.187	-0.752*	-0.547*

* $P < 0.05$, it can be thought of correlation analysis with statistical significance.

Table 3: The relative risk (RR) and 95% CI of $PM_{2.5}$ (per $10\mu g/m^3$) on daily outpatient visits

	<i>Time</i>	<i>RR</i>	<i>95%CI</i>	<i>P value</i>
Cough	lag0	0.998	0.9971-0.9995	* $P < 0.001$
	lag4	1.002	1.001-1.003	* $P < 0.001$
Respiratory division	lag0	0.997	0.996-0.998	* $P < 0.001$
	lag4	1.001	1.002-1.0018	* $P = 0.013$
Angina	lag0	1.007	1.003-1.012	* $P = 0.003$
	lag1	1.005	1.001-1.009	* $P = 0.021$
Cardiovascular division	lag0	1	0.999-1.001	$P = 0.742$
	lag1	1.002	1.001-1.002	* $P < 0.001$

RR= relative risk, CI= confidence interval, * $P < 0.05$, can be thought of correlation analysis with statistical significance. lag0= current day=the first day, lag1= the second day, lag4= the fifth day

The results from the one-day lag effect analysis showed that $PM_{2.5}$ exposure had statistically significant influences on both angina and total cardiovascular division visit right on the first day ($P < 0.05$) (Fig. 3A and 3B). No significant effect

was observed on the other days. Interestingly, $PM_{2.5}$ exposure had statistically significant effects on cough and total respiratory division visit on the fifth day, instead of the first day ($P < 0.05$) (Fig. 3C and 3D).

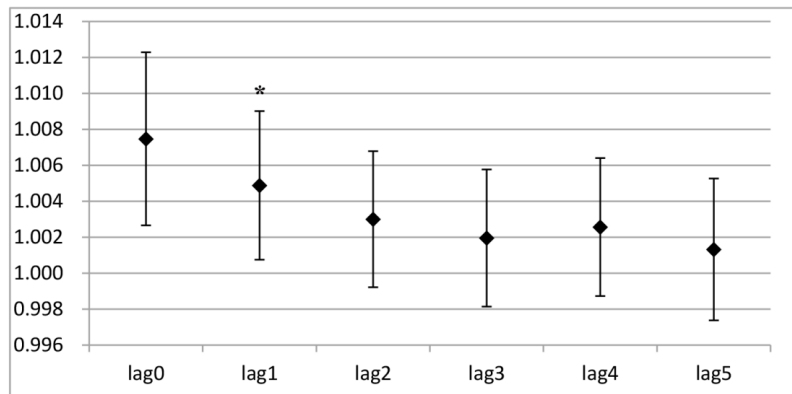


Fig. 3: A: The RRs of $PM_{2.5}$ in a single stranded effect on daily angina outpatient visits Y-axis indicates relative risk (RR) in the one-day lag effect analysis; * indicates $P < 0.05$.

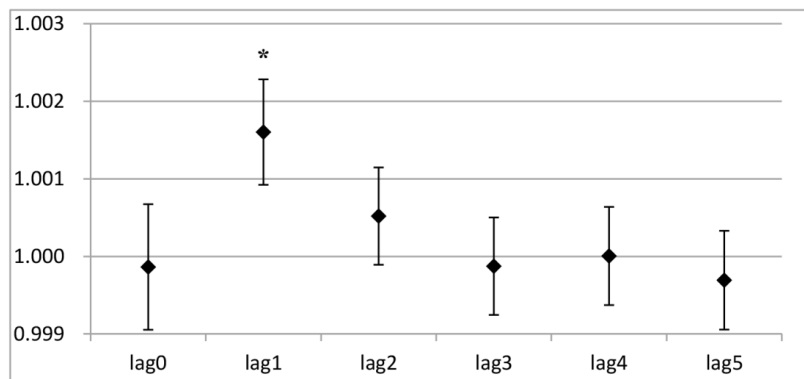


Fig. 3: B: The RRs of $PM_{2.5}$ in a single stranded effect on daily cardiovascular division outpatient visits

Y-axis indicates relative risk (RR) in the one-day lag effect analysis; * indicates $P < 0.05$.

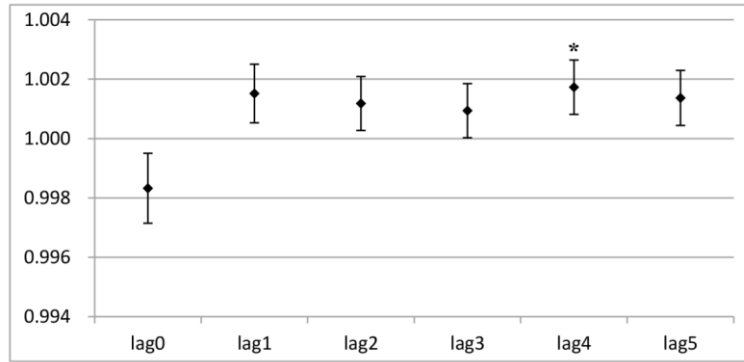


Fig. 3: C: The RRs of $PM_{2.5}$ in a single stranded effect on daily cough outpatient visits
Y-axis indicates relative risk (RR) in the one-day lag effect analysis; * indicates $P < 0.05$.

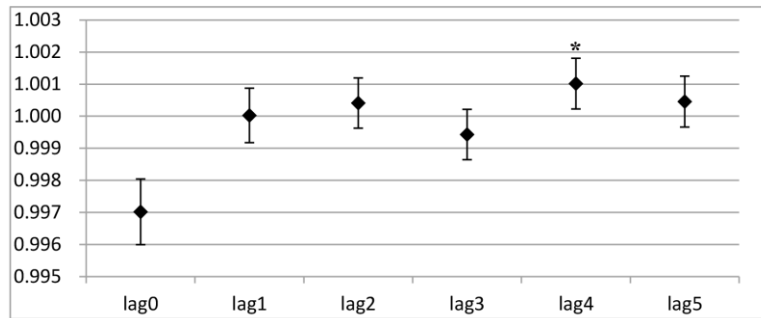


Fig. 3: D: The RRs of $PM_{2.5}$ in a single stranded effect on daily respiratory division outpatient visits
Y-axis indicates relative risk (RR) in the one-day lag effect analysis; * indicates $P < 0.05$.

After short-term exposure, a $10 \mu\text{g}/\text{m}^3$ increase in $PM_{2.5}$ was positively associated with a 0.74% increase in angina visits on the first day, as well as a 0.50% increase on the second day ($P < 0.05$) (Table 4). As shown in Table 4, with a $10 \mu\text{g}/\text{m}^3$ increase in short-term exposure to $PM_{2.5}$ on the first day (lag0), the relative risk of outpatient visits for cough and total respiratory division signifi-

cantly decreased by 0.17% and 0.30% ($P < 0.05$). However, the cough and total respiratory division visits increased significantly by 0.17% and 0.10% ($P < 0.05$) on the fifth day (lag4). No significant effect on the outpatient visits for cough and total respiratory diseases were found on the other days ($P > 0.05$) (Table 4).

Table 4: Comparison of percentage increase (and 95% CI) in relative risk of outpatient visits associated with short-term $PM_{2.5}$ exposure (per $10 \mu\text{g}/\text{m}^3$)

		<i>Increased visits (%)</i>	<i>95%CI</i>	<i>P value</i>
Cough	lag0	-0.168	-0.286% - 0.049%	* $P < 0.05$
	lag4	0.173	0.082% - 0.264%	* $P < 0.05$
Respiratory division	lag0	-0.299	-0.402% - 0.197%	* $P < 0.05$
	lag4	0.101	0.022% - 0.180%	* $P < 0.05$
Angina	lag0	0.743	0.265% - 1.221%	* $P < 0.05$
	lag1	0.486	0.074% - 0.897%	* $P < 0.05$
Cardiovascular division	lag0	--	--	-

lag1	0.16	0.092% - 0.228%	P>0.05
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Discussion

The mechanisms underlying adverse effects of PM_{2.5} on respiratory and cardiovascular systems are still not fully understood. Pulmonary and systematic oxidative stress, inflammation, atherosclerosis, and related cardiovascular disease might be involved in. The increase in short-term air pollution exposure might provoke alveolar inflammation, with release of mediators capable of causing exacerbations of lung disease (23, 24).

Interestingly, we found that short-term PM_{2.5} exposure had a significantly instant effect on cardiovascular outpatient visits while a delayed effect on respiratory visits in Beijing. Our results showed increased angina visits on the first day, reflecting the acute effect (several hours to days) on cardiovascular response. The direct effect of air pollution might be attributed to the occurrence of rapid cardiovascular responses (within a few hours); such as increased heart rate and hypertension, leading to acute exacerbation of cardiovascular disease (25-27). One of the possibilities underlying mechanisms might be attributed to autonomic nervous system (ANS) dysfunction, resulting in increased sympathetic activity and decreased parasympathetic activity, oxidative stress, and systemic inflammation. Reactive oxygen species (ROS) might also serve as acute potential mediators of PM_{2.5} effects on heart rate variability and other cardiovascular endpoints (28, 29). On the other hand, we observed the reduction of a cough and respiratory division visits on the first day and the increased visits on the fifth day. Similarly, a study in the United States showed that PM_{2.5} had lag effect on low respiratory infection (LRI) during the twenty-five months period (8). One of the explanations might be that patients usually restricted their outdoor activities including going to visit doctors on the foggy days, thus contributing to the decreased visits. Other unknown physiopathological pathways underlying mechanism of the delayed effect by short-term PM_{2.5} exposure might exist and needed to be further elucidated.

In addition, our study has the following limitations. Firstly, the nature of design for the retrospective and time series study limited our ability to draw a definite conclusion on causal effect between PM_{2.5} and outpatient visits. Secondly, we were unable to observe other types of air pollutants because the data were not available and these pollutants were not our major focus. Thirdly, the data for PM_{2.5} levels in Beijing were obtained from the monitoring station at the US Embassy in Beijing, because that was the PM_{2.5} assessment date only available for us during that time, data could reflect air quality of the entire city of Beijing. More accurate and adequate data for PM_{2.5} concentrations would be available for further analysis since Chinese government had set up more stations to monitor air quality in not only Beijing but also other surrounding areas. Fourthly, the present study was performed only in a single represented hospital in Beijing (the Guang'anmen Hospital) which might be not generalizable to all hospitals. However, we did investigate a long span of time with a larger number of visits, which reflected the effect of air pollution in Beijing on human health to a certain extent. Finally, the medical database for PM₁₀ level in our hospital was limited. Due to this limitation, we did not investigate the relationship between PM₁₀ and patient health alone, thus hard to discriminate from its complications from PM_{2.5}. That would be considered in further analysis once we have both PM₁₀ and PM_{2.5} datasets available.

Furthermore, biomedical function studies on PM_{2.5} induced genomic instability, DNA damage, autonomic dysfunction, oxidative stress, inflammation and homeostasis would be required to elucidate molecular mechanisms by which PM_{2.5} might affect human cardiovascular and respiratory health. More direct or indirect evidence on individual-level data, including changes in genomics, epigenomics, proteomics and metabolomics caused by PM_{2.5}, would be helpful to understand their physiopathological pathways and to prevent from those PM_{2.5}-associated disease

occurrences. We hence are planning to generate those data for further studies. Our findings would trigger the government to be aware of severe environment threatens and make corresponding healthy policies. That would also help to develop more effective biochemical tests and defensive medical devices.

Conclusion

The short-term exposure to high level of PM_{2.5} pollution had an instant effect on cardiovascular outpatient visits whereas a lag effect on respiratory visits in Beijing. It might severely affect human cardiovascular and respiratory health, leading to a significant increase in outpatient visits for related diseases in Beijing.

Ethical considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

Acknowledgments

We thank Dr. Hui Li, YuyanGuo, Shigang Liu helped to collect the data and do the contribution for our paper. China Academy of Chinese Medical Sciences (CACMS) Innovation Grant, ZZ0708077, supported this work.

Conflict of Interest

The authors declare that there is no conflict of interest.

References

1. ZHANG Rui, TAO Jing, WEI Jian-rong, et al (2014). Pollution levels and distribution characteristics of PM_{2.5} in indoor air. *J Environ Health*, 31(12):1082-1084.
2. Lin YC, Hsu SC, Chou CC et al (2016). Winter-time haze deterioration in Beijing by industrial pollution deduced from trace metal fingerprints and enhanced health risk by heavy metals. *Environ Pollut*, 208(Pt A):284-293.
3. FanZhang, Hai-rongCheng, Zu-wuWang, et al (2014). Fine particles (PM_{2.5}) at a CAWNET background site in Central China: Chemical compositions, seasonal variations and regional pollution events. *Atmos Environ*, 86:193-202.
4. Yang S, Dong J, Cheng B (2000). Characteristics of air particulate matter and their sources in urban and rural area of Beijing. *J Environ Sci*, 12(4):402- 409.
5. Samoli E, Peng R, Ramsay T et al (2008). Acute effects of ambient particulate matter on mortality in Europe and North America: Results from the APHENA study. *Environ Health Perspect*, 116(11):1480-6.
6. Anenberg SC, Horowitz LW, Tong DQ, West JJ (2010). An estimate of the global burden of anthropogenic ozone and fine particulate matter on premature human mortality using atmospheric modeling. *Environ Health Perspect*, 118(9):1189-95.
7. Fleischer NL, Meriardi M, van Donkelaar A et al (2014). Outdoor air pollution, preterm birth, and low birth weight: Analysis of the world health organization global survey on maternal and perinatal health. *Environ Health Perspect*, 122(4):425-30.
8. Sinclair AH, Edgerton ES, Wyzga R, Tolsma D (2010). A two-time-period comparison of the effects of ambient air pollution on outpatient visits for acute respiratory illnesses. *J Air Waste Manag Assoc*, 60(2):163-75.
9. Pope CA 3rd, Dockery DW (2006). Health effects of fine particulate air pollution: Lines that connect. *J Air Waste Manag Assoc*, 56(6):709-42.
10. Pateraki St, Asimakopoulos DN, Flocas HA, Maggos Th, Vasilakos Ch (2012). The role of meteorology on different sized aerosol fractions (PM₁₀, PM_{2.5}, PM_{2.5-10}). *Sci Total Environ*, 419:124-135.
11. David YH Pui, Sheng-ChiehChen, ZhiliZuo (2014). PM_{2.5} in China: Measurements, sources, visibility and health effects, and mitigation. *Particuology*, 13:1-26.

12. Chen SC, Tsai CJ, Chou CCK et al (2010). Ultra-fine particles at three different sampling locations in Taiwan. *Atmos Environ*, 44(4):533-540.
13. Chen SC, Tsai CJ, Huang CY et al (2010). Chemical mass closure and chemical characteristics of ambient ultrafine particles and other PM fractions. *Aerosol Sci Technol*, 44(9):713-723.
14. Yang K, Huanjing Weisheng Xue (2003). People's Medical Publishing House, 61-3.
15. Beelen R, Hoek G, van den Brandt PA et al (2008). Long-term effects of traffic-related air pollution on mortality in a Dutch cohort (NLCS-Air study). *Environ Health Perspect*, 116(2): 196-202
16. Beelen R, Stafoggia M, Raaschou-Nielsen O et al (2014). Long-term exposure to air pollution and cardiovascular mortality: An analysis of 22 European cohorts. *Epidemiology*, 25(3):368-78.
17. Gehring U, Heinrich J, Kramer U et al (2006). Long-term exposure to ambient air pollution and cardiopulmonary mortality in women. *Epidemiology*, 17(5):545-551.
18. Naess O, Nafstad P, Aamodt G et al (2007). Relation between concentration of air pollution and cause-specific mortality: Four-year exposures to nitrogen dioxide and particulate matter pollutants in 470 neighborhoods in Oslo, Norway. *Am J Epidemiol*, 165(4):435-43.
19. Cao J, Li W, Tan J et al (2009). Association of ambient air pollution with hospital outpatient and emergency room visits in Shanghai, China. *Sci Total Environ*, 407(21):5531-6.
20. Li P, Xin J, Wang Y et al (2013). The acute effects of fine particles on respiratory mortality and morbidity in Beijing from 2004 to 2009. *Environ Sci Pollut Res Int*, 20(9):6433-6444.
21. Samet JM, Dominici F, Zeger SL et al (2000). The national morbidity, mortality, and air pollution study. Part I: Methods and methodologic issues. *Res Rep Health Eff Inst*, (94 Pt 1):5-14; discussion 75-84.
22. Samet JM, Zeger SL, Dominici F et al (2000). The national morbidity, mortality, and air pollution study. Part II: Morbidity and mortality from air pollution in the united states. *Res Rep Health Eff Inst*, 94(Pt 2):5-70; discussion 71-9.
23. Maitre A, Bonnetterre V, Huillard L et al (2006). Impact of urban atmospheric pollution on coronary disease. *Eur Heart J*, 27(19):2275-84.
24. Peters A, Perz S, Doring A et al (1999). Increases in heart rate during an air pollution episode. *Am J Epidemiol*, 150(10):1094-8.
25. Fang SC, Cavallari JM, Eisen EA et al (2009). Vascular function, inflammation, and variations in cardiac autonomic responses to particulate matter among welders. *Am J Epidemiol*, 169(7):848-56.
26. Guo Y, Tong S, Zhang Y et al (2010). The relationship between particulate air pollution and emergency hospital visits for hypertension in Beijing, China. *Sci Total Environ*, 408(20):4446-50.
27. Zhang J, Zhu T, Kipen H et al (2013). Cardio respiratory biomarker responses in healthy young adults to drastic air quality changes surrounding the 2008 Beijing Olympics. *Res Rep Health Eff Inst*, (174):5-174.
28. Brook RD, Franklin B, Cascio W et al (2004). Air pollution and cardiovascular disease: A statement for healthcare professionals from the expert panel on population and prevention science of the American heart association. *Circulation*, 109(21):2655-71.
29. Nel A (2005). Atmosphere. Air pollution-related illness: Effects of particles. *Science*, 308(5723):804-6.