Individual Exposure to Ambient PM2.5 and Hospital Admissions for COPD in 110 Hospitals: A Case-Crossover Study in Guangzhou, China

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Individual exposure to ambient PM$_{2.5}$ and hospital admissions for COPD in 110 hospitals: a case-crossover study in Guangzhou, China

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ABSTRACT

Few studies have evaluated the short-term association between hospital admissions and individual exposure to ambient particulate matter (PM$_{2.5}$). Particularly, no studies focused on hospital admissions for chronic obstructive pulmonary disease (COPD) at individual level. We assessed the short-term effects of PM$_{2.5}$ on hospitalization admissions for COPD in Guangzhou, China, during 2014-2015, based on satellite-derived estimates of ambient PM$_{2.5}$ concentrations at 1-km resolution near the residential address as individual-level exposure for each patient. 40,002 patients with COPD admitted to 110 hospitals were included in this study. A time-stratified case-crossover design with conditional logistic regression models was applied to assess the effects of PM$_{2.5}$ based on 1-km grid data of aerosol optical depth provided by National Aeronautics and Space Administration on hospital admissions for COPD. Further, we performed stratified analyses by individual demographic characteristics and season of hospital admission. 10 $\mu g/m^3$ increase in individual-level PM$_{2.5}$ was associated with an increase of 1.6% (95% confidence interval [CI]: 0.6%, 2.7%) in hospitalization for COPD at lag of 0-5 days. The impact of PM$_{2.5}$ on hospitalization for COPD was greater significantly in male and patients admitted in summer and accordingly the impacts may be exacerbated in the context of global warming. Our study strengthened the evidence for the adverse effect of PM$_{2.5}$ based on satellite-based individual-level exposure data.

Key words: PM$_{2.5}$; satellite; COPD; hospitalization; case-crossover design
Capsule: short-term effects of PM$_{2.5}$ on hospitalization admissions for COPD in individual level.
1. Introduction

Fine particulate matter with aerodynamic diameters <2.5 μm (PM$_{2.5}$) is a great concern for public health, since it can penetrate into the lung deeply and induce respiratory diseases (Chen et al. 2017; Jiang et al. 2016; Kloog et al. 2012; Liu et al. 2018). Chronic obstructive pulmonary disease (COPD) is a major chronic respiratory disease, and the prevalence of COPD reached 251 million globally in 2016 (Hopke et al. 2019; Salimi et al. 2018; World Health Organization 2017). Elucidating the impact of exposure to PM$_{2.5}$ on hospitalizations for COPD can help for developing interventions and thereafter reducing the burden of diseases.

An increasing number of studies have associated exposure to PM$_{2.5}$ with hospital admissions for respiratory diseases, including COPD (Harrison and Yin 2000; Hopke et al. 2019; Kim et al. 2015; Lin et al. 2020). However, the estimates of the association between PM$_{2.5}$ and hospital admissions were not always consistent (Belleudi et al. 2010; Kim et al. 2015; Kloog et al. 2014; Ko et al. 2007; Lin et al. 2020; Rice et al. 2015). Geographical variations in the estimates of associations suggested in prior studies may be due to the disparities in the level of air pollutant concentration, regional climates and socio-economical levels, and characteristics of local residents (Kumar et al. 2018). Thus, reports of different study locations can be beneficial for delineating a comprehensive contour of the adverse health effect of PM$_{2.5}$.

More importantly, previous studies examined health effects of ambient PM$_{2.5}$ exposure by using the PM$_{2.5}$ level of the nearest station as individual exposure, or more
commonly using the average PM$_{2.5}$ level of a few monitoring stations as a proxy of exposure for the whole population (Harrison and Yin 2000; Hopke et al. 2019; Kim et al. 2015; Lin et al. 2020; Santus et al. 2012; Zhang et al. 2019). The limited number of monitoring stations are not necessarily representative enough for the exposure level of the population in a location and thus there may be bias in such proxy (Goldman et al. 2011; Liu et al. 2017; Samet et al. 2000). In addition, the PM$_{2.5}$ level calculated from selected monitoring stations ignores the spatial gradient of the exposure level among patients which may lead to misclassification of the exposure as well (Faustini et al. 2012; Liu et al. 2018; Moolgavkar and Suresh 2000; Tian et al. 2018). With the development of satellite monitoring technology, some models have been developed to estimate the level of ambient PM$_{2.5}$ based on satellite data (Danesh et al. 2019; Guo et al. 2018; Lin et al. 2018). We previously proposed a method for a high-coverage and accurate estimation of daily PM$_{2.5}$ at 1-km resolution in mainland China based on the satellite data of atmospheric aerosol optical depth (AOD) with solving the problem of high missing rate, which is usually ignored in previous studies and leads to inaccurate estimation of PM$_{2.5}$ (Chen et al. 2020). The 1-km estimates of PM$_{2.5}$ which can be matched with the residential addresses are expected to be a more precise proxy for the exposure level of PM$_{2.5}$ for the subjects involved in studies on health effect of air pollution and the effect estimates tends to be more reliable (Hennig et al. 2020; Wong et al. 2015; Woo et al. 2020). Several cohort studies have applied satellite-derived exposure data to quantify long-term effects of PM$_{2.5}$ on health outcomes, with the data of addresses of subjects (Danesh et al. 2019; Guo et al. 2018; Lin et al. 2018). To our
knowledge, there is no previous study assessing the short-term effects of PM$_{2.5}$ on hospital admissions for COPD using satellite-based estimates of PM$_{2.5}$ at 1-km resolution or higher as individual exposure level, although Kloog et al. (2014) estimated the short-term effects on all-cause hospital admissions using PM$_{2.5}$ at a $10 \times 10$ km spatial resolution in the Mid-Atlantic.

Guangzhou is one of the largest cities in the south of China (latitude: 23°07′N; longitude 113°15′E), covering an area of 7434.4 km$^2$ with 14.9 million permanent residents. The average annual PM$_{2.5}$ concentration in Guangzhou was from 37.0-46.8 $\mu g/m^3$ between 2014 and 2015, which was much higher than the air quality guideline of WHO, 10 $\mu g/m^3$ (World Health Organization, 2005). The present study aims to assess the short-term effects of ambient PM$_{2.5}$ on hospital admissions for COPD in Guangzhou, China, during 2014-2015, based on satellite-derived estimates of daily PM$_{2.5}$ concentrations at 1-km resolution near the residential address as individual-level exposure for each individual.

2. Materials and methods

2.1. Data sources

The data on the home page of electronic medical records for all individual hospitalization due to COPD admitted in 110 hospitals during 2014–2015 in Guangzhou were retrieved from the Guangzhou Health Information Center, which is a part of the National Health Statistics Network Direct Report system having standard
operation procedure and sophisticated measures for quality control (National Health and Family Planning Commission of the People's Republic of China 2007). Principal diagnosis was coded according to the International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10). We extracted the information for all individuals admitted due to COPD (ICD-10 code: J40-J44), including sex, age, residential address, occupational class, marital status and date of admission. Daily meteorological data, including daily mean temperature and relative humidity, were download from the National Meteorological Center (http://data.cma.cn/).

The study was approved by the ethical committee of Southern Medical University, and patient informed consent was waived, since only de-identified data derived from the official health information system were provided and analyzed anonymously.

2.2. Exposure assessment

In our previous study, we applied extreme gradient boosted (XGBoost) imputation to fill the missing gap of 1-km multiangle implementation of AOD obtained from National Aeronautics and Space Administration, and the coverage of AOD was significantly increased from 15.46% to 98.64% on average in mainland China (Chen et al. 2020). Then, a combined method of non-linear exposure-lag-response model and XGBoost was applied to predict daily 1×1 km PM$_{2.5}$ concentrations using meteorological variables and the XGBoost-interpolated AOD, with high predictive accuracy (Cross-validation $R^2=0.81$ for Guangzhou) (Chen et al. 2020). Daily levels of PM$_{2.5}$ were well estimated for all grids including those without monitoring stations. Next, each patient’s
residential address was matched to the 1-km grid cell according to the longitude and
latitude, and then the corresponding daily PM$_{2.5}$ concentrations in the grid cell was
treated as the proxy of daily exposure for the patient.

2.3. Statistical analysis

We adopted a time-stratified case-crossover design to assess the associations between
PM$_{2.5}$ and hospital admissions for COPD. This approach has been widely applied to
evaluate health effects of air pollution in which each case serves as his/her own control
(Levy et al. 2001; Szyszkowicz et al. 2018; Tsai et al. 2013). In this study, the case days
were defined as the dates of admission while the referent days were those fell on the
same day of the week within the same month as the case day. Since the case period and
the referent period is very close in time, this design avoids the influence of individual
characteristics and long-term and seasonal trends on the effect estimation (Bateson and
Schwartz 1999; Janes et al. 2005).

We used conditional logistic regression models to quantify the impacts of PM$_{2.5}$
on hospitalizations due to COPD. The model was of the following form:

$$\text{logit}(P_i) = \alpha_i + \text{NS}(T_{06}, df = 3) + \text{NS}(RH_{06}, df = 3) + \delta\text{Holiday} + \beta\text{PM}_{2.5}$$

$P_i$ and $\alpha_i$ are the probability of hospitalization and the intercept for stratum $i$.

According to previous studies, a natural cubic spline (NS) with three degrees of
freedom ($df$s) was applied for the moving average of temperature ($T$) and relative
humidity ($RH$) at a lag of 0-6 days (Liu et al. 2017; Lu et al. 2019; Tian et al. 2018). In
addition, an indicator variable of public holidays ($Holiday$) was also included (Hwang
\( \delta \) is the regression coefficient for Holiday. Here, we considered the effects of PM\(_{2.5}\) on hospitalizations for COPD at lags up to six days. Both of single-day and multiple-day lags were considered in this study (Devries et al. 2016; Hwang et al. 2017; Liu et al. 2018).

Next, we conducted a stratified analysis by sex, age (<65 and \( \geq \)65 years), occupational class (the unemployed, blue-collar workers, and white-collar workers), marital status (married, unmarried, and divorce/widowed) and season of hospital admission (winter [December to February], spring [March to May], summer [June to August], and autumn [September to November]) (Ma et al. 2019). The differences in the effects of PM\(_{2.5}\) on hospital admissions for COPD between two subgroups were tested via the \( Z \) test with the following formula:

\[
Z = \frac{\beta_1 - \beta_2}{\sqrt{SE(\beta_1)^2 + SE(\beta_2)^2}}
\]

where \( \beta_1 \) and \( \beta_2 \) represent the regression coefficients of PM\(_{2.5}\) for two subgroups, and \( SE(\beta_1) \) and \( SE(\beta_2) \) are the corresponding standard errors. Sensitivity analyses were conducted to assess the robustness of the results by changing \( df \)s for temperature and relative humidity from 3 to 2–6.

All statistical tests were two-sided and \( P < 0.05 \) was considered statistically significant. We performed all data analyses using R software (version 3.5.1, R Foundation for Statistical Computing).

3. Results
A total of 40,002 patients admitted to 110 hospitals with COPD from 2014 to 2015 were
included in the analysis (Figure 1). Patients hospitalized for COPD were predominately
males (74.1%) and those aged ≥65 years (83.8%) (Table 1). The unemployed and
married individuals accounted for 81.5% and 93.3% of the hospital admissions for
COPD. It seemed that the differences in the proportions of hospitalizations for COPD
across four seasons were small (Table 1). Average satellite-derived 1-km-resolution
PM$_{2.5}$ concentrations during the study period were 42.6 $\mu g/m^3$ (ranges from 6.0 to
164.4 $\mu g/m^3$) for COPD patients. Daily temperature and relative humidity were on
average 22.2°C (ranges from 5.2 to 31.4°C) and 79.8% (ranges from 31.5 to 97.5%)
during the study period (Table 2).

The effect of PM$_{2.5}$ on hospital admission for COPD was higher on the current day
in the single-day model, meanwhile the effect was the greatest for the moving average
of 0-5 days than for other lagged days (Table 3). It was estimated that 10 $\mu g/m^3$ increase
in PM$_{2.5}$ was associated with an increase of 1.6% (OR=1.016, 95% confidence interval
[CI]: 1.006, 1.027) in hospitalization for COPD at a lag of 0-5 days.

We estimated the ORs of hospitalizations for COPD per 10 $\mu g/m^3$ increase in
individual exposure level of PM$_{2.5}$, at lag0-5 days, for different subgroups. The effect
of PM$_{2.5}$ on hospital admission for COPD was statistically significant for males (OR:
1.023, 95% CI: 1.011, 1.036), while the effect was statistically non-significant for
females, and the difference in the effects of PM$_{2.5}$ was statistically significant by sex. It
was witnessed that hospitalizations for COPD (OR: 1.020, 95% CI: 1.008, 1.032)
increased with PM$_{2.5}$ among people ≥65 years of age. However, the difference in the
effects of PM$_{2.5}$ was not statistically significant by age. It seemed that the effect of PM$_{2.5}$ on hospitalizations for COPD was weaker for the unemployed and divorce/widowed people than for other subgroups. A larger OR (1.052 [95% CI: 1.021, 1.084]) was estimated for patients admitted due to COPD in summer than in other seasons (Figure 2 and Table S1).

According to the results of sensitivity analysis, the effect estimates were not substantially changed when changing the df/s for temperature and relative humidity from 3 to 2-6 (Table S2).

4. Discussion

We estimated the short-term effect of ambient PM$_{2.5}$ on hospital admissions for COPD based on satellite-derived 1-km-resolution estimates of PM$_{2.5}$ in Guangzhou, China. We found the significant association between hospital admissions for COPD with the ambient PM$_{2.5}$ at individual exposure level, and the effect of PM$_{2.5}$ was stronger in male and patients admitted during the warm season. Our findings provided more solid evidence for the association between ambient PM$_{2.5}$ and hospital admissions for COPD with individual exposure data.

In this study, we estimated that 10 $\mu g/m^3$ increase in PM$_{2.5}$ was associated with an increase of 1.6% in hospitalization for COPD at a lag of 0-5 days. Statistically significant associations between PM$_{2.5}$ and hospital admissions for COPD were also reported in other studies using ground-level monitoring data of PM$_{2.5}$ but the magnitude
of estimates varied across study locations. For example, the corresponding effect estimates for COPD admissions were 2.06% at lag 0-6 days in Ningbo, China (Zhang et al. 2019) and 3.10% at lag 0-2 days in Milan Italy (Santus et al. 2012). Lin et al (2020) shown that the effect of PM$_{2.5}$ on hospital admissions for COPD was highest at a distributed lag of 0-7 days (relative risks=1.073, 95% CI: 1.016, 1.133) in Yinzhou District, China. Inconsistency was further observed in studies which reported statistically non-significant associations of PM$_{2.5}$ with hospital admissions for COPD in some other cities (Belleudi et al. 2010; Liu et al. 2018; Peel et al. 2005; Slaughter et al. 2005; Stieb et al. 2009). A certain number of previous studies examined the associations with the data of a single or a few hospitals in which the sample size may be insufficient for the inference and therefore non-significant results were obtained (Peel et al. 2005; Slaughter et al. 2005). Previous studies on short-term associations between exposure to air pollutants and health outcomes commonly used the average measurements obtained from a few monitoring stations as the proxy of exposure (Lin et al. 2020; Santus et al. 2012; Tian et al. 2018; Zuo et al. 2019). Measurements of air pollutant concentrations obtained from monitoring stations can capture the temporal variation of the average exposure level. However, using the average measurements from a limited number of monitoring stations cannot fully reflect the spatial variation in exposure level of subjects which may lead to bias in the estimates of associations between air pollutants and health outcomes due to the measurement error of exposure (Hwang et al. 2017; Liu et al. 2017; Tian et al. 2018; Xie et al. 2019; Zuo et al. 2019). On this issue, an accurate proxy of individual exposure using satellite-based PM$_{2.5}$ with
high resolution is crucial when investigating health effects of air pollution. In addition, different levels of air pollutant concentrations, demographic characteristics and healthcare facilities, and the criteria for hospital admission may explain the variations in estimates of the associations between PM$_{2.5}$ and hospital admissions for COPD (Kumar et al. 2018).

Exploring the potential effect modifiers of PM$_{2.5}$ on hospital admissions can be helpful for identifying potentially susceptible population and for developing a more accurately targeted intervention. The differences in the effects of PM$_{2.5}$ on hospital admissions for COPD by sex was statistically significant in our study, which was in accordance with prior studies (Lin et al. 2018). A higher effect was observed in male, and the difference between gender may be due to lifestyle behaviors (tobacco and alcohol consumption, exercise and diet) (Xie et al. 2019). As for the disparities by age, we found that the effects of PM$_{2.5}$ on hospitalizations were statistically significant in individuals ≥65 years of age for COPD, while non-significant results were observed in those <65 years. Such finding was also observed in a study which explored the association between PM$_{2.5}$ and hospital admissions for acute exacerbation of COPD in southwestern Taiwan, China (Hwang et al. 2017). A study in Hefei, China, claimed that the effect of PM$_{2.5}$ on COPD hospitalization differed by age, although the statistical significance of the difference was not examined (Xie et al. 2019). Regarding the disparities in the associations of PM$_{2.5}$ with hospitalizations for COPD by occupational class and marital status, relatively small sample size for some subgroups in the present study may account for the lack of statistical power to detect significance effects.
We found that the effects of PM$_{2.5}$ on hospitalizations for COPD varied by season, with the highest estimates of the effects occurring in summer. The variation in the effects of PM$_{2.5}$ by season could be due to that people tend to participate in outdoor activities and may open windows more frequently during warm months, leading to more exposure to ambient air pollutants (Stafoggia et al. 2016; Tian et al. 2018). In the context of global warming, temperature is expected to increase, and heat wave will occur more frequently (Lee et al. 2018; Zhang et al. 2017). Consequently, adverse health impacts of exposure to PM$_{2.5}$ are very likely to be exacerbated in the future given the higher effects of PM$_{2.5}$ on hospitalizations for COPD observed in summer. Further studies are required to clarify the underlying mechanism of the variation in effects of PM$_{2.5}$ by season and then inform better preparedness for the potentially elevated burden associated with PM$_{2.5}$ in the future.

The current study was subject to several limitations. First, we did not assess the effects of exposure to other air pollutants on hospitalizations for COPD, since the individual exposure data tailored for each patient were not available. Second, the sample sizes were relatively small for some subgroups which may be insufficient for the inference of the effects of PM$_{2.5}$ for these subgroups. Third, the current study controlled for the effects of temperature, relative humidity and holiday on hospitalizations for COPD, but other potentially influential factors, such as respiratory virus activity, were not considered because of the unavailability of data. Fourth, although compared with the PM$_{2.5}$ averaged from the monitoring stations, the satellite-based PM$_{2.5}$ is more accurate reflected spatial gradient at 1×1 km solution, this address-
level exposure estimation is still a proxy of individual exposure to outdoor PM$_{2.5}$, and we cannot rule out the residual measurement error. Further studies can be conducted to achieve more accurate estimates of effects of PM$_{2.5}$ with the use of personal exposure data accounting for both of outdoor and indoor exposure levels.

5. Conclusions

We found the significant association between hospital admissions for COPD with the ambient PM$_{2.5}$, and our study strengthened the evidence for the adverse effect of PM$_{2.5}$ based on satellite-based individual-level exposure data. The impact of PM$_{2.5}$ on hospitalization for COPD was greater in male and patients admitted in summer and accordingly the impacts may be exacerbated in the context of global warming.

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Author contribution

Jie-Qi Jin: Conceptualization, Writing-original draft, Formal analysis. Dong Han: Resources, Writing-review & editing. Qi Tian: Writing-review & editing. Zhao-Yue Chen: Resources, Writing-review & editing. Yun-Shao Ye: Resources, Writing-review & editing. Qiao-Xuan Lin: Writing-review & editing. Chun-Quan Ou:
Data availability

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Consent for publication

Not applicable.

Ethics approval and consent to participate

The study was approved by the ethical committee of Southern Medical University, and patient informed consent was waived, since only de-identified data were collected and the data were analyzed anonymously.

Competing interests

The authors declare they have no competing financial interests.
References

Bateson, T.F., Schwartz, J., 1999. Control for Seasonal Variation and Time Trend in Case-Crossover Studies of Acute Effects of Environmental Exposures. Epidemiology (Cambridge, Mass.) 10, 539-544.

Belleudi, V., Faustini, A., Stafoggia, M., Cattani, G., Marconi, A., Perucci, C.A., Forastiere, F., 2010. Impact of Fine and Ultrafine Particles on Emergency Hospital Admissions for Cardiac and Respiratory Diseases. EPIDEMIOLOGY 21, 414-423.

Chen, R., Yin, P., Meng, X., Liu, C., Wang, L., Xu, X., Ross, J.A., Tse, L.A., Zhao, Z., Kan, H., Zhou, M., 2017. Fine Particulate Air Pollution and Daily Mortality. A Nationwide Analysis in 272 Chinese Cities. Am J Respir Crit Care Med 196, 73-81.

Chen, Z., Jin, J., Zhang, R., Zhang, T., Chen, J., Yang, J., Ou, C., Guo, Y., 2020. Comparison of Different Missing-Imputation Methods for MAIAC (Multiangle Implementation of Atmospheric Correction) AOD in Estimating Daily PM2.5 Levels. Remote Sensing 12, 3008.

Danesh, Y.M., Wang, Y., Di Q, Zanobetti, A., Schwartz, J., 2019. Long-term exposure to PM2.5 and ozone and hospital admissions of Medicare participants in the Southeast USA. ENVIRONMENT INTERNATIONAL 130, 104879.

DeVries, R., Kriebel, D., Sama, S., 2016. Low level air pollution and exacerbation of existing copd: a case crossover analysis. Environmental Health 15.

Faustini, A., Stafoggia, M., Cappai, G., Forastiere, F., 2012. Short-Term Effects of Air Pollution in a Cohort of Patients With Chronic Obstructive Pulmonary Disease.
Goldman, G.T., Mulholland, J.A., Russell, A.G., Strickland, M.J., Klein, M., Waller, L.A., Tolbert, P.E., 2011. Impact of exposure measurement error in air pollution epidemiology: effect of error type in time-series studies. Environ Health 10, 61.

Guo, C., Zhang, Z., Lau, A., Lin, C.Q., Chuang, Y.C., Chan, J., Jiang, W.K., Tam, T., Yeoh, E.K., Chan, T.C., Chang, L.Y., Lao, X.Q., 2018. Effect of long-term exposure to fine particulate matter on lung function decline and risk of chronic obstructive pulmonary disease in Taiwan: a longitudinal, cohort study. Lancet Planet Health 2, e114-e125.

Harrison, R.M., Yin, J., 2000. Particulate matter in the atmosphere: which particle properties are important for its effects on health? SCIENCE OF THE TOTAL ENVIRONMENT 249, 85-101.

Hennig, F., Geisel, M.H., Kälsch, H., Lucht, S., Mahabadi, A.A., Moebus, S., Erbel, R., Lehmann, N., Jöckel, K., Scherag, A., Hoffmann, B., 2020. Air Pollution and Progression of Atherosclerosis in Different Vessel Beds—Results from a Prospective Cohort Study in the Ruhr Area, Germany. ENVIRONMENTAL HEALTH PERSPECTIVES 128, 107003.

Hopke, P.K., Croft, D., Zhang, W., Lin, S., Masiol, M., Squizzato, S., Thurston, S.W., van Wijngaarden, E., Utell, M.J., Rich, D.Q., 2019. Changes in the acute response of respiratory diseases to PM2.5 in New York State from 2005 to 2016. SCIENCE OF THE TOTAL ENVIRONMENT 677, 328-339.

Hwang, S., Lin, Y., Guo, S., Chou, C., Lin, C., Chi, M., 2017. Fine particulate matter
on hospital admissions for acute exacerbation of chronic obstructive pulmonary
disease in southwestern Taiwan during 2006 - 2012. INTERNATIONAL
JOURNAL OF ENVIRONMENTAL HEALTH RESEARCH 27, 95-105.
Janes, H., Sheppard, L., Lumley, T., 2005. Case-Crossover Analyses of Air Pollution
Exposure Data. EPIDEMIOLOGY 16, 717-726.
Jiang, X., Mei, X., Feng, D., 2016. Air pollution and chronic airway diseases: what
should people know and do? Journal of Thoracic Disease 8, E31-E40.
Kim, K., Kabir, E., Kabir, S., 2015. A review on the human health impact of airborne
particulate matter. ENVIRONMENT INTERNATIONAL 74, 136-143.
Kloog, I., Coull, B.A., Zanobetti, A., Koutrakis, P., Schwartz, J.D., 2012. Acute and
chronic effects of particles on hospital admissions in New-England. PLoS One 7,
e34664.
Kloog, I., Nordio, F., Zanobetti, A., Coull, B.A., Koutrakis, P., Schwartz, J.D., 2014.
Short Term Effects of Particle Exposure on Hospital Admissions in the Mid-
Atlantic States: A Population Estimate. PLoS One 9, e88578.
Ko, F.W.S., Tam, W., Wong, T.W., Chan, D.P.S., Tung, A.H., Lai, C.K.W., Hui, D.S.C.,
2007. Temporal relationship between air pollutants and hospital admissions for
chronic obstructive pulmonary disease in Hong Kong. THORAX 62, 780-785.
Kumar, L.D., Han, L.J., Cheol, K.H., 2018. Associations between Ambient Particulate
Matter and Nitrogen Dioxide and Chronic Obstructive Pulmonary Diseases in
Adults and Effect Modification by Demographic and Lifestyle Factors.
International Journal of Environmental Research and Public Health 15, 363.
Lee, W.; Choi, H.M.; Lee, J.Y.; Kim, D.H.; Honda, Y.; Kim, H., 2018. Temporal changes in mortality impacts of heat wave and cold spell in Korea and Japan. ENVIRONMENT INTERNATIONAL 116, 136-146.

Levy, D.; Lumley, T.; Sheppard, L.; Kaufman, J.; Checkoway, H., 2001. Referent Selection in Case-Crossover Analyses of Acute Health Effects of Air Pollution. Epidemiology (Cambridge, Mass.) 12, 186-192.

Lin, H.; Qian, Z.M.; Guo, Y.; Zheng, Y.; Ai, S.; Hang, J.; Wang, X.; Zhang, L.; Liu, T.; Guan, W.; Li, X.; Xiao, J.; Zeng, W.; Xian, H.; Howard, S.W.; Ma, W.; Wu, F., 2018. The attributable risk of chronic obstructive pulmonary disease due to ambient fine particulate pollution among older adults. ENVIRONMENT INTERNATIONAL 113, 143-148.

Lin, C.; Li, D.; Lu, J.; Yu, Z.; Zhu, Y.; Shen, P.; Tang, M.; Jin, M.; Lin, H.; Shui, L.; Chen, K.; Wang, J. Short-term associations between ambient fine particulate matter pollution and hospital visits for chronic obstructive pulmonary disease in Yinzhou District, China. Environ. Sci. Pollut. R. 2020, 27(17), 21647-21653.

Liu, Y.; Sun, J.; Gou, Y.; Sun, X.; Li, X.; Yuan, Z.; Kong, L.; Xue, F., 2018. A Multicity Analysis of the Short-Term Effects of Air Pollution on the Chronic Obstructive Pulmonary Disease Hospital Admissions in Shandong, China. International Journal of Environmental Research and Public Health 15, 774.

Liu, Y.; Xie, S.; Yu, Q.; Huo, X.; Ming, X.; Wang, J.; Zhou, Y.; Peng, Z.; Zhang, H.; Cui, X.; Xiang, H.; Huang, X.; Zhou, T.; Chen, W.; Shi, T., 2017. Short-term effects of ambient air pollution on pediatric outpatient visits for respiratory...
diseases in Yichang city, China. ENVIRONMENTAL POLLUTION 227, 116-124.

Lu, P., Zhang, Y., Lin, J., Xia, G., Zhang, W., Knibbs, L.D., Morgan, G.G., Jalaludin, B., Marks, G., Abramson, M., Li, S., Guo, Y., 2019. Multi-city study on air pollution and hospital outpatient visits for asthma in China. ENVIRONMENTAL POLLUTION 257, 113638.

Ma, Y., Yu, Z., Jiao, H., Zhang, Y., Ma, B., Wang, F., Zhou, J., 2019. Short-term effect of PM2.5 on pediatric asthma incidence in Shanghai, China. ENVIRONMENTAL SCIENCE AND POLLUTION RESEARCH 26, 27832-27841.

Moolgavkar, S.H., 2000. AIR POLLUTION AND HOSPITAL ADMISSIONS FOR CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN THREE METROPOLITAN AREAS IN THE UNITED STATES. INHALATION TOXICOLOGY 12, 75-90.

NationalHealthandFamilyPlanningCommissionofthePeople'SRepublicofChina, 2007. Notice of the General Office of the Ministry of Health on Implementing the Direct Reporting Work of the National Health Statistics Network.

Organization, W.H., 2005. WHO Air Quality Guidelines for Particulate Matter, Ozone, Nitrogen Dioxide and Sulfur Dioxide. Global Update 2005. Summary of Risk Assessment.

Organization, W.H., 2017. COPD. https://www.who.int/news-room/fact-sheets/detail/chronic-obstructive-pulmonary-disease-(copd). (accessed 8.14, 2020).
Peel, J.L., Tolbert, P.E., Klein, M., Metzger, K.B., Flanders, W.D., Todd, K., Mulholland, J.A., Ryan, P.B., Frumkin, H., 2005. Ambient Air Pollution and Respiratory Emergency Department Visits. EPIDEMIOLOGY 16, 164-174.

Rice, M.B., Ljungman, P.L., Wilker, E.H., Dorans, K.S., Gold, D.R., Schwartz, J., Koutrakis, P., Washko, G.R., O’Connor, G.T., Mittleman, M.A., 2015. Long-term exposure to traffic emissions and fine particulate matter and lung function decline in the Framingham heart study. Am J Respir Crit Care Med 191, 656-664.

Salimi, F., Morgan, G., Rolfe, M., Samoli, E., Cowie, C.T., Hanigan, I., Knibbs, L., Cope, M., Johnston, F.H., Guo, Y., Marks, G.B., Heyworth, J., Jalaludin, B., 2018. Long-term exposure to low concentrations of air pollutants and hospitalisation for respiratory diseases: A prospective cohort study in Australia. ENVIRONMENT INTERNATIONAL 121, 415-420.

Samet, J.M., Dominici, F., Zeger, S.L., Schwartz, J., Dockery, D.W., 2000. The National Morbidity, Mortality, and Air Pollution Study. Research report (Health Effects Institute) 94, 5-14, 75-84.

Santus, P., Russo, A., Madonini, E., Allegra, L., Blasi, F., Centanni, S., Miadonna, A., Schiraldi, G., Amaducci, S., 2012. How air pollution influences clinical management of respiratory diseases. A case-crossover study in Milan. RESPIRATORY RESEARCH 13, 95.

Slaughter, J.C., Kim, E., Sheppard, L., Sullivan, J.H., Larson, T.V., Claiborn, C., 2005. Association between particulate matter and emergency room visits, hospital admissions and mortality in Spokane, Washington. J Expo Anal Environ
Stafoggia, M., Zauli-Sajani, S., Pey, J., Samoli, E., Alessandrini, E., Basagaña, X., Cernigliaro, A., Chiusolo, M., Demaria, M., Díaz, J., Faustini, A., Katsouyanni, K., Kelessis, A.G., Linares, C., Marchesi, S., Medina, S., Pandolfi, P., Pérez, N., Querol, X., Randi, G., Ranzi, A., Tobias, A., Forastiere, F., 2016. Desert Dust Outbreaks in Southern Europe: Contribution to Daily PM10 Concentrations and Short-Term Associations with Mortality and Hospital Admissions. ENVIRONMENTAL HEALTH PERSPECTIVES 124, 413-419.

Stieb, D.M., Szyszkowicz, M., Rowe, B.H., Leech, J.A., 2009. Air pollution and emergency department visits for cardiac and respiratory conditions: a multi-city time-series analysis. Environmental Health 8, 25.

Szyszkowicz, M., Kousha, T., Castner, J., Dales, R., 2018. Air pollution and emergency department visits for respiratory diseases: A multi-city case crossover study. ENVIRONMENTAL RESEARCH 163, 263-269.

Tian, Y., Xiang, X., Juan, J., Song, J., Cao, Y., Huang, C., Li, M., Hu, Y., 2018. Short-term effects of ambient fine particulate matter pollution on hospital visits for chronic obstructive pulmonary disease in Beijing, China. Environmental Health 17.

Tsai, S., Chang, C., Yang, C., 2013. Fine Particulate Air Pollution and Hospital Admissions for Chronic Obstructive Pulmonary Disease: A Case-Crossover Study in Taipei. International Journal of Environmental Research and Public Health 10, 6015-6026.
Wong, C.M., Lai, H.K., Tsang, H., Thach, T.Q., Thomas, G.N., Lam, K.B.H., Chan, K.P., Yang, L., Lau, A.K.H., Ayres, J.G., Lee, S.Y., Man Chan, W., Hedley, A.J., Lam, T.H., 2015. Satellite-Based Estimates of Long-Term Exposure to Fine Particles and Association with Mortality in Elderly Hong Kong Residents. ENVIRONMENTAL HEALTH PERSPECTIVES 123, 1167-1172.

Woo, K.S., Chook, P., Hu, Y.J., Lao, X.Q., Lin, C.Q., Lee, P.W.A., Kwok, C.Y.T., Wei, A.N., Guo, D.S., Yin, Y.H., Lau, K.H.A., Leung, K.S., Leung, Y., Celermajer, D.S., 2020. The impact of particulate matter air pollution (PM2.5) on atherosclerosis in modernizing China: a report from the CATHAY study. INTERNATIONAL JOURNAL OF EPIDEMIOLOGY.

Xie, J., Teng, J., Fan, Y., Xie, R., Shen, A., 2019. The short-term effects of air pollutants on hospitalizations for respiratory disease in Hefei, China. INTERNATIONAL JOURNAL OF BIOMeteorology 63, 315-326.

Zhang, R., Chen, Z., Ou, C., Zhuang, Y., 2017. Trends of Heat Waves and Cold Spells over 1951 - 2015 in Guangzhou, China. Atmosphere 8, 37.

Zhang, Z., Chai, P., Wang, J., Ye, Z., Shen, P., Lu, H., Jin, M., Gu, M., Li, D., Lin, H., Chen, K., 2019. Association of particulate matter air pollution and hospital visits for respiratory diseases: a time-series study from China. ENVIRONMENTAL SCIENCE AND POLLUTION RESEARCH 26, 12280-12287.

Zuo, B., Liu, C., Chen, R., Kan, H., Sun, J., Zhao, J., Wang, C., Sun, Q., Bai, H., 2019. Associations between short-term exposure to fine particulate matter and acute exacerbation of asthma in Yancheng, China. CHEMOSPHERE 237, 124497.
Table 1. Characteristics of included patients admitted with chronic obstructive pulmonary disease.

| Variable       | Group          | N (%)       |
|----------------|----------------|-------------|
| Sex            | Male           | 29,652 (74.1) |
|                | Female         | 10,350 (25.9)  |
| Age            | <65 years      | 6,497 (16.2)  |
|                | ≥65 years      | 33,505 (83.8) |
|                | Unemployed     | 22,509 (81.5) |
| Occupational class | White collar  | 1,170 (4.2)    |
|                | Blue collar    | 3,948 (14.3)   |
|                | Married        | 36,671 (93.3)  |
| Marital Status | Unmarried      | 1,668 (4.2)     |
|                | Divorce/widowed| 969 (2.5)       |
|                | Winter         | 9,749 (24.4)    |
|                | Spring         | 11,306 (28.3)   |
|                | Summer         | 10,088 (25.2)   |
|                | Autumn         | 8,859 (22.1)    |
Table 2. Summary statistics of exposure level of satellite-based PM$_{2.5}$ and meteorological conditions for patients with chronic obstructive pulmonary disease in Guangzhou, China, 2014-2015.

| Variable                  | Minimum | Median | Maximum | Mean  | SD  |
|---------------------------|---------|--------|---------|-------|-----|
| PM$_{2.5}$ (mg/m$^3$)     | 6.0     | 38.7   | 164.4   | 42.6  | 21.0|
| Temperature (°C)          | 5.2     | 23.7   | 31.4    | 22.2  | 6.1 |
| Relative humidity (%)     | 31.5    | 80.5   | 97.5    | 79.8  | 9.9 |

Abbreviations: COPD, chronic obstructive pulmonary disease; SD: the standard deviation. T: Temperature; RH: Relative humidity.
Table 3. Odds ratios of hospital admissions for chronic obstructive pulmonary disease per 10 μg/m³ increase in PM$_{2.5}$ at different lag days.

| Lag (days) | OR (95% CI)     | P-value |
|-----------|-----------------|---------|
| 0         | 1.012 (1.004, 1.019) | 0.002   |
| 1         | 1.007 (1.000, 1.014) | 0.056   |
| 2         | 1.006 (0.999, 1.013) | 0.097   |
| 3         | 1.006 (0.999, 1.013) | 0.115   |
| 4         | 1.008 (1.001, 1.015) | 0.027   |
| 5         | 1.006 (0.999, 1.013) | 0.100   |
| 6         | 1.001 (0.994, 1.007) | 0.873   |
| 0-1       | 1.012 (1.004, 1.021) | 0.004   |
| 0-2       | 1.013 (1.004, 1.022) | 0.005   |
| 0-3       | 1.014 (1.004, 1.024) | 0.005   |
| 0-4       | 1.016 (1.005, 1.026) | 0.003   |
| 0-5       | 1.016 (1.006, 1.027) | 0.002   |
| 0-6       | 1.015 (1.004, 1.027) | 0.006   |

Abbreviations: OR, odds ratio; 95% CI, 95% confidence interval;
Figures captions

Figure 1. Locations of monitoring stations of PM$_{2.5}$ and places of residence of the included patients admitted with chronic obstructive pulmonary disease.

Figure 2. Odds ratios of hospitalizations for chronic obstructive pulmonary disease (COPD) per 10 $\mu g/m^3$ increase of individual exposure level of PM$_{2.5}$ at a lag of 0-5 days. Points and lines are point estimates and the corresponding 95% confidence intervals of odds ratios. The dashed line indicates odds ratio = 1.
Figure 1

Locations of monitoring stations of PM2.5 and places of residence of the included patients admitted with chronic obstructive pulmonary disease.
Figure 2

Odds ratios of hospitalizations for chronic obstructive pulmonary disease (COPD) per 10 µg/m3 increase of individual exposure level of PM2.5 at a lag of 0-5 days. Points and lines are point estimates and the corresponding 95% confidence intervals of odds ratios. The dashed line indicates odds ratio = 1.

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