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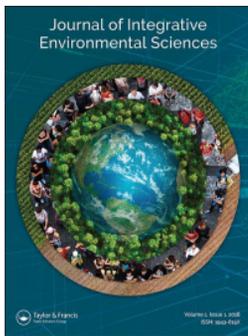
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RESEARCH ARTICLE



# Risk assessment of mortality from acute exposure to ambient fine particles based on the different toxicities of chemical compositions in China

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## ABSTRACT

Health risks, including mortalities and morbidities, attributed to chronic or acute exposure to ambient fine particulate matter (PM<sub>2.5</sub>), have been assessed based on the increments in ambient concentrations. Different toxicities of the various chemical compositions in PM<sub>2.5</sub> mixtures have been confirmed by epidemiological evidence but have rarely been considered. We proposed an approach to calculate the disease burden of both the chemical components and concentrations of PM<sub>2.5</sub> by combining their pre-established dose–response relationships with a multivariate Gaussian model. We estimated that PM<sub>2.5</sub> mixtures account for 0.43 (95% CI: 0.29 ~ 0.56) million premature deaths in China in 2013, consistent with estimates based on single-pollutant models in quantifying the total risk but with differing risk distributions. The residential, an elemental carbon-rich emission sector, accounted for approximately a quarter of PM<sub>2.5</sub> emissions, but for half of the premature deaths attributable to air pollution, due to the stronger toxicity of carbonaceous particles than other PM<sub>2.5</sub> compositions. Conventional risk assessments based on PM<sub>2.5</sub> mass assume equality in the toxicity of PM<sub>2.5</sub> compositions and may therefore fundamentally underestimate the skewness of the risk distribution and the adverse health effects of particles from the residential emissions. The different toxicities of the of PM<sub>2.5</sub> compositions modify the risk estimates and thus should be included in emission reduction plans.

## ARTICLE HISTORY

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## KEYWORDS

fine particles; elemental carbon; health risk; different toxicities; source apportionment

## 1. Introduction

Ambient exposure to air pollutants, especially particulate matter with an aerodynamic diameter less than 2.5 μm (PM<sub>2.5</sub>), has been associated with multiple adverse health outcomes, including cardiovascular and respiratory diseases (Franklin et al. 2007), lung

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cancer (Pope et al. 2011), and birth defects (Wilhelm and Ritz 2005).  $PM_{2.5}$  has been identified as a major public health hazard, particularly in developing countries (Lim et al. 2013). Risk assessments on the disease burdens of  $PM_{2.5}$  have been conducted globally (Apte et al. 2015), nationally (Fann et al. 2012; Liu et al. 2016; Li et al. 2019) and regionally (Kheirbek et al. 2013). For example, Lelieveld et al. (2015) estimated that worldwide, long-term exposure to ambient  $PM_{2.5}$  lead to 3.2 (95% CI: 1.5–4.6) million premature deaths per year. In those studies, the disease burdens were evaluated by pre-established dose–response relationships between the total concentrations of  $PM_{2.5}$  mixtures and the health outcomes of interest, and equally toxicity was assumed for different chemical components. However, multiple epidemiological studies have confirmed that the chemical compositions of  $PM_{2.5}$  exert different toxicities that modulate the health effects (Franklin et al. 2008; Atkinson et al. 2015). Carbonaceous particles and metals in  $PM_{2.5}$  are more toxic than other compositions (Maynard et al. 2007; Dai et al. 2016). Without incorporating the effect modifications of individual chemical components into risk assessments, the health effects of  $PM_{2.5}$  can be “falsely averaged”: among subpopulations that are exposed to relatively more toxic particles, the risks are underestimated, whereas among those that are exposed to less toxic particles, the risks are overestimated. In other words, the different toxicities of  $PM_{2.5}$  compositions are important sources of risk inequality (Bell and Ebisu 2012), and therefore affect the efficacy of air quality policies (Fann et al. 2011). Additionally, considering the varied mixtures of  $PM_{2.5}$  sources, the specific toxicities of the chemical compositions also determine the health risks associated with different emission sectors. For example, more consistent associations have been reported between traffic-related components and adverse health outcomes (Kelly and Fussell 2012). Therefore, to optimize emission reduction policies, the effect modifications exerted by individual  $PM_{2.5}$  compositions should be taken into account in risk assessments to identify the sources that contribute the most to the disease burden of  $PM_{2.5}$ .

The health effects of the major components of  $PM_{2.5}$  – nitrate ( $NO_3^-$ ), sulphate ( $SO_4^{2-}$ ), elemental carbon (EC) and organic carbon (OC), have been examined individually using single-pollutant models (Atkinson et al. 2015). However, because of common collinearities among these pollutants, the health effects of  $PM_{2.5}$  compositions have rarely been reported simultaneously, rendering multi-pollutant risk assessments difficult. The health effects estimated by a single-pollutant model may be also reflect the risk of other, correlating pollutants. Therefore, simply summing the health risks of different chemical compositions may overestimate the total risk of  $PM_{2.5}$  because the health risks of correlated pollutants are counted twice. In the present study, we addressed this issue by combining the risks from multiple pollutants in a multivariate Gaussian model that characterized their correlations using a pre-estimated variance-covariance matrix. The approach can also be extended to evaluate the health risks of other correlated pollutants, and thus, the method is named as the risk assessment of multiple pollutants (RAMP).

To illustrate the approach, we used RAMP to evaluate the mortality attributable to acute exposure to ambient  $PM_{2.5}$  in China in 2013. We selected acute mortality as the main health outcome because previous meta-analyses established the dose–response relationships for both  $PM_{2.5}$  mass and the four major compositions of  $PM_{2.5}$  ( $NO_3^-$ ,  $SO_4^{2-}$ , EC and OC) (Atkinson et al. 2014, 2015; Li et al. 2019). Long-term exposure to ambient  $PM_{2.5}$ , due to poor air quality, has been identified as the fourth leading contributor to the global disease burden (Yang et al. 2013) and may cause 1.37 million premature deaths

per year in China (Liu et al. 2016). Particulate pollutants species in China are complex and varied, and their sources in China are heterogeneous sources because of the uneven levels of urbanization and industrialization between regions. The RAMP approach can account for the different toxicities of PM<sub>2.5</sub> compositions, providing useful information on the distribution of PM<sub>2.5</sub>-related risks in China. By combining pre-established dose-response relationships, baseline mortality from county-level census data, an annual PM<sub>2.5</sub> map that was estimated from monitoring, remote sensing, and Community Multiscale Air Quality (CMAQ) modelling data and the compositions, and sources of PM<sub>2.5</sub> simulated by the Comprehensive Air Quality Model with extensions (CAMx) and Particulate Source Apportionment Technology (PAST), we quantified the long-term mortality risk attributable to PM<sub>2.5</sub> from various sectors and investigated the spatial distribution of the risk in China.

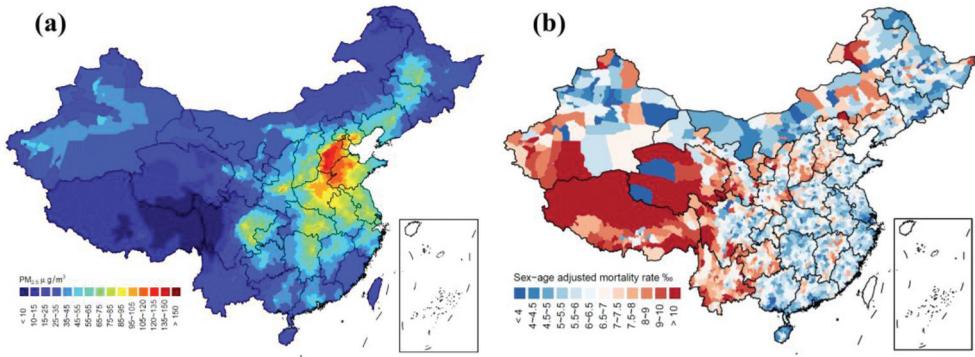
## 2. Methods

### 2.1. Baseline data

We approximated the population baseline in our study year (2013) with the nearest census data. We obtained county-level demographic data, including population counts stratified by sex, age and mortality rate, from the 2010 population census of the People's Republic of China (2010 census). The community-based mortality counts were screened in the 2010 census data and mainly reflected the total deaths that occurred between 1 November, 2009, and 31 October, 2010. The raw mortality rates were available at the county level, and the specific mortality rates were reported by sex and by age at the national level. To calibrate the potential confounding effects of demographic factors on the baseline risk, we calculated the sex- and age-adjusted mortality rates using an indirect method (Anderson and Rosenberg 1998) in each county (Figure 1). After completing the survey, 402 communities were randomly resampled to evaluate the uncertainty in the census data, and the nonresponse rate was estimated to be 0.1%. Therefore, the uncertainty in the census data was negligible compared with the uncertainty in the other inputs in this risk assessment.

### 2.2. PM<sub>2.5</sub> concentrations

We estimated the daily mass concentrations of PM<sub>2.5</sub> with a spatial resolution of 0.1° across China in 2013. Briefly, the products combined the in-situ observed, satellite-derived and CAMQ-simulated PM<sub>2.5</sub> using a data fusion approach. The details of the approach and the related datasets are presented in Xue et al. (2017). The predicted daily PM<sub>2.5</sub> concentrations were consistent ( $R^2 = 0.78$ ) with the out-of-sample cross-validated observations of in situ PM<sub>2.5</sub> concentrations. Root mean squared error (RMSE) is an unbiased estimator for modelling error and was reported as 29.5 µg/m<sup>3</sup>. Figure S1 presents more details of the cross-validation. The gridded daily maps of PM<sub>2.5</sub> concentrations were further averaged by the county-level administrative boundaries to matched with the demographic data geographically. The uncertainty in PM<sub>2.5</sub> was characterized using the Monte Carlo method by the standard errors of daily estimates.



**Figure 1.** County-level maps of 2013 concentrations of  $PM_{2.5}$  (a) and baseline mortality rates adjusted by sex and age (b) in China.

### 2.3. $PM_{2.5}$ components and sources

The  $PM_{2.5}$  concentrations were further split by their components and sources with the same method that we employed in our previous study (Li et al. 2015) with CAMx and PSAT (ENVIRON, 2013). Seven  $PM_{2.5}$  components were simulated simultaneously ( $NO_3^-$ ,  $SO_4^{2-}$ ,  $NH_4^+$ , EC, OC, other anthropogenic fine particles and mineral dust). In the emission configuration, both natural and anthropogenic sources of these components were considered. Natural sources were wind-blown emissions (Wang et al. 2012) of mineral dust and biogenic emissions (Guenther et al. 2012) of non-methane volatile organic compounds. Anthropogenic sources were divided into five categories: agriculture, industry, power plants, residential, and transportation. CAMx/PSAT tracked  $PM_{2.5}$  and its precursor gases that were emitted from the six sources (natural source and the five anthropogenic sources) throughout all the chemical and physical processes to apportion the simulated concentrations of each  $PM_{2.5}$  component between sources. We previously simulated the components and sources of  $PM_{2.5}$  in 2006 and 2013 (Li et al. 2015). In the present study, we averaged the products of the 2013 data into annual means. Compared with the observed annual mean concentrations of aerosol components from China Atmosphere Watch Network (CAWNET, Zhang et al. 2015), proportions of mineral dust and OC predicted by CAMx were underestimated, while proportions of  $NO_3^-$ ,  $SO_4^{2-}$ , and EC were generally consistent with the observations. Figure S2 presents more details of the comparison.

### 2.4. RAMP statistical model

In risk assessments of single pollutants, the premature deaths attributable to  $PM_{2.5}$  or one specific composition are quantified using the following function within each geographic unit:

$$H_{i,c} = [1 - 1/\exp(\Delta y_{i,c} \cdot \beta_i)] \cdot B_c \cdot P_c \quad (1)$$

where  $i$  denotes the index for  $PM_{2.5}$  or one specific composition;  $c$  denotes the geographic index (i.e. the county identifier in this study);  $P_c$  and  $B_c$  denote the total population and total incidence in each county, respectively;  $\Delta \mathbf{y}_i$  ( $\Delta \mathbf{y}_i \equiv [\Delta y_{i,1}, \Delta y_{i,2}, \dots, \Delta y_{i,k}]'$ ) denotes the increment of the target pollutant  $i$ , and was quantified as the anthropogenic

concentration of the pollutant, which was calculated by subtracting the environmental background concentration from the total concentration; and  $\beta$  denotes the coefficient to relate  $\Delta y_i$  with the logarithm scale of relative risk and was obtained from a previous meta-analysis (Atkinson et al. 2014, 2015). Figure S3 shows the  $\beta$  values and their 95% CIs.  $H_{i,c}$  denotes the number of premature deaths attributable to pollutant  $i$  within county  $c$ .

The overall number of deaths attributable to  $PM_{2.5}$  is not equal to the sum of deaths attributable to the individual compositions, because the health risks are not independent of each other. To avoid double counting the health risks from the correlated compositions, we used the RAMP approach, which assumes that the collinearities of multiple anthropogenic pollutants ( $\Delta y_i$ ) can be characterized by a multivariate Gaussian distribution as follows:

$$[\Delta y_1, \Delta y_2, \dots, \Delta y_k]^T \equiv \mathbf{y} \sim N(\boldsymbol{\mu}, \boldsymbol{\sigma}^2); \boldsymbol{\mu} = [\mu_1, \mu_2, \dots, \mu_k]^T; \sigma_{ij} = Cov(\Delta y_i, \Delta y_j) \quad (2)$$

In a single-pollutant model, the logarithm scale of relative risk for a certain pollutant  $i$  can be derived as  $\Delta y_i \cdot \beta_i$ . Let  $\boldsymbol{\gamma}$  ( $\boldsymbol{\gamma} \equiv [\gamma_1, \gamma_2, \dots, \gamma_k]^T$ ) denotes the latent independent health effects of the different pollutants. As  $\Delta y_i \cdot \beta_i$  quantifies not only the latent health effects from pollutant  $i$ , but also those from other correlated pollutants,  $\Delta y_i \cdot \beta_i$  are often greater than  $\Delta y_i \cdot \gamma_i$ . Given an increment of  $\Delta y_i$  in pollutant  $i$ , correlated pollutants increase by  $E(\Delta y_{-i} | \Delta y_i)$ ; thus, the corresponding health risks can be estimated as  $E(\Delta y_{-i} | \Delta y_i) \cdot \boldsymbol{\gamma}_{-i}$ , where  $\Delta y_{-i}$  and  $\boldsymbol{\gamma}_{-i}$  denote the other pollutants (excluding  $i$ ) and their latent health effects, respectively. Therefore, the following equation can be derived:

$$\begin{aligned} \Delta y_i \cdot \gamma_i + E(\Delta y_{-i} | \Delta y_i) \cdot \boldsymbol{\gamma}_{-i} &= \Delta y_i \cdot \beta_i; E(\Delta y_{-i} | \Delta y_i) \\ &= \boldsymbol{\mu}_{-i} + Cov(\Delta y_{-i}, \Delta y_i) \cdot \boldsymbol{\sigma}_{ii}^{-1} \cdot (\Delta y_i - \mu_i) \end{aligned} \quad (3)$$

By solving the equations for each pollutant conditioned on pre-estimated  $\boldsymbol{\mu}$  and  $\boldsymbol{\sigma}$ , the latent health effects ( $\boldsymbol{\gamma}$ ) can be calculated. Finally, the total health risks attributed to multiple pollutants can be quantified as follows:

$$H = [1 - 1/exp(\Delta y_i \boldsymbol{\gamma})] * B * P \quad (4)$$

In this study, we first calculated the premature deaths attributable to  $PM_{2.5}$ ,  $NO_3^-$ ,  $SO_4^{2-}$ , EC and OC separately at the county level in 2013 using Equation (1). Then,  $\boldsymbol{\mu}$  and  $\boldsymbol{\sigma}$  were estimated from county-level mass concentrations of four  $PM_{2.5}$  compositions ( $NO_3^-$ ,  $SO_4^{2-}$ , EC and OC; Table S1). The corresponding  $\boldsymbol{\gamma}$  values were solved by a regression model consisting of Equation (3) for  $PM_{2.5}$ ,  $NO_3^-$ ,  $SO_4^{2-}$ , EC and OC in each county. Figure S3 shows the estimated  $\boldsymbol{\gamma}$  values. By applying Equation (4) on a county-level, we quantified the premature deaths attributable to  $PM_{2.5}$  mixtures in the RAMP.

### 3. Results

Figure 1 shows county-level inputs, including the annual means of  $PM_{2.5}$  concentrations and sex-and age-adjusted mortality rates. The heavily polluted areas ( $PM_{2.5} > 95 \mu g/m^3$ ) covered the North China Plain (including the southern part of Hebei Province, the south-eastern part of Beijing Municipality, Tianjin Municipality, the northeastern part of Henan Province and the western part of Shandong Province, Figure 1(a)). The mortality risk was lower in developed regions, such as the metropolitan areas of Beijing, Tianjin, Shanghai and Guangzhou, whereas it was higher in undeveloped regions, such as Southwest China

(Figure 1(b)). Figures S4 and S5 are maps of  $PM_{2.5}$  concentrations from natural and anthropogenic sources, respectively.  $PM_{2.5}$  sources were determined by industrialization and urbanization levels and varied geographically (Figure S6). Figure S7 shows the spatial patterns of the four major compositions of  $PM_{2.5}$ .

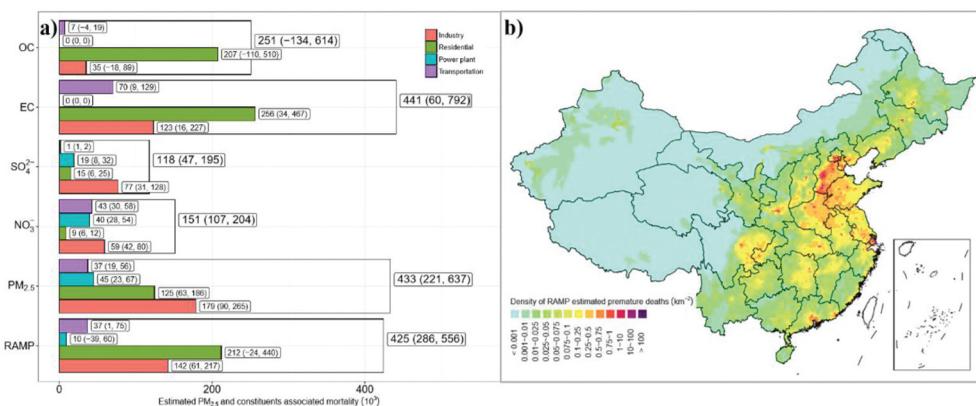
Table 1 presents the population-weighted concentrations of  $PM_{2.5}$  and its four chemical compositions by emission sources. During 2013, the population-weighted exposure to  $PM_{2.5}$ ,  $NO_3^-$ ,  $SO_4^{2-}$ , EC and OC was  $61.5 \mu\text{g}/\text{m}^3$ ,  $12.4 \mu\text{g}/\text{m}^3$ ,  $10.7 \mu\text{g}/\text{m}^3$ ,  $4.9 \mu\text{g}/\text{m}^3$  and  $9.5 \mu\text{g}/\text{m}^3$ , respectively. The primary source of  $PM_{2.5}$  was industry (39.5%), followed by the residential (26.5%); this population-weighted source apportionment result has been discussed in our previous work (Li et al. 2015, 2017). The primary source of inorganic particles ( $NO_3^-$  and  $SO_4^{2-}$ ) was industry, and that of carbonaceous particles (EC and OC) was residential. Table 1 lists the relative risk values calculated for all-caused mortality per increment of  $10 \mu\text{g}/\text{m}^3$  in  $PM_{2.5}$  and its four chemical compositions derived from previous meta-analyses (Atkinson et al. 2014, 2015). Atkinson et al. (2014) derived pooled estimates for the short-term effect of outdoor  $PM_{2.5}$  on all-caused mortality from 23 estimates from 56 related studies. In a follow-up study (Atkinson et al. 2015), the authors applied a similar approach for the  $NO_3^-$ ,  $SO_4^{2-}$ , EC and OC, using 12, six, six and four independent estimates, respectively, of their acute effects on all-caused mortality; in single-pollutant modelling, the health effect of EC was reported to be the highest.

Figure 2(a) graphs the numbers of premature deaths in China attributable to acute exposure to  $PM_{2.5}$  mass,  $NO_3^-$ ,  $SO_4^{2-}$ , EC and OC, which are 0.43 (95% CI: 0.22 ~ 0.64), 0.15 (0.11 ~ 0.20), 0.12 (0.05 ~ 0.20), 0.44 (0.06 ~ 0.79) and 0.25 (−0.13 ~ 0.61) million throughout China, respectively, and stratified by source. The data suggest that the deaths attributable to  $PM_{2.5}$  mass or to inorganic particles ( $NO_3^-$  and  $SO_4^{2-}$ ) were mainly caused by industry emissions, while the deaths attributable to carbonaceous particles (EC and OC) were mainly caused by residential emissions. RAMP analysis showed that  $PM_{2.5}$  mixtures may have accounted for 0.43 (0.29 ~ 0.56) million premature deaths, similar to the estimation for  $PM_{2.5}$  mass. However, RAMP analysis also showed that residential emissions may be dominant contributors (about one-half) to the mortality risks of  $PM_{2.5}$  mixtures, although the number of deaths attributed to residential  $PM_{2.5}$  (0.21 million, with a 95% CI of −0.02 to 0.44 million) did not differ significantly from zero because of the large uncertainty in the health effects of carbonaceous particles (Figure S1). The spatial pattern of the number of RAMP-estimated premature deaths per square kilometre in China (Figure 2(b)), suggested that the  $PM_{2.5}$

**Table 1.** Relative risk (RR) values for an increment of  $10 \mu\text{g}/\text{m}^3$  in mass concentration of fine particulate matter ( $PM_{2.5}$ ) and its four major compositions and their population-weighted sources apportionment.

	RR for an increment of $10 \mu\text{g}/\text{m}^3$	Population-weighted concentrations of pollutants from various sources ( $\mu\text{g}/\text{m}^3$ )						
		Total	Industry	Power plants	Residential	Transportation	Nature	Others
$NO_3^-$	1.0171 (1.0121, 1.0232)	12.44	4.75	3.14	0.68	3.4	0.32	0.15
$SO_4^{2-}$	1.0151 (1.0060, 1.0253)	10.72	7.07	1.72	1.3	0.13	<0.01	0.49
EC	1.1379 (1.0171, 1.2714)	4.90	1.34	<0.01	2.73	0.77	0.05	0.01
OC	1.0376 (0.9812, 1.0981)	9.50	1.33	<0.01	7.65	0.28	0.16	0.08
$PM_{2.5}$	1.0104 (1.0052, 1.0156)	61.45	24.28	5.85	16.3	4.92	2.47	7.63

The data were obtained from previous meta-analyses (Atkinson et al. 2014, 2015).  $NO_3^-$ , nitrate;  $SO_4^{2-}$ , sulphate; EC, elemental carbon; OC, organic carbon.

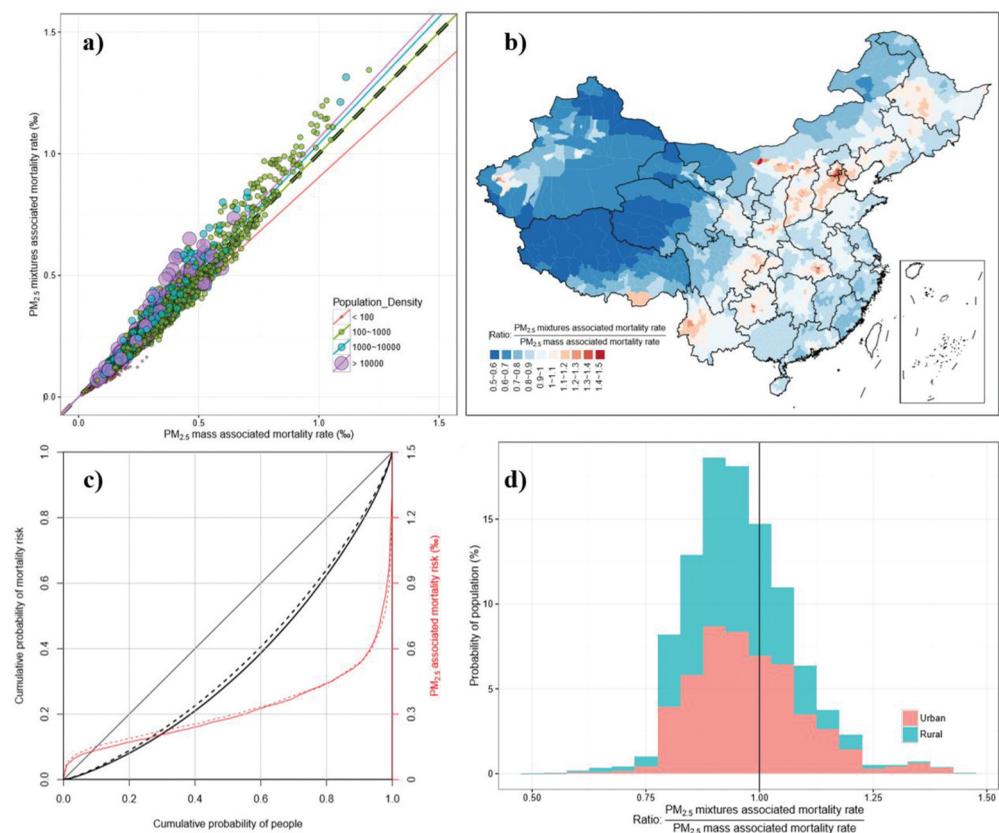


**Figure 2.** Premature deaths attributable to fine particulate matter (PM<sub>2.5</sub>) estimated by single-pollutant models and risk assessment of multiple pollutants (RAMP) analysis. (a) Total counts of premature deaths attributable to each pollutant and stratified by emission source. (b) Death counts attributable to PM<sub>2.5</sub> mixtures per square kilometre, estimated by RAMP.

mixture-associated deaths were mostly distributed in the heavily polluted or densely populated areas.

We used the pollutant-associated mortality rate, defined as the number of premature deaths normalized by population size, to quantify the pollutant-increased risk. **Figure 3(a)** plots the PM<sub>2.5</sub> mass-associated mortality rates against the PM<sub>2.5</sub> mixture-associated mortality rates by county. The results suggest that the risks attributable to PM<sub>2.5</sub> mixtures may be underestimated by risk assessments that are based on PM<sub>2.5</sub> mass in large cities (population density > 1,000/km<sup>2</sup>). **Figure 3(b)** shows the county-level ratio of the PM<sub>2.5</sub> mixture-associated mortality rate to the PM<sub>2.5</sub> mass-associated mortality rate; the findings indicate that a risk assessment based on PM<sub>2.5</sub> mass may underestimate the risks in heavily polluted areas (including the Beijing-Tianjin-Hebei metropolitan region, the southeastern part of the Loess Plateau, the Northeast China Plain, the Sichuan Basin, the western part of Yunnan Province, and the metropolitan areas around Wuhan, Changsha, Guiyang and Guangzhou) but overestimate the risks in less polluted areas, such as the western part of China, coastal areas, and other rural areas). **Figure 3(c)** displays the probability distribution of those ratios between urban and rural populations. Without incorporating the effect modifications of chemical compositions, the mortality risk of PM<sub>2.5</sub> mixtures for 68.6% of the population (including 63.6% of urban and 73.7% of rural residents) may be overestimated, whereas that for the remaining 31.4% (including 36.4% of urban and 26.4% of rural residents), may be underestimated. In comparison with risk assessments based on PM<sub>2.5</sub> mass, RAMP analysis may yield a more skewed distribution of the mortality risks attributable to PM<sub>2.5</sub> mixtures.

To further evaluate the risk distribution, we visualized the cumulative probability distributions and Lorenz curves (**Figure 3(c)**). In the risk assessment based on PM<sub>2.5</sub> mass, low-risk ( $\leq 0.3\text{‰}$ ) areas were inhabited by 51.9% of the population, and high-risk ( $\geq 0.9\text{‰}$ ) areas were inhabited by 0.9% of the population. In RAMP analysis, the low-risk areas were inhabited by 55.0% of the population and the high-risk areas were inhabited by 1.6% of the population (Table S2). The mortality risks calculated using RAMP analysis



**Figure 3.** (a) Scatterplot of PM<sub>2.5</sub> mass-associated mortality rates and PM<sub>2.5</sub> mixture-associated mortality rates estimated by risk assessment of multiple pollutants. Dot radius represents the population density of each county, and the regression lines were calculated for four population density levels. (b) Spatial pattern of the ratio of PM<sub>2.5</sub> mass-associated mortality rates and PM<sub>2.5</sub> mixture-associated mortality rates. (c) Cumulative probability distributions (red) and Lorenz curves (black) for PM<sub>2.5</sub> mass-associated mortality rates (dashed lines) and PM<sub>2.5</sub> mixture-associated mortality rates (solid lines). (d) Probability distribution of the population ratios in urban (red) and rural (blue) areas.

were less equally distributed, which can be confirmed by Lorenz curves, defined as the proportions of overall risk (on the y-axis) to the bottom proportions of population (on the x-axis). The inequality of risk distribution can be reflected by the area between the diagonal line and the Lorenz curve, and the results suggest higher inequality in the RAMP-estimated values. Table S3 lists detailed data on the correlations between constituent concentrations and mortality ratios.

#### 4. Discussion

In this paper, we illustrated a novel approach, RAMP analysis, to incorporate the effect modifications of chemical compositions into a risk assessment of PM<sub>2.5</sub> mixtures. We

calculated that acute exposure to  $PM_{2.5}$  contributed to 0.43 (0.29–0.56) million premature deaths, accounting for 5.7% of total deaths in China in 2013. Most previous risk assessments in China have focused on mortality caused by long-term exposure to  $PM_{2.5}$  using the integrated exposure-response function (Burnett et al. 2014), and the reported annual totals were 1.23 million (Lim et al. 2013), 1.36 million for  $PM_{2.5}$  and ozone (Lelieveld et al. 2015), and 1.37 million (Liu et al. 2016); those totals are approximately twice as higher as our estimate. However, the health effects of long-term exposure to  $PM_{2.5}$  are expected to manifest after a latency period of several decades.

By incorporating composition-specific mortality into the risk assessment, we showed how the mortality attributable to  $PM_{2.5}$  can be modified when the assumption of equally toxic particles is avoided. Our findings suggest that heterogeneous toxicities do not significantly change the overall risk associated with  $PM_{2.5}$  but do determine the detailed distribution of risk among populations. RAMP analysis demonstrated the differential risks of  $PM_{2.5}$  compositions; the risk distribution was more skewed, and environmental inequality was enhanced. Conventional risk assessments can mask risk hotspots associated with certain suspected toxic substances, such as EC. Schwartz et al. (2011) noted that differential exposure risk was a knowledge gap that could be filled with more precise risk assessments and provided alternative policy guidelines to achieve more efficient risk reductions and greater health status equity between populations.

Carbonaceous particles mostly originate from combustion and have been found to contribute significantly to haze events of particulate pollution in China (Huang et al. 2014). Although multiple epidemiological studies have shown consistently stronger associations between carbonaceous particles and outcomes, such as mortality (Atkinson et al. 2015), there are no conclusive explanations for the greater toxicity of carbonaceous particles. Possible reasons include the toxic organic compounds of carbonaceous particles (e.g. polycyclic aromatic hydrocarbons), the ultrafine size of those particles, and the adsorbed toxic species on those particles, such as endotoxins (Kelly and Fussell 2012). In our study, RAMP analysis showed that carbonaceous particles, especially EC, are critically involved in the mortality caused by inhaling  $PM_{2.5}$  mixtures. EC contributed 8.2% of the population-weighted anthropogenic  $PM_{2.5}$  but was estimated to cause 48.4% of the overall premature deaths. Because EC was most strongly correlated with both the toxicity of  $PM_{2.5}$  (mixture-associated mortality rate) and population density, the two factors that determine the deaths counts, EC may be the most representative species in measuring the health risks of particulate pollution in China. The correlations between concentrations of EC and mortality ratios also suggest that in an EC-rich atmosphere, the health risks of  $PM_{2.5}$  tend to be underestimated by conventional risk assessments that are based on  $PM_{2.5}$  mass alone. Residential emissions were the leading source of elemental carbon (55.7%), representing coal and wood combustion for heating and cooking. Residential emissions accounted for approximately a quarter (27.6%) of  $PM_{2.5}$  emissions but for half (49.9%) of the premature deaths attributable to  $PM_{2.5}$ , underscoring the importance of this emission source that was neglected in previous risk assessments based on  $PM_{2.5}$  mass, which may have misinformed emission reduction policies in China by underestimating the risks in urban areas and overestimating the risks in rural areas.

Unlike previous reports, our study offers the following advantages: (1) county-level baseline data; (2) advanced exposure estimation; and (3) composition-specific mortality

estimates. In previous studies, health baseline data such as the mortality rate were obtained at the national (Lelieveld et al. 2015; Lim et al. 2013) or province (Liu et al. 2016) level, and small-scale spatial variations, particularly the differences between urban and rural areas, were ignored. In our previous study (Xue et al. 2017), we derived the optimal daily estimates of  $PM_{2.5}$  throughout China by combining monitoring, satellite remote sensing, and air quality modelling data, which reduced the uncertainty in the risk assessment. Our study quantified the mortality from  $PM_{2.5}$  mixtures by individual compositions for the first time; the results revealed risk distributions between populations that differed from conventional risk assessments that were based on  $PM_{2.5}$  mass alone. Nonetheless, our findings were weakened by the large uncertainty from the use of multiple datasets and complex models. First, because of the limited number of epidemiological studies on  $PM_{2.5}$  compositions, the 95% CIs were wide, especially for EC and OC. Second, although validation against the observation has been made in this study, uncertainties in emission inventories, meteorological predictions, and the formulations and parameterizations used in the chemistry transport model affect the accuracy of the results. Third, due to the limitations in extant epidemiological evidences, the toxicities for some key components of  $PM_{2.5}$  are still unknown. For instance, our analysis ignored the specific association between mortality and ammonium, the major component for the  $PM_{2.5}$  from agricultural sector. In our RAMP model, the exposure-response function for ammonium was approximated as equal to that derived from studies on total  $PM_{2.5}$ . We estimated that agricultural sector contributed to 0.026 (95% CI: 0.002, 0.049) million premature deaths, approximately accounting for 6.2% of the total  $PM_{2.5}$ -related deaths, which might be biased due to the ignorance of ammonium-specific toxicity. Last but not least, RAMP analysis depends on the correlation matrix of  $PM_{2.5}$  constituents as input data, which should have been sourced from original epidemiological studies but was replaced by an estimate from our previous dataset. To minimize the uncertainty in the RAMP results, more epidemiological studies on  $PM_{2.5}$  compositions are required.

## 5. Conclusions

This study proposed an integrative approach to incorporate the effect modifications of chemical compositions into a risk assessment of  $PM_{2.5}$  mixtures, which was used to estimate the premature deaths attributable to  $PM_{2.5}$  in China by emission sources. Approximately 0.43 (95% CI: 0.29 ~ 0.56) million deaths could be attributed to acute exposure to  $PM_{2.5}$  mixtures in 2013. Overall, RAMP analysis indicated that conventional risk assessments based on  $PM_{2.5}$  mass may underestimate the skewness of the risk distribution and the health risk of residential emissions. Combining the constituent-specific mortality rates in the risk assessment revealed that the health effects of  $PM_{2.5}$  may mostly impact a small subpopulation exposed to relatively more toxic chemical compositions (e.g. EC), suggesting the need for more targeted strategies for emission reductions, especially in the residential sector.

## Disclosure statement

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