

# Urban-rural disparity of the short-term association of PM<sub>2.5</sub> with mortality and its attributable burden

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## Graphical abstract



## Public summary

- PM<sub>2.5</sub> had greater effects on CVD/CED mortality in urban cities than in rural areas
- PM<sub>2.5</sub> had stronger effects on RESP mortality in rural areas than in urban cities
- An annual mean of 16.5/100,000 deaths was attributable to PM<sub>2.5</sub> in urban cities
- An annual mean of 3.4/100,000 deaths was attributable to PM<sub>2.5</sub> in rural areas
- Spatially targeted measures are needed to reduce PM<sub>2.5</sub>-related mortality in China



# Urban-rural disparity of the short-term association of PM<sub>2.5</sub> with mortality and its attributable burden

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Although studies have investigated the associations between PM<sub>2.5</sub> and mortality risk, evidence from rural areas is scarce. We aimed to compare the PM<sub>2.5</sub>-mortality associations between urban cities and rural areas in China. Daily mortality and air pollution data were collected from 215 locations during 2014–2017 in China. A two-stage approach was employed to estimate the location-specific and combined cumulative associations between short-term exposure to PM<sub>2.5</sub> (lag 0–3 days) and mortality risks. The excess risks (ER) of all-cause, respiratory disease (RESP), cardiovascular disease (CVD), and cerebrovascular disease (CED) mortality for each 10 µg/m<sup>3</sup> increment in PM<sub>2.5</sub> across all locations were 0.54% (95% confidence interval [CI]: 0.38%, 0.70%), 0.51% (0.10%, 0.93%), 0.74% (0.50%, 0.97%), and 0.52% (0.20%, 0.83%), respectively. Slightly stronger associations for CVD (0.80% versus 0.60%) and CED (0.61% versus 0.26%) mortality were observed in urban cities than in rural areas, and slightly greater associations for RESP mortality (0.51% versus 0.43%) were found in rural areas than in urban cities. A mean of 2.11% (attributable fraction [AF], 95% CI: 1.48%, 2.76%) of all-cause mortality was attributable to PM<sub>2.5</sub> exposure in China, with a larger AF in urban cities (2.89% [2.12%, 3.67%]) than in rural areas (0.61% [–0.60%, 1.84%]). Disparities in PM<sub>2.5</sub>-mortality associations between urban cities and rural areas were also found in some subgroups classified by sex and age. This study provided robust evidence on the associations of PM<sub>2.5</sub> with mortality risks in China and demonstrated urban-rural disparities of PM<sub>2.5</sub>-mortality associations for various causes of death.

**Keywords:** fine particulate matter; mortality; urban-rural disparity; China

## INTRODUCTION

Numerous studies have examined the associations between short-term exposure to ambient particulate matter with an aerodynamic diameter of 2.5 µm or less (PM<sub>2.5</sub>) and daily mortality.<sup>1–3</sup> For example, Liu et al. found that each 10 µg/m<sup>3</sup> increase in PM<sub>2.5</sub> was associated with a 0.68% higher risk of all-cause mortality, a 0.55% higher risk of cardiovascular (CVD) mortality, and a 0.47% higher risk of respiratory (RESP) mortality using data from 652 cities worldwide.<sup>1</sup> These studies demonstrated a robust association between PM<sub>2.5</sub> and mortality risk worldwide.

Previous studies suggested that the associations between air pollution and health may be different between urban cities and rural areas. Residents in rural areas usually use traditional stoves, have fewer self-protection mea-

asures, and participate in more outdoor activities, which may increase their exposure to air pollution and lead to more premature deaths.<sup>4</sup> In addition, the lack of planning in rural areas exacerbates residential environmental exposures.<sup>5</sup> Correspondingly, urban residents usually consume more materials and energy than rural residents, which may lead to higher per capita emissions of air pollutants and higher air pollution concentrations. Moreover, urban population growth and in-migration indicate that population exposure to air pollution increases even without substantial air quality changes.<sup>6</sup> These complex dynamics indicate the necessity to further illustrate the urban-rural disparity of the associations between PM<sub>2.5</sub> and human health.

However, to date, few studies have compared the discrepancy of the mortality-PM<sub>2.5</sub> association between urban cities and rural areas, and the existing results are inconsistent. In addition, most previous studies assessed the urban-rural disparity of associations of long-term exposures to PM<sub>2.5</sub> with health,<sup>5,7–9</sup> and no study was found to investigate the short-term effect difference of PM<sub>2.5</sub> between urban cities and rural areas. For example, a study conducted in China reported a higher mortality risk attributable to long-term PM<sub>2.5</sub> exposures in dense urban cities than in rural areas.<sup>7</sup> In contrast, Zhao et al. observed a stronger long-term effect of PM<sub>2.5</sub> on mortality in rural areas than in urban cities in China.<sup>8</sup> Therefore, more multilocation studies are needed to corroborate the difference in the associations of short-term exposure to PM<sub>2.5</sub> with mortality between urban cities and rural areas.

A better understanding of the urban-rural disparity of air pollution-related mortality risk and burden is important for effective decision making in designing spatially targeted interventions and mitigation policies. This is especially relevant for developing countries such as China, which is suffering from severe air pollution and has a large number of rural residents. Given these knowledge gaps, we collected data in 215 locations from four provinces in China to compare the associations of short-term exposure to PM<sub>2.5</sub> with mortality risk and burden between urban cities and rural areas.

## RESULTS

### General characteristics of study samples

A total of 2,604,828 deaths were included in this study (403,725 deaths caused by RESP, 1,050,326 deaths caused by CVD, and 524,790 deaths caused by CED). The mean number of daily all-cause deaths was 8.3 (SD = 5.8) in all locations, with a mean of 8.9 (SD = 5.9) and 7.7 (SD = 5.6) deaths in urban cities and rural areas, respectively. The average daily RESP, CVD, and CED deaths in all locations were 1.3 (SD = 1.7), 3.3 (SD = 2.8), and 1.7 (SD = 1.7), respectively. We observed higher mean PM<sub>2.5</sub>, NO<sub>2</sub>, and SO<sub>2</sub>

**Table 1.** Characteristics of the studied variables in 215 locations in China

	Mean (SD)	Minimum	P <sub>25</sub>	Median	P <sub>75</sub>	Maximum
<b>All-cause mortality</b>						
Total	8.3 (5.8)	0	4	7	11	119
Urban	8.9 (5.9)	0	5	8	12	62
Rural	7.7 (5.6)	0	4	6	10	119
<b>RESP mortality</b>						
Total	1.3 (1.7)	0	0	1	2	73
Urban	1.2 (1.5)	0	0	1	2	16
Rural	1.3 (1.8)	0	0	1	2	73
<b>CVD mortality</b>						
Total	3.3(2.8)	0	1	3	5	109
Urban	3.4(2.7)	0	1	3	5	41
Rural	3.3(2.9)	0	1	3	5	109
<b>CED mortality</b>						
Total	1.7 (1.7)	0	0	1	2	30
Urban	1.7 (1.7)	0	0	1	2	30
Rural	1.6 (1.7)	0	0	1	2	27
<b>PM<sub>2.5</sub> (μg/m<sup>3</sup>)</b>						
Total	38.3 (25.1)	4.0	21.5	31.6	47.8	451.1
Urban	41.7 (27.2)	4.0	23.1	35.1	52.1	451.1
Rural	35.0 (22.3)	4.9	20.3	29.0	43.5	429.5
<b>NO<sub>2</sub> (μg/m<sup>3</sup>)</b>						
Total	28.9 (15.7)	3.8	17.3	24.3	36.6	141.1
Urban	34.0 (17.3)	4.6	20.6	30.4	44.2	141.1
Rural	23.9 (12.1)	3.8	15.6	20.5	28.4	122.3
<b>SO<sub>2</sub> (μg/m<sup>3</sup>)</b>						
Total	17.3 (11.2)	2.2	11.0	14.5	20.4	188.7
Urban	17.7 (13.2)	2.8	10.3	14.2	20.7	188.7
Rural	17.0 (8.8)	2.2	11.5	14.8	20.2	116.4
<b>O<sub>3</sub> (μg/m<sup>3</sup>)</b>						
Total	59.5 (24.1)	2.8	41.5	56.9	75.0	224.6
Urban	59.2 (25.4)	2.8	40.3	56.8	75.6	224.6
Rural	59.8 (22.6)	5.5	42.6	57.0	74.3	223.4
<b>CO (mg/m<sup>3</sup>)</b>						
Total	0.9 (0.3)	0.3	0.7	0.8	1.0	3.8
Urban	0.9 (0.3)	0.3	0.7	0.9	1.0	3.8
Rural	0.9 (0.3)	0.3	0.7	0.8	1.0	3.5
<b>Mean temperature (°C)</b>						
Total	16.7 (9.6)	-28.9	11.2	18.2	23.4	35.6
Urban	16.5 (10.4)	-28.9	10.6	18.3	24.1	35.6
Rural	16.8 (8.8)	-27.7	11.7	18.1	22.7	35.6

**Table 1.** Continued

	Mean (SD)	Minimum	P <sub>25</sub>	Median	P <sub>75</sub>	Maximum
<b>Relative humidity (%)</b>						
Total	74.8 (14.2)	8.0	66.0	77.0	85.0	100.0
Urban	74.8 (14.4)	8.0	66.0	77.0	86.0	100.0
Rural	74.9 (14.0)	14.0	67.0	77.0	85.0	100.0

SD: standard deviation.

concentrations, slightly lower mean O<sub>3</sub> concentrations, and identical mean CO concentrations in urban cities than in rural areas (Figure 1 and Table 1). Daily PM<sub>2.5</sub> concentration was positively associated with daily O<sub>3</sub> ( $r = 0.11$ ,  $p < 0.05$ ), CO ( $r = 0.47$ ,  $p < 0.05$ ), NO<sub>2</sub> ( $r = 0.62$ ,  $p < 0.05$ ), and SO<sub>2</sub> ( $r = 0.51$ ,  $p < 0.05$ ), and it was negatively associated with daily TM ( $r = -0.32$ ,  $p < 0.05$ ) and RH ( $r = -0.26$ ,  $p < 0.05$ ) (Table S2).

### Cumulative exposure-response associations of daily PM<sub>2.5</sub> with mortality risk

We observed a general positive association between PM<sub>2.5</sub> and mortality in all locations, with a steeper slope at low PM<sub>2.5</sub> concentrations (<30 μg/m<sup>3</sup>), particularly for CVD and CED mortality. However, the nonlinear association patterns between PM<sub>2.5</sub> and mortality were different across areas and causes. For example, a steeper slope at higher PM<sub>2.5</sub> concentrations (>80 μg/m<sup>3</sup>) was found in rural areas than in urban areas for the association between PM<sub>2.5</sub> and RESP mortality risk. In urban areas, we observed greater associations of PM<sub>2.5</sub> with CVD mortality than with RESP mortality on days with higher PM<sub>2.5</sub> concentrations (Figure 2).

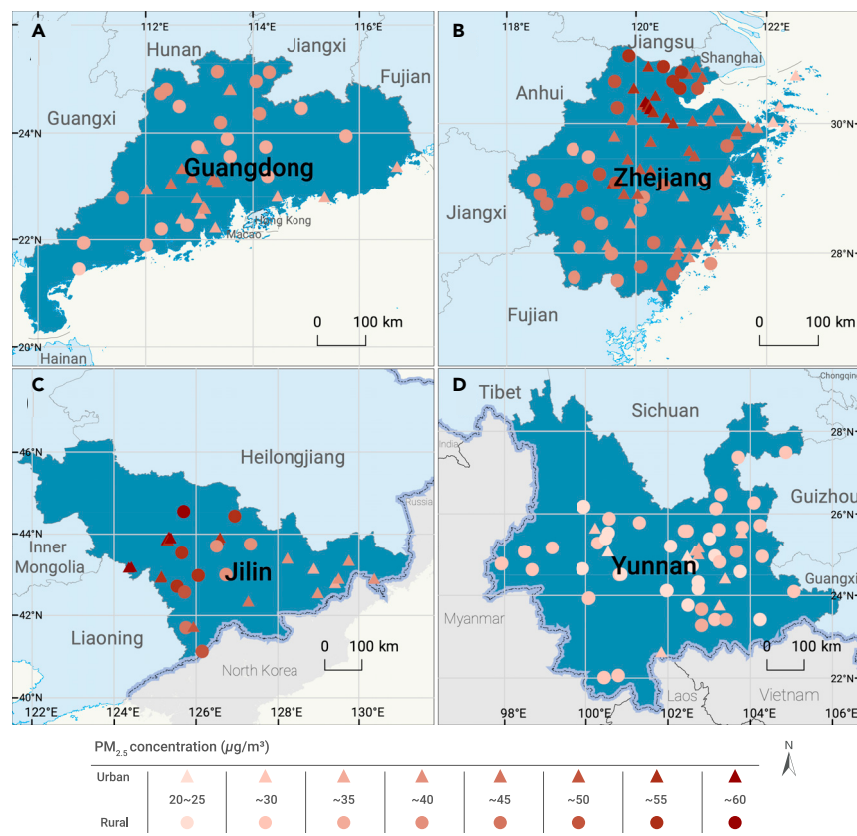
Table 2 shows the cumulative (lag 0–3 days) ERs of mortality for each 10 μg/m<sup>3</sup> increase in PM<sub>2.5</sub> concentrations. The ERs of all-cause mortality, RESP, CVD, and CED mortality in all locations were 0.54% (95% CI: 0.38%, 0.70%), 0.51% (0.10%, 0.93%), 0.74% (0.50%, 0.97%), and 0.52% (0.20%, 0.83%), respectively. Stratification analyses showed greater associations between PM<sub>2.5</sub> and mortality in urban cities than in rural areas for all-cause mortality (0.68% [0.50%, 0.86%] versus 0.17% [−0.17%, 0.52%]) and in most subgroups, including CVD mortality (0.80% [0.51%, 1.08%] versus 0.60% [0.18%, 1.03%]), CED mortality (0.61% [0.23%, 0.98%] versus 0.26% [−0.32%, 0.83%]), males (0.64% [0.43%, 0.85%] versus 0.12% [−0.21%, 0.44%]), and people aged 0 to 74 years (0.43% [0.20%, 0.66%] versus 0.00% [−0.32%, 0.32%]). In particular, we found statistically significant urban-rural differences in the associations of PM<sub>2.5</sub> with all-cause mortality among the total participants ( $p = 0.011$ ), males ( $p = 0.009$ ), and people aged 0 to 74 years ( $p = 0.034$ ).

In contrast, we found slightly greater associations between PM<sub>2.5</sub> and RESP mortality in rural areas than in urban cities (0.51% [−0.14%, 1.16%] versus 0.43% [−0.11%, 0.98%]), particularly in females (0.91% [0.02%, 1.81%] versus 0.09% [−0.67%, 0.85%]), and in people aged 0 to 74 years (0.40% [−0.62%, 1.42%] versus −0.07% [−1.06%, 0.93%]).

### Attributable fraction of mortality caused by ambient PM<sub>2.5</sub>

We observed that 2.11% (95% CI: 1.48%, 2.76%) of all-cause mortality was attributable to PM<sub>2.5</sub> exposure in 215 locations, with a larger AF in urban cities than in rural areas (2.89% [2.12%, 3.67%] versus 0.61% [−0.60%, 1.84%]). Greater AFs comparing urban cities with rural areas were also found on RESP (1.82% [−0.47%, 4.18%] versus 1.70% [−0.47%, 3.94%]), CVD (3.35% [2.13%, 4.59%] versus 2.13% [0.63%, 3.65%]) and CED mortality (2.56% [0.98%, 4.17%] versus 0.90% [−1.09%, 2.94%]). However, we observed larger AFs of RESP mortality in rural females (3.08% [95% CI: 0.06%, 6.22%]) than in urban females (0.37% [95% CI: −2.76%, 3.64%]) (Table 3).

An annual mean of 12.0 (95% CI: 8.4, 15.6) deaths per 100,000 population were attributable to PM<sub>2.5</sub> exposure in all locations, with a mean of 16.5 (12.1, 21.0) deaths per 100,000 in urban cities and 3.4 (−3.3, 10.3) deaths per 100,000 in rural areas (Table 4).



**Figure 1. The distribution of 215 Chinese locations and their mean daily PM<sub>2.5</sub> concentration during 2014–2017 (A) Guangdong; (B) Zhejiang; (C) Jilin; (D) Yunnan.**

### Sensitivity analyses

Sensitivity analyses showed that our results were robust to the changes of *dfs* of long-term trend, using different cutoffs of urbanization ratio to define rural areas, using different definitions of extreme PM<sub>2.5</sub> concentrations, and adjustment for other air pollutants including O<sub>3</sub> and CO. However, the associations of PM<sub>2.5</sub> with mortality were reduced after adjustment for NO<sub>2</sub> and SO<sub>2</sub> (Table S3). We did not find substantial changes in the associations between PM<sub>2.5</sub> and mortality risks in all locations and in urban cities after limiting the study days with daily mean PM<sub>2.5</sub> concentrations less than the maximum PM<sub>2.5</sub> concentration of rural locations (Figure S5).

### DISCUSSION

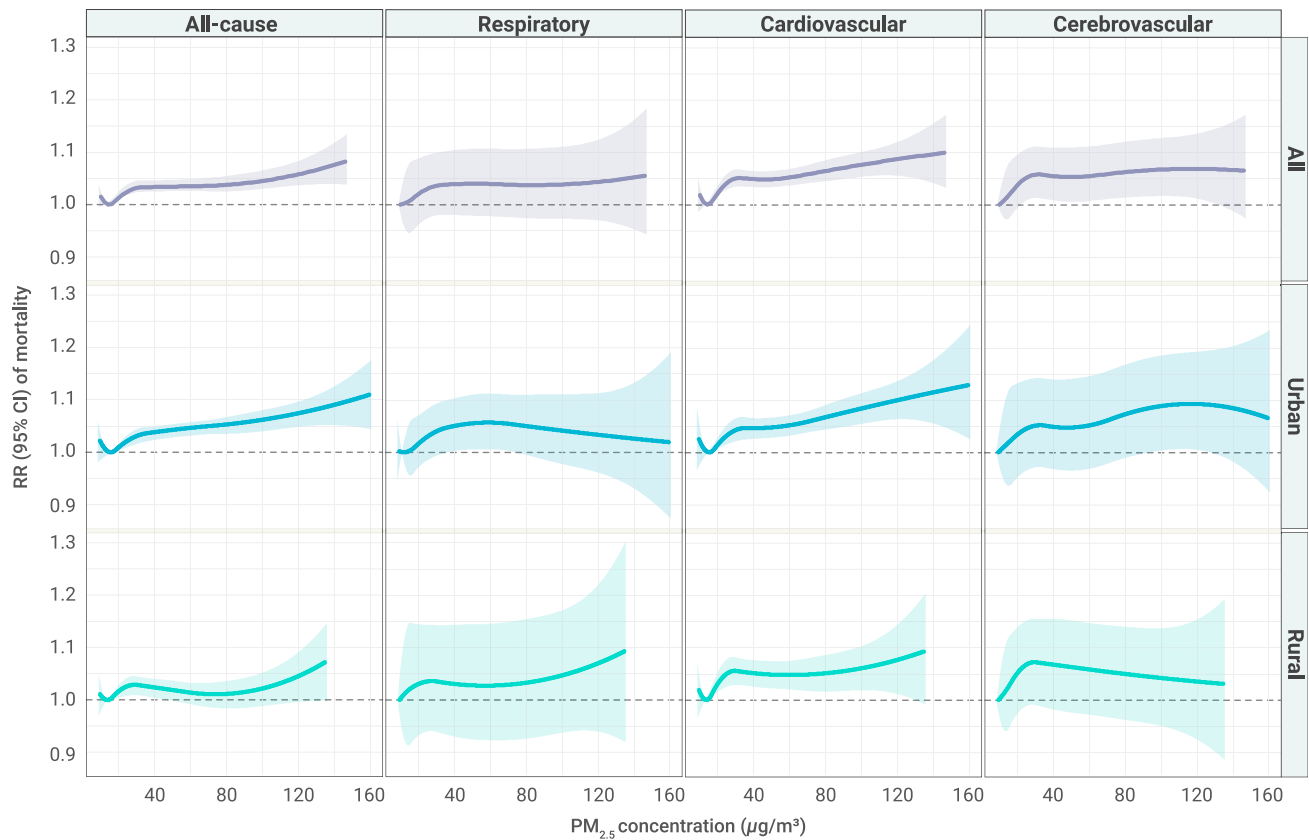
This study comprehensively compared the associations of short-term exposures to PM<sub>2.5</sub> and mortality risks between urban cities and rural areas in China. We found that short-term exposure to PM<sub>2.5</sub> was positively associated with risks of all-cause, RESP, CVD, and CED mortality. The associations of PM<sub>2.5</sub> with all-cause, CVD, and CED mortality were slightly greater in urban cities than in rural areas. In contrast, for RESP mortality, the effect of PM<sub>2.5</sub> was more pronounced in rural areas than in urban cities. These disparities in PM<sub>2.5</sub>-mortality associations between urban cities and rural areas were also found in some subgroups by sex and age.

Many previous studies have illustrated the positive associations between short-term exposure to PM<sub>2.5</sub> and mortality risk. A global meta-analysis demonstrated that each 10 µg/m<sup>3</sup> increase in PM<sub>2.5</sub> concentration was associated with 0.65%, 0.73%, 0.92%, and 0.72% increases in all-cause, RESP, CVD, and CED mortality risk, respectively.<sup>10</sup> A recent comprehensive review conducted by the U.S. Environmental Protection Agency also reported a positive relationship between PM<sub>2.5</sub> and mortality.<sup>11</sup> However, the risk estimates reported in Western countries were generally larger than our findings, which may be related to the higher air pollution levels in China. Previous studies have illustrated that the effects of PM<sub>2.5</sub> depend on the mean level of air pollution, with greater sizes at low PM<sub>2.5</sub> concentrations.<sup>1</sup> The results of the nonlinear exposure-response association between PM<sub>2.5</sub> and mortality in

this study also showed a steeper slope at low PM<sub>2.5</sub> concentrations (<30 µg/m<sup>3</sup>), particularly for CVD and CED mortality.

Compared with those in rural areas, we found slightly greater associations of PM<sub>2.5</sub> with CVD and CED mortality in urban cities. A few studies also reported consistent results with the present study.<sup>12,13</sup> For example, Garcia et al. observed a slightly larger effect of PM<sub>2.5</sub> exposure on mortality from ischemic heart disease in urban cities in California than in rural areas.<sup>12</sup> The reasons for this phenomenon are not completely clear, and they may be related to the differences in the sources and chemical compositions of PM<sub>2.5</sub>. In urban cities, particularly in metropolises, the major emission sources of PM<sub>2.5</sub> are traffic and industries, which cause emissions to usually contain more toxic components, such as elemental carbon (EC), organic carbon (OC), sulfate, nitrate, and heavy metals. These compositions could lead to higher levels of inflammation and oxidative stress and result in greater impairments to the human cardiovascular system.<sup>11,14,15</sup> A study conducted in Germany reported that exposure to PM<sub>2.5</sub> from a smelter area induced a greater inflammatory response than exposure to PM<sub>2.5</sub> from a control area in healthy volunteers.<sup>14</sup> We previously observed stronger associations of cardiovascular mortality with compositions of PM<sub>2.5</sub>, including OC, EC, sulfate, and nitrate, than other compositions.<sup>16</sup> In addition, rapid urbanization across China promoted the in-migration of a substantial population, particularly young people, to urban cities. However, these in-migrated people tend to reside in more polluted areas and hence intensify the health damage of air pollution.<sup>6</sup> The influence of in-migration may be an important reason for the larger urban-rural disparity of association between PM<sub>2.5</sub> and CVD mortality in younger people than in the elderly (Table 2).

In contrast to CVD and CED mortality, we observed more pronounced effects of PM<sub>2.5</sub> on RESP mortality, particularly at higher PM<sub>2.5</sub> concentrations in rural areas compared with urban cities, although the differences were not statistically significant. A few previous studies also suggested stronger effects of PM<sub>2.5</sub> on RESP mortality in suburban or rural areas than in urban cities in China.<sup>5,8,17</sup> For instance, Zhao et al. found that the relative risk of PM<sub>2.5</sub>-related RESP mortality was stronger in rural areas than in urban cities



**Figure 2. The cumulative exposure-response curves between  $PM_{2.5}$  and mortality over lag 0–3 days in all urban and rural locations** Note: The solid lines represent the cumulative relative risk of mortality over 4 days (lag 0–3 days) for  $PM_{2.5}$  concentrations, which are the combined effects of exposure and lag dimensions.

across China and that  $PM_{2.5}$  pollution was the dominant driving force of RESP mortality in rural areas.<sup>8</sup> These findings indicate that the RESP mortality burden caused by  $PM_{2.5}$  might be underestimated in countries with large rural populations if we use concentration–response relationships derived from urban cities to assess the mortality burden of  $PM_{2.5}$ . This finding has important implications for air pollution control in China because there are more than 500 million people living in rural China.

The reasons for the greater associations of  $PM_{2.5}$  with RESP mortality risk in rural areas than in urban cities remain unclear and may be explained by several reasons. First, compared with urban residents, rural populations have disadvantaged socioeconomic conditions, sanitation, health care systems, living environments, and health status with more respiratory diseases (Table S4),<sup>18</sup> which can increase their susceptibility to  $PM_{2.5}$ .<sup>17</sup> Second, rural residents, particularly women, usually have higher levels of exposure to indoor air pollution from solid fuels for cooking and heating without adequate ventilation compared with urban residents.<sup>19,20</sup> As a result, the exposure to ambient  $PM_{2.5}$  in rural areas might be underestimated, and indoor air pollutants may synergize with the RESP mortality risks caused by a per-unit increase in ambient  $PM_{2.5}$  concentrations. A recent global meta-analysis also reported stronger effects of household air pollution on respiratory diseases than on cardiovascular diseases.<sup>21</sup> Third, higher levels of some chemical components, such as neonicotinoid insecticide, of  $PM_{2.5}$  in rural areas may also contribute to the greater health impacts of  $PM_{2.5}$ .<sup>22,23</sup> Fourth, the greater effects of  $PM_{2.5}$  in rural areas may also be related to a higher prevalence of smoking and second-hand smoke,<sup>24,25</sup> which may intensify the effects of ambient air pollution on RESP mortality risks.

Urban-rural disparities in the associations between  $PM_{2.5}$  and mortality were also observed in people of different sexes and ages. For example, a much stronger association of  $PM_{2.5}$  with RESP mortality was found in rural females than in urban females, which may be related to their differences in

exposures, socioeconomic conditions, and health status. Compared with urban females, rural females usually have harder physical activities,<sup>26</sup> more indoor air pollution from passive smoking and solid fuels for cooking and heating,<sup>24,25</sup> and poorer health status,<sup>27</sup> which may increase their exposure and susceptibility to air pollution. In addition, our results showed that the effects of  $PM_{2.5}$  were generally greater in females than in males and in older people than in younger people, which was consistent with previous studies.<sup>3,28</sup>

Our findings indicate that air pollution can result in discrepant adverse health between urban and rural people. Different measures are needed to design urban and rural residents. In urban areas, efforts should be spent on upgrading industry structures and technologies, upgrading energy structures (such as developing economically and socially sustainable alternatives to fossil fuel used), and promoting green transportation (such as public and electric transportation). In rural areas, more efforts should focus on legislation to ban smoking, reduce indoor pollution exposure, improve ventilation, and promote the usage of protective measurements for air pollution. Moreover, the different patterns of  $PM_{2.5}$ -mortality associations in urban cities versus rural areas should be considered in future epidemiological studies and the estimations of disease burden attributable to air pollution.

Many previous studies have estimated the mortality burden attributable to  $PM_{2.5}$  exposure globally. However, most studies have focused on long-term exposure to  $PM_{2.5}$ ,<sup>29–33</sup> and information on the mortality burden attributable to short-term  $PM_{2.5}$  exposure is scarce.<sup>34</sup> In this study, we observed that an annual mean of 12.0 deaths per 100,000 population were attributable to  $PM_{2.5}$  exposure in all included locations, and the corresponding AF was 2.11%. Our finding was lower than that in the study by Li et al., which reported that the additional death rate was 13.78 per 100,000 people throughout China.<sup>34</sup> This difference may be partially because the present study

**Table 2.** The cumulative ER<sup>a</sup> (%; 95% CI) of mortality for each 10 µg/m<sup>3</sup> increase in PM<sub>2.5</sub> concentration over lag 0–3 days by region

	Total	Sex		Age (years)	
		Male	Female	0–74	75–
<b>All-cause mortality</b>					
Total	0.54 (0.38, 0.70)	0.46 (0.29, 0.64)	0.66 (0.43, 0.89)	0.26 (0.08, 0.45)	0.77 (0.57, 0.98)
Urban	0.68 (0.50, 0.86)	0.64 (0.43, 0.85)	0.75 (0.48, 1.02)	0.43 (0.20, 0.66)	0.87 (0.63, 1.11)
Rural	0.17 (–0.17, 0.52)	0.12 (–0.21, 0.44)	0.46 (0.05, 0.87)	0.00 (–0.32, 0.32)	0.45 (0.05, 0.85)
p <sup>b</sup>	0.011	0.009	0.248	0.034	0.079
<b>RESP mortality</b>					
Total	0.51 (0.10, 0.93)	0.66 (0.20, 1.13)	0.39 (–0.19, 0.97)	0.19 (–0.52, 0.90)	0.60 (0.13, 1.06)
Urban	0.43 (–0.11, 0.98)	0.72 (0.11, 1.34)	0.09 (–0.67, 0.85)	–0.07 (–1.06, 0.93)	0.58 (–0.01, 1.17)
Rural	0.51 (–0.14, 1.16)	0.33 (–0.39, 1.05)	0.91 (0.02, 1.81)	0.40 (–0.62, 1.42)	0.46 (–0.31, 1.23)
p <sup>b</sup>	0.854	0.420	0.172	0.519	0.809
<b>CVD mortality</b>					
Total	0.74 (0.50, 0.97)	0.69 (0.41, 0.97)	0.76 (0.44, 1.09)	0.24 (–0.09, 0.57)	0.99 (0.72, 1.25)
Urban	0.80 (0.51, 1.08)	0.78 (0.42, 1.14)	0.80 (0.40, 1.20)	0.37 (–0.06, 0.79)	0.98 (0.66, 1.30)
Rural	0.60 (0.18, 1.03)	0.55 (0.08, 1.03)	0.68 (0.11, 1.26)	0.09 (–0.45, 0.63)	0.96 (0.49, 1.43)
p <sup>b</sup>	0.444	0.450	0.737	0.425	0.945
<b>CED mortality</b>					
Total	0.52 (0.20, 0.83)	0.54 (0.19, 0.89)	0.47 (0.02, 0.93)	–0.12 (–0.63, 0.40)	0.87 (0.54, 1.19)
Urban	0.61 (0.23, 0.98)	0.50 (0.05, 0.95)	0.71 (0.14, 1.28)	–0.01 (–0.66, 0.65)	0.87 (0.46, 1.28)
Rural	0.26 (–0.32, 0.83)	0.51 (–0.17, 1.20)	–0.04 (–0.82, 0.75)	–0.19 (–1.00, 0.63)	0.61 (–0.03, 1.24)
p <sup>b</sup>	0.319	0.981	0.131	0.736	0.501

<sup>a</sup>The 95% CI of an ER including zero indicates no statistical significance.

<sup>b</sup>The p values were for difference tests in the associations between urban and rural areas.

considered the disparities in PM<sub>2.5</sub>-mortality associations between urban and rural areas. We found a larger death rate (16.5/100,000 people) in urban areas than in rural areas (3.4/100,000 people). However, Li et al. applied a unique exposure-response association to estimate the mortality burden related to PM<sub>2.5</sub> throughout China,<sup>34</sup> which may lead to an overestimation. The larger mortality burden in urban areas may be due to the stronger association between PM<sub>2.5</sub> and all-cause mortality and the higher PM<sub>2.5</sub> concentrations. Therefore, the urban-rural disparities of PM<sub>2.5</sub>-mortality associations should not be ignored in estimating the disease burden of air pollution.

### Strengths and limitations

This study has several strengths. First, our study compared the effects of PM<sub>2.5</sub> exposure on all causes and cause-specific mortality in both urban cities and rural areas in China and provided new insights into the urban-rural difference in the effects of PM<sub>2.5</sub> on mortality. Second, the large-scale study including 215 locations in different regions of China increased the external representativeness of our findings. Third, we employed a random forest model to assess the daily PM<sub>2.5</sub> concentrations in each location, which could reduce the misclassification bias.

There are also several limitations. First, similar to many previous time-series studies, this study was an ecological study. Therefore, the association between PM<sub>2.5</sub> and mortality should be interpreted with caution. Second, we did not find an official definition of rural areas in China and alternatively employed the urbanization ratio to define urban cities and rural areas. Nevertheless, the results of sensitivity analyses showed the robustness of our findings to the cutoffs of the urbanization ratio. Third, as we discussed above, people in rural areas of China usually have higher rates of indoor

air pollution than urban residents.<sup>19,20</sup> Unfortunately, the present study cannot adjust for indoor pollution, which may lead to bias in our findings.

### Conclusion

We observed slightly stronger associations of PM<sub>2.5</sub> with CVD and CED mortality risks in urban cities than in rural areas and slightly greater associations with RESP mortality in rural areas than in urban cities. Our findings suggest that the disparities in PM<sub>2.5</sub>-mortality associations between urban cities and rural areas should be considered in the assessment of mortality burden attributable to air pollution. Spatially targeted measures are needed to reduce PM<sub>2.5</sub>-related mortality in China.

### MATERIALS AND METHODS

#### Study locations

The present study included 215 locations covering Guangdong, Zhejiang, Jilin, and Yunnan provinces (Figure 1). We selected these locations from the provincial mortality surveillance system, which was administered by the corresponding provincial Center for Disease Control and Prevention (CDC) following the same protocol as China's Disease Surveillance Points System.<sup>35</sup> At each surveillance point, all deaths certified by clinical doctors or local CDC professionals are reported to the CDC using an Internet-based reporting system. To ensure adequate statistical power, only the surveillance points with population sizes exceeding 200,000 or annual mortality rates >4‰ were included in our study, which has been described in previous studies.<sup>36–38</sup> We further divided these locations into urban areas (n = 106 locations) and rural regions (n = 109 locations) according to whether the urbanization ratio exceeds 50% because the history of urbanization development worldwide showed that 50% was an important turning point, which not only indicates that the economy would continue to develop rapidly but also may cause changes in disease patterns.<sup>39</sup> The urbanization ratio reflects the ratio of the urban population to the total population size.<sup>40</sup> The

**Table 3.** The AF<sup>a</sup> (%; 95% CI) of mortality attributable to ambient PM<sub>2.5</sub> pollution by region

	Total	Sex		Age (years)	
		Male	Female	0–74	75–
<b>All-cause mortality</b>					
Total	2.11 (1.48, 2.76)	1.81 (1.11, 2.51)	2.59 (1.68, 3.50)	1.01 (0.31, 1.72)	3.07 (2.25, 3.90)
Urban	2.89 (2.12, 3.67)	2.71 (1.83, 3.61)	3.18 (2.02, 4.35)	1.80 (0.83, 2.78)	3.75 (2.71, 4.80)
Rural	0.61 (–0.60, 1.84)	0.41 (–0.75, 1.57)	1.62 (0.16, 3.11)	–0.02 (–1.12, 1.11)	1.62 (0.18, 3.08)
p <sup>b</sup>	0.002	0.002	0.105	0.017	0.020
<b>RESP mortality</b>					
Total	1.93 (0.36, 3.52)	2.49 (0.74, 4.28)	1.47 (–0.71, 3.71)	0.66 (–1.78, 3.18)	2.30 (0.51, 4.13)
Urban	1.82 (–0.47, 4.18)	3.03 (0.44, 5.71)	0.37 (–2.76, 3.64)	–0.28 (–4.12, 3.77)	2.47 (–0.03, 5.05)
Rural	1.70 (–0.47, 3.94)	1.11 (–1.28, 3.58)	3.08 (0.06, 6.22)	1.27 (–1.94, 4.62)	1.57 (–1.03, 4.27)
p <sup>b</sup>	0.942	0.295	0.233	0.554	0.631
<b>CVD mortality</b>					
Total	2.85 (1.93, 3.77)	2.66 (1.57, 3.77)	2.97 (1.68, 4.28)	0.90 (–0.33, 2.15)	3.91 (2.85, 4.98)
Urban	3.35 (2.13, 4.59)	3.27 (1.76, 4.82)	3.36 (1.66, 5.11)	1.49 (–0.24, 3.26)	4.16 (2.79, 5.57)
Rural	2.13 (0.63, 3.65)	1.95 (0.27, 3.66)	2.42 (0.38, 4.51)	0.29 (–1.53, 2.16)	3.45 (1.74, 5.21)
p <sup>b</sup>	0.221	0.258	0.494	0.356	0.532
<b>CED mortality</b>					
Total	1.99 (0.78, 3.23)	2.07 (0.73, 3.44)	1.83 (0.06, 3.65)	–0.44 (–2.32, 1.49)	3.44 (2.14, 4.76)
Urban	2.56 (0.98, 4.17)	2.10 (0.22, 4.02)	3.01 (0.60, 5.49)	–0.03 (–2.72, 2.75)	3.72 (1.97, 5.52)
Rural	0.90 (–1.09, 2.94)	1.81 (–0.60, 4.29)	–0.13 (–2.83, 2.66)	–0.65 (–3.37, 2.17)	2.16 (–0.10, 4.49)
p <sup>b</sup>	0.207	0.855	0.091	0.755	0.293

<sup>a</sup>The 95% CI of an AF including zero indicates no statistical significance.

<sup>b</sup>The p values were for difference tests in the associations between urban and rural areas.

urbanization ratios for the urban and rural areas are 0.71 (standard deviation [SD] = 0.16) and 0.36 (SD = 0.10), respectively.

#### Data collection

Daily mortality data from January 1, 2014, to December 31, 2017, in every included location were obtained from the corresponding provincial CDC. Based on the codes of the 10th revision of the International Classification of Diseases (ICD-10), we extracted daily mortality data from all nonaccidental causes (codes A00-R99), RESP (codes J00-J99), CVD (codes I00-I99), and CED (codes I60-I69). We then classified daily death counts into several subgroups by sex and age (0–74 and ≥75 years).

Because some selected locations were not covered by the air quality monitoring system, we collected daily average air pollution data at national air pollutant monitoring stations from the National Urban Air Quality Real-time Publishing Platform (<http://106.37.208.233:20035/>), and then a random forest model was applied to simulate the daily average air pollution data at each study location.<sup>41,42</sup> We input predictors including type of land use, road density, population density, meteorological factors, and gross domestic product (GDP) per capita in the model to reduce misclassification bias.<sup>41,42</sup> The coefficient of determination ( $R^2$ ) from a linear fitting of predictions and observations of ground monitors was 0.83, and the root mean squared prediction error (RMSE) of daily PM<sub>2.5</sub> was 10.61 μg/m<sup>3</sup>. Information on other air pollutant estimations can be found in the [supplemental information](#) (Supplemental section 1.1 and [Figures S1 and S2](#)).

Daily meteorological data, including the mean temperature (TM, °C) and relative humidity (RH, %), of 698 weather stations across China were derived from the China Meteorological Data Sharing Service System (<http://data.cma.cn/>). We employed Australian National University Splines thin plate smoothing software to interpolate the daily TM and RH at a 0.01° × 0.01° resolution for all of China.<sup>37</sup> The results of 10-fold cross-validation show good prediction accuracy of the interpolation method for daily TM ( $R^2 = 0.96$ , RMSE = 2.37°C) and RH ( $R^2 = 0.81$ , RMSE = 7.70%) (see [Supplemental text section 1.2](#) and [Figure S3](#)

in [supplemental information](#)). Daily TM and RH of 215 locations were extracted from the interpolated grid.

Population data (from 2014 to 2017) and GDP per capita (in 2015) for each study location were obtained from the Statistical Yearbook.<sup>43</sup> Socioeconomic characteristics, including average years of education and urban population size, were obtained from the 2010 Population Census in China.<sup>43</sup> The data source of predictors (raster data) in the random forest model can be seen in [Supplemental text section 1.1](#) of the [supplemental information](#).

#### Statistical analyses

We applied a two-stage approach, which has been widely applied in previous studies.<sup>37,44</sup> In the first stage, we estimated the location-specific nonlinear PM<sub>2.5</sub>-mortality associations using a distributed lag nonlinear model (DLNM) combined with a quasi-Poisson distribution function. A quadratic B-spline (*bs*) function was employed to estimate the nonlinear and lag effects of PM<sub>2.5</sub>. A *bs* function was used to estimate and control for nonlinear and lag effects of contemporaneous daily TM. A natural cubic spline (*ns*) with 3 degrees of freedom (*df*) was used to control for RH, a *ns* with seven *df* per year to control for the seasonal and long-term trends in mortality, and a categorical variable to control for the day of the week.

In the second stage, we pooled the location-specific overall exposure-response curves using a multivariate meta-analysis with random effects models. The minimum mortality pollution was taken as a reference in the pooled exposure-response curve. To avoid the potential impacts of extreme PM<sub>2.5</sub> concentrations on model fitting, days with PM<sub>2.5</sub> concentrations below the 0.5% centile or above the 99.5% centile in the distribution of PM<sub>2.5</sub> concentrations were removed from the DLNM modeling.

The pooled exposure-response curves between PM<sub>2.5</sub> and mortality showed approximately linear relationships. Therefore, in the first stage, we also applied a distributed lag model (DLM) to estimate the location-specific linear PM<sub>2.5</sub>-mortality associations, in which a linear function and a *bs* function were employed to estimate the linear and lag effects of PM<sub>2.5</sub>, respectively. The

**Table 4.** Annual mean number of deaths (95% CI, per 100,000 people) attributable to ambient PM<sub>2.5</sub> pollution by region

	Total	Sex		Age (years)	
		Male	Female	0–74	75–
<b>All-cause mortality</b>					
Total	12.0 (8.4, 15.6)	5.9 (3.6, 8.2)	6.2 (4.1, 8.4)	2.5 (0.8, 4.3)	9.8 (7.2, 12.4)
Urban	16.5 (12.1, 21.0)	8.8 (5.9, 11.8)	7.8 (5.0, 10.7)	4.3 (2.0, 6.6)	12.6 (9.1, 16.1)
Rural	3.4 (–3.3, 10.3)	1.3 (–2.4, 5.1)	3.8 (0.4, 7.3)	0.0 (–2.9, 2.9)	4.8 (0.5, 9.2)
<b>RESP mortality</b>					
Total	1.7 (0.3, 3.1)	1.2 (0.4, 2.1)	0.6 (–0.3, 1.4)	0.1 (–0.4, 0.6)	1.6 (0.3, 2.8)
Urban	1.5 (–0.4, 3.4)	1.4 (0.2, 2.6)	0.1 (–1.0, 1.3)	0.0 (–0.6, 0.6)	1.6 (0.0, 3.3)
Rural	1.6 (–0.5, 3.8)	0.6 (–0.7, 2.0)	1.3 (0.0, 2.6)	0.3 (–0.5, 1.2)	1.1 (–0.7, 3.0)
<b>CVD mortality</b>					
Total	6.5 (4.4, 8.6)	3.3 (1.9, 4.6)	3.1 (1.8, 4.5)	0.7 (–0.3, 1.7)	5.7 (4.2, 7.3)
Urban	7.3 (4.6, 10.0)	3.8 (2.0, 5.6)	3.4 (1.7, 5.2)	1.0 (–0.2, 2.2)	6.2 (4.2, 8.3)
Rural	5.1 (1.5, 8.8)	2.6 (0.4, 4.8)	2.6 (0.4, 4.9)	0.3 (–1.5, 2.1)	5.0 (2.5, 7.5)
<b>CED mortality</b>					
Total	2.3 (0.9, 3.7)	1.3 (0.5, 2.2)	0.9 (0.0, 1.9)	–0.2 (–1.0, 0.6)	2.5 (1.5, 3.4)
Urban	2.8 (1.1, 4.6)	1.2 (0.1, 2.4)	1.5 (0.3, 2.8)	0.0 (–1.4, 1.4)	2.8 (1.5, 4.1)
Rural	1.1 (–1.3, 3.5)	1.2 (–0.4, 2.9)	–0.1 (–1.5, 1.4)	–0.3 (–1.7, 1.1)	1.5 (–0.1, 3.2)

parameters of other variables in the DLM were the same as those in the DLNM. The results of preliminary analyses showed that the greatest cumulative excess risk (ER) of mortality for each 10  $\mu\text{g}/\text{m}^3$  increase in PM<sub>2.5</sub> was observed within lag 0–3 days (Table S1 and Figure S4). Thus, we estimated the 4-day (lag 0–3 days) cumulative ER (%),  $(\text{RR}-1) \times 100\%$  of all-cause and cause-specific mortality for exposure to PM<sub>2.5</sub> concentrations in both DLNM and DLM analyses, which was consistent with previous studies.<sup>45,46</sup> In particular, the cumulative ER (%; 95% confidence interval [CI]) of mortality risk attributable to each 10  $\mu\text{g}/\text{m}^3$  increase in PM<sub>2.5</sub> during lag 0–3 days in the DLM analyses was reported, which was the combined effect of exposure and lag dimensions (Supplemental text section 1.3 of the supplemental information).

Based on the pooled exposure-response relationships, we estimated their corresponding attributable fractions (AF) of mortality and number of deaths (/100,000) attributable to PM<sub>2.5</sub> exposure (Supplemental text section 1.4 of the supplemental information). All of the above analyses were separately implemented in all locations, urban locations, rural locations, males, females, people <75 years old, people  $\geq 75$  years old, and mortality, including all-cause, RESP, CVD, and CED mortality. We applied 2-sample z-tests using stratification-specific point estimates and their SEs to test the potential effect modification of regions (urban versus rural).<sup>47</sup>

#### Sensitivity analyses

To test the robustness of our results, we changed the *dfs* for the time trend from 6 to 8 per year, cutoffs of urbanization ratio (0.45, 0.50, and 0.55) to define rural areas, and percentiles (<2.0% or >98.0%, <1.0% or >99.0%, <0.5% or >99.5%) to define extreme PM<sub>2.5</sub> concentrations. Two-pollutant models were used to adjust for O<sub>3</sub>, CO, NO<sub>2</sub>, and SO<sub>2</sub>. Previous studies have shown that the exposure-response association between PM<sub>2.5</sub> and mortality was also affected by PM<sub>2.5</sub> concentrations.<sup>1</sup> In this study, we found higher mean PM<sub>2.5</sub> concentrations in urban cities than in rural areas. Therefore, we estimated the nonlinear and linear exposure-response association between PM<sub>2.5</sub> and mortality risks in all locations and urban cities only on days with daily PM<sub>2.5</sub> concentrations less than the maximum PM<sub>2.5</sub> concentration (134.7  $\mu\text{g}/\text{m}^3$ ) in rural areas.

R software version 3.6.1 (<https://cran.r-project.org/bin/windows/base/old/3.6.1/>) was used to conduct data analysis. A *p* value of less than 0.05 was considered to indicate statistical significance.

#### Ethical approval

This study was approved by the Ethics Committee of Guangdong Provincial CDC (No. 2019025). Data were analyzed at the aggregate level, and no participants were contacted.

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#### AUTHOR CONTRIBUTIONS

W.M. and T.L. conceptualized the study; T.L., H.M., M.Y., J.H., J.X., S.C., W.Z., X.L., G.H., Z.R., and W.M. developed the methodology; H.M., S.C., W.Z., and X.L. performed the formal analysis; T.L., H.M., M.Y., and W.M. prepared the original draft; T.L., H.M., M.Y., Y.Xiao, B.H., L.L., H.Z., R.H., Z.H., Y.Xu, L.Y., M.Q., Q.Z., X.X., W.G., J.H., J.X., S.C., W.Z., X.L., G.H., Z.R., C.H., Y.D., and W.M. reviewed and edited the manuscript; W.M., T.L., and C.H. acquired the funding; M.Y., Y.Xiao, B.H., L.L., H.Z., R.H., Z.H., Y.Xu, L.Y., M.Q., Q.Z., X.X., W.G., and Y.D. acquired the resources; and W.M., T.L., L.L., and C.H. supervised the study.

#### DECLARATION OF INTERESTS

The authors declare no competing interests.

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#### SUPPLEMENTAL INFORMATION

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