



ELSEVIER

Contents lists available at ScienceDirect

The Lancet Regional Health - Western Pacific

journal homepage: www.elsevier.com/locate/lanwpc

Research paper

Short-Term Ambient Particulate Air Pollution and Hospitalization Expenditures of Cause-Specific Cardiorespiratory Diseases in China: A Multicity Analysis

Yang Xie^a, Zichuan Li^b, Hua Zhong^a, Xing Lin Feng^c, Pantao Lu^d, Zhouyang Xu^b, Tongjun Guo^b, Yaqin Si^e, Jinxi Wang^f, Libo Chen^e, Chen Wei^e, Furong Deng^b, Andrea A. Baccarelli^g, Zhijie Zheng^h, Xinbiao Guo^b, Shaowei Wu^{i,*}

^a School of Economics and Management, Beihang University, Beijing, China

^b Department of Occupational and Environmental Health Sciences, School of Public Health, Peking University, Beijing, China

^c Department of Health Policy and Management, School of Public Health, Peking University, Beijing, China

^d College of Environmental Sciences and Engineering, Peking University, Beijing, China

^e Beijing HealthCom Data Technology Co. Ltd, Beijing, China

^f Shanghai Songsheng Business Consulting Co., Ltd, Shanghai, China

^g Department of Environmental Health Sciences, Columbia University Mailman School of Public Health, New York, NY, United States

^h Department of Global Health, School of Public Health, Peking University, Beijing, China

ⁱ Department of Occupational and Environmental Health, School of Public Health, Xi'an Jiaotong University Health Science Center, Xi'an, Shaanxi, China.

ARTICLE INFO

Article history:

Received 16 March 2021

Revised 1 July 2021

Accepted 12 July 2021

Keywords:

Air pollution

PM_{2.5}

hospital admissions

hospitalization expenditures

economic loss

ABSTRACT

Background: Ambient air pollution is leading risk factor for health burden in China. Few studies in China have investigated the economic loss related to short-term exposure to ambient PM_{2.5}, which could trigger acute onset of cardiorespiratory diseases within a few days.

Methods: Daily ambient air pollutants data are obtained for each city from the National Air Quality Monitoring System and daily hospitalization data are obtained from the urban employee-based basic medical insurance scheme database in 74 Chinese cities with an average coverage of 88.5 million urban employees during 2016–2017. A three-stage time-series analytic approach is used in this study to investigate the impact of short-term exposure to ambient fine particulate (PM_{2.5}) air pollution on hospital admissions, expenses and hospital stays of three cause-specific cardiorespiratory diseases, including lower respiratory infections (LRI), coronary heart disease (CHD) and stroke in the included cities.

Findings: Based on the time-series analysis using daily hospitalization data, 28,560 LRI cases, 54,600 CHD cases, and 23,989 stroke cases are attributable to ambient PM_{2.5} in the 74 cities during the study period, and the related attributable expenses are 220 million CNY (US\$ 32.9 million) for LRI, 458 million CNY (US\$ 68.5 million) for CHD, and 410 million CNY (US\$ 65.8 million) for stroke, respectively. These attributable numbers account for 1.45% to 2.05% of total hospital admissions and 1.10% to 1.51% of total expenses for the three diseases during 2016–2017, respectively. The attributable numbers for the three cause-specific cardiorespiratory diseases would increase to 362,007 hospital admission cases and 3.68 billion CNY expenses (\$US550 million) in the entire urban employee population (299 million) in China during 2016–2017, and the related direct economic loss of absence from work would be 798 million CNY (US\$ 119.3 million).

* Corresponding Author: Shaowei Wu, PhD, Department of Occupational and Environmental Health, School of Public Health, Xi'an Jiaotong University Health Science Center, 76 Yanta West Road, Yanta District, Xi'an, Shaanxi 710061, China, Tell: 86-13810867605
E-mail address: shaowei_wu@xjtu.edu.cn (S. Wu).

Interpretation: Our results support that short-term exposure to ambient PM_{2.5} pollution could lead to significant health and economic impacts in China. Reducing levels of ambient PM_{2.5} can avoid substantial health damage and expenditures, and generate appreciable economic benefits from decreasing absence from work.

Funding: Natural Science Foundation of China (82073509, 71903010, 71903011), and the National Key Research and Development Program of China (2017YFC0211600, 2017YFC0211601).

© 2021 The Authors. Published by Elsevier Ltd.

This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>)

Research in context

Evidence before this study

Billions of people live in over polluted regions with ambient PM_{2.5} levels over the WHO guideline (annual mean: 10 µg/m³), whereas evidence is lacking for the economic loss related to short-term exposure to ambient air pollution, especially in developing countries with high ambient air pollution. Most existing studies have evaluated the health and economic losses related to long-term exposure to ambient air pollution based on the total mortality or morbidity data, and few studies have evaluated the economic loss related to short-term exposure to ambient air pollution based on detailed hospitalization expenditure data.

Added value of this study

To our best knowledge, our study provides the first detailed evaluation about the excess hospitalization burden attributable to short-term exposure to ambient PM_{2.5} based on daily hospital admission data over multiple cities in China. This study estimates that short-term exposure to ambient PM_{2.5} leads to significant increases in hospital admissions and hospitalization expenses for three major cause-specific cardiorespiratory diseases responsible for population disease burden including lower respiratory infections, coronary heart disease and stroke in urban employees in 74 Chinese cities during 2016–2017. The attributable number estimates would increase to 362,007 hospital admission cases and 3.68 billion CNY expenses (\$US550 million) for the three cause-specific cardiorespiratory diseases in the entire urban employee population (299 million) in China during 2016–2017, and the related direct economic loss of absence from work for the younger adults (15–64 years) subgroup would be 798 million CNY (US\$ 119.3 million).

Implications of all the available evidence

Given that billions of people live in the over polluted regions with ambient PM_{2.5} levels over the WHO guideline, especially in developing countries, the potential economic loss due to short-term exposure to ambient PM_{2.5} would be enormous over the world. Accurately estimating the impact of ambient air pollution is crucial for the establishment of effective air quality regulations, and our study findings may provide important evidence for ambient air pollution control action from the angle of input-output (policy cost-benefit) balance.

Introduction

Ambient air pollution is leading millions of premature deaths all over the world, especially in developing countries, and has become the eighth leading risk factor for death according to the Global Burden of Diseases (GBD) in 2017^{1,2}. Ambient particulate matter with an aerodynamic diameter of 2.5 micrometers or less (PM_{2.5}) is the major air pollutant receiving world-wide attention due to its high toxicity. More than 90% people live in the over polluted regions, where PM_{2.5} exceeds the guideline (annual mean:

10 µg/m³) proposed by the World Health Organization (WHO)³. In addition, numerous studies indicate that ambient PM_{2.5} pollution is associated with a broad range of chronic and acute health effects^{1,3–8}. Exposure to ambient air pollution not only damages public health but also causes economic loss, resulting in increased healthcare expenditures and decreased work hours^{9,10}. The welfare damages for ambient air pollution and household air pollution were estimated to be \$3767 billion, accounting for 5.06% of world gross domestic products (GDP) in 2015¹¹.

Ambient air pollution, especially ambient PM_{2.5}, has significant contribution on cardiorespiratory mortality^{12,13}. China has the largest population in the world and is facing severe ambient air pollution issue¹⁴. The Global Burden of Disease 2017 study shows that approximately 1.1 million people died prematurely, and 21.8 million years of life lost were lost in China in 2015 due to long-term exposure to ambient air pollution¹⁵. One study using national mortality-specific baseline incidence rates derived from the GBD study estimated that the national long-term PM_{2.5}-attributable mortality in 2016 was 0.96 million, accounting for about 9.98% of the total reported deaths nationwide¹⁶. In addition, the specific hospital admission morbidities for cardiovascular disease and respiratory disease related to PM_{2.5} were 0.36 million and 0.61 million, respectively, based on baseline incidence rates derived from previous references¹⁶. The result also shows that long-term PM_{2.5} exposure caused an economic loss of 101.4 billion US\$, accounting for 0.9% of the national GDP in 2016, based on provincial health cost and per capita GDP information¹⁶.

Although several studies also reported economic loss related to long-term exposure to ambient air pollution based on data on hospital admissions and average expense per time^{16,17}, few studies have evaluated the economic loss related to short-term exposure to ambient air pollution based on detailed hospitalization expenditure data. Numerous studies have shown that short-term exposure to ambient PM_{2.5} within a few days could trigger acute onset of cardiorespiratory diseases including lower respiratory infections (LRI), coronary heart disease (CHD), and stroke^{18–20}, which are among the major cardiorespiratory diseases responsible for population disease burden². Several previous studies also show that short-term exposure to PM_{2.5} could lead to more intensive care admissions and more hospital admissions of cardiorespiratory diseases^{21–23}. Therefore, short-term exposure to ambient PM_{2.5} has important adverse health effects in addition to that of long-term exposure to ambient PM_{2.5}. The evaluation on the health and economic burdens of both types of exposure constitutes an integrated perspective on the adverse socioeconomic impact related to ambient PM_{2.5}. To date, detailed evaluation on the hospitalization expenditures related to short-term exposure to ambient PM_{2.5} for these specific diseases has been lacking in China.

In addition, the levels of ambient particulate air pollution and spectrum of disease may vary geographically, especially in China, a large country with the largest population in the world, and it is necessary to investigate the variation in the impact of air pollution on these cause-specific cardiorespiratory diseases (e.g., LRI,

CHD, and stroke) across different regions for targeted disease prevention. A previous investigation finds that a 10 $\mu\text{g}/\text{m}^3$ increase in inhalable particulate matter (PM_{10}) reduces life expectancy by 0.64 years based on quasiexperimental variation in PM_{10} generated by China's Huai River policy, which provides free or heavily subsidized coal for indoor heating during the winter to cities north of the Huai River but not to those in the south²⁴. The large variations in both ambient particulate air pollution levels and spectrum of disease across China provide a unique opportunity to investigate the relationship between ambient $\text{PM}_{2.5}$ and three cause-specific cardiorespiratory diseases in different regions, e.g., northern region and southern region divided by the Huai River.

This study thus evaluates the health and hospitalization expenditures related to ambient $\text{PM}_{2.5}$ with respect to these cause-specific cardiorespiratory diseases in 74 cities of China in 2016–2017 based on detailed daily morbidity data obtained from the urban employee-based basic medical insurance scheme (UEBMI) of China.

Materials and Methods

This study evaluated the relationship between ambient particulate air pollution and hospital admissions, expenditures and hospital stays of three cause-specific cardiorespiratory diseases, including LRI, CHD and stroke, based on detailed hospital admissions data obtained from the UEBMI in China. Our study extracted daily hospital admission data from 74 administrative divisions of prefecture-level cities (out of 338 prefecture-level cities in total) in China during January 1, 2016 and December 31, 2017.

Health Data

This study population includes all the urban Chinese populations who joined the UEBMI in the included cities. The UEBMI covers all the current urban employees and retirees of past urban employees. Insurance policy is the same after employees retired in China^{25,26}. Specifically, daily hospital admissions and hospital expenditure data are obtained for 74 cities and hospital stay data are obtained for 69 cities from the UEBMI (covering 299 million employees). Three major cardiorespiratory diseases including LRI, CHD, and stroke are our targeted diseases, which are coded according to the ICD-10 codes (LRI: J12–J22; CHD: I20–I25; stroke: I60–I61, I63–I64)^{27,28}. For each disease, the hospital expenditure and hospital stay for a given day during the study are defined as the average expenses and days per person in that day multiplied by the number of patients who were admitted to the hospital because of the disease in that day. The UEBMI also includes outpatient visits information. However, the disease diagnosis for outpatient visits is less reliable than hospital admissions, and thus we do not include outpatient visits in our study. This study is exempted from institutional review board approval by the Ethics Committee of Peking University Health Science Center, because all data used for the study are collected for administrative purposes without any individual identifiers.

Ambient air pollution data

Daily ambient air pollutants data, including fine particulate matter ($\text{PM}_{2.5}$), nitrogen dioxide (NO_2), ozone (O_3), sulfur dioxide (SO_2) and carbon monoxide (CO), are obtained for each city from the National Air Quality Monitoring System^{25,26}. Environmental air quality monitoring stations are usually set at fixed-sites which have good regional representativeness and can objectively reflect the ambient air quality level and change rules in a certain

space²⁹. Daily mean concentrations for all ambient air pollutants in each city are calculated by averaging all valid monitoring measurements if there is more than one monitor in that city. We also collect daily meteorological data on mean temperature ($^{\circ}\text{C}$) and relative humidity (%) from the National Meteorological Data Service Center of China (<http://data.cma.cn/>, accessed 2019-01-01).

Statistical analysis

In this study, we use a three-stage time-series analytic approach to assess the city-specific and overall estimates of the association between ambient $\text{PM}_{2.5}$ and daily hospital admissions, total hospital stays and total expenses for LRI, CHD and stroke. In the first stage, we estimate city-specific associations using a Constrained Distributed Lag Model (CDLM)³⁰ with a time-series quasi-Poisson regression^{25,26} as below:

$$\begin{aligned} \text{Log}(E(Y_t)) = & \alpha + bs_t(\text{air pollutants}) + \text{Day of week} + \text{Holiday} \\ & + ns_t(\text{calendar time, df} = 7 \text{ per year}) \\ & + ns_t(\text{temperature, df} = 6) \\ & + ns_t(\text{relative humidity, df} = 3) \end{aligned} \quad (1)$$

where $E(Y_t)$ is the expected count of health variables in the analyzed city on day t ; $bs_t(\text{air pollutants})$ is the concentrations of $\text{PM}_{2.5}$ in the analyzed city on day t using a CDLM with 3 degrees of freedom (df) polynomials for 2 lag days; Day of week is the indicator variable for day of week to account for possible variations over weekdays and weekends; Holiday is the indicator variable for public holidays to account for possible variations over holidays and non-holidays; $ns_t(\text{calendar time})$ is the natural cubic spline for calendar time with 7 df per year to exclude unmeasured time trends longer than 2 months; $ns_t(\text{temperature})$ and $ns_t(\text{relative humidity})$ are natural cubic splines with 6 df for 3-day moving average temperature and 3 df for 3-day moving average relative humidity on day t to control for potential non-linear and delayed confounding effects of meteorological conditions, respectively²⁵. Specifically, non-linear effects are controlled for by using natural cubic splines, and delayed effects are controlled for by using moving average data. Associations between short-term exposure to ambient $\text{PM}_{2.5}$ and six health variables (hospital admissions and total hospital stays for LRI, CHD and stroke) are assessed separately using the above single-pollutant models. The city-specific effect estimates are expressed as relative risks (RR) and related 95% confidence intervals (CI) by using the equation $\text{RR} = e^{\beta}$, where β is the coefficient derived from the above model.

In the second stage, we pool the city-specific effect estimates to obtain the overall effect estimates that represent the effects for all included cities using a random-effect model. The lag 0–2 effects of $\text{PM}_{2.5}$ on health variables are estimated and expressed as RR and related 95% CI associated with a 10 $\mu\text{g}/\text{m}^3$ increase in $\text{PM}_{2.5}$. Lag 0–2 is chosen as the main exposure metric because many previous studies found most apparent associations between ambient $\text{PM}_{2.5}$ and health outcomes within this time frame^{26,31,32}, and sensitivity analyses are performed from lag0–1 to lag0–6. Moreover, we calculate health variable-specific overall excess risk in percent change (%) $((\text{RR} - 1) * 100)$ related to a 10 $\mu\text{g}/\text{m}^3$ increase in ambient $\text{PM}_{2.5}$ at lag 0–2.

In the third stage, we first use overall effect estimates from the second stage to calculate attributable fraction (AF) and attributable number (AN) of health variables during the study period based on the estimated RR at lag 0–2. $\text{AN}_{i,c}$ in each year i for city c are computed through the formula^{33,34}:

$$\text{AN}_{i,c} = N_{i,c} * (\text{RR}_{i,c} - 1) / \text{RR}_{i,c}, \text{ with } \text{RR}_{i,c} = e^{(\beta * D_{i,c} / 10)} \quad (2)$$

where $N_{i,c}$ is the annual total number of health variable in year i for city c , β is health variable-specific overall coefficients derived

from the second stage and D_{ic} is the annual average concentration of $PM_{2.5}$ in year i for city c . Annual AN for a given health variable is then summed over years and cities. AF is calculated by dividing the AN by the sum of the corresponding health variable over years and cities. In addition, the upper and lower 95% CI values of the pooled β are used to calculate the 95% CIs of AN and AF using the above equations³⁵.

Besides, we estimate AFs and ANs of total expenses for LRI, CHD and stroke using the formula³⁶:

$$AN_{ec} = AN_{ac} * AE_c \quad (3)$$

where AN_{ac} is the AN of hospital admissions for city c during the study period, and AE_c is the average expense across all admissions for city c during the study period. AF is calculated by dividing the AN by the sum of total expenses over cities.

In order to estimate the national level health burden of ambient $PM_{2.5}$ pollution, we also project the hospital admissions, total hospital stays, and total expenses attributable to $PM_{2.5}$ in the entire urban employee population (299 million averaged over 2016-2017) who joined the UEBMI based on results of 74 cities included in the study assuming the same exposure-response relationship between short-term exposure to ambient $PM_{2.5}$ and the examined health outcomes across China. In addition, we also estimate the direct economic loss of absence from work for the younger adults (15-64 years) subgroup using the city-level average wage from Chinese Statistical Yearbook during the study period^{37,38}. We multiply total hospital stay in days attributable to $PM_{2.5}$ by average daily wage in each city, and then multiply the proportion of younger UEBMI participants (15-64 years) in the city to calculate the city-specific economic loss for absence from work. Then we summarize the total economic loss attributable to $PM_{2.5}$ over 74 cities.

We then conduct subgroup analyses by geographical region, gender and age (15-64 and ≥ 65). All included cities are divided into northern and southern regions according to the Huai River-Qinling Mountains line. To further understand the potential impact of other air pollutants on the results, two-pollutant models are fitted with average concentrations of NO_2 , O_3 , SO_2 , or CO along with $PM_{2.5}$ at the same lags in the regression models. The R software (version 3.6.2) is used for all statistical analyses and plotting. R packages `dlnm` (author: A. Gasparrini) and `meta` (author: Sara Balduzzi and Gerta Rücker and Guido Schwarzer) are used, and a 2-sided P value < 0.05 is considered statistically significant.

Role of the funding source

The sponsors of this study played no role in the study design, data collection, or analysis of data; interpretation of results; or in the writing of this manuscript. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

Figure 1 shows the geographic locations of all 74 Chinese cities included in this study. The UEBMI covers an average of 88.5 million population during 2016-2017 across these cities. Table 1 shows the distribution in daily levels of ambient $PM_{2.5}$ and meteorological variables during the study period. The average daily concentrations of ambient $PM_{2.5}$ in the 74 cities during the study period is $49.7 \mu g/m^3$ (Column 1), and is higher in the northern region ($57.6 \mu g/m^3$) than in the southern region ($41.7 \mu g/m^3$).

Table 2 summarizes descriptive statistics for hospital admission variables during the study period. A total of 6.03 million hospital admission cases, including 1.97 million LRI cases, 2.67 million CHD cases and 1.39 million stroke cases, are identified in the

UEBMI database across 74 cities during the study period. The total expenses reach 78,972 million CNY (US\$ 11,804 million) for the three cause-specific cardiorespiratory diseases. Among the three diseases, CHD has the largest total expenses of 30,307 million CNY (US\$ 4,530 million), higher than those for LRI [19,963 million CNY (US\$ 2,984 million)] and stroke [28,702 million CNY (US\$ 4,283 million)]. The total hospital stays reach 57.5 million days for the three cause-specific cardiorespiratory diseases in 69 cities during our study period. CHD also has the largest total hospital stays (22.8 million days) among the three diseases, higher than those for LRI (16.8 million days) and stroke (17.9 million days).

Overall excess risks of hospital admissions and total hospital stays for LRI, CHD and stroke at different cumulative lags are shown in Figure 2. The excess risks are generally significant from lag0-2 to lag0-4 for all six health outcomes except the excess risk at lag0-4 for LRI hospital admission. The excess risks are attenuated at lag0-5 to lag0-6.

Table 3 and Table 4 show the results for the analyses of the associations between ambient $PM_{2.5}$ (lag0-2) and hospital admissions, total hospital stays and total expenses of LRI, CHD and stroke during 2016-2017. The excess risks in % per $10 \mu g/m^3$ increase in ambient $PM_{2.5}$ (lag0-2) are 0.26%, 0.34% and 0.33% for hospital admissions of LRI, CHD and stroke, respectively, and 0.38%, 0.60% and 0.52% for total hospital stays of LRI, CHD and stroke, respectively (all $P < 0.05$). Overall, the fractions of hospital admissions and total hospital stays attributable to ambient $PM_{2.5}$ range from 1.45% to 2.05%, and 1.87% to 3.01%, and the fractions of total expenses attributable to ambient $PM_{2.5}$ range from 1.10% to 1.51% for the three diseases during 2016-2017, respectively.

The largest AF of hospital admissions associated with $PM_{2.5}$ among the three diseases is the CHD-related AF (2.05%, 95% CI: 0.63%, 3.44%), and the corresponding AN is 54,600 (95% CI: 16,808, 91,820). Moreover, CHD-related AF (3.01%, 95% CI: 1.59%, 4.40%) for total hospital stays is larger than those for the other two diseases as well. For total expenses, CHD-related AF (1.51%, 95% CI: 0.46%, 2.55%) associated with $PM_{2.5}$ is also more apparent than LRI-related AF (1.10%, 95% CI: 0.15%, 2.05%) and stroke-related AF (1.43%, 95% CI: 0.43%, 2.42%), and the corresponding AN for CHD expenses is 458 million CNY (95% CI: 141, 772), also higher than that for LRI expenses (220 million CNY, 95% CI: 29, 408) and stroke expenses (410 million CNY, 95% CI: 123, 694). In two-pollutant models adjusting for other air pollutants, most AF estimates remain positive but are attenuated, whereas some estimates become even more significant when compared to the results in the single-pollutant models (Tables S1 and S2).

Results of projection of hospital admissions, total expenses and total hospital stays attributable to ambient $PM_{2.5}$ to the national level show that the AN estimates would increase to 362,007 hospital admission cases, 3.68 billion CNY expenses (\$US 550 million) and 5.21 million hospital days for the entire urban employee population in China during 2016-2017 (Table 5).

In the subgroup analyses by region for the AF estimates attributable to ambient $PM_{2.5}$ at lag 0-2, four of the six AF estimates for hospital admissions and total hospital stays (CHD-related hospital admissions, and LRI-, CHD- and stroke-related total hospital stays) are higher in the northern region than in the southern region (Table S3). Results for subgroup analyses by gender show that four of the six AF estimates for hospital admissions and total hospital stays (LRI-, CHD- and stroke-related hospital admissions, and CHD-related total hospital stays) are higher in males than in females (Table S4), and all AF estimates for hospital admissions and total hospital stays are higher in older adults (age ≥ 65 years) subgroup than in younger adults (age 15-64 years) subgroup (Table S5).

In the subgroup analyses for total expenses, the AF for CHD in the northern region (1.90%, 95% CI: 0.25%, 3.52%) is higher than



Figure 1. Map of the included cities (n=74) in mainland China. The black points represent cities in the northern region (n=37), and the gray points represent cities in the southern region (n=37).

Table 1
Description for daily ambient PM_{2.5}, temperature and relative humidity in 74 Chinese cities during 2016-2017

Measure and Region	Mean	SD	Minimum	Median	Maximum	Interquartile Range
PM _{2.5} (μg/m ³)						
Overall	49.7	37.7	3.0	39.3	389.0	37.1
Northern region ^a	57.6	43.4	3.5	45.1	389.0	42.8
Southern region	41.7	28.7	3.0	34.3	342.6	31.6
Temperature (°C)						
Overall	15.2	10.2	-22.8	16.7	36.5	15.2
Northern region	12.4	11.3	-22.8	13.6	35.3	19.0
Southern region	18.0	8.0	-7.8	18.8	36.5	12.6
Relative humidity (%)						
Overall	68.5	17.9	7.0	71.0	100.0	25.9
Northern region	60.6	18.6	7.0	61.0	100.0	29.0
Southern region	76.4	13.2	17.0	77.0	100.0	18.0

Abbreviation: PM_{2.5}: particulate matter with an aerodynamic diameter of 2.5 micrometers or less.

^aThere are 37 cities and 37 cities in the southern and northern region, respectively.

Table 2
Demographic characteristics of hospital admission cases in the included Chinese cities^a during 2016-2017

Disease	Total	Northern region	Southern region	Males	Females	Age 15-64 years	Age ≥65 years
Hospital admissions (million case)							
LRI	1.97	0.98	0.99	0.89	0.75	0.75	0.89
CHD	2.67	2.01	0.66	1.27	0.98	0.82	1.43
Stroke	1.39	0.81	0.59	0.77	0.40	0.42	0.75
Total expenses (million CNY)							
LRI	19,963	3,669	16,294	10,354	7,606	6,053	11,906
CHD	30,307	9,201	21,106	16,650	10,549	9,616	17,582
Stroke	28,702	7,490	21,212	16,157	9,787	8,586	17,358
Total hospital stays (million days)							
LRI	16.8	7.6	9.2	6.3	8.0	6.1	8.1
CHD	22.8	15.8	7.0	8.8	10.7	6.4	13.1
Stroke	17.9	9.5	8.4	5.2	9.8	5.2	9.8

Abbreviations: CHD: coronary heart disease; CNY: Chinese Yuan; LRI: lower respiratory infections.

^aTwo years' average numbers of the UEBMI participants are 88.5 million for hospital admissions and total expenses (74 cities) and 84.6 million for total hospital stays (69 cities) during 2016-2017; subgroup numbers may not add up to the total number because of rounding, and subgroup numbers excluded admission cases without sex or age information.

that in the southern region (1.46%, 95% CI: -0.20%, 3.09%), whereas the AF for LRI in the southern region (1.80%, 95% CI: 0.11%, 3.47%) is higher than that in the northern region (0.82%, 95% CI: -0.56%, 2.18%) (Table S6). The AF estimates for total expenses of three diseases are all higher in males than in females, and are all higher in older adults than in younger adults.

The direct economic loss of absence from work for the younger adults (15-64 years) subgroup due to the three cause-specific cardiorespiratory diseases attributable to ambient PM_{2.5} would be 226 million CNY (US\$ 33.8 million) in the included cities, and would increase to 798 million CNY (US\$ 119.3 million) for the entire urban employee population in China (Table 5).

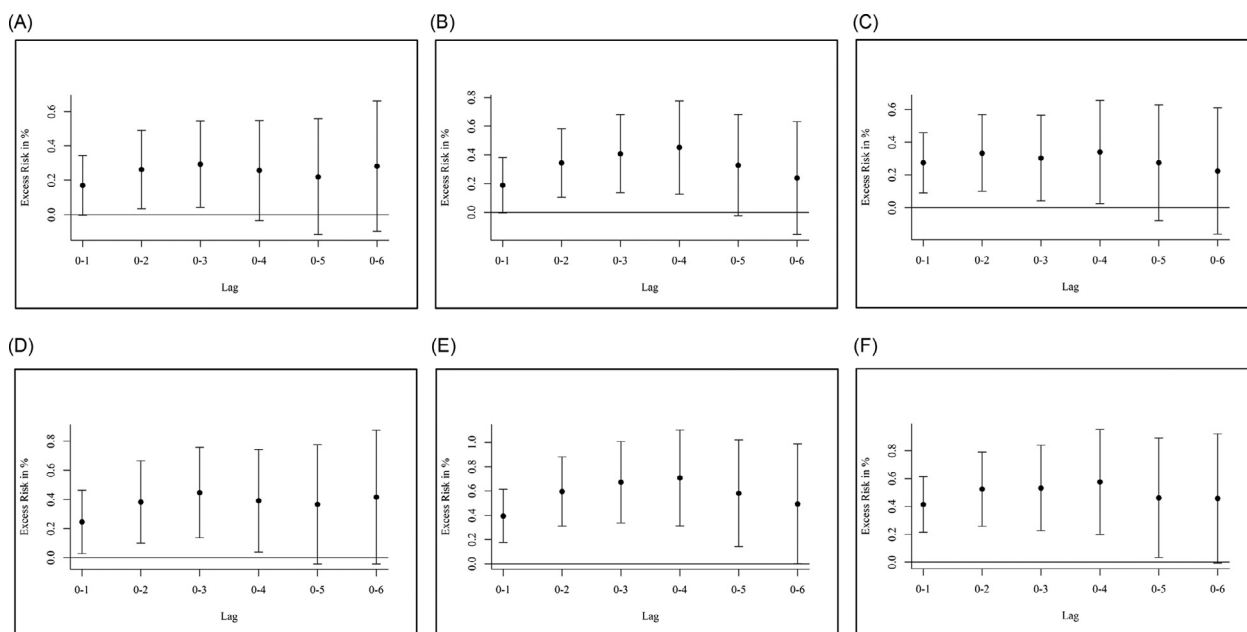


Figure 2. Overall excess risks in % of hospital admissions and total hospital stays per 10 $\mu\text{g}/\text{m}^3$ increase in ambient $\text{PM}_{2.5}$ at different cumulative lag days in included cities. (A) Hospital admissions for LRI; (B) Hospital admissions for CHD; (C) Hospital admissions for stroke; (D) Total hospital stays for LRI; (E) Total hospital stays for CHD; (F) Total hospital stays for stroke.

Table 3

Attributable numbers and fractions of hospital admissions and total hospital stays associated with ambient $\text{PM}_{2.5}$ at lag 0-2 in the included cities^a during 2016-2017

Disease	Health variable	Excess risk in % (95% CI) ^b	Attributable number (95% CI)	Attributable fraction in % (95% CI)
LRI	Hospital admissions (case)	0.26 (0.03, 0.49)	28 560 (3 796, 52 990)	1.45 (0.19, 2.69)
	Total hospital stays (thousand day)	0.38 (0.10, 0.67)	314 (82, 543)	1.87 (0.49, 3.23)
CHD	Hospital admissions (case)	0.34 (0.10, 0.58)	54 600 (16 808, 91 820)	2.05 (0.63, 3.44)
	Total hospital stays (thousand day)	0.60 (0.31, 0.88)	686 (363, 1003)	3.01 (1.59, 4.40)
Stroke	Hospital admissions (case)	0.33 (0.10, 0.57)	23 989 (7 212, 40 551)	1.72 (0.52, 2.91)
	Total hospital stays (thousand day)	0.52 (0.26, 0.79)	473 (234, 707)	2.64 (1.31, 3.95)

Abbreviations: CHD: coronary heart disease; LRI: lower respiratory infections; ^aTwo years' average numbers of the UEBMI participants are 88.5 million for hospital admissions (74 cities) and 84.6 million for total hospital stays (69 cities) during 2016-2017; ^b Per 10 $\mu\text{g}/\text{m}^3$ increase in ambient $\text{PM}_{2.5}$.

Table 4

Attributable numbers and fractions of total expenses (million CNY) associated with ambient $\text{PM}_{2.5}$ at lag 0-2 in the included cities^a during 2016-2017

Disease	Attributable number (95% CI)	Attributable fraction in % (95% CI)
LRI	220 (29, 408)	1.10 (0.15, 2.05)
CHD	458 (141, 772)	1.51 (0.46, 2.55)
Stroke	410 (123, 694)	1.43 (0.43, 2.42)

Abbreviations: CHD: coronary heart disease; CNY: Chinese Yuan; LRI: lower respiratory infections.

^aTwo years' average number of the UEBMI participants is 88.5 million in 74 cities during 2016-2017.

Discussion

In general, our study provides the first detailed evaluation about the excess hospitalization expenditure burden attributable to short-term exposure to ambient $\text{PM}_{2.5}$ based on daily hospital admission data from a large population over multiple cities in the context of high air pollution in China. Our results show that ambient $\text{PM}_{2.5}$ would significantly increase the hospital admissions, total expenses and total hospital stays for three major cause-specific cardiorespiratory diseases responsible for population disease burden including LRI, CHD and stroke. The attributable hospital admissions, total expenses and total hospital stays would reach 362,007 hospital admission cases, 3.68 billion CNY expenses (\$US 550 million) and 5.21 million hospital days for the entire urban employee population (299 million averaged over 2016-2017) in China assum-

ing the same exposure-response relationship between short-term exposure to ambient $\text{PM}_{2.5}$ and the examined health outcomes as found in the present study. These results suggest that short-term exposure to ambient $\text{PM}_{2.5}$ pollution could lead to significant health and economic impacts in China.

Health expenditure has been increasing in China. A previous study reported that the governmental health expenditures on health care quadrupled from 359 billion CNY to 1.52 trillion CNY from 2008 to 2017³⁹. Ambient air pollution is among the leading risk factors for increasing health expenditure¹¹. A number of existing studies have evaluated the health and economic burden associated with long-term exposure to ambient air pollution based on measures of mortality and statistics of life (e.g., disability-adjusted life years), whereas few studies have focused on the impact of short-term exposure to ambient air pollution due to a range of barriers. For example, a previous study shows that the total respiratory disease and cardiovascular disease-specific hospital admission morbidities attributable to long-term exposure to ambient $\text{PM}_{2.5}$ are 0.61 million and 0.36 million in China in 2016, respectively, based on baseline incidence rates derived from previous references¹⁶.

Short-term exposure to ambient $\text{PM}_{2.5}$ may also lead to substantial health burden in addition to long-term exposure to ambient $\text{PM}_{2.5}$ ^{32,40}, and therefore the potential socioeconomic impact of ambient air pollution may have been underestimated in the literature because of sparse evidence on the economic evaluation for short-term exposure^{41,42}. A recent study evaluates the

Table 5

Projection of attributable numbers of hospital admissions, total expenses and total hospital stays associated with ambient PM_{2.5} at lag 0-2 from the included cities to the national level during 2016-2017

Disease	Health variable	Included cities ^a (95% CI)	National level ^b (95% CI)
LRI	Hospital admissions (case)	28 560 (3 796, 52 990)	96 491 (12 825, 179 028)
	Total expenses (million CNY)	220 (29, 408)	743 (98, 1 378)
	Total hospital stays (thousand day)	314 (82, 543)	1 110 (291, 1 918)
	Economic loss from work day loss (million CNY)	50 (13, 86)	177 (46, 303)
CHD	Hospital admissions (case)	54 600 (16 808, 91 820)	184 468 (56 786, 310 217)
	Total expenses (million CNY)	458 (141, 772)	1 547 (476, 2 608)
	Total hospital stays (thousand day)	686 (363, 1003)	2 426 (1 281, 3 546)
	Economic loss from work day loss (million CNY)	103 (56, 153)	363 (196, 539)
Stroke	Hospital admissions (case)	23 989 (7 212, 40 551)	81 048 (24 366, 137 003)
	Total expenses (million CNY)	410 (123, 694)	1 385 (416, 2 345)
	Total hospital stays (thousand day)	473 (234, 707)	1 670 (829, 2 499)
	Economic loss from work day loss (million CNY)	73 (36, 108)	258 (127, 382)

Abbreviations: CHD: coronary heart disease; CNY: Chinese Yuan; LRI: lower respiratory infections.

^aAttributable hospital admissions and total expenses are calculated based on data from 74 cities with an average coverage of 88.5 million population during 2016-2017, whereas attributable total hospital stays and economic loss from work day loss are calculated based on data from 69 cities with an average coverage of 84.6 million population during 2016-2017.

^bThe UEBMI covers an average urban employee population of 299 million in China during 2016-2017.

health burden and economic loss attributable to short-term exposure to ambient air pollution in China based on data obtained from the national statistical yearbook and other similar sources and exposure-response functions for different ambient air pollutants published in previous epidemiological studies⁴¹. They estimate that the summed economic loss of hospital admissions for cardiovascular and respiratory diseases attributable to short-term exposure to six major ambient air pollutants is 71.81 billion CNY in 2017 in China⁴¹. This estimate is much higher than our estimate of 3.68 billion CNY for ambient PM_{2.5} alone for three cause-specific cardiorespiratory diseases during 2016-2017. Nevertheless, our study does not include other cardiorespiratory diseases beyond the three major cardiorespiratory diseases (i.e., LRI, CHD, stroke) and our study population is also limited to urban employees. However, it should be noted that the exposure-response functions obtained from different studies may be heterogeneous, and levels of different ambient air pollutants are usually highly correlated with each other, and the attributable economic loss estimates for different air pollutants may be substantially overlapped under such conditions. In contrast, our study uses detailed daily hospital admission data from the UEBMI database which could help generate reliable exposure-response function for the estimation of related hospitalization expenditures, and thus may serve as a novel dimension to improve the assessment of economic burden of air pollution on human health. Nevertheless, our study only reflects the direct expenditures on the hospital admissions for the LRI, CHD and stroke, which may still underestimate the economic burden related to short-term exposure to ambient PM_{2.5}.

In addition to the direct expenses due to hospital admissions, ambient PM_{2.5} will also increase the economic loss due to absence from work for the hospitalized patients. The related direct economic loss of absence from work for the younger adults (15-64 years) subgroup would be 226 million CNY (US\$ 33.8 million) in the included cities during the study period, and would increase to 798 million CNY (US\$ 119.3 million) for the entire urban employee population in China during the study period (Table 5).

Furthermore, there are also additional costs for other healthcare behaviors such as wages for nursing workers or economic loss due to absence from work for close relatives of the hospitalized patients. In support of these results, one previous study based on the survey data from the Health and Retirement Study and hospitalization data in the US finds that hospital admissions increase out-of-pocket medical spending, unpaid medical bills, and bankruptcy, and reduce earnings which are substantial compared to the out-of-pocket spending increase⁴³. Another study on health burden in the European Union also shows that the productivity loss because

of early death cost and lost working days account for 41% of total health cost of cancer in EU, which is a little bit higher than the health care cost proportion of 40%⁴⁴. Furthermore, if we include the outpatient visits, the direct expenses would be much higher than the present estimation.

Our study also provides specific evaluation for subgroups divided by region, gender and age, and finds some interesting results. First, the AF estimates of hospital admissions and total expenses for CHD and stroke in the northern region are significant and generally higher than those in the southern region, whereas the AF estimates of hospital admissions and total expenses for LRI in the southern region are higher than those in the northern region. This finding suggests that short-term exposure to ambient PM_{2.5} may have different impact patterns over the northern and southern regions of China, and CHD and stroke are more likely to be affected by ambient PM_{2.5} in the northern region whereas LRI is more likely to be affected by ambient PM_{2.5} in the southern region. The major reason for the regional difference in the AF estimates for CHD and stroke would be the higher average ambient PM_{2.5} concentration in the northern region than in the southern region, because the AF estimates are calculated based on the average ambient PM_{2.5} concentration. As for the regional difference in the AF estimates for LRI, it is plausible that high relative humidity in the southern region could provide suitable microenvironment for growth of microorganism, which could be absorbed on the surface of ambient PM_{2.5} and may further increase the risk of LRI when inhaled into the body. Therefore, a same unit increase in ambient PM_{2.5} in the southern region may have a higher potential to increase the risk of LRI than in the northern region. In addition, the AN estimates for the total expenses of all three diseases in the southern region are all higher than in the northern region. The higher absolute values of total expenses attributable to ambient PM_{2.5} in the southern region suggest that hospitalized patients in the southern region may have a stronger affordability than in the northern region, which may be determined by local economic development levels, as per capita GDP and average income are higher in the southern region. This finding suggests that additional reduction of ambient PM_{2.5} would save more expenses in the southern region than in the northern region. Nevertheless, the difference between different regions may also be associated with the severity of the investigated diseases, which is unavailable in the present study, and future studies are encouraged to investigate this issue in detail.

We also find that the AF estimates tend to be higher in males than in females, and also tend to be higher in older adults (≥65 years) subgroup than in younger adults (15-64 years) subgroup. These results provide clues for the susceptible population in the

context of high ambient air pollution. Males are likely to have more outdoor activities compared to females due to differences in occupation characteristics, and thus may have higher exposures to ambient PM_{2.5}. The work intensity and activity level of males are also higher than those of females, resulting in increased respiratory rates in males than in females. Therefore, males are likely to absorb more ambient PM_{2.5} than females under the same air pollution condition. In addition, animal experiments in mice find that male offspring of dams exposing to diesel exhaust (a major source for ambient PM_{2.5}) along with stress restriction during pregnancy have a greater pro-inflammatory change in microglial-derived cytokine levels compared to female offspring in their adulthood, suggesting a potentially higher health susceptibility of male offspring in response to air pollution exposure vs. female offspring⁴⁵. A human exposure study also supports a more apparent increase in inflammation-related gene expression profiles in males than in females after exposure to wood smoke, another source for ambient air pollution⁴⁶. Individuals aged ≥ 65 years have declined body function compared to younger individuals, and thus would be more vulnerable to ambient air pollution.

This study has several limitations. First, we only use the city level ambient PM_{2.5} concentrations from fixed-site air monitoring stations which do not reflect personal exposures to ambient PM_{2.5}, and there exists certain exposure measurement error. Nevertheless, it has been shown that fixed-site air monitoring measurements could reflect ambient air pollution levels of the urban background to a certain extent⁴⁷, and the monitoring data have been commonly used as a proxy for population exposure to ambient air pollution in previous time-series analyses^{25,26,48}. Second, this study only covers the health data in 2016 and 2017 and cannot assess the long-term impact of ambient PM_{2.5} over multiple years. The digitization is happening quite near in China, and it is difficult to get detailed daily hospital admission data over multiple cities in the past. Future studies with daily hospital admission data over multiple years will provide useful information about the changes in AF estimates associated with exposure to ambient air pollution over stages with different air pollution conditions, and help evaluate the effectiveness of air pollution control action implemented by the government. Third, the UEBMI database used in this study covers the urban employee population but does not include children under 15 years old and the population in the rural areas, which may underestimate the health and economic losses associated with short-term exposure to ambient PM_{2.5} in China. Fourth, some potential confounding variables, such as traffic noise, light pollution, have also been found to affect human health^{49,50}, but related data are not available in our study. Future studies are encouraged to investigate the potential confounding effects of these factors in the context of ambient air pollution. Finally, this study only estimates the health and economic losses associated with ambient PM_{2.5} concentrations, and is unable to consider the impact of different chemical components or emission sources of ambient PM_{2.5}, which may vary over different regions of China. Ambient PM_{2.5} is a mixture consisting of various chemical components with different toxicological potentials from different emission sources, all of which may have contributed to the observed results.

In summary, our study provides evidence for the increased hospital admissions, total expenses and total hospital stays of three cause-specific cardiorespiratory diseases, including LRI, CHD and stroke, in association with short-term exposure to ambient PM_{2.5} in a large urban population in China. The projected attributable numbers for short-term exposure to ambient PM_{2.5} would be 362,007 hospital admission cases, 3.68 billion CNY expenses (\$US 550 million) and 5.21 million hospital days for the entire urban employee population (299 million) in China during 2016–2017. Our results also show that ambient PM_{2.5} pollution may lead to higher attributable proportions of health and economic

losses for CHD and stroke in the northern region, and higher attributable proportions of health and economic losses for LRI in the southern region. Most existing studies on the economic evaluation related to ambient air pollution are conducted in developed countries, where ambient PM_{2.5} concentrations are much lower than that in developing countries. Given that billions of people live in the over polluted regions with ambient PM_{2.5} levels over the WHO guideline, especially in developing countries, the potential economic loss due to short-term exposure to ambient PM_{2.5} would be enormous over the world. Our findings may provide important evidence for ambient air pollution control action from the angle of input-output (policy cost-benefit) balance especially in developing countries, because accurately estimating the impact of ambient air pollution is crucial to the establishment of effective air quality regulations.

Contributors

YX, HZ, XLF and SW designed the study; YX, ZL, HZ, and PL performed the data analysis; ZX and TG collected the exposure data; YS, JW, LC and CW provided the health data; YX, ZL, HZ and SW wrote the paper; FD, AAB, ZZ, and XG provided critical comments; SW provided study supervision, and all authors approved the paper for submission. The authors declare no conflict of interest.

Data sharing statement

The environmental data used in this study are publicly available. The health data required for the analysis in this study were obtained from the urban employee-based basic medical insurance scheme (UEBMI) of China operated by Ministry of Human Resources and Social Security of the People's Republic of China. The study is carried out under privacy protection. The health data owner confirmed that the data cannot be made to the public due to privacy reasons.

Editor note: The Lancet Group takes a neutral position with respect to territorial claims in published maps and institutional affiliations.

Declaration of Competing Interest

We declare no competing interests.

Acknowledgments

None.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:[10.1016/j.lanwpc.2021.100232](https://doi.org/10.1016/j.lanwpc.2021.100232).

References

- [1] Burnett R, Chen H, Szyszkowicz M, et al. Global estimates of mortality associated with long-term exposure to outdoor fine particulate matter. In: *Proceedings of the National Academy of Sciences*, 115; 2018. p. 9592–7.
- [2] Collaborators GRFGlobal, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *The Lancet* 2018;392(10159):1923–94.
- [3] WHO. Burden of disease from ambient and household air pollution. 2015.
- [4] Burnett RT, Pope CA, Ezzati M, et al. An integrated risk function for estimating the global burden of disease attributable to ambient fine particulate matter exposure. *Environmental Health Perspectives* 2014;122(4):397–403.
- [5] Cr Pope, Burnett RT, Turner MC, et al. Lung cancer and cardiovascular disease mortality associated with ambient air pollution and cigarette smoke: shape of the exposure-response relationships. *Environ Health Perspect* 2011;119(11):1616–21.

- [6] Krewski D, Jerrett M, Burnett RT, et al. Extended follow-up and spatial analysis of the American Cancer Society study linking particulate air pollution and mortality. MA: Health Effects Institute Boston; 2009.
- [7] Cohen AJ, Ross Anderson H, Ostro B, et al. The Global Burden of Disease Due to Outdoor Air Pollution. *Journal of Toxicology and Environmental Health, Part A* 2005;68(13-14):1301-7.
- [8] Pope III CA, Burnett MJ, Thun, et al. Lung cancer, cardiopulmonary mortality, and long-term exposure to fine particulate air pollution. *JAMA* 2002;287(9):1132-41.
- [9] Markandya A, Sampietro J, Smith SJ, et al. Health co-benefits from air pollution and mitigation costs of the Paris Agreement: a modelling study. *The Lancet Planetary Health* 2018;2(3):e126-ee33.
- [10] Lanzi E, Dellink R, Chateau J. The sectoral and regional economic consequences of outdoor air pollution to 2060. *Energy Economics* 2018.
- [11] Landrigan PJ, Fuller R, Acosta NJR, et al. The Lancet Commission on pollution and health. *Lancet* 2018;391(10119):462-512.
- [12] Lelieveld J, Pozzer A, Pöschl U, Fnaiss M, Haines A, Münzel T. Loss of life expectancy from air pollution compared to other risk factors: a worldwide perspective. *Cardiovasc Res* 2020;116(11):1910-17.
- [13] Lelieveld J, Klingmüller K, Pozzer A, et al. Cardiovascular disease burden from ambient air pollution in Europe reassessed using novel hazard ratio functions. *Eur Heart J* 2019;40(20):1590-6.
- [14] Hu J, Huang L, Chen M, et al. Premature mortality attributable to particulate matter in China: source contributions and responses to reductions. *Environmental Science & Technology*; 2017.
- [15] Cohen A, Brauer M, Burnett RT, et al. Estimates and 25-year trends of the global burden of disease attributable to ambient air pollution: an analysis of data from the Global Burden of Diseases Study. *The Lancet* 2015;389(10082):1907-18 2017.
- [16] Maji KJ, Ye W-F, Arora M, Nagendra SS. PM_{2.5}-related health and economic loss assessment for 338 Chinese cities. *Environment International* 2018;121:392-403.
- [17] Yang J, Zhang B. Air pollution and healthcare expenditure: Implication for the benefit of air pollution control in China. *Environment International* 2018;120:443-55.
- [18] Horne BD, Joy EA, Hofmann MG, et al. Short-term elevation of fine particulate matter air pollution and acute lower respiratory infection. *Am J Respir Crit Care Med* 2018;198(6):759-66.
- [19] Mustafic H, Jabre P, Caussin C, et al. Main Air Pollutants and Myocardial Infarction: A Systematic Review and Meta-analysis. *JAMA* 2012;307(7):713-21.
- [20] Shah ASV, Lee KK, McAllister DA, et al. Short term exposure to air pollution and stroke: systematic review and meta-analysis. *BMJ* 2015;350:h1295.
- [21] Groves CP, Butland BK, Atkinson RW, Delaney AP, DVJlcm Pilcher. Intensive care admissions and outcomes associated with short-term exposure to ambient air pollution: a time series analysis. *Intensive Care Med* 2020;46(6):1213-21.
- [22] Host S, Larrieu S, Pascal L, et al. Short-term associations between fine and coarse particles and hospital admissions for cardiorespiratory diseases in six French cities. *Occup Environ Med* 2008;65(8):544-51.
- [23] Burnett RT, Cakmak S, Brook JR, Krewski D. The role of particulate size and chemistry in the association between summertime ambient air pollution and hospitalization for cardiorespiratory diseases. *Environmental health perspectives* 1997;105(6):614-20.
- [24] Ebenstein A, Fan M, Greenstone M, He G, Zhou M. New evidence on the impact of sustained exposure to air pollution on life expectancy from China's Huai. *PNAS* 2017;114:6.
- [25] Tian Y, Liu H, Zhao Z, et al. Association between ambient air pollution and daily hospital admissions for ischemic stroke: A nationwide time-series analysis. *PLoS Med* 2018;15(10):e1002668.
- [26] Gu X, Guo T, Si Y, et al. Association between ambient air pollution and daily hospital admissions for depression in 75 Chinese cities. *Am J Psychiatry* 2020;177(8):735-43.
- [27] Moore HC, de Klerk N, Jacoby P, Richmond P, Lehmann D. Can linked emergency department data help assess the out-of-hospital burden of acute lower respiratory infections? A population-based cohort study. *BMC Public Health* 2012;12:703.
- [28] Ricci C, Wood A, Muller D, et al. Alcohol intake in relation to non-fatal and fatal coronary heart disease and stroke: EPIC-CVD case-cohort study. *BMJ* 2018;361:k934.
- [29] Ministry of Environmental Protection of China Technical regulation for selection of ambient air quality monitoring stations (on trial). Beijing: China Environmental Science Press; 2013.
- [30] Gasparrini A. Modeling exposure-lag-response associations with distributed lag non-linear models. *Stat Med* 2014;33(5):881-99.
- [31] Liu C, Chen R, Sera F, et al. Ambient particulate air pollution and daily mortality in 652 cities. *N Engl J Med* 2019;381(8):705-15.
- [32] Di Q, Dai L, Wang Y, et al. Association of short-term exposure to air pollution with mortality in older adults. *JAMA* 2017;318(24):2446-56.
- [33] Tian Y, Liu H, Wu Y, et al. Association between ambient fine particulate pollution and hospital admissions for cause specific cardiovascular disease: time series study in 184 major Chinese cities. *BMJ* 2019;367:l6572.
- [34] Gasparrini A, Armstrong B, Kovats S, Wilkinson P. The effect of high temperatures on cause-specific mortality in England and Wales. *Occup Environ Med* 2012;69(1):56-61.
- [35] Chen G, Zhang Y, Zhang W, et al. Attributable risks of emergency hospital visits due to air pollutants in China: A multi-city study. *Environmental pollution* 2017;228:43-9.
- [36] Wei Y, Wang Y, Di Q, et al. Short term exposure to fine particulate matter and hospital admission risks and costs in the medicare population: time stratified, case crossover study. *BMJ* 2019;367:l6258.
- [37] National Bureau of Statistics of China CHINA STATISTICAL YEARBOOK. China Statistics Press; 2017.
- [38] National Bureau of Statistics of China CHINA STATISTICAL YEARBOOK. China Statistics Press; 2016.
- [39] Yip W, Fu H, Chen AT, et al. 10 years of health-care reform in China: progress and gaps in universal health coverage. *The Lancet* 2019;394(10204):1192-204.
- [40] Di Q, Wang Y, Zanobetti A, et al. Air pollution and mortality in the medicare population. *N Engl J Med* 2017;376(26):2135-6.
- [41] Yao M, Wu G, Zhao X, Zhang J. Estimating health burden and economic loss attributable to short-term exposure to multiple air pollutants in China. *Environmental Research* 2020;183:109184.
- [42] Li X, Tang K, Jin XR, et al. Short-term air pollution exposure is associated with hospital length of stay and hospitalization costs among inpatients with type 2 diabetes: a hospital-based study. *J Toxicol Env Heal A* 2018;81(17):819-29.
- [43] Dobkin C, Finkelstein A, Kluender R, Notowidigdo MJ. The economic consequences of hospital admissions. *The American Economic Review* 2018;108(2):308-52.
- [44] Luengofernandez R, Leal J, Gray A, Sullivan R. Economic burden of cancer across the European Union: a population-based cost analysis. *Lancet Oncology* 2013;14(12):1165-74.
- [45] Bolton JL, Huff NC, Smith SH, et al. Maternal stress and effects of prenatal air pollution on offspring mental health outcomes in mice. *Environmental health perspectives* 2013;121(9):1075-82.
- [46] Rebuli ME, Speen AM, Martin EM, et al. Wood smoke exposure alters human inflammatory responses to viral infection in a sex-specific manner: a randomized, placebo-controlled study. *Am J Respir Crit Care Med* 2019;199(8):996-1007.
- [47] Chen R, Kan H, Chen B, et al. Association of particulate air pollution with daily mortality: the China Air Pollution and Health Effects Study. *Am J Epidemiol* 2012;175(11):1173-81.
- [48] Vicedo-Cabrera AM, Sera F, Liu C, et al. Short term association between ozone and mortality: global two stage time series study in 406 locations in 20 countries. *BMJ* 2020;368:m108.
- [49] Münzel T, Daiber A. Environmental stressors and their impact on health and disease with focus on oxidative stress. *Antioxid Redox Signal* 2018;28(9):735-40.
- [50] Münzel T, Hahad O, Daiber A. The dark side of nocturnal light pollution. Outdoor light at night increases risk of coronary heart disease. *Eur Heart J* 2021;42(8):831-4.