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We would like to submit the paper "The impact of ambient particulate matter on hospital outpatient visits for respiratory and circulatory system disease in an urban Chinese population" by Ce Wang*, Lan Feng and Kai Chen for publication in Science of the Total Environmental.

Significance and Novelty:

There are limited evidence on the association between short-term exposure to ambient particulate matter (PM) and overall hospital outpatient visits for respiratory system disease (RESD) and cardio-cerebrovascular system disease (CCD) in high-polluted countries like China. It is unclear whether this linear exposure-response relationship hold in high pollution area. A time-series study during 2013-2016 was conducted to investigate 245,442 and 430,486 hospital visits for RESD and CCD respectively from Nanjing city, China. The results showed that $PM_{2.5}$ and PM_{10} were associated with health outcome, and also implied that environmental policies should focus on the multi-pollutants joint prevention and control other than those related to PM only.

We considered this paper based on a huge Chinese dataset, with focusing on a very relevant environmental topic as fitting exactly in your journal's scope. All authors approved the paper, which has not been published previously nor is being considered by another peer-reviewed journal. This manuscript includes 6000 words, five figures and two tables, and supplementary material contains five tables and two figures.

We hope you consider our paper worthwhile of peer review and publication, and are looking forward to your response.

Sincerely,
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- PM was associated with overall outpatient visits of cardiopulmonary health.
- The health impact of air pollution in Nanjing may be due to mixed-pollution.
- The relationship curve presented non-linear across the full range of exposures.
- Estimated risks in warm season were higher than those in cold season.

The impact of ambient particulate matter on hospital outpatient visits for respiratory and circulatory system disease in an urban Chinese population

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Abstract

There are limited evidence on the association between short-term exposure to ambient particulate matter (PM) and overall hospital outpatient visits for respiratory system disease (RESD) and cardio-cerebrovascular system disease (CCD) in high-polluted countries like China. Though previous epidemiological studies of RESD and CCD generally applied a linear relationship of the acute PM effects, it is unclear whether this linear exposure-response relationship hold in high pollution area. In this study, a time-series study during 2013 through 2016 was conducted to investigate 245,442 and 430,486 hospital visits for RESD and CCD respectively from Nanjing city, China. A combination of logistic generalized additive model (GAM) and distributed lag nonlinear models (DLNM) was used to evaluate the exposure-response associations. The results disclosed that a 10 $\mu g/m^3$ increase in $PM_{2.5}$ and PM_{10} concentration on the current day of exposure (lag 0) was associated with 0.36% (95% CI: -0.02%-0.73%) and 0.33% (0.07%-0.60%) increase in RESD; and 0.42% (0.00%-0.85%) and 0.37% (0.08%-0.67%) increase in CCD. The exposure-response association was approximately linear within 0-150 $\mu g/m^3$ of PM concentration and non-linear across the full range of exposures. There were no any obvious threshold concentration below which air pollutant had no effect on RESD and CCD. The effects of PM on RESD and CCD were sensitive to additional adjustment for co-pollutants, indicating the health effects of air pollution mixture in Nanjing city. Though not statistically significant, the estimated risks in warm season were higher than those in cold season, suggesting potential synergistic effects of ambient PM pollution and temperature on triggering

RESD and CCD.

Keywords: respiratory; cardiovascular; outpatient visits; air pollution; $PM_{2.5}$; PM_{10}

1. Introduction

It has been shown that short-term and long-term exposure to ambient particulate matter (PM) are associated with adverse health outcomes for respiratory (e.g., asthma, chronic obstructive pulmonary disease) and cardio-cerebrovascular disease (e.g., coronary heart disease, stroke), and even mortality (Apte et al., 2015; Burnett et al., 2014; Chen et al., 2017a; Miller et al., 2007; Wang et al., 2018a; Zheng et al., 2018b). Previous epidemiological studies have estimated the relative risk (RR) and excess risk (ER) of short-term PM exposure on respiratory system disease (hereafter referred to RESD) and cardio-cerebrovascular system disease (hereafter referred to CCD) to evaluate population health (Chan et al., 2006; Kim et al., 2012; Tao et al., 2014; Tramuto et al., 2011; Vahedian et al., 2017). These results in general presented “heterogeneity” characteristic, probably due to different species compositions, air pollution sources and population characteristics, etc. For establishing effective control policy, it is necessary to evaluate the local impact of ambient PM pollution on population health, particularly in heavy polluted regions.

In general, China was subjected to air pollution since 1950s, and received sufficient attention during two decades (Fang et al., 2016; Liu et al., 2017a). Besides healthy years of life lost, it also caused a large amount of economic costs, e.g., approximately 25.2 billion USD in health expenditure caused by $PM_{2.5}$ pollution in 2030 (Cohen et al., 2017; Xie et al., 2016; Zhang et al., 2008). More regular observation of air pollutants ($PM_{2.5}$, PM_{10}, SO_2, NO_2, CO, O_3) was implemented since 2013 based on a wide national monitoring network (Liang et al., 2017; Wang et al., 2018c). During 2013, China experienced serious air pollution episode and PM was considered as the primary air pollutants. Then, the government issued an *Action Plan on Prevention and Control of Air Pollution* which was intended to intensify the comprehensive treatment to reduce the multi-pollutant emissions (State Council, 2013; Chen et al., 2018a). However, till now, very few studies in China had assessed the association between PM concentrations and outpatient visits of overall cardiopulmonary morbidity (Cai et al., 2015; Yang et al., 2016; Zhang et al., 2018; Zhao et al., 2017). Furthermore, before 2013, precise estimated impacts of PM pollution exposure were insufficient due to limited availability of air quality observations in China. Different from western countries, regular outpatient visit (first-come first-served) in China greatly outnumbered hospital admission which meant patient’s condition was serious, and would broadly reflected the acute health effect associated with air pollution (Guo et al., 2018; Tian et al., 2018b). As a result, it can be considered as a more comprehensive “indicator” to characterize the exposure-response relationship. Hence, it is essential to implement an overall epidemiologic evidence of adverse health effects caused by ambient PM pollution based on a refined air pollution monitoring and health outcome records since 2013.

Nanjing city, which is the capital of Jiangsu Province, China, has an area of approximately 6587 km^2 and the population has increased from 6.43 million in 2013 to 6.63 million in 2016 (NMBS, 2014-2017). According to daily average concentration of each pollutant in 2013, day counts for exceeding the Ambient Air Quality Standards (AAQS) Grade II were 310 days for particulate matter with an aerodynamic diameter of 2.5μm or less ($PM_{2.5}$) (AAQS: 35 $\mu g/m^3$), 314 days for particulate matter with an aerodynamic diameter between 2.5μm and 10μm (PM_{10}) (AAQS: 70 $\mu g/m^3$), respectively (MEE, 2016). The overall pollution level was abated in the following years. However, compared with western countries, the city was still subjected to high level of air pollution. In this study, we examined the exposure-response relationship between PM ($PM_{2.5}$ and PM_{10}) and outpatient visit for RESD and CCD across all ages, as well as combined effects of other air pollutants, during 2013 through 2016 in Nanjing City.

2. Methods

2.1 Data collection

Daily hospital outpatient visit for RESD (all diseases related to respiratory system) and CCD (all diseases related to circulatory system) from 2013 through 2016 were collected from Nanjing Drum Tower Hospital. For some missing historical records on Chinese holidays, (e.g., Spring Festival, Mid-Autumn Festival, National Day), which accounted for 2.3% of the total records, piecewise cubic Hermite interpolation was applied to transform the original records to equidistant data at daily intervals. During weekends, the population could only get access to regular hospital visit till noon, resulting in much lower records on weekends than those on weekdays (see

Supplemental Fig.S1 and Fig.S2). Thus, we excluded the visits on weekends in this analysis. The daily concentrations of air pollutants at nine air quality monitoring stations across the city (see Fig.1), i.e., 24-hour average concentration of $PM_{2.5}$, PM_{10}, SO_2, NO_2, and CO, and the maximum daily 8-hour moving average concentration of O_3, from 2013 to 2016 were obtained from Qingyue Open Environmental Data Center (https://data.epmap.org). There are no missing data for daily air pollution concentrations. The matched meteorological observations, i.e., air temperature (ATEMP) and relative humidity (RHUM), were derived from China Meteorological Data Service Center (CMDC) (http://data.cma.cn).

2.2 Statistical analysis

Generalized additive model (GAM) (see Equ. (1)) was established to estimate the RR of PM pollution on RESD and CCD with a quasi-Poisson regression, controlling for measured confounders (e.g., RHUM) and unmeasured confounders (e.g., time trends) (Dominici et al., 2002; Peng and Dominici, 2008). Distributed Lag Non-Linear Model (DLNM) was used to evaluate the cumulative effects of air temperature (ATEMP) which considered the non-linear and delayed effect of ATEMP on health (Gasparrini, 2011). The single lag model was specified with daily $PM_{2.5}$ and PM_{10} concentration in various lag days (lag 0-lag 7), and the ER was presented as percent increase with 95% confidence interval (CI) in hospital visit per 10 $\mu g/m^3$ increase in air pollutant concentration (see Equ. (2)). Then, moving average lag model (lag 01-lag 07) was used to evaluate the cumulative effect of PM pollution within eight days (Arbex et al., 2009; Liu et al., 2013). For evaluating the stability of pollutant effect, the multi-pollutant model was applied to estimate confounding effect of multiple air pollutants (Duan et al., 2015; Mostofsky et al., 2012; Zhang et al., 2017). The lag which yielded the largest effect for the air pollutant of interest in single lag model was applied in the multi-pollutant model when adjusted for co-pollutant, i.e., SO_2, NO_2, CO and O_3 (Chen et al., 2016b; Zhu et al., 2018). $PM_{2.5}$ and PM_{10} were separately input the multi-pollutant model as they showed highly collinearity (Table S1). We also explored potential effect of RESD and CCD by cold (October to March) and warm season (April to September), and tested for important differences between two seasons (Zeka et al., 2006). The exposure-response curves were illustrated to show the shape of relationship between PM ($PM_{2.5}$ and PM_{10}) concentrations against hospital visits (RESD and CCD) using univariate penalized cubic regression spline smooths (degree of freedom, $df = 3$).

$$Log\left[E\left(Y_t\right)\right] = \alpha + \beta x_{t-l} + \eta Cb.temp_L + \delta DOW + s\left(TIME, df\right) + s\left(RHUM, df\right) \quad (1)$$

$$ER = 100 \times \left[e^{IQR \times \left(\beta_{t-l} \pm 1.96SE\right)} - 1\right] \quad (2)$$

$E\left(Y_t\right)$ represented the expected count of hospital visits for RESD and CCD at day t. The pollutant x_{t-l} (e.g., $PM_{2.5}$) was included in the model at a lag l that might range from 0 to 7 days lag in single lag model. α was the interception. β represented the log-relative risk of RESD and CCD associated with a unit increase of air pollutant concentration. SE showed the standard error of β . $Cb.temp_L$ was cross-basis function representing an exposure-lag-response bi-dimensional function for $PM_{2.5}$ and PM_{10}, respectively, and L referred to the maximum lag day. DOW was the dummy variable for day of week (Monday to Friday) and adjusted as categorical variables.

$TIME$ was numeric value of 1-1461 (a total of 4 years). Penalized cubic regression splines (S) were used to control calendar time ($TIME$) and relative humidity ($RHUM$). η and δ were the coefficients for $Cb.temp_L$ and DOW receptively. We used 3 df for $RHUM$, and the cross-basis matrix was generated using a natural cubic spline with 4 df for ATEMP and 4 df for lag days (Chen et al., 2016a; Liu et al., 2017b; Tian et al., 2017). The df for long-term time trend ($df = 6$ per year) was selected because of data reduction on hospital visits during weekends (Guo et al., 2018; Guo et al., 2010), and the maximum lag of ATEMP (max $lag = 14$) were chosen in main analysis. We also assessed the robustness of the results in terms of the df values for time trend (5 and 7 per year) and maximum lag (7 and 21) (SM Table S2-S3). All analysis of GAM and DLNM were implemented using MGCV package in R-language software version 3.4.4 (R Core Team, 2016). The statistical tests were two-sided and *p*-value < 0.05 was considered as statistically significant. In order to facilitate comparison, the results were presented as the percent change in daily hospital visit per 10 μg/m^3 increase of air pollutant concentration.

3. Results

3.1 Hospital visits and environmental observations

During 2013-1016, the total hospital visits for RESD and CCD were 279,416 and 479,397, respectively, and daily records ranged from 35-462 and 31-624 person-time, respectively. The annual averages of $PM_{2.5}$, PM_{10} and NO_2 concentrations were still in violation of corresponding AAQS, and the maximum concentration of $PM_{2.5}$, PM_{10},

SO_2, NO_2, CO and O_3 were 327, 446, 139, 142, 4752 and 280 μg/m^3, respectively (see Table 1). Interquartile range (IQR) of $PM_{2.5}$ and PM_{10} concentration were 47μg/m^3 and 76.5 μg/m^3 during study period. $PM_{2.5}$ concentrations were highly positively associated with PM_{10} ($r = 0.926$, $p<0.05$), and both of them showed moderately positive correlation with SO_2, NO_2 and CO concentrations ($r = 0.634$-0.728, $p<0.05$), however, they slightly negatively associated with O_3. In general, air pollutants were negatively correlated with ATEMP and RHUM, except for O_3 concentrations which were directly proportional to ATEMP (see SM Table S1). In general, both hospital visits and environmental variables displayed periodic variations (see Supplemental Fig.S2).

3.2 Exposure-response relationships

Fig.2 illustrated the percent changes for RESD and CCD associated with a 10 μg/m^3 increase in each air pollutant concentration at different lag structures. In general, after adjustment for calendar time, day of the week and weather conditions, the increments of hospital visits were highest on current day (lag 0) for $PM_{2.5}$ and PM_{10} concentration, i.e., a 10 μg/m^3 increase in $PM_{2.5}$ and PM_{10} was associated with a 0.36% (95% CI: -0.02%, 0.73%) ($p=0.065$) and 0.33% (0.07%, 0.60%) increase in daily hospital visits on RESD, respectively; 0.42% (0.00%, 0.85%) and 0.37% (0.08%, 0.67%) increase in daily hospital visits on CCD, respectively. PM_{10} also exerted a high effect for RESD (0.33% increase; 95% CI: -0.15%-0.82%) and CCD (0.37%; -0.17%-0.92%) when 7 days moving average exposures (lag 07), however, no significance relationship could be found. The more detailed results were listed in Table S4.

We also examined the robustness of exposure-responses relationship with inclusion of potential confounding factors, i.e., SO_2, NO_2, CO and O_3, based on multi-pollutant model (see Table 2). In general, the significant positive associations were still maintained between cardiopulmonary health and PM in multi-pollutant models after adjusted for O_3, and the associations became non-significant after adjusted for SO_2, NO_2 and CO (except for the effect of PM_{10} on RESD). Specifically, ER of RESD and CCD caused by $PM_{2.5}$ was slightly increased by 0.08% and 0.09% after inclusion of O_3; For PM_{10}, ER of RESD was slightly increased by 0.05% and 0.04% after inclusion of CO and O_3, respectively, and ER on CCD was slightly increased by 0.04% after inclusion of O_3. For the other cases, the estimated effects of $PM_{2.5}$ and PM_{10} were alleviated and became insignificant with inclusion of corresponding co-pollutants in multi-pollutant models.

Fig.3 illustrated the exposure-response relationships associated with each air pollutant exposure (0-99th percentile of concentration ranges of $PM_{2.5}$: 0-220 $\mu g/m^3$; PM_{10}: 0-320 $\mu g/m^3$). The curves shared the similar tendency for RESD and CCD when exposed to the same air pollutant. Approximately, they presented essentially linear relationships within 0-150 $\mu g/m^3$ of PM concentrations. The curves for $PM_{2.5}$ and PM_{10} tended to become nonlinear at the higher concentration probably due to the data scarcity at this range. The uncertainty of relative risk presented increase at higher concentration of PM (>150 $\mu g/m^3$). There were no any obvious threshold concentration below which air pollutant had no effect on RESD and CCD.

3.3 Effect modification by season

It was clearly shown that the association between air pollutants (lag 0 for $PM_{2.5}$ and PM_{10}) and hospital visits presented similarity in cold and warm season (Fig.4). Mostly, the significant positive associations were found, only except for the impact of $PM_{2.5}$ on RESD in cold season. In general, PM had slightly greater impact on RESD and CCD in warm season than in cold season. Particularly, ER of RESD and CCD was increased by 0.18% (0.05%, 0.31%) in cold season and 0.35% (0.20%, 0.50%) in warm season associated with a 10 $\mu g/m^3$ increase in PM_{10}, respectively. There was no evidence of effect modification by season because of the marginally difference of log-relative risk (see Table S5).

4. Discussion

This was the first study in China to apply outpatient visits of overall respiratory and circulatory system diseases. From a representative hospital in Nanjing city, short-term exposure to PM was significantly associated with cardiopulmonary morbidity which covered 279,416 and 479,397 outpatient visits for RESD and CCD, respectively. The exposure-response association was approximately linear within 0-150 $\mu g/m^3$ of PM concentration and non-linear across the full range of exposures. This tendency was similar with the health effect of long-term exposure to air pollution (Burnett et al., 2018). Our findings also demonstrated mixed-pollution in Nanjing city other than PM only. It implied the control of other gaseous pollutants should not be ignored for programmatically protect human health. It should also be noted that apparent health effects of PM were still observed even the concentrations were below the current AAQS of China ($PM_{2.5}$: 35 μg/m^3; PM_{10}: 70 μg/m^3).

Hospital admission was frequently used as morbidity outcome in developed counties. In USA and Europe, several investigations showed the impacts of PM on hospital admission of RESD and CCD from residential population across all ages (Capraz et al., 2017; Granados-Canal et al., 2005; Host et al., 2008; Talbott et al., 2014; Tomaskova et al., 2016; Wordley et al., 1997), e.g., a 10 μg/m^3 increase in $PM_{2.5}$ concentration was associated with an increase of 1.50%-2.50% and 0.50%-1.20% in RESD and CCD admissions, respectively; while a 10 μg/m^3 increase in PM_{10} concentration resulted in an increase of 0.61%-2.40% and 1.24%-2.10% in RESD and CCD admissions, respectively. In general, the estimated epidemiological evidences were relatively higher in western countries compared with results in this study, possibly due to: Firstly, it might involve the different compositions of air pollutants with complex chemical components, which potentially presented spatial heterogeneity (Mo et al., 2018; Qiao et al., 2014); Secondly, the saturation effect and harvest effect might be present when PM pollution maintained a high level (Chen et al., 2017b). In fact, the exposure-response relationships (see Fig.3) displayed non-linear across the full range of exposures, particularly in high polluted region (Pope, 2015); Thirdly, outpatient visits were applied rather than hospital admissions in main analysis. In addition, the inconsistency might also be attributed to the influence of population structure and susceptibility, e.g., heterogeneous in socioeconomic status, educational levels, age distribution (Tony Cox, 2013). We obtained a similar ERs compared with limited researches in China. A case-crossover study across 26 largest cities showed that RESD and CCD admissions with ER of 0.26% (0.22%-0.31%) and 0.23% (0.20%-0.26%) respectively were significantly associated with 10 μg/m^3 increase in PM$_{2.5}$ concentration, and for PM$_{10}$, the results presented 0.21% (0.17%-0.24%) and 0.15% (0.13%-0.17%), respectively (Liu et al., 2018). ER of outpatient visits for respiratory diseases increased by 0.37% (0.26%-0.48%) with a 10 μg/m^3 increase in PM$_{2.5}$ concentration in Shanghai (patients aged≧15 years) (Wang et al., 2018d). A case in Ningbo observed the adverse effects of PM$_{2.5}$ on CCD hospital visits, i.e., 10 μg/m^3 increase in PM$_{2.5}$ concentration was significantly associated with an ER of 0.60% (0.00%, 1.10%) (patients aged ≥18 years) (Zheng et al., 2018a). For each 10 μg/m^3 increase in the PM$_{2.5}$ concentration, outpatient visits for RESD were increased by 0.53% (0.22%-0.84%) in Lanzhou (Chai et al., 2019).

In this study, the single-pollutant models (see Fig.2 and Table S4) disclosed the maximum effect of air pollutants at current-day (lag 0) exposures to PM$_{2.5}$ and PM$_{10.}$ It indicated that the population in Nanjing city were susceptible to exposures to these pollutants and suffered acute response during very short period. It was consistent with previous studies (Phung et al., 2016; Tian et al., 2018a). E.g., a case study from London demonstrated that the highest association with total cardiovascular diseases was observed with PM$_{10}$ at current day (Atkinson et al., 1999). Some specific-city studies also obtained lagged response to PM but with different maximum lag effects (Luo et al., 2018; Qiu et al., 2018). In general, we found that the risk estimates for PM lost statistical significant after adjusted for co-pollutants in multi-pollutant models except for O_3 (see Table 2), potentially due to its weak correlation with other air pollutants ($r = -0.206 \sim -0.053$) which resulted in the reduction in the possibility of confounding. Meanwhile, the confidence intervals of RRs were widened, potentially because collinearity among air pollutants and the loss of precision from additional covariates. Particularly, for both RESD and CCD, the adverse effect of PM was greatly influenced after adjusted for SO_2 and NO_2, which was similar with previous study in Wuhan city (Wang et al., 2018b). It was difficult to exactly evaluate the independent effect of PM due to a strong correlation between PM and SO_2, NO_2, CO. These findings implied that air pollution in Nanjing city could be considered as the consequence of “mixed-pollution”. We could infer that multiple air pollutants including other gaseous pollutants appeared most responsible for increased risk on cardiopulmonary health of population in Nanjing city. As a result, the corresponding health effect are indispensable in the future works. Relatively, PM had more serious impact on cardiopulmonary health of population in Nanjing city during warm season than cold season (see Fig.4). Nanjing city is known as one of “four ovens” cities in China, with generally hot summers. It is thus necessary to explore the synergistic effects of air pollution and temperature on triggering RESD and CCD, particular on high temperature days (Chen et al., 2018b; Lee et al., 2018; Sun et al., 2019).

The study had several limitations. Firstly, as in most time-series studies, the average daily concentrations of air pollutant across monitoring stations were used for population exposure level. This might result in measurement error because individual exposure depended on many cases, e.g., outdoor activities, location of dwelling.

However, this error tends to be non-differential and might result in an underestimation of the PM effects (Chen et al., 2017b).Secondly, the historical records of hospital visits were collected from only one hospital in the city, therefore, and it might affect the generalizability of the epidemiological results. Thirdly, this study only covered four years because the regular monitoring of air pollutants was implemented since 2013. Fourthly, the records on weekends which only covered "half a day" resulted in data discontinuity. Therefore, the main analysis did not include weekends. Finally, more studies on the potential non-linear associations between high-level air pollution and respiratory and circulatory system diseases are needed.

5. Conclusions

This time-series study of cause-specific hospital visits provided an opportunity to determine associations of PM exposures with overall respiratory and circulatory system diseases in Nanjing, China. This is one of the few studies on short-term effects of ambient air pollutants on hospital outpatient visits based on a largescale electronic registry database in China. Multiple air pollutants could be responsible for the adverse health outcomes in Nanjing city. In the future, more comprehensive exposure data is needed to explore non-linear exposure-response associations and synergistic effects. Overall, our findings also implied that, to deal with air pollution mixture, environmental policies should focus on the multi-pollutants joint prevention and control other than those related to PM only.

Conflict of interest

All authors declare that they have no actual or potential competing financial interests.

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Figure caption

Fig.1 The location of Nanjing City, air quality monitoring stations and Nanjing Drum Tower Hospital (9 stations located in downtown area: S1 - Mai gao qiao, S2 - Cao chang men, S3 - Shan xi lu, S4 - Zhong hua men, S5 - Rui jin lu, S6 - Xuan wu hu, S7 - Pu kou, S8 - Ao ti zhong xin, S9 - Xian lin da xue cheng; symbol of red-cross represents the hospital)

Fig.2 Percent change (95% CI) of hospital admissions on RESD and CCD associated with each IQR increase in air pollutant concentrations with different lag days (red triangle represented single lag effect and square represented moving average lag effect)

Fig.3 The exposure-response curve of pollutants concentrations and hospital admissions on RESD and CCD ($PM_{2.5}$ (Lag 0), PM_{10} (Lag 0))

Fig.4 Percent change (95% CI) of RESD and CCD associated with each IQR increase in $PM_{2.5}$ (Lag 0) and PM_{10} (Lag 0) concentration by season (cool and warm)

Table 1

Table 1 Statistics of hospital visits on RESD, CCD, air pollutants and meteorological observations during 2013 through 2016 in Nanjing City

Variable	RESD	CCD	PM$_{2.5}$	PM$_{10}$	SO$_2$	NO$_2$	CO	O$_3$	ATEMP	RHUM
Units	persons	persons	μg/m^3	μg/m^3	μg/m^3	μg/m^3	mg/m^3	μg/m^3	°C	%
Min result	35	31	4	8	4	14	0.327	5	-6.7	26
Max result	462	624	327	446	139	142	4.752	280	34.6	97
Mean	235.10	412.34	64.02	110.66	24.27	50.39	1.01	96.25	16.66	72.09
Median	236	425	53	98	20	45	0.916	89	17.8	73
Std dev	62.92	99.70	42.09	63.10	16.04	20.85	0.41	49.30	9.03	13.89
Pct5	130	215.6	17	34	8	24	0.53	28	2.2	48
Pct25	196	367	35	65	14	35	0.741	57	8.7	63
Pct50	236	425	53	98	20	45	0.916	89	17.8	73
Pct75	277.75	480	82	141.5	30	62	1.181	129	23.9	83
Pct95	342	539	145	232	53	91	1.859	190.9	30.89	93
IQR	81.75	113	47	76.5	16	27	0.44	72	15.2	20

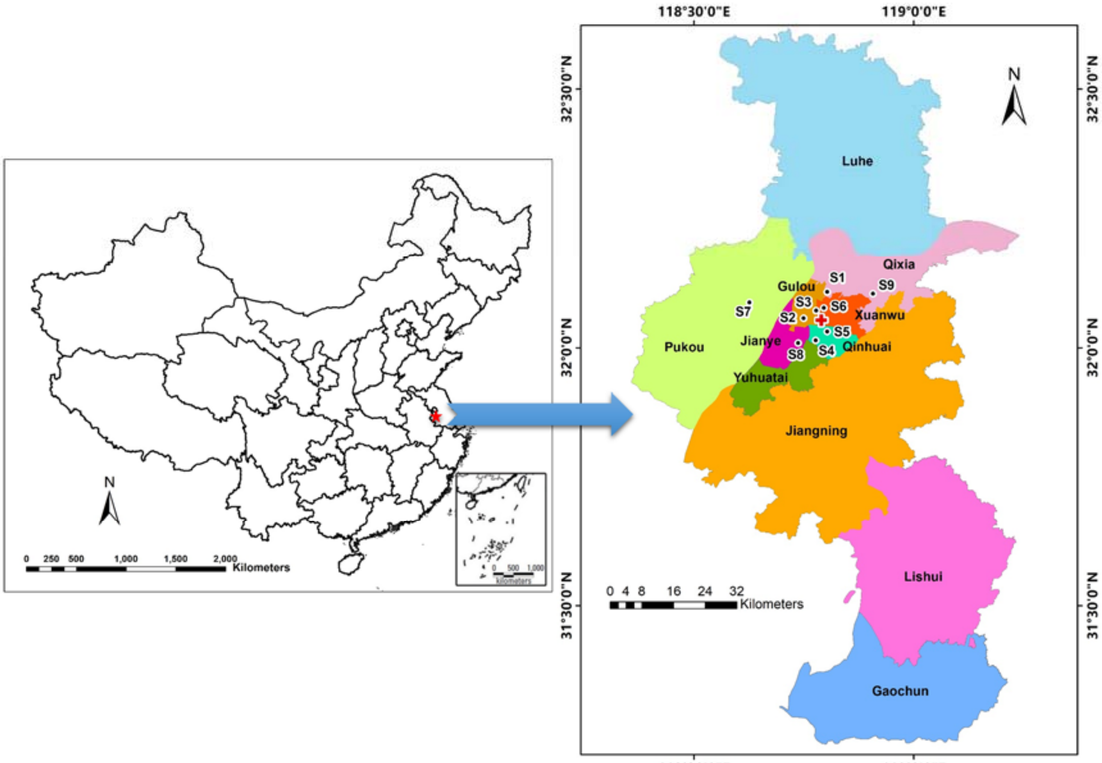
Note: Std dev represents standard deviation; Pct represents percentile; RESD represents overall respiratory system disease; CCD represents overall cardio-cerebrovascular system disease; ATEMP represents air temperature; RHUM represents relative humidity.

Table 2

Table 2 ER of RESD and CCD associated with each IQR increase in air pollutant concentrations based on two-pollutant models

Air pollutants		ER in RESD (%)	95% CI (%)	ER in CCD (%)	95% CI (%)
$PM_{2.5}$		0.35	-0.02, 0.73	0.42	0.00, 0.85
	$+SO_2$	-0.03	-0.47, 0.41	-0.16	-0.65, 0.33
	$+NO_2$	-0.20	-0.64, 0.24	-0.15	-0.64, 0.35
	+CO	0.37	-0.15, 0.84	0.23	-0.32, 0.77
	$+O_3$	0.43	0.05, 0.81	0.51	0.08, 0.94
PM_{10}		0.33	0.07, 0.60	0.37	0.08, 0.67
	$+SO_2$	0.08	-0.23, 0.39	-0.03	-0.38, 0.32
	$+NO_2$	-0.08	-0.40, 0.25	-0.05	-0.41, 0.31
	+CO	0.38	0.04, 0.72	0.28	-0.09, 0.65
	$+O_3$	0.37	0.10, 0.63	0.41	0.11, 0.70

Note: in two-pollutant model, $PM_{2.5}$ (Lag 0), PM_{10} (Lag 0), SO_2 (Lag 0), NO_2 (Lag 0), CO (Lag 0) and O_3 (Lag 0) concentration was used respectively.


N
0 250 500 1,000 1,500 2,000 Kilometers
0 500 1,000 kilometers
118°30'0"E
119°0'0"E
32°30'0"N
32°0'0"N
31°30'0"N
N
Luhe
Qixia
S1
S9
Gulou
S3
S6
S7
S2
Xuanwu
S5
Pukou
Jianye
Qinhuai
S8
S4
Yuhuatai
Jiangning
Lishui
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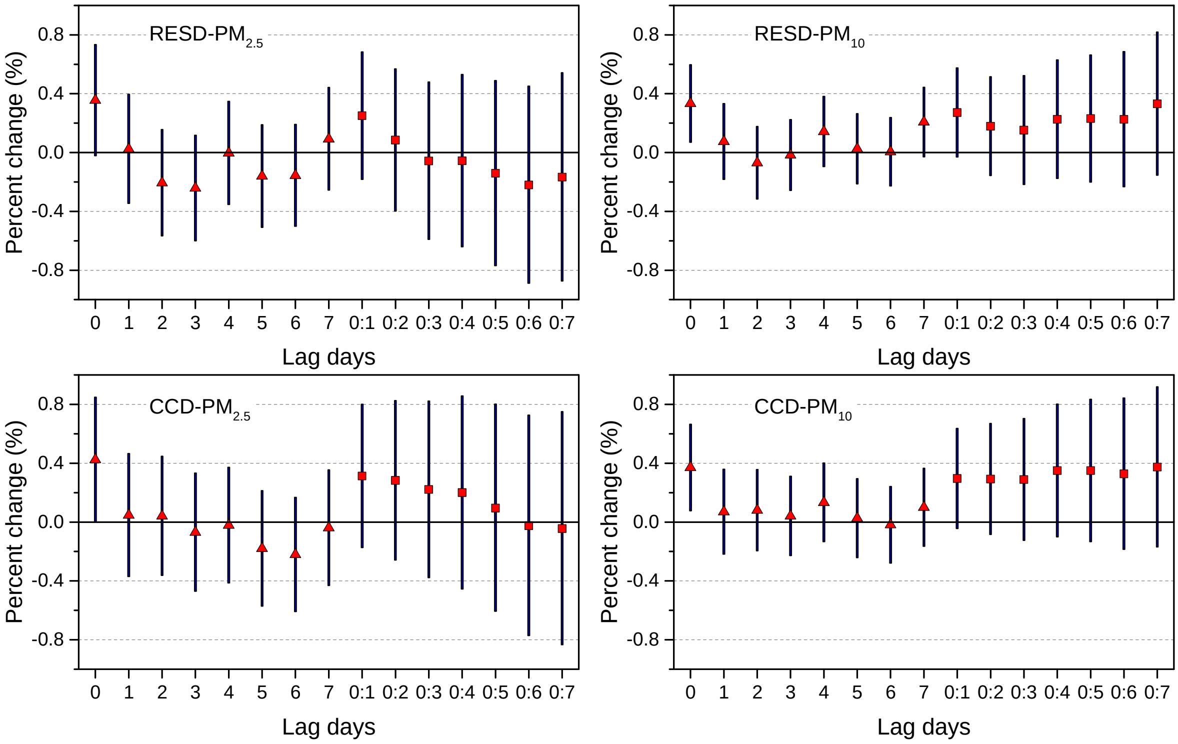
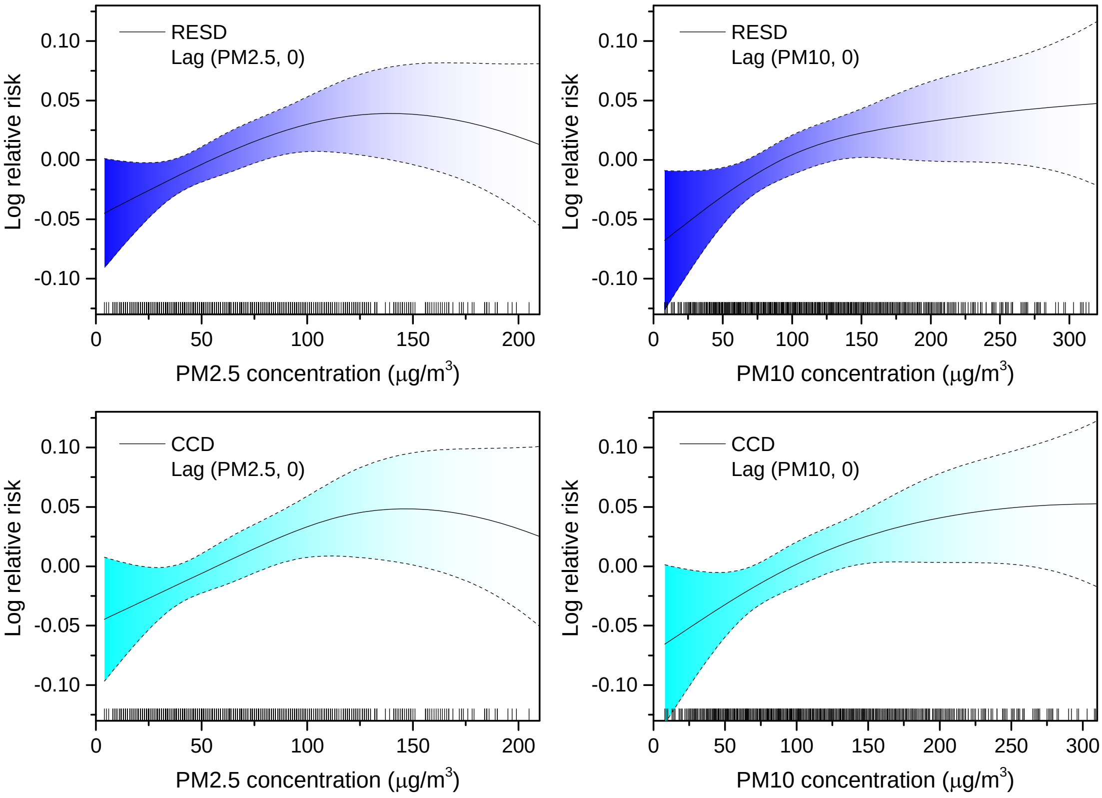
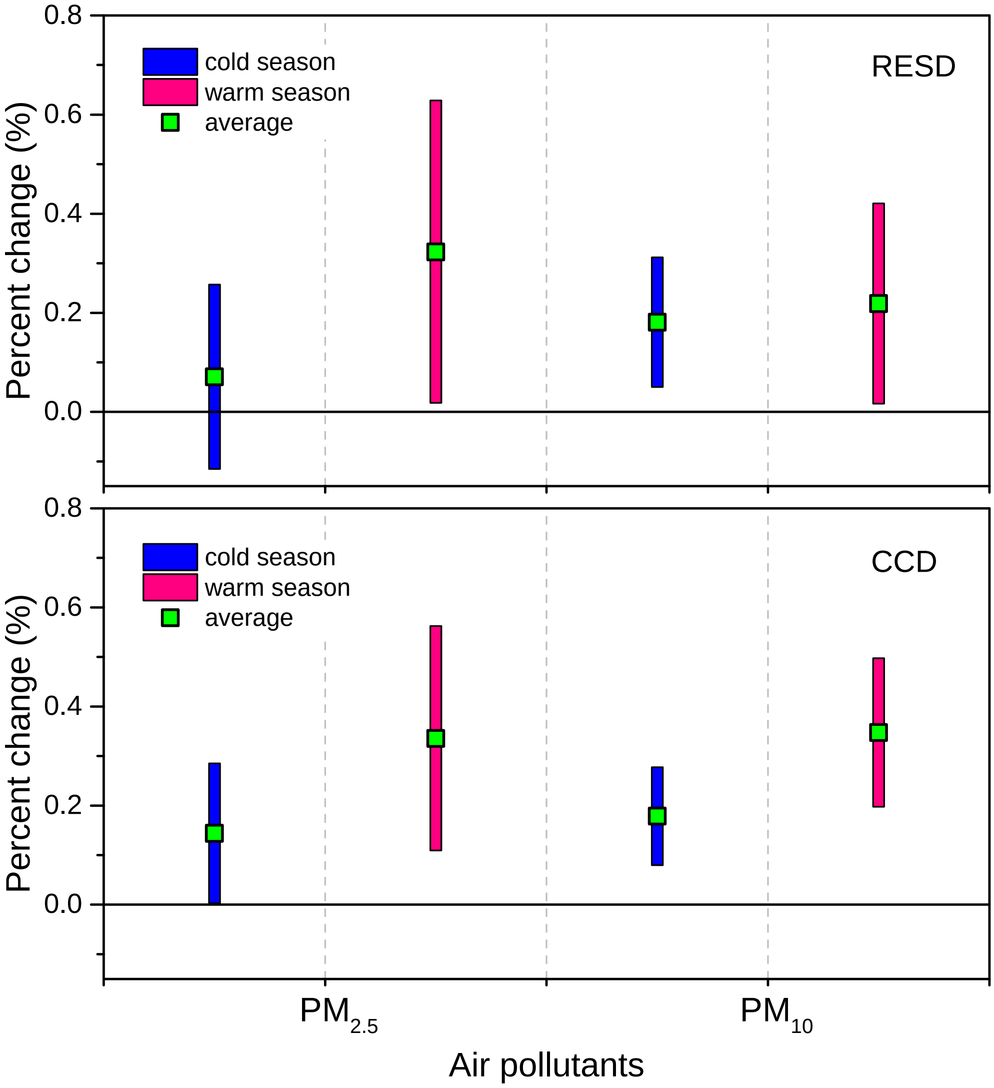

RESD-PM$_{2.5}$
RESD-PM$_{10}$
CCD-PM$_{2.5}$
CCD-PM$_{10}$
Percent change (%)
0.8
0.4
0.0
-0.4
-0.8
0
1
2
3
4
5
6
7
0:1
0:2
0:3
0:4
0:5
0:6
0:7
Lag days


RESD
Lag (PM2.5, 0)
Log relative risk
0.10
0.05
0.00
-0.05
-0.10
0
50
100
150
200
PM2.5 concentration (μg/m3)
RESD
Lag (PM10, 0)
Log relative risk
0
50
100
150
200
250
300
PM10 concentration (μg/m3)
CCD
Lag (PM2.5, 0)
Log relative risk
PM2.5 concentration (μg/m3)
CCD
Lag (PM10, 0)
Log relative risk
PM10 concentration (μg/m3)


0.8
0.6
0.4
0.2
0.0
Percent change (%)
cold season
warm season
average
RESD
0.8
0.6
0.4
0.2
0.0
Percent change (%)
cold season
warm season
average
CCD
PM2.5
PM10
Air pollutants

Supplementary Material

The impact of ambient particulate matter on hospital outpatient visits for respiratory and circulatory system disease in an urban Chinese population

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Table S1

Table S1 Pearson correlations between concentrations of air pollutants and meteorological observations

Variables	SO_2	NO_2	CO	O_3	$PM_{2.5}$	PM_{10}	ATEMP	RHUM
SO_2	1							
NO_2	0.651[a]	1						
CO	0.563[a]	0.594[a]	1					
O_3	-0.100[a]	-0.166[a]	-0.206[a]	1				
$PM_{2.5}$	0.634[a]	0.652[a]	0.709[a]	-0.116[a]	1			
PM_{10}	0.713[a]	0.728[a]	0.662[a]	-0.053[a]	0.926[a]	1		
ATEMP	-0.346[a]	-0.364[a]	-0.353[a]	0.494[a]	-0.338[a]	-0.320[a]	1	
RHUM	-0.469[a]	-0.302[a]	-0.037	-0.297[a]	-0.102[a]	-0.327[a]	0.134[a]	1

a: two-tailed test of significance is used (p<0.05)

Table S2

Table S2 ER of RESD and CCD caused by $PM_{2.5}$ and PM_{10} with a maximum lag of 7, 14 and 21days (6 df per year of calendar time was used in DLNM)

df = 6, per year of calendar time	RESD		CCD	
Maximum lag = 7	ER (%)	95% CI (%)	ER (%)	95% CI (%)
Lag (PM25, 0)	0.34	-0.04, 0.72	0.42	-0.00, 0.85
Lag (PM10, 0)	0.33	0.07, 0.59	0.39	0.09, 0.68
Maximum lag = 14	ER (%)	95% CI (%)	ER (%)	95% CI (%)
Lag (PM25, 0)	0.36	-0.02, 0.73	0.42	0.00, 0.85
Lag (PM10, 0)	0.33	0.07, 0.60	0.37	0.08, 0.67
Maximum lag = 21	ER (%)	95% CI (%)	ER (%)	95% CI (%)
Lag (PM25, 0)	0.30	-0.08, 0.68	0.38	-0.04, 0.81
Lag (PM10, 0)	0.27	0.00, 0.53	0.31	0.01, 0.60

Table S3

Table S3 ER of RESD and CCD caused by $PM_{2.5}$ by different df per year of calendar time (maximum lag = 14 was used in DLNM)

df, per year for calendar time	RESD		CCD	
	ER (%)	95% CI (%)	ER (%)	95% CI (%)
df = 5	0.39	0.02, 0.77	0.47	0.05, 0.89
df = 6	0.36	-0.02, 0.73	0.42	0.00, 0.85
df = 7	0.35	-0.04, 0.73	0.43	0.00, 0.86

Note: Lag (PM25, 0) was used to display percent increase of hospital visits on RESD and CCD associated with an IQR increase of $PM_{2.5}$ concentration by different degrees of freedom per year.

Table S4

Table S4 ER (%) and 95% CI of RESD and CCD for an IQR increase in pollutants concentrations with different lag days in single-pollutant models

Lag Days	RESD		CCD	
	$PM_{2.5}$	PM_{10}	$PM_{2.5}$	PM_{10}
Lag 0	0.36 (-0.02, 0.73)	0.33 (0.07, 0.60)	0.42 (0.00, 0.85)	0.37 (0.08, 0.67)
Lag 1	0.02 (-0.35, 0.40)	0.07 (-0.18, 0.33)	0.05 (-0.37, 0.47)	0.07 (-0.22, 0.36)
Lag 2	-0.21 (-0.57, 0.16)	-0.07 (-0.32, 0.18)	0.04 (-0.36, 0.45)	0.08 (-0.20, 0.36)
Lag 3	-0.24 (-0.60, 0.12)	-0.02 (-0.26, 0.22)	-0.07 (-0.47, 0.33)	0.04 (-0.23, 0.31)
Lag 4	0.00 (-0.35, 0.35)	0.14 (-0.10, 0.38)	-0.02 (-0.41, 0.37)	0.13 (-0.13, 0.40)
Lag 5	-0.16 (-0.51, 0.19)	0.03 (-0.21, 0.27)	-0.18 (-0.57, 0.21)	0.03 (-0.24, 0.30)
Lag 6	-0.16 (-0.50, 0.19)	0.01 (-0.23, 0.24)	-0.22 (-0.61, 0.17)	-0.02 (-0.28, 0.24)
Lag 7	0.09 (-0.26, 0.44)	0.21 (-0.03, 0.44)	-0.04 (-0.43, 0.35)	0.10 (-0.16, 0.37)
Lag 01	0.25 (-0.18, 0.68)	0.27 (-0.03, 0.58)	0.31 (-0.17, 0.80)	0.30 (-0.04, 0.64)
Lag 02	0.08 (-0.40, 0.57)	0.18 (-0.16, 0.52)	0.28 (-0.26, 0.83)	0.29 (-0.08, 0.67)
Lag 03	-0.06 (-0.59, 0.48)	0.15 (-0.22, 0.52)	0.22 (-0.38, 0.82)	0.29 (-0.12, 0.70)
Lag 04	-0.06 (-0.64, 0.53)	0.23 (-0.18, 0.63)	0.20 (-0.45, 0.86)	0.35 (-0.10, 0.80)
Lag 05	-0.14 (-0.77, 0.49)	0.23 (-0.20, 0.66)	0.10 (-0.61, 0.80)	0.35 (-0.13, 0.84)
Lag 06	-0.22 (-0.89, 0.45)	0.23 (-0.23, 0.69)	-0.03 (-0.77, 0.73)	0.33 (-0.19, 0.84)
Lag 07	-0.17 (-0.87, 0.54)	0.33 (-0.15, 0.82)	-0.04 (-0.83, 0.75)	0.37 (-0.17, 0.92)

Table S5

Table S5 ER (%) and 95% CI of RESD and CCD for an IQR increase in pollutants concentrations with cold and warm season in single-pollutant models

Pollutant and statistics	RESD		CCD	
	Cold	Warm	Cold	Warm
$PM_{2.5}$	0.07 (-0.12, 0.26)	0.32 (0.02, 0.63)	0.14 (0.00, 0.29)	0.34 (0.11, 0.56)
Estimate	7.07×10^{-5}	3.22×10^{-4}	1.44×10^{-4}	3.35×10^{-4}
SE	9.49×10^{-5}	1.55×10^{-4}	7.20×10^{-5}	1.15×10^{-4}
Difference of estimates and 95% CI	-2.52×10^{-4} (-3.57×10^{-4}, 3.56×10^{-4})		-1.91×10^{-4} (-2.66×10^{-4}, 2.66×10^{-4})	
PM_{10}	0.18 (0.05, 0.31)	0.22 (0.02, 0.42)	0.18 (0.08, 0.28)	0.35 (0.20, 0.50)
Estimate	1.81×10^{-4}	2.18×10^{-4}	1.78×10^{-4}	3.47×10^{-4}
SE	6.67×10^{-5}	1.03×10^{-4}	5.03×10^{-5}	7.62×10^{-5}
Difference of estimates and 95% CI	-3.74×10^{-5} (-2.40×10^{-4}, 2.40×10^{-4})		-1.69×10^{-4} (-1.79×10^{-4}, 1.79×10^{-4})	

Note: in single-pollutant model, $PM_{2.5}$ (Lag 0) and PM_{10} (Lag 0) concentration was used respectively.

Figure S1

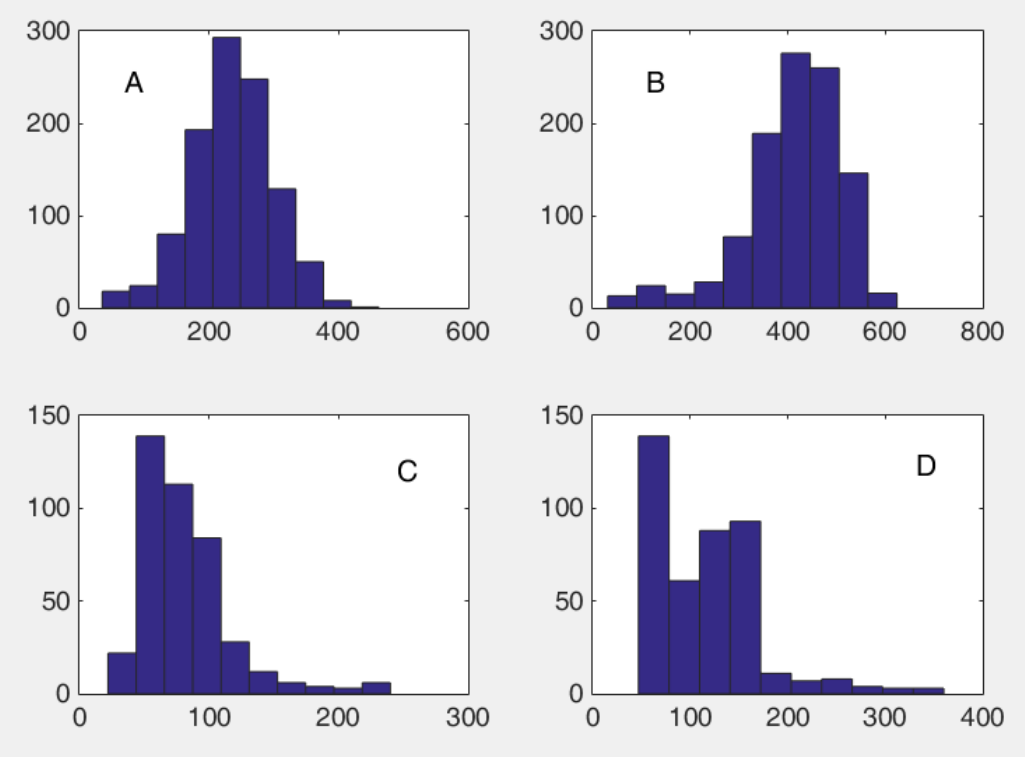

Fig.S1 Histogram plots for RESD and CCD during 2013 through 2016. (A) RESD on weekdays; (B) CCD on weekdays; (C) RESD on weekends; (D) CCD on weekends.

Figure S2

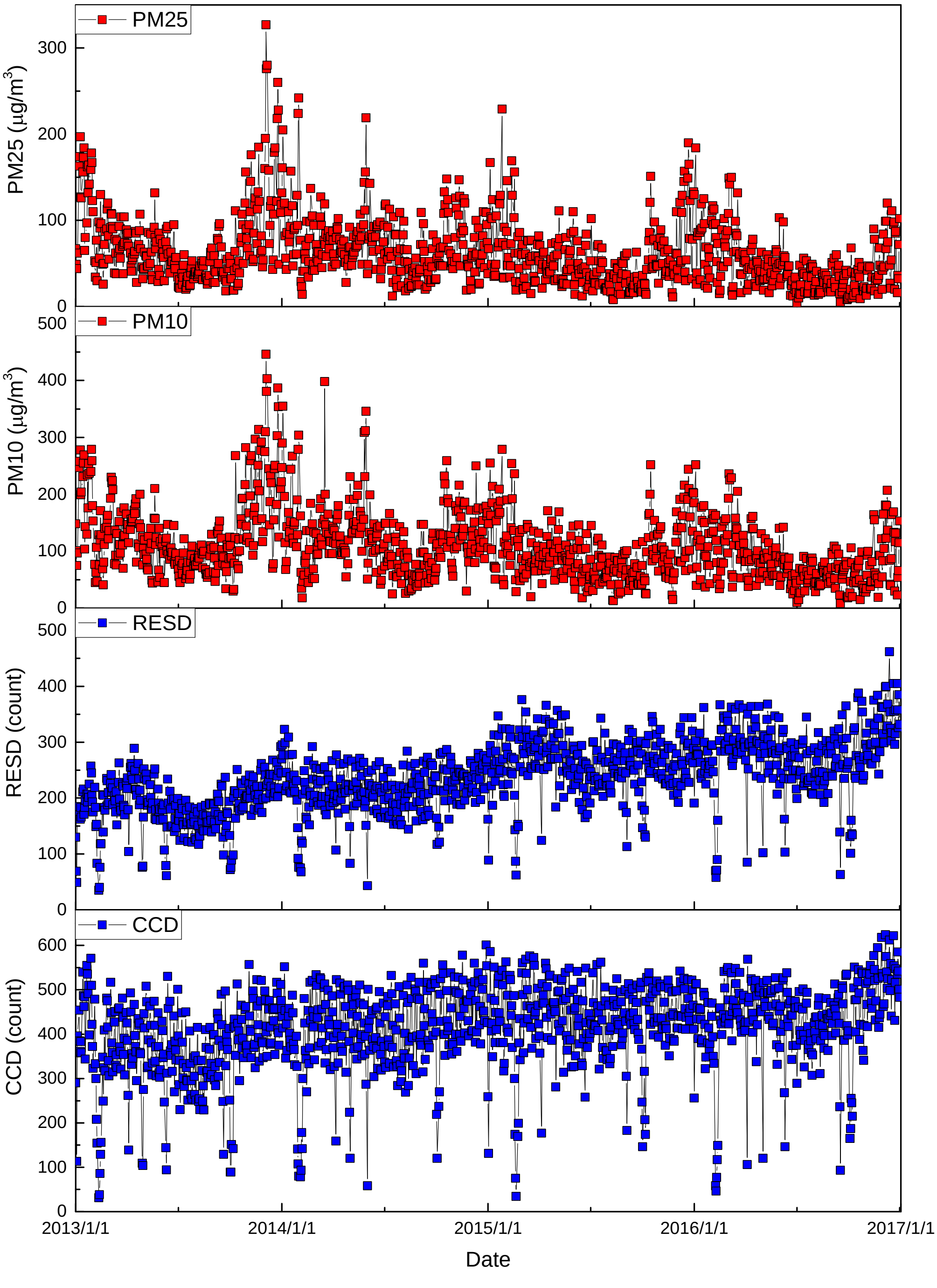

Fig.S2 Time-series of outpatient visits for RESD and CCD, and concentrations of $PM_{2.5}$ and PM_{10} during 2013 through 2016 in Nanjing city