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Estimating mortality burden attributable to short-term PM_{2.5} exposure: A national observational study in China

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Abstract

Studies worldwide have estimated the number of deaths attributable to long-term exposure to fine airborne particles (PM_{2.5}), but limited information is available on short-term exposure, particularly in China. In addition, most existing studies have assumed that short-term PM2.5-mortality associations were linear. For this reason, the use of linear exposure-response functions for calculating disease burden of short-term exposure to PM_{2.5} in China may not be appropriate. There is an urgent need for a comprehensive, evidence-based assessment of the disease burden related to short-term PM_{2.5} exposure in China. Here, we explored the non-linear association between short-term PM_{2.5} exposure and all-cause mortality in 104 counties in China; estimated countyspecific mortality burdens attributable to short-term PM2.5 exposure for all counties in the country and analyzed spatial characteristics of the mortality burden due to short-term PM2.5 exposure in China. The pooled $PM_{2.5}$ -mortality association was non-linear, with a reversed J-shape. We found an approximately linear increased risk of mortality from 0 to 62 μg/m³ and decreased risk from 62 to 250 µg/m³. We estimated a total of 169,862 additional deaths from short-term PM_{2.5} exposure throughout China in 2015. Models using linear exposure-response functions for the PM_{2.5}-mortality association estimated 32,186 deaths attributable to PM_{2.5} exposure, which is 5.3 times lower than estimates from the non-linear effect model. Short-term PM2.5 exposure contributed greatly to the death burden in China, approximately one seventh of the estimates from the chronic effect. It is essential and crucial to incorporate short-term PM2.5-related mortality estimations when considering the disease burden attributable to PM2.5 in developing countries

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such as China. Traditional linear effect models likely underestimated the mortality burden due to short-term exposure to $PM_{2.5}$.

Keywords

PM_{2.5}; Short-term; Mortality burden; Non-linear

1. Introduction

Fine particulate matter (particles $2.5 \, \mu m$ in aerodynamic diameter; $PM_{2.5}$) has been a major public health concern in China over the past few decades, ranking fifth among risk factors for disease burden in China in 2010 (Forouzanfar et al., 2016). According to the most recent Global Burden of Disease (GBD) study, exposure to ambient $PM_{2.5}$ caused 4.2 million deaths globally in 2015 (Cohen et al., 2017). China leads the world in disease burden attributable to $PM_{2.5}$, which accounted for more than one-quarter of total $PM_{2.5}$ -attributable deaths in the world in 2015 (Cohen et al., 2017). Many studies performed using the GBD methodology have confirmed that over one million deaths are attributable to $PM_{2.5}$ exposure in China (Wang et al., 2018; Lelieveld et al., 2015; Lim et al., 2012; J. Liu et al., 2016; M. Liu et al., 2016). Notably, all of these results from previous studies have focused on the estimations of deaths attributable to the chronic effects of $PM_{2.5}$.

Many studies have shown that short-term exposure to $PM_{2.5}$ is related to increased risks of mortality (Atkinson et al., 2014; Chen et al., 2018; Chen et al., 2017). Thus, the mortality burden due to short-term exposure to $PM_{2.5}$ may also be serious in China because of the combined impact of the high magnitude of $PM_{2.5}$ exposure and the large population. A quantitative estimate of the disease burden related to short-term $PM_{2.5}$ exposure is urgently needed in China to develop better emission control, disease control, and health policies.

Although a large number of air pollution epidemiologic studies have shown that short-term exposure to $PM_{2.5}$ is associated with mortality, the assumption for the exposure-response relationship is critical for calculating the burden of disease. Generally, a linear exposure-response function is used to calculate the burden of disease due to short-term $PM_{2.5}$ exposure (Atkinson et al., 2014). However, recently, little evidence has suggested that the association between short-term $PM_{2.5}$ exposure and mortality is non-linear in China (Chen et al., 2017; Chen et al., 2011), which has not been found in previous studies in developed countries with low exposure levels (Daniels et al., 2000; Schwartz and Zanobetti, 2000; Schwartz et al., 2002). As such, the use of linear exposure-response functions for calculating disease burden of short-term exposure to $PM_{2.5}$ in China may not be appropriate.

To address the limitations listed above, this study investigated the national level mortality burden attributable to short-term exposure of $PM_{2.5}$ in China. Our objectives are as follows: (1) to explore the nonlinear association between short-term $PM_{2.5}$ exposure and all-cause mortality in 104 counties in China; (2) to estimate county-specific mortality burdens attributable to short-term $PM_{2.5}$ exposure for all counties in the country; and (3) to analyze spatial characteristics of the mortality burden due to short-term $PM_{2.5}$ exposure in China.

2. Methods

2.1. Data

We collected daily county level (a key unit for administration and policy making in China) mortality, PM_{2.5} and meteorological data from 2013 to 2015 in 104 counties in China from SHEAP dataset (SHEAP data is from the project of short-term health effect of air pollution in China). The locations of the counties are shown in Fig. 1. Daily county-specific all-cause mortality data were collected from the Chinese Center for Disease Control and Prevention. Daily county-specific mean temperature and relative humidity were collected from the China Meteorological Data Sharing Service System. Daily county-specific PM_{2.5} data were estimated from Moderate Resolution Imaging Spectroradiometer (MODIS) collection 6 level 2 aerosol optical depth (AOD) at 10 km resolution. We used multiple imputation to fill in missing satellite data and then divided the study domain into seven clusters to control for unobserved spatial heterogeneity. We trained a cluster-based random forest model with daily convolution layer of PM2.5 constructed from ground PM2.5 measurements as an input to account for the spatial autocorrelation of PM_{2.5}. The centroid of each 10 km grid was spatially joined with the selected 104 counties. An unweighted average of PM_{2.5} concentrations was calculated when a county contained more than one PM_{2.5} grid. If no PM_{2.5} grids fell within the county, then the closest grid was assigned as the PM_{2.5} concentration for that county.

Fig. S1 shows the workflow of PM2.5 modeling. First, we filled missing satellite data by multiple imputation including the Moderate Resolution Imaging Spectroradiometer (MODIS) aerosol optical depth (AOD) from Aqua and Terra satellites, the MODIS cloud fraction (Platnick et al., 2003), the Community Multi-scale Air Quality (CMAQ) AOD simulations (Appel et al., 2012), and elevation data (Xiao et al., 2017). After gap-filling, the coverage of satellite retrieval increased to 100% in space and time. Second, the modeling domain was divided into seven clusters using geographically weighted regression (GWR), the K-means algorithm, and GIS methods. Dividing a large modeling domain into sub-regions controlled unobserved spatial heterogeneity and improved model performance. This cluster pattern was stable in time. Random forest models were trained in each region separately. Finally, we used the fitted random forest models to estimate daily PM_{2.5} concentrations at grid cells without monitor. To evaluate model performance, the ten-fold cross validation results are shown in Fig. S2. The random forest model predictions were closely consistent with ground measurements, with R2 larger than 0.90 and slope close to 1.0.

To estimate the additional deaths attributable to $PM_{2.5}$ in China in 2015, we also extracted county-specific population and total mortality rate data for all of the counties in China from the sixth nationwide population census (National Bureau of Statistics of China, 2015). The county-specific daily $PM_{2.5}$ of all 2851 counties in China in 2015 was also modeled using the method mentioned above.

2.2. Statistical analysis

2.2.1. Non-linear effect model—A three-stage analysis was performed in this study. In the first stage, we estimated the county-specific non-linear PM_{2.5}-mortality relationships in 104 counties in China. During the second stage, we pooled the estimated county-specific exposure-response functions using a meta-regression model. In the third stage, we estimated the additional deaths due to short-term exposure to PM_{2.5} in China in 2015 by combining the pooled PM_{2.5}-mortality association and county-level daily PM_{2.5} exposure.

2.2.1.1. First stage analysis.: We implemented a standard time series quasi-Poisson regression for each county to evaluate the effect of sameday $PM_{2.5}$ on all-cause mortality. We modeled the exposure-response curve with natural cubic splines with two internal knots at 35 µg/m³ and 75 µg/m³ of $PM_{2.5}$ concentrations for the main analysis. We applied a county-specific 95% percentile of $PM_{2.5}$ concentration as the cut-off point for $PM_{2.5}$ values to avoid extremely high values which affected the model performance. We controlled for day of the week as a categorical variable, daily mean temperature and relative humidity using a natural cubic spline with 3 degrees of freedom (df) respectively, and seasonal and long-term trends with a natural cubic spline with 5 df per year. We then predicted the county-specific log relative risk (RR) and standard error (SE) for daily $PM_{2.5}$ exposure.

2.2.1.2. Second stage analysis.: In the second stage, we pooled the associations between PM_{2.5} and mortality for 104 counties using a random-effect meta-regression with restricted maximum likelihood (REML) estimation.

The main model above is defined as Model 1. We conducted several sensitivity analyses to check the non-linear association. We used a linear model to examine the linear association between PM_{2.5} and mortality (Model 2). We set natural cubic splines with three knots at 35 $\mu g/m^3$, 50 $\mu g/m^3$, and 75 $\mu g/m^3$ (Model 3), and with four knots at 35 $\mu g/m^3$, 50 $\mu g/m^3$, 75 $\mu g/m^3$, and 125 $\mu g/m^3$ (Model 4). The knots were also changed in the first stage analysis for Model 3 and Model 4. We used I² statistics to quantify the heterogeneity among models (Supplementary Table S3), and we selected model 1, which provided the lowest I² value in the main analysis. We used 0 $\mu g/m^3$ as the centering value and the reference PM_{2.5} concentration to calculate the relative risks.

2.2.1.3. Third stage analysis.: We finally applied model 1 to predict $PM_{2.5}$ and all-cause mortality associations in all 2851 counties in China to calculate the additional short-term all-cause deaths related to $PM_{2.5}$ in 2015 by incorporating county-specific modeled daily $PM_{2.5}$ concentrations, county-specific populations, and mortality rates from the sixth nationwide population census.

Daily additional deaths attributable to $PM_{2.5}$ for county *i* were calculated as follows:

$$\Delta Mortality_i = Y_i \times ERC_i \times POP_i. \tag{1}$$

Here, Mortality_i is the daily $PM_{2.5}$ -related additional deaths in county i, Y_i represents the baseline daily mortality rate in county i, POP_i is the population in county i. ERC_i is the

attributable percentage variation in mortality for a specified variation in $PM_{2.5}$, derived from the calculated relative risk at each $PM_{2.5}$ concentration from the meta-regression model in the second stage of analysis.

We calculated the daily death attributable to $PM_{2.5}$ by this method for all 365 days in 2015 in each county. We then calculated the sum of $PM_{2.5}$ -related deaths in all counties in China in 2015.

2.2.2. Linear effect model—We also conducted the same analysis using a linear effect model for the $PM_{2.5}$ -mortality association and mortality burden estimation for comparison with the non-linear effect models. A three-stage analysis was used to investigate the relationship of the $PM_{2.5}$ and morality and the mortality burden of $PM_{2.5}$.

In the first stage, generalized linear models assuming a quasi-Poisson distribution were used to generate county-specific PM_{2.5}-mortality associations. Same-day PM_{2.5} concentrations were used in the main analysis (Table S2). We controlled for daily average temperature, relative humidity, day of the week, and calendar date in the model. The covariates were adjusted according to the following: a natural cubic spline with 3 degrees of freedom (df) for daily mean temperature and daily mean relative humidity, a natural cubic spline with 5 df per year for the long-term trend and day of the week. Sensitivity analyses were also conducted to check the robustness of the results in the main analysis (Table S1). In the second stage, we pooled the county-specific associations to generate an overall association between PM_{2.5} and mortality by conducting a random-effect meta-analysis. In the third stage, we used the association from the second stage to calculate the additional short-term all-cause deaths related to PM_{2.5} in 2015 by incorporating the county-specific modeled daily PM_{2.5} concentrations, county-specific populations, and mortality rates from the sixth nationwide population census. We calculated the daily death attributable to PM_{2.5} by this method for all 365 days in 2015 in each county. We then calculated the sum of PM_{2.5}-related deaths in all of the counties in China in 2015.

All of the analyses were performed using the R statistical software (version 3.3.1, 64-bit, Foundation for Statistical Computing, Vienna, Austria). The "mvmeta" and "dlnm" package in R software was used in this study.

3. Results

Fig. 1 presents $PM_{2.5}$ concentrations during the study period (2013–2015). The blue points show centroids of the 104 counties used in the first stage of analysis. The 104 counties cover all seven geographic regions in China (Eastern, Northern, Central, Southern, Southwestern, Northwestern, and Northeastern) and 31 provinces (except Hong Kong, Macao, and Taiwan). The highest $PM_{2.5}$ concentrations were observed in the Beijing-Tianjin-Hebei region, with annual mean concentrations above $100 \, \mu \text{g/m}^3$. Table S2 shows the descriptive statistics for mortality, $PM_{2.5}$, and meteorological data for the 104 counties. The dataset included 1,069,911 deaths. Approximately 9 all-cause deaths per day on average occurred during the study period, with the highest number of daily average, 28 deaths per day, recorded in Yongqiao County in Anhui Province. The overall mean daily concentrations of $PM_{2.5}$ were

61.6 $\mu g/m^3$ in these 104 counties. The highest county-specific daily mean concentration of PM_{2.5} is 106.7 $\mu g/m^3$, which was recorded in Xingtai County in Hebei Province. The lowest county-specific daily mean concentration of PM_{2.5} was 23.2 $\mu g/m^3$, which was recorded in Meilan County in Hainan Province.

The association between daily $PM_{2.5}$ concentration and relative risk of total mortality from model 1 is shown in Fig. 2. The association was non-linear, with approximately linear increasing mortality risk from 0 to 62 μ g/m³. From 62 to 250 μ g/m³, the risk decreases gradually. The RRs are 1.026 (95% CI: 1.014–1.038) and 1.031 (95% CI: 1.021–1.042) for $PM_{2.5}$ concentration of 35 μ g/m³ and 75 μ g/m³ versus 0 μ g/m³, respectively. The I^2 of model 1 is 22%, which accounts for the minimum heterogeneity among all the models. The I^2 statistics of all models is shown in Table S3, and model 2 (linear effect model) showed the most heterogeneity. The associations between $PM_{2.5}$ and mortality estimated by model 2, model 3, and model 4 are shown in Figs. S3, S4, and S5, respectively.

Regional statistics of county level population, mortality rate, and annual $PM_{2.5}$ concentration are shown in Table S4. The predicted number of additional deaths attributable to $PM_{2.5}$ and the corresponding additional death rate in the seven regions of China in 2015 are shown in Table 1. The number of predicted additional deaths attributable to short-term $PM_{2.5}$ exposure was 169,862 (95% CI: 97,994, 240,967), and the additional death rate was 13.78 (95% CI: 7.95–19.55) per 100,000 people throughout China in 2015. The highest additional death was observed in Eastern China, with 52,502 (95% CI: 30,505–74,266) deaths. The population of Eastern China is 358,863,351, and the average mortality rate is 6.0% with a mean annual $PM_{2.5}$ concentration of 49.5 μ g/m³. The highest additional death rate was 15.03 (95% CI: 8.51–21.49) per 100,000 people in Southwestern China, which has a population of 185,917,082, an average mortality rate of 6.5%, and a mean annual $PM_{2.5}$ concentration of 35.1 μ g/m³. The mortality burden of $PM_{2.5}$ estimated from linear effect model was 32,186 (95% CI: 10,705–53,631) in China, which is much lower than the estimation from the non-linear effect model.

We estimated and mapped county-specific additional deaths associated with short-term exposure to $PM_{2.5}$, as well as additional deaths rate (1/100,000) and additional deaths per $100~\rm km^2$ (Figs. 3, 4, and S6). Regions of high additional deaths included the Beijing-Tianjin-Hebei area in Northern China, the Yangtze River Delta in Eastern China, the Changsha-Zhuzhou-Xiangtan and Wuhan area in Central China, the Sichuan Basin in Southwestern China, and the southwest coast of Guangdong Province in Southern China. The spatial pattern of the increase in death rates showed little difference than those for additional deaths. Aside from the Beijing-Tianjin-Hebei area in Northern China, the Yangtze River Delta in Eastern China and Sichuan Basin in Southwestern China, the North Tibet area in Southwestern China, the South Sinkiang area in Northwestern China and Liaoning Province in Northeastern China also exhibited high additional death rates. The spatial pattern of additional deaths per $100~\rm km^2$ was similar to that of additional deaths except for southwest region.

4. Discussion

To the best of our knowledge, this is the first study to evaluate county-specific additional deaths due to short-term $PM_{2.5}$ exposure in China using a non-linear effect model. The impacts of short-term exposure to $PM_{2.5}$ on mortality were linearly positive from 0 to 62 $\mu g/m^3$, and then decreasing RR from 62 to 250 $\mu g/m^3$. We estimated the number of deaths related to short-term exposure of $PM_{2.5}$ from the non-linear model to be 169,862 (95% CI: 97,994 and 240,967) for the entire country in 2015. However, the linear effect model estimated only 32,186 deaths for the entire country in 2015.

Our findings suggest that in developing countries like China, often with a wide range of PM_{2.5} concentrations, the relationship between PM_{2.5} and mortality is non-linear. This study delivers the first insight into the burden of disease associated with short-term exposure to PM_{2.5} in areas with high exposure to PM_{2.5}, which may provide a scientific foundation for implementing public health intervention policies. The use of a linear function may greatly underestimate the mortality burden attributable to short-term PM_{2.5} exposure in China.

Although a large number of previous studies have assumed a linear relationship (Atkinson et al., 2014; Lu et al., 2015; Franklin et al., 2007) between PM_{2.5} and mortality, some studies have provided clues suggesting that the shape of the PM_{2.5}-mortality exposureresponse relationship is non-linear (Chen et al., 2017; Daniels et al., 2000; Schwartz and Zanobetti, 2000; Schwartz et al., 2002). Some US studies have investigated the shape of the relationship between short-term particulate matter and mortality. These studies focused on the evidence of a threshold at low concentrations. However, these studies found that the exposure-response relationship to be nearly linear, with no evidence of the presence of a threshold at low concentrations (Daniels et al., 2000; Schwartz and Zanobetti, 2000; Schwartz et al., 2002). The concentrations of PM_{2.5} in these US studies were very low, normally daily PM_{2.5} concentrations below 35 µg/m³ (Franklin et al., 2007). However, the PM_{2.5} exposure in China has an extensive range of concentrations, the daily concentration of PM_{2.5} normally ranged from a few to many hundreds. A recent short-term PM_{2.5} and mortality study in 272 Chinese cities showed that the shape of PM_{2.5} and mortality relationship is nonlinear, with the effect that magnitude tended to be lower at higher concentrations (Chen et al., 2017), which is very similar to our results in this study. We found that the non-linear model accounts for smaller heterogeneity than the linear model in China. In model 1, two knots showed very low heterogeneity with an I² of 22%, which means that this non-linear model may explain the majority of the heterogeneity among effects under different exposure levels. Our study and previous evidence from Chinese studies confirmed that the shape of the association between PM2 5 and mortality could be a non-linear curve in China, where the concentration of PM_{2.5} can range from very low to extremely high. At low PM_{2.5} exposure levels, our study found an approximately linear relationship between PM_{2.5} and mortality, which is consistent with previous US studies. At the middle and high levels of PM_{2.5}, we found the magnitude of the effect to decrease as the concentration of PM_{2.5} increased. The number of days during which PM_{2.5} concentration was below $62 \,\mu\text{g/m}^3$ is quite high (about 68%). This phenomenon may be attributable to the "harvesting effect," which means the most sensitive individuals among the population may have already died at lower levels of exposure (Costa et al., 2016).

Most studies have focused on estimation of the disease burden due to long-term exposure to PM_{2.5} (Wang et al., 2018; Lelieveld et al., 2015; Lim et al., 2012; J. Liu et al., 2016; M. Liu et al., 2016). Earlier studies used exposure-response functions from Western countries with lower levels of PM_{2.5} exposure to estimate the global burden of disease from long-term exposure to PM_{2.5} (Cohen et al., 2005). In a country like China with high levels of exposure to PM_{2.5}, using a linear exposure-response relationship derived from the cohort studies performed in Western countries may overestimate the magnitude of the health effects. More and more studies have revealed that the association between long-term PM2.5 exposure and mortality is non-linear (Yin et al., 2017; Burnett et al., 2014). In order to address this limitation, a GBD study developed the integrated exposure-response (IER) curve to estimate the long-term PM_{2.5} exposure-response association from low exposure level to concentration as high as 1000 µg/m³ (Burnett et al., 2014). Many studies have used the IER model to estimate the number of long-term PM_{2.5}-related deaths in China (Wang et al., 2018). GBD 2010 studies reported 1.23 million additional deaths (Lim et al., 2012), while other studies reported additional deaths ranging from 1.23 to 1.37 million (Wang et al., 2018; Lelieveld et al., 2015; Lim et al., 2012; J. Liu et al., 2016; M. Liu et al., 2016).

While many studies already estimate deaths attributable to longterm PM_{2.5} exposure, there are almost no studies that focus on the estimation of the number of additional deaths attributable to short-term PM_{2.5} at the global and country levels. In China, no study has reported the short-term PM_{2.5}-related additional deaths throughout the entire country. One possible reason for this is that the health effects of acute PM_{2.5} are far less pronounced than those of chronic exposure (Atkinson et al., 2014; Chen et al., 2017; Yin et al., 2017; Di et al., 2017), which may explain the very small burden of disease in developed countries with low levels of exposure and relatively small populations. In developing countries, however, the situation is completely different. Even with the relative small acute health effect, the burden of disease from short-term PM_{2.5} exposure should not be disregarded with high levels of PM_{2.5} exposure and a huge population, especially in China. We found approximately 0.17 million short-term PM_{2.5}-related additional deaths in China, which is about one seventh the size attributable to chronic effects. It is essential to include short-term PM_{2.5}-related mortality when considering the overall PM_{2.5}-related disease burden in China. For the most part, the linear exposure-response association was expected in few short-term PM_{2.5}-related health impact studies (Chen et al., 2017; Zhao et al., 2017; Lin et al., 2017). However, using the linear PM_{2.5} and mortality associations rather than a non-linear relationship could substantially change the estimation of disease burden (Roberts and Martin, 2006). Previously, limited health impact estimation studies in China had considerable uncertainty because these studies did not use a nonlinear association between PM_{2.5} and mortality (Chen et al., 2017; Zhao et al., 2017; Lin et al., 2017). In our study, we reported the 95% confidence interval for additional deaths attributable to short-term exposure to PM_{2.5}. Our work also showed a fairly wide range of estimated values, but it nonetheless provides more accurate results than most previous studies, which only reported estimates without acknowledging uncertainty.

The spatial distribution of PM_{2.5} concentration, additional deaths, and death rate were somewhat different, mainly because the exposureresponse differed across different PM_{2.5} exposure concentration for a given population density in different counties. The spatial

distribution of high levels of mortality related to short-term PM_{2.5} exposure is consistent with previous estimations of the health impact of the effects of chronic exposure to PM_{2.5} (Wang et al., 2018). The Chinese government has released a series of air pollution prevention measures, such as those in the Air Pollution Prevention and Control Action Plan and the Three-year Plan on Defending the Blue Sky (2018–2020) (The State Council, 2017) and has already taken measures to correct these problems over the past several years, especially in the three key areas and 10 urban agglomerations identified in the action plan. These areas are essentially the same as those recognized as the high disease burden area in our study (State Department of People's Republic of China, 2013). By population, China is the largest country in the world (Cohen et al., 2017). In 2015, the Chinese government announced a two-child policy to address the country's accelerating aging problem (The 18th CPC central committee, 2015). For this reason, the disease burden attributable to PM_{2.5} in China may remain high even as air quality improves because of the increasing size and age of the population. Although air pollution control measures have played a part in the government's efforts, our findings and the future demographic trends indicate that prompt action to improve the air quality in China is urgently needed, which could rapidly reduce the acute health impacts from short-term PM2.5 and also mitigate the disease burden in China attributable to long-term PM_{2.5} exposure.

Our work has some limitations. The census data of county-level population and mortality rate in 2010 were used in this study to calculate the burden of disease in 2015. These are the latest and only available county-level statistical data in China from the nationwide extensive demographic census every 10 years. Our study provided only short-term $PM_{2.5}$ -related all-cause mortality burden and does not address the disease burden of cause of death because of the lack of causespecific mortality data. Finally, we used modeled $PM_{2.5}$ concentration in this study because China's $PM_{2.5}$ monitoring system cannot cover the entire country and $PM_{2.5}$ was the sole pollutant included. However, previous studies in China either used $PM_{2.5}$ alone to analyze the acute mortality effect (Chen et al., 2017) or showed that the acute mortality effect of $PM_{2.5}$ remained robust regardless of whether adding other pollutants (Chen et al., 2018).

Overall, this study adds significant new evidence on the short-term $PM_{2.5}$ exposure and mortality association across a broad $PM_{2.5}$ exposure range. Our estimates of disease burden attributable to short-term $PM_{2.5}$ exposure may inform future studies in developing countries that have high concentrations of $PM_{2.5}$.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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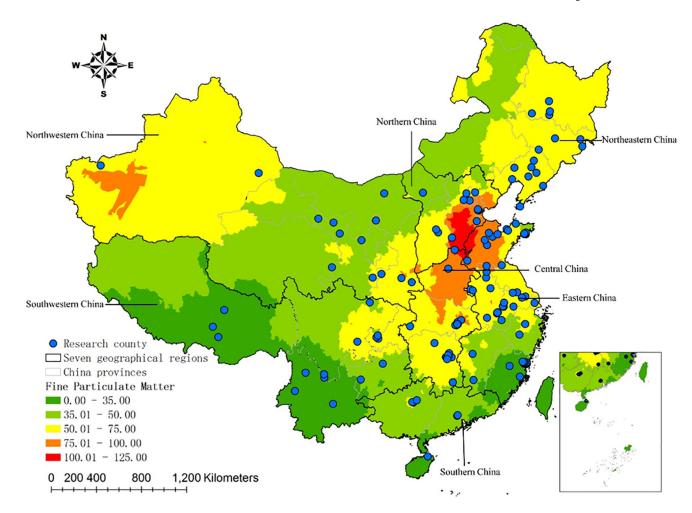
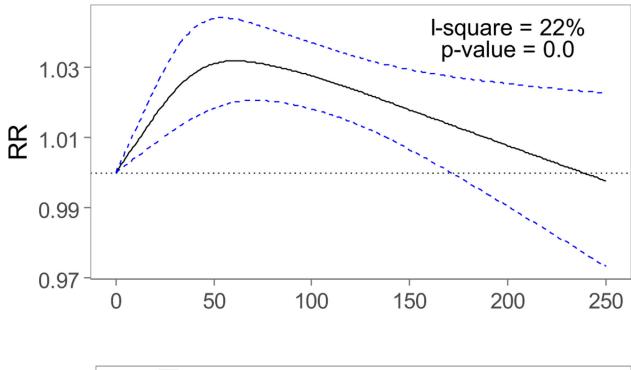


Fig. 1. Map of $PM_{2.5}$ concentration during the study period (2013–2015). Blue points indicate the geographic centers of 104 counties. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)



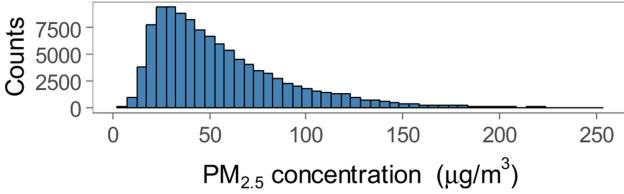


Fig. 2. Association between daily $PM_{2.5}$ concentration and relative risk of total mortality using random-effect meta-regression with a natural cubic spline model for $PM_{2.5}$ with 2 knots (Model 1).

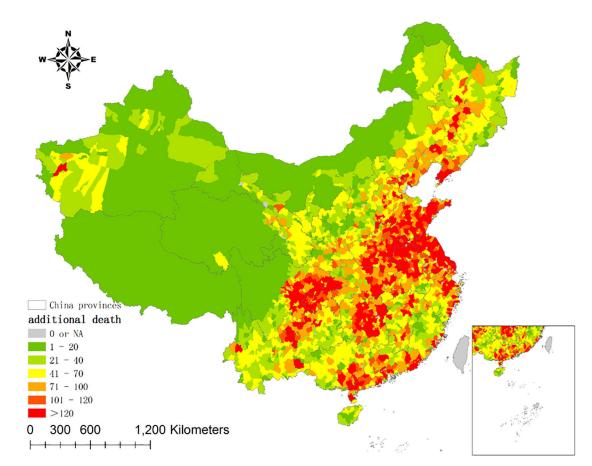


Fig. 3. Predicted short-term PM_{2.5}-related additional deaths in China in 2015 as indicated by Model

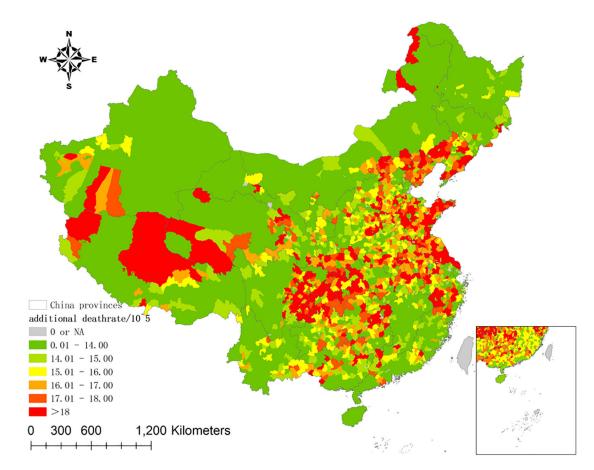


Fig. 4. Predicted short-term $PM_{2.5}$ -related increase in the death rate (1/100,000) in China in 2015 as indicated by Model 1.

Table 1

Predicted $PM_{2.5}$ -related additional deaths and increase in death rates in different regions of China in 2015, with non-linear $PM_{2.5}$ - mortality association estimated using Model 1.

Region	Additional deaths	Increase in death rate (1/100,000)
Eastern China	52,502 (95%CI: 30,505-74,266)	14.63 (95%CI: 8.50–20.69)
Northern China	18,032 (95%CI: 10,396-25,580)	13.67 (95%CI: 7.88–19.39)
Central China	29,899 (95%CI: 17,669-41,992)	14.59 (95%CI: 8.62-20.49)
Southern China	15,263 (95%CI: 8622-21,851)	10.41 (95%CI: 5.88-14.91)
Southwestern China	27,945 (95%CI: 15,823-39,948)	15.03 (95%CI: 8.51-21.49)
Northwestern China	11,944 (95%CI: 6842-16,984)	12.60 (95%CI: 7.22-17.92)
Northeastern China	14,277 (95%CI: 8137-20,346)	13.00 (95%CI: 7.41-18.52)
China	169,862 (95%CI: 97,994–240,967)	13.78 (95%CI: 7.95–19.55)