



# Does air pollution contribute to urban–rural disparity in male lung cancer diseases in China?

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## Abstract

It remains unknown whether exposure to ambient air pollution can be a mediator linking socioeconomic indicator to health outcome. The present study aims to examine the mediation effect of PM<sub>2.5</sub> air pollution on the association between urban–rural division and the incidence (mortality) rate of male lung cancer. We performed a nationwide analysis in 353 counties (districts) of China between 2006 and 2015. A structural equation model was developed to determine the mediation effect of exposure to PM<sub>2.5</sub>. We also tested whether the findings of the mediation effect of exposure to PM<sub>2.5</sub> are sensitive to the controls of smoking factors and additional air pollutant, and PM<sub>2.5</sub> exposures with different lag structures. According to the results, we found that exposure to PM<sub>2.5</sub> significantly mediated the association between urban–rural division and the incidence rate of male lung cancer. Specifically, there were significant associations between urban–rural division, exposure to PM<sub>2.5</sub>, and the incidence rate of male lung cancer, with PM<sub>2.5</sub> exposure accounting for 29.80% of total urban–rural difference in incidence rates of male lung cancer. A similar pattern of results was observed for the mortality rate of male lung cancer. That is, there was a significant mediation effect by PM<sub>2.5</sub> on the association of the mortality rate with urban–rural division. The findings of exposure to PM<sub>2.5</sub> as a mediator were robust in the three sensitivity analyses. In conclusion, urban–rural difference in exposures to PM<sub>2.5</sub> may be a potential factor that contributes to urban–rural disparity in male lung cancer diseases in China. The findings inform that air pollution management and control may be effective measures to alleviate the great difference in male lung cancer diseases between urban and rural areas in China.

**Keywords** Urban–rural division · Air pollution · Mediation effect · Lung cancer · China

## Introduction

Socioeconomic disparities in health outcomes have been well documented. However, socioeconomic statuses do not affect human health directly. Hence, it is essential to understand mediators (pathways) linking socioeconomic factors

to health outcomes. Exposure to air pollution is a potential mediator that can explain socioeconomic disparities in health outcomes. However, whether air pollution exposure mediates the relationship between socioeconomic status and human health has not been well and fully understood in China.

Previous studies have investigated associations between socioeconomic status, air pollution and health outcome.

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With respect to socioeconomic disparities in air pollution exposures, how disparity in exposures to air pollution occurs has been understood on the basis of several theories, such as market dynamics, racial discrimination and urbanization (Brulle and Pellow 2006; Mohai et al. 2009; Cesaroni et al. 2010; Padilla et al. 2014). Empirically, some studies have reported the significant association between socioeconomic status and air pollution exposure (Hajat et al. 2013; Bravo et al. 2016; Xu et al. 2019). In particular, collecting data from the project EURO-HEALTHY, a European study suggested that unemployment rate is positively associated with  $\text{NO}_2$  concentration in nine metropolitan areas of Europe (Samoli et al. 2019). Combining data of mobile phone location, estimated  $\text{PM}_{2.5}$  concentrations and housing price, a study reported that there is a significant association between economic status and individual total  $\text{PM}_{2.5}$  exposure in Shenzhen, China (Guo et al. 2020a, b).

Regarding the association between air pollution and health outcome, biologically, air pollution can cause detrimental effects on human health through the increase in genetic damage such as cytogenetic abnormalities (International Agency for Research on Cancer (Volume 109), 2016a), oxidative stress, and inflammation (Lodovici and Bigagli 2011). A large number of studies have also indicated the adverse effects of air pollution on human's physical health (Pope et al. 2002; Pope and Dockery 2006; Chen et al. 2017) as well as psychological health (Power et al. 2015; Salinas-Rodríguez et al. 2018). It has also been reported that health consequences vary with race (Redmond et al. 2011), behavior factors (International Agency for Research on Cancer (Volume 83), 2016c; Rasmussen-Torvik et al. 2016) and socioeconomic indicators including urban–rural division, income and educational attainment (Cohen and Pope 3rd 1995; Fang et al. 2010; Evandrou et al. 2014).

Building on the work above, few studies have attempted to examine the mediation effect of air pollution exposure. It is hypothesized that socioeconomic status is associated with air pollution exposure, which in turn affects the physical and psychological health of human beings. Empirically, most of the studies generally suggest the mediation role of air pollution exposure on socioeconomic disparities in health outcomes, although the number of studies is small. Collecting health data of 6,463 adults from the Multi-ethnic Study of Atherosclerosis (MESA), Song et al. (2020) reported the significant mediation effect of exposure to ambient  $\text{PM}_{2.5}$  on the association between race/ethnicity and systolic blood pressure across six cities of USA. Using county-level birth certificate data acquired from the National Centre for Health Statistics of the USA, Woodruff et al. (2003) indicated that the difference in exposures to air pollution among racial groups can partly account for racial disparity in preterm deliveries. Benmarhnia et al. (2017) suggested that  $\text{PM}_{2.5}$  does explain a proportion of racial disparity in preterm

births in California of the USA, although the effect of this air pollutant is quite small.

Despite these efforts, more studies are required due to the following reasons. Firstly, such studies are quite limited, hence it is not sufficient to conclude the mediation effect of air pollution exposure. Secondly, most of studies investigating the mediation effect of air pollution exposure focus on racial disparity (Woodruff et al. 2003; Hackbarth et al. 2011; Song et al. 2020), although racial issue is not popular or does not exist in many countries such as China. This highlights the more and further examinations in other contexts. Thirdly, few studies have investigated the determinants of urban–rural disparity in lung cancer diseases in China. Lung cancer has been the number one cause of cancer incidences (and mortalities) in China with age-adjusted incidence rate of lung cancer at 36.54 per 100,000 people in 2014 (He and Chen 2018). Also, the large difference in lung cancer diseases between urban and rural areas (counties Vs. districts) has been well documented in China and other countries (Cohen and Pope 3rd 1995; Dikshit et al. 2012; He and Chen 2018; International Agency for Research on Cancer (Volume 168), 2019) with age-adjusted incidence rate of male lung cancer at 54.15 per 100,000 people in urban areas and at 49.06 per 100,000 people in rural China in the present study. Meanwhile, a number of studies have suggested the adverse effects of air pollution (especially  $\text{PM}_{2.5}$  which is highly severe and prominent in Chinese cities) on lung cancer diseases (Pope et al. 2002; International Agency for Research on Cancer (Volume 109), 2016a; Guo et al. 2020a). However, it remains unknown whether air pollution exposure can explain urban–rural disparity in lung cancer diseases in China.

To fill the gaps above, this work aims to investigate the mediation effect of exposure to  $\text{PM}_{2.5}$  on the association between urban–rural division and the incidence (mortality) rate of male lung cancer in 353 Chinese cancer registries (counties/districts). The mediation effect was examined using a structural equation model which controlled for time, location and socioeconomic indicators. Moreover, we tested whether the findings of the mediation effect of air pollution exposure are sensitive to the controls of health and behavior factors (e.g., smoking behavior) and additional air pollutant, and  $\text{PM}_{2.5}$  exposures with different lag structures (single- and moving-average lags).

## Materials and methods

### Research area

The present study is to investigate the mediation effect of exposure to  $\text{PM}_{2.5}$  on urban–rural disparity in lung cancer diseases in 353 cancer registries of China. The number of

urban (districts) and rural (counties) registries were 88 and 265, respectively. The 353 cancer registries were selected mainly due to the available data on health outcomes and socioeconomic indicators. Home to about 190.21 million in 2014, these registries are located in 31 of 34 Chinese provinces, autonomous regions and municipalities. Figure 1 presents the spatial distributions of 353 Chinese cancer registries.

## Data collection

### Annual mean $PM_{2.5}$ concentrations

The targeted variable of air pollution is annual mean  $PM_{2.5}$  concentrations, which are aggregated in each registry. Severe  $PM_{2.5}$  air pollution in Chinese cities has received great attention from the public, scholars, and governments. Numerous studies have also provided the mechanisms and empirical evidences of  $PM_{2.5}$  effects on human health including lung cancer diseases as health outcome in this work (International Agency for Research on Cancer (Volume 109), 2016a; Yin et al. 2017; Guo et al. 2020a). Accordingly,  $PM_{2.5}$  is selected as the variable of air pollution to examine its mediation effect in the present study.

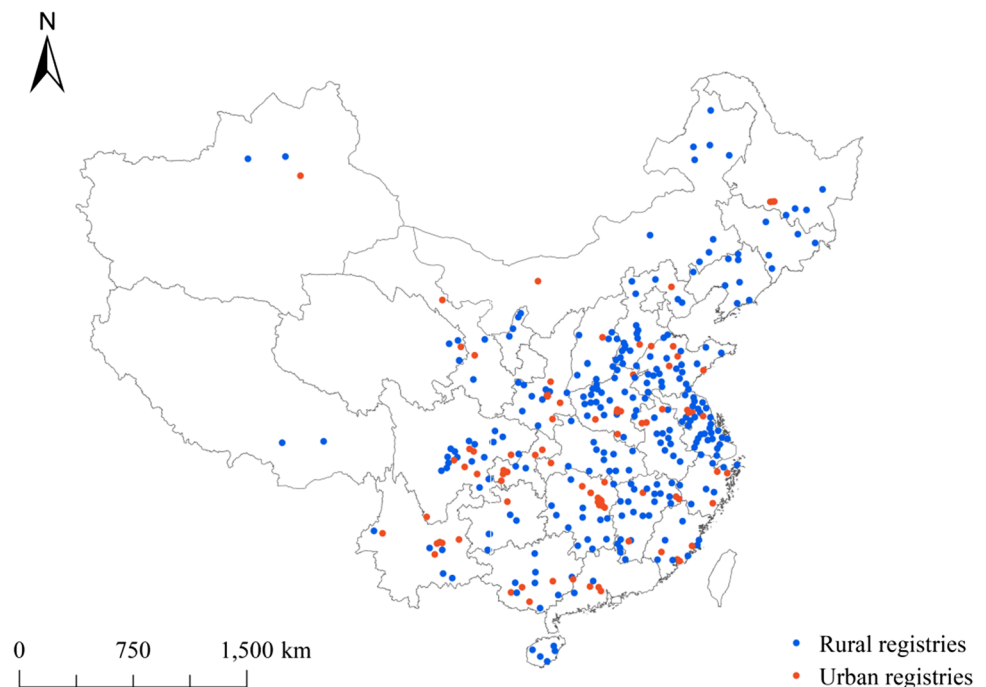
Data on annual ground  $PM_{2.5}$  concentrations with spatial resolution at  $1\text{ km}^2$  from 2000 to 2015, were collected from the dataset of China Regional Estimates (V4.CH.02) publicly released by the Atmospheric Composition Analysis Group of Dalhousie University ([http://fizz.phys.dal.ca/~atmos/martin/?page\\_id=140](http://fizz.phys.dal.ca/~atmos/martin/?page_id=140)). Notably, data between 2006 and 2015 are used to examine the mediation effect of

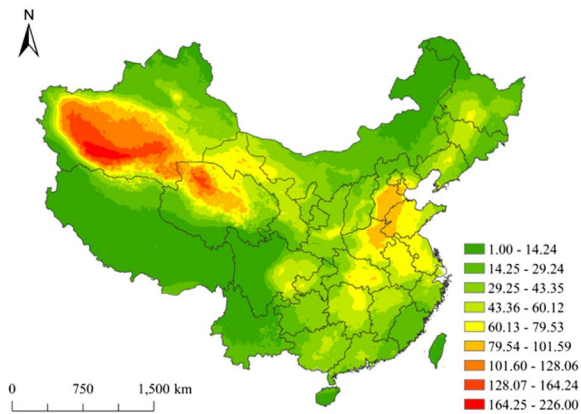
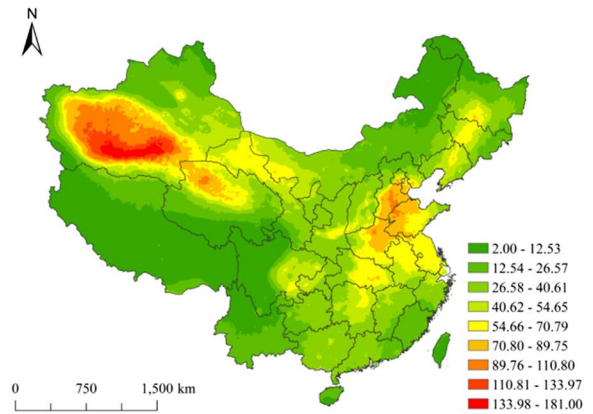
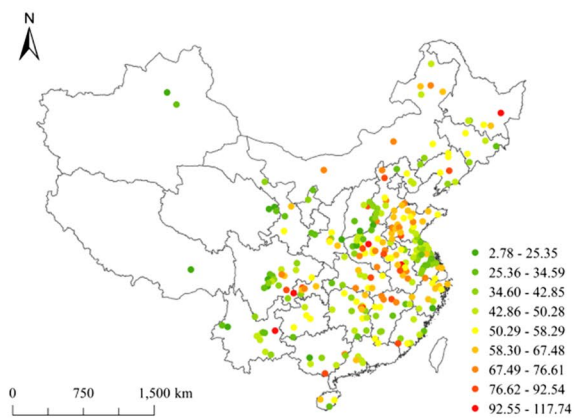
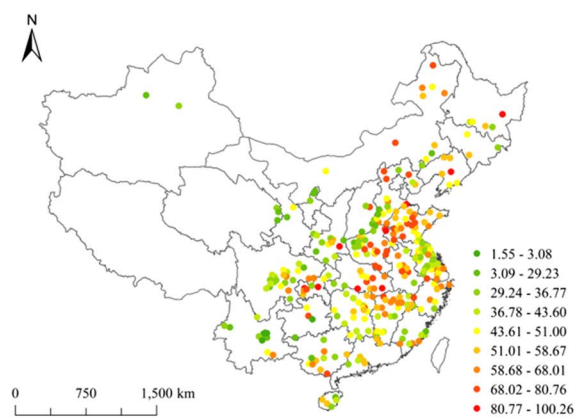
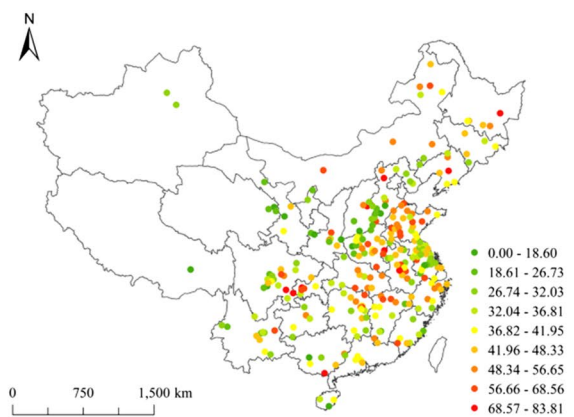
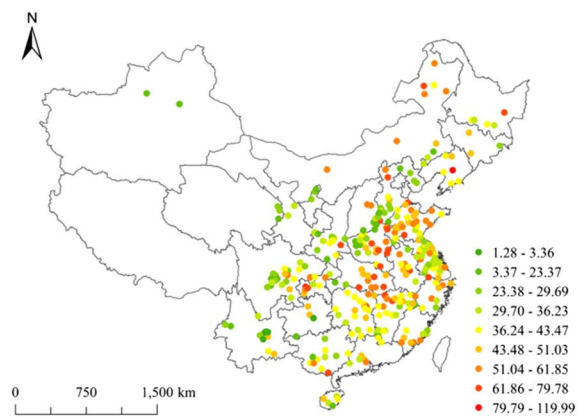
exposure to  $PM_{2.5}$ , while those from 2000 to 2015 are utilised to test the robustness of  $PM_{2.5}$  mediation effect in the sensitivity analysis. More details of  $PM_{2.5}$  data produced can refer to Van Donkelaar et al. (2016). Briefly, three satellite instruments, namely the NASA Moderate Resolution Imaging Spectroradiometer, Multi-angle Imaging Spectroradiometer and Sea-Viewing Wide Field-of-View Sensor, were used to retrieve AOD. Then, a GEOS-Chem chemical transport model was used to associate the retrieved AOD to near-surface  $PM_{2.5}$  concentrations, which subsequently produced the time-series dataset of ground  $PM_{2.5}$  concentrations at  $1\text{ km}^2$  spatial resolution from 2000 to 2017. Notably, there was residual bias in the initial satellite-derived values of  $PM_{2.5}$ . As a response, a geographically weighted regression model, in combination with ground-based measurements, was used to adjust for such residual bias. According to the results of validation, the estimated  $PM_{2.5}$  was highly in line with the value derived from the monitoring measurement with  $R^2$  equal to 0.81 (Van Donkelaar et al. 2015). To date, this dataset has been widely used in  $PM_{2.5}$ -associated studies (Han et al. 2018; Li et al. 2018; Wang et al. 2019; Liu et al. 2020). Figure 2(A–B) shows the spatial distributions of  $PM_{2.5}$  concentrations in 2014 and 2015, respectively.

### Annual age-standardized incidence (mortality) rate of male lung cancer

Data on annual age-standardized incidence (mortality) rate of male lung cancer (i.e., male trachea, bronchus and lung cancer) for each of 353 counties (districts) from 2006 to 2015 were acquired from the 2009–2018 China Cancer Registry

Fig. 1 Research area



**(A) PM<sub>2.5</sub> in 2014 ( $\mu\text{g}/\text{m}^3$ )****(B) PM<sub>2.5</sub> in 2015 ( $\mu\text{g}/\text{m}^3$ )****(C) Incidence case per 10<sup>5</sup> people in 2014****(D) Incidence case per 10<sup>5</sup> people in 2015****(E) Mortality case per 10<sup>5</sup> people in 2014****(F) Mortality case per 10<sup>5</sup> people in 2015****Fig. 2** Spatial distributions of PM<sub>2.5</sub> and the incidence (mortality) rate of male lung cancer in 2014 and 2015

Annual Report. The age-standardized incidence (mortality) rate is defined as the number of incidents (deaths) of male lung cancer per 100,000 people per year in a given county (district), and then the number was age-standardized according to the Segi's world population. The reports used in the present study were released by the Chinese Cancer Registry, National Cancer Centre of China. In these reports, the causes (e.g., lung cancer) of cancers have been specified according to the International Classification of Diseases version 10. The aim of the establishment of cancer registry in China is mainly to provide the timely and important information of cancer development across China (e.g., the number and rate of cancer incidence), which thus is highly representative at national scale. In particular, the 2017 China Cancer Registry Annual Report publicly released data of cause-specific cancer incidence (mortality) for 339 cancer registries (i.e., city, counties, districts, suburban areas of city) in 2014 (He and Chen 2018). These registries covering a population of more than 288 million residents in 2014, are dispersed over 31 of 34 Chinese province-level administrative units (He and Chen 2018). Figure 2(C–F) presents the spatial distributions of the incidence (mortality) rate of male lung cancer in 2014 and 2015.

#### Socioeconomic indicators, time and location covariates

We extracted socioeconomic data from multiple sources, namely the China Statistical Yearbook (County level), Tabulation of the 2010 Population Census of the People's Republic of China and China Cancer Registry Annual Report. Socioeconomic covariates controlled in the present study include urban–rural division (dummy variable), finance per capita ( $10^8$  RMB), proportion of manufacturing workers (%), proportion of construction workers (%) and population size ( $10^4$  people). These variables were selected to adjust for the differential health outcomes in relation to economic status, occupation and socioeconomic status based on the availability of data and the findings of previous studies (Cohen and Pope 3rd 1995; Elo 2009; Zhou et al. 2015).

Notably, the information of urban and rural division was derived from the China Cancer Registry Annual Report which uses districts and counties to represent urban and rural situations in China, respectively (He and Chen 2018). In China, it is of great significance to monitor and understand cancer burden in the respective urban and rural settings. Such operationalization is used to inform the design of policies and strategies for cancer preventions and controls which are tailored for the respective urban and rural settings at national scale. In the present study, the mean urbanization rates for districts and counties were 71.27% and 38.26%, respectively, which can well represent the urban and rural settings in China. The operationalization of the use of districts and counties to examine urban–rural disparities has

been extensively adopted in many Chinese studies (Liu et al. 2015; Cui et al. 2016; Hu et al. 2019a, b).

#### Health and behavior factors

The variables of health and behavior include smoking prevalence, smoking strength (i.e. number of cigarettes smoked per day), alcohol consumption, and diabetes, which have shown their significant associations with lung cancer diseases in previous studies (International Agency for Research on Cancer (Volumes 44 and 83), 2016c). Data of the four variables were extracted from the 2015 China Health and Retirement Longitudinal Study (CHARLS) wave3 (specifically, the module of health status and functioning), publicly released by the National School of Development of Peking University. As a high-quality nationally representative survey, CHARLS wave3 is to assess the health conditions of Chinese residents with ages 45 or older. This survey recruited 12,400 households and 23,000 individuals that are located in 28 of 34 Chinese province-level administrative regions.

#### Statistical analysis

Structural equation model (SEM) was used to investigate the mediation effect of air pollution exposure on the association between urban–rural division and the incidence (mortality) rate of male lung cancer. SEM is a simultaneous equations system, which simultaneously combines multiple analyses such as regression analysis and path analysis. This model can not only facilitate the investigation of associations within and among groups of endogenous and exogenous factors, but also help to examine these factors' direct, indirect and total effects on each other. More details of SEM can refer to Bollen and Long (1993) and Golob (2003). To date, SEM has been widely used in many fields such as built environment and travel behavior (Bagley and Mokhtarian 2002; Cao et al. 2007). Also, this model has been increasingly used in environmental health studies (Fyhri and Klæboe 2009; Liu et al. 2019; Song et al. 2020).

In the present study, SEM was used to simultaneously examine the association between urban–rural division and the incidence (mortality) rate of male lung cancer (total association), the effect of urban–rural division on the incidence (mortality) rate of male lung cancer while controlling for ambient  $PM_{2.5}$  exposure and other covariates (direct association), and the extent that the difference in  $PM_{2.5}$  exposures between urban and rural areas can explain urban–rural disparity in incidence (mortality) rates of male lung cancer (indirect association). That is, the effect of urban–rural division on the incidence (mortality) rate of male lung cancer can be decomposed into an indirect effect (through air pollution exposure) and a direct effect

(through other pathways). It is hypothesized that the difference in urban–rural statuses can not only cause differential  $PM_{2.5}$  exposures, but also lead to disparity in incidence (mortality) rates of male lung cancer. Since ambient  $PM_{2.5}$  can adversely affect lung cancer outcomes, the difference in  $PM_{2.5}$  exposures between urban and rural areas may account for urban–rural difference in incidence (mortality) rates of male lung cancer. More specifically, two equations were modelled. The first one modelled exposure to ambient  $PM_{2.5}$  as a function of urban–rural division, adjusting for time, location and other socioeconomic factors including finance per capita, proportion of manufacturing workers, proportion of construction workers and population size. The second equation modelled the incidence (mortality) rate of male lung cancer as a function of urban–rural division, controlling for exposure to ambient  $PM_{2.5}$  and all covariates included in the first equation. Notably, the selection of socioeconomic indicators in the two equations was based on the findings of previous environmental health studies (Hajat et al. 2013; Evandrou et al. 2014; Huang et al. 2019).

Three sensitivity analyses were performed. Firstly, we tested the sensitiveness of the mediation effect of exposure to  $PM_{2.5}$  to the control of health and behavior factors. Based on data availability and the findings of previous lung cancer studies (International Agency for Research on Cancer (Volumes 44 and 83), 2016), four factors including smoking prevalence, smoking strength (i.e. number of cigarettes smoked per day), alcohol consumption and diabetes were selected for such adjustments. Since the CHARLS survey does not cover all counties/districts of the present study, we kept samples located in the cities of the CHARLS survey, which left around half of original samples for the sensitivity analysis. Also, data of health and behavior we can access are available at the level of prefectural city, so we attributed districts/counties within the same city with the same health and behavior characteristics. Secondly, we examined whether the mediation effect of exposure to ambient  $PM_{2.5}$  is robust to the adjustment of additional air pollutant (i.e.,  $SO_2$ ), because some studies suggested that the lack of additional air pollutant control may obscure the mediation effect of the targeted air pollution (Song et al. 2020). Thirdly, we tested whether the mediation effect of exposure to ambient  $PM_{2.5}$  is sensitive to  $PM_{2.5}$  exposures with different lag structures (i.e., single- and moving-average lags), because there is the potential latency of the development of lung cancer consequences as indicated in many previous studies (Garshick et al. 2012; Guo et al. 2020a; Chung et al. 2021).

## Results

### Descriptive analysis

The results of the descriptive statistics of air pollutants, health outcomes, and some socioeconomic factors between urban and rural areas are shown in Table 1. The mean  $PM_{2.5}$  concentrations was  $51.71 \mu\text{g}/\text{m}^3$  in urban areas, which was higher than that of rural areas at  $49.97 \mu\text{g}/\text{m}^3$  (Table 1); moreover,  $PM_{2.5}$  concentrations also varied greatly among urban and rural groups with the standard deviation at 18.62 and 18.82, respectively (Table 1). With regard to the mean incidence rate of male lung cancer, it was 54.15 per 100,000 people and 49.06 per 100,000 people in urban and rural areas, respectively, which demonstrated the potential of urban–rural disparity in incidence rates (Table 1); the great variations in incidence rates of urban and rural groups were also observed. A similar pattern of results was found for the mortality rate of male lung cancer. In particular, as shown in Table 1, the mean mortality rate was higher in urban than in rural areas with observed values at 43.91 per 100,000 people and 39.52 per 100,000 people, respectively. Also, there were great difference in additional air pollutants and some socioeconomic indicators between urban and rural groups (Table 1).

### Mediation effects of air pollution

Tables 2 and 4 present the results of  $PM_{2.5}$  as a mediator linking urban–rural division and the incidence rate. In general,  $PM_{2.5}$  significantly mediated the association between

**Table 1** Descriptive statistics of air pollutants, health outcomes and some socioeconomic factors between urban and rural areas

Variables	Areas	Min	Mean	SD	Max
$PM_{2.5}$ ( $\mu\text{g}/\text{m}^3$ )	Urban	11.21	51.71	18.62	90.91
	Rural	2.40	49.97	18.82	100.73
$SO_2$ ( $\mu\text{g}/\text{m}^3$ )	Urban	1.38	26.28	12.80	49.76
	Rural	0.09	29.29	14.52	65.73
Incidence rate (per $10^5$ people)	Urban	1.55	54.15	17.52	125.51
	Rural	2.78	49.06	16.63	117.74
Mortality rate (per $10^5$ people)	Urban	1.28	43.91	15.54	119.99
	Rural	0.00	39.52	13.65	94.32
Finance per capita (108 RMB)	Urban	0.28	29.63	61.95	802.73
	Rural	0.22	19.85	21.07	284.76
Construction (%)	Urban	0.09%	0.37%	0.24%	3.14%
	Rural	0.04%	0.33%	0.19%	1.02%
Manufacturing (%)	Urban	0.13%	0.93%	0.75%	3.96%
	Rural	0.02%	0.88%	0.82%	4.21%

**Table 2** Association between urban–rural division and incidence rate: PM<sub>2.5</sub> as a mediator

Variables	Direct		Indirect		Total	
	$\beta$	95% CI	$\beta$	95% CI	$\beta$	95% CI
Urban–rural	3.39 ***	(1.49, 5.35)	1.44 ***	(0.91, 2.05)	4.83 ***	(2.85, 6.85)
Air pollution	0.31 ***	(0.25, 0.38)	-	-	0.31 ***	(0.25, 0.38)
Lat	-6.18 ***	(-7.81, -4.66)	5.08 ***	(4.10, 6.19)	-1.11 *	(-2.29, 0.00)
Lat <sup>2</sup>	0.09 ***	(0.07, 0.11)	-0.07 ***	(-0.09, -0.06)	0.02 **	(0.00, 0.04)
Year 2007	2.37	(-5.55, 10.54)	0.42	(-1.42, 2.15)	2.79	(-4.99, 10.82)
Year 2008	3.87	(-3.69, 11.11)	-0.99	(-2.74, 0.45)	2.88	(-4.63, 10.24)
Year 2009	3.59	(-3.01, 10.02)	-1.03	(-2.74, 0.31)	2.56	(-4.01, 8.95)
Year 2010	5.54	(-0.41, 11.61)	-0.63	(-2.20, 0.62)	4.91	(-0.85, 10.99)
Year 2011	8.52 **	(2.69, 14.61)	-1.95 **	(-3.56, -0.76)	6.56 **	(0.72, 12.45)
Year 2012	11.87 ***	(6.05, 18.06)	-3.04 ***	(-4.76, -1.77)	8.84 ***	(3.01, 14.98)
Year 2013	9.50 ***	(3.70, 15.26)	-0.68	(-2.26, 0.55)	8.82 ***	(2.94, 14.42)
Year 2014	9.33 ***	(3.79, 15.25)	-1.05	(-2.58, 0.16)	8.28 ***	(2.86, 14.16)
Year 2015	8.04 ***	(2.56, 14.28)	-1.92 ***	(-3.51, -0.73)	6.12 **	(0.49, 12.10)
Finance	-0.00	(-0.03, 0.03)	-0.00	(-0.01, 0.01)	-0.00	(-0.03, 0.02)
Construction <sup>a</sup>	4.48 **	(0.52, 8.75)	-2.17 ***	(-3.39, -1.21)	2.31	(-1.63, 6.55)
Manufacturing <sup>a</sup>	-0.28	(-1.40, 0.83)	0.16	(-0.14, 0.45)	-0.13	(-1.25, 0.92)
Population	0.05 ***	(0.02, 0.07)	0.04 ***	(0.03, 0.05)	0.09 ***	(0.06, 0.11)

\* for  $P < 0.1$ , \*\* for  $P < 0.05$  and \*\*\* for  $P < 0.01$ . <sup>a</sup> for value = original value  $\times$  100

urban–rural division and the incidence rate. The incidence rate of male lung cancer significantly varied between urban and rural areas, which indicated the existence of urban–rural disparity in incidence rates of male lung cancer. The total and direct effects of urban–rural division were 4.83 (95% CI: 2.85, 6.85), and 3.39 (95% CI: 1.49, 5.35), respectively, which suggested that there was an indirect effect. Regarding the indirect effect of urban–rural division through the impact on exposure to PM<sub>2.5</sub>, exposure significantly varied between urban and rural areas ( $\beta = 4.64$ , 95% CI: 3.08, 6.26) with residents living in urban areas exposed to high levels of air pollution concentrations (Table 4); also, the association between PM<sub>2.5</sub> exposure and the incidence rate of male lung cancer was significant (Table 2); more importantly, there was a significant difference in incidence rates by urban–rural division that was associated with PM<sub>2.5</sub> exposure (the indirect effect) ( $\beta = 1.44$ , 95% CI: 0.91, 2.05), namely air pollution exposure accounted for 29.80% of total urban–rural difference in incidence rates of male lung cancer in China (Table 2).

The results of the mediation effect by PM<sub>2.5</sub> on the association of mortality rate with urban–rural division are shown in Tables 3 and 4. Generally, there was a significant mediation effect by PM<sub>2.5</sub>. As shown in Table 3, there was a significant difference in mortality rates of male lung cancer between urban and rural areas. This suggested the existence of disparity in mortality rates by urban–rural division. The direct and indirect effects of urban–rural division were 2.97 (95% CI: 1.37, 4.76) and 4.07 (95% CI: 2.38, 5.84), respectively. Regarding the indirect effect of urban–rural

division (rural areas as the reference), such division was positively associated with exposure to PM<sub>2.5</sub> air pollution ( $\beta = 4.64$ , 95% CI: 3.08, 6.26), namely people residing in urban areas suffered from disproportionate exposures to air pollution (Table 4); there was a positive effect of PM<sub>2.5</sub> on the mortality rate of male lung cancer (as shown in Table 3); PM<sub>2.5</sub>-associated difference in mortality rates between urban and rural areas was also significant ( $\beta = 1.09$ , 95% CI: 0.68, 1.56), namely the proportion of urban–rural difference in mortality rates of male lung cancer attributable to PM<sub>2.5</sub> exposures was 26.85%.

## Sensitivity analysis

### Adjustment of health and behavior factors

Figure 3 presents the results of the sensitivity analysis adjusting for health and behavior factors. In general, the findings of the mediation role of PM<sub>2.5</sub> was not sensitive to the control of such factors. Without the adjustment of health and behavior covariates (Fig. 3(A)), there was a significant difference in incidence rates of male lung cancer by urban–rural division due to differential exposures to PM<sub>2.5</sub> between urban–rural areas; PM<sub>2.5</sub> was positively associated with the incidence rate (Fig. 3(A)). After the control of health and behavior covariates (Fig. 3(B)), urban–rural difference in incidence rates of male lung cancer, which was related to differential PM<sub>2.5</sub> exposures (i.e., the indirect effect of urban–rural division through the impact on exposure to PM<sub>2.5</sub>), was still significant;

**Table.3** Association between urban–rural division and mortality rate: PM<sub>2.5</sub> as a mediator

Variables	Direct		Indirect		Total	
	$\beta$	95% CI	$\beta$	95% CI	$\beta$	95% CI
Urban–rural	2.97 ***	(1.37, 4.76)	1.09***	(0.68, 1.56)	4.07***	(2.38, 5.84)
Air pollution	0.24***	(0.19, 0.29)	-	-	0.24***	(0.19, 0.29)
Lat	-5.18***	(-6.51, -3.99)	3.85***	(3.04, 4.78)	-1.33***	(-2.30, -0.40)
Lat <sup>2</sup>	0.08***	(0.06, 0.10)	-0.06***	(-0.07, -0.04)	0.02***	(0.01, 0.04)
Year 2007	3.92	(-3.11, 11.14)	0.32	(-1.07, 1.65)	4.24	(-2.65, 11.56)
Year 2008	3.45	(-3.18, 10.24)	-0.75	(-2.07, 0.34)	2.70	(-3.90, 9.44)
Year 2009	3.49	(-1.82, 8.84)	-0.78	(-2.14, 0.22)	2.71	(-2.70, 8.05)
Year 2010	2.86	(-2.13, 8.04)	-0.48	(-1.65, 0.48)	2.38	(-2.54, 7.64)
Year 2011	5.08	(-0.04, 10.14)	-1.48***	(-2.73, -0.56)	3.60	(-1.45, 8.69)
Year 2012	8.56***	(3.24, 13.66)	-2.31***	(-3.67, -1.31)	6.26**	(1.14, 11.46)
Year 2013	6.47**	(1.34, 11.42)	-0.52	(-1.73, 0.42)	5.96**	(0.93, 10.83)
Year 2014	6.78**	(1.82, 11.61)	-0.80	(-2.03, 0.09)	5.98**	(1.03, 10.90)
Year 2015	7.01**	(2.03, 12.01)	-1.46***	(-2.75, -0.54)	5.55**	(0.64, 10.56)
Finance	0.00	(-0.02, 0.02)	-0.00	(-0.01, 0.00)	0.00	(-0.02, 0.02)
Construction <sup>a</sup>	3.29	(-0.44, 7.53)	-1.64***	(-2.57, -0.89)	1.64	(-2.08, 5.91)
Manufacturing <sup>a</sup>	0.83	(-0.06, 1.61)	0.12	(-0.10, 0.34)	0.95*	(0.08, 1.70)
Population	0.05***	(0.03, 0.07)	0.03***	(0.02, 0.04)	0.08***	(0.06, 0.10)

\* for  $P < 0.1$ , \*\* for  $P < 0.05$  and \*\*\* for  $P < 0.01$ . <sup>a</sup> for value = original value  $\times 100$

**Table.4** Association between urban–rural division and PM<sub>2.5</sub>

Variables	$\beta$	95% CI
Urban–rural	4.64***	(3.08, 6.26)
Lat	16.39***	(15.46, 17.44)
Lat <sup>2</sup>	-0.23***	(-0.25, -0.22)
Year 2007	1.35	(-4.75, 6.84)
Year 2008	-3.20	(-8.57, 1.56)
Year 2009	-3.32	(-8.81, 1.12)
Year 2010	-2.05	(-6.82, 2.12)
Year 2011	-6.31**	(-10.95, -2.34)
Year 2012	-9.80***	(-14.59, -5.56)
Year 2013	-2.19	(-6.85, 1.95)
Year 2014	-3.39	(-8.04, 0.62)
Year 2015	-6.21***	(-10.71, -2.26)
Finance	-0.01	(-0.04, 0.02)
Construction <sup>a</sup>	-6.99***	(-10.27, -3.56)
Manufacturing <sup>a</sup>	0.51	(-0.45, 1.38)
Population	0.14***	(0.11, 0.15)

\* for  $P < 0.1$ , \*\* for  $P < 0.05$  and \*\*\* for  $P < 0.01$ . <sup>a</sup> for value = original value  $\times 100$

there was a significant effect of PM<sub>2.5</sub> on the incidence rate (Fig. 3(B)); significant associations between health and behavior factors and the incidence rate of male lung cancer were also observed (Fig. 3(B)). A similar pattern of results was observed for the mortality rate of male lung cancer (Fig. 3(C) and Fig. 3(D)). In particular, PM<sub>2.5</sub>-related difference in mortality rates of male lung cancer between

urban and rural areas was still significant after the adjustment of health and behavior covariates (Fig. 3(D)).

#### PM<sub>2.5</sub> exposures with different lag structures

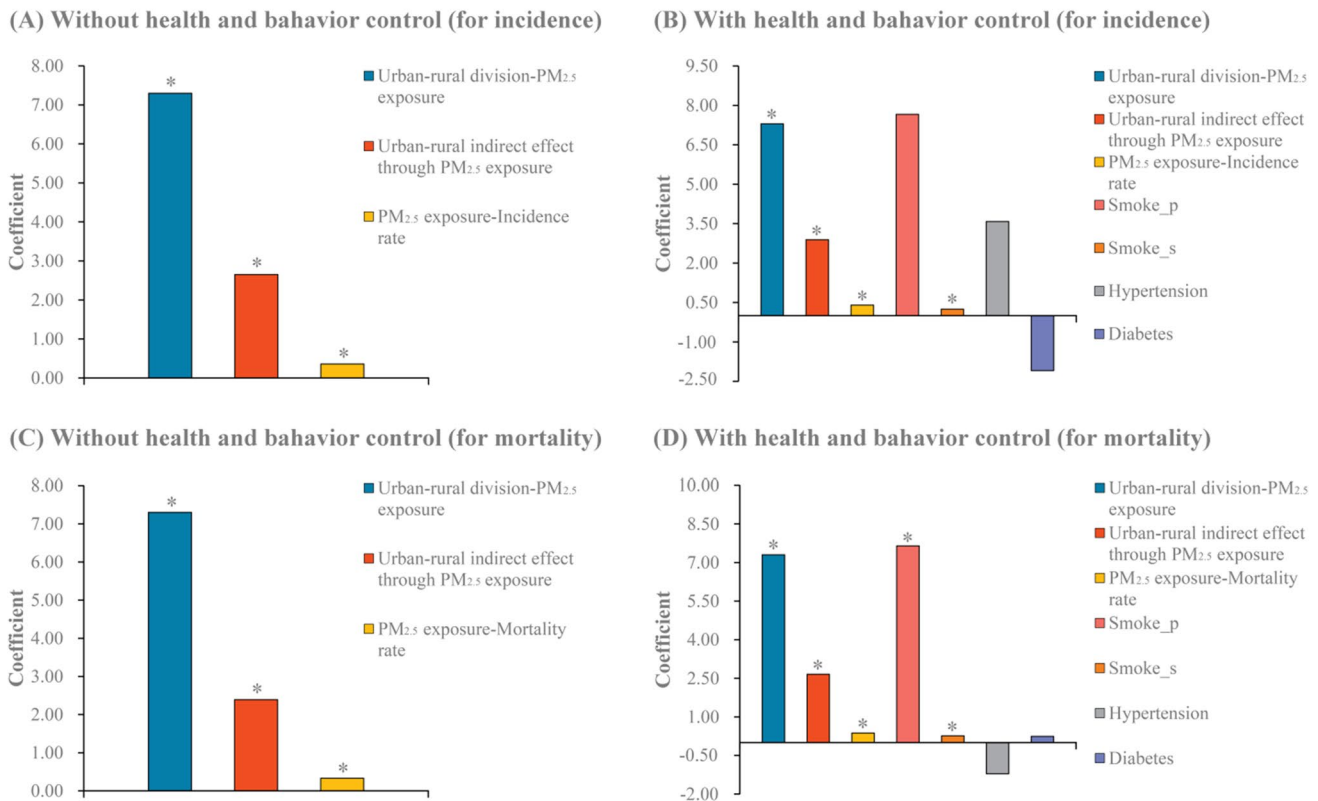
The results of the sensitivity analysis using PM<sub>2.5</sub> exposures with different lag structures are shown in Fig. 4. In general, the mediation effect of PM<sub>2.5</sub> was robust to the different operationalization of PM<sub>2.5</sub> exposures. As shown in Fig. 4(A), there were significant associations of PM<sub>2.5</sub> at lag 1 with urban–rural division and the incidence rate of male lung cancer; the indirect effect of urban–rural division on the incidence rate through the impact on PM<sub>2.5</sub> at lag 1 (i.e., the difference in incidence rates by urban–rural division, which is associated with different exposures to PM<sub>2.5</sub> at lag 1) was positive (Fig. 4(A)); a similar pattern of results was observed for PM<sub>2.5</sub> exposures at each of single- and moving-average lags (i.e., lag 1 to lag 6, lag 01 to lag 06) in Fig. 4(A). With respect to the mortality rate (Fig. 4(B)), we found a pattern of results similar to those of incidence rate (Fig. 4(B)). In particular, the indirect effect of urban–rural division through the impact on exposures to PM<sub>2.5</sub> at each of PM<sub>2.5</sub> lags was still significant (Fig. 4(B)).

#### Adjustment of additional air pollutant

Figure 5 presents the results of the sensitiveness of PM<sub>2.5</sub> mediation effect to the adjustment of additional air pollutant (i.e., SO<sub>2</sub>). In general, the results of the mediation role of PM<sub>2.5</sub> were robust to the control of additional air pollution



\* Significant effect



**Fig. 3** Sensitivity analysis of PM<sub>2.5</sub> mediation effect to the adjustment of health and behavior factors

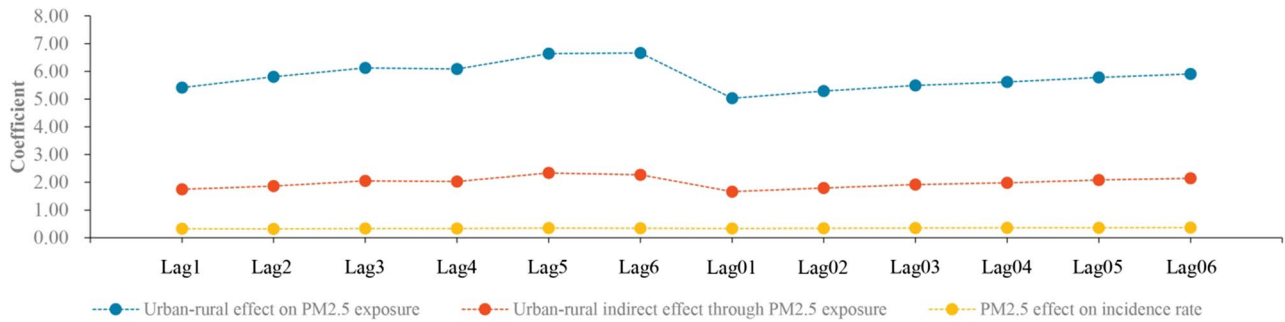
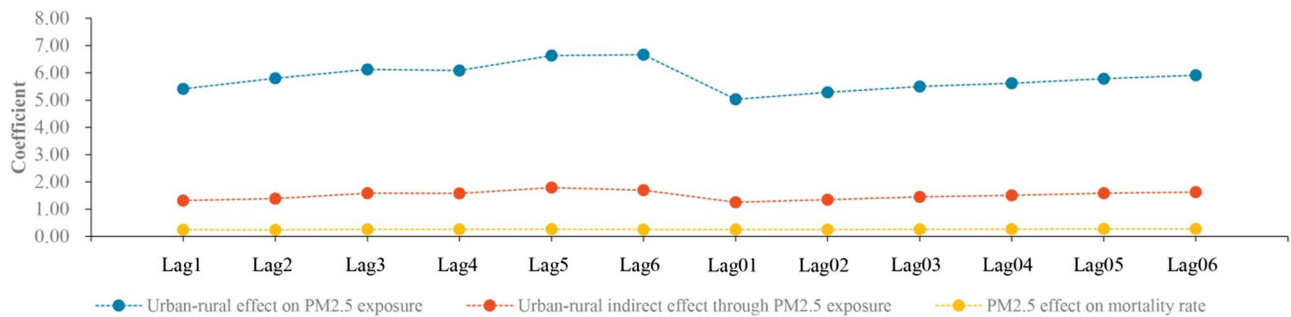
(namely SO<sub>2</sub>). With the control of additional air pollutant (i.e., SO<sub>2</sub>) in the structural equation model (Fig. 5(A)), PM<sub>2.5</sub> exposures varied between urban and rural areas, and the association between PM<sub>2.5</sub> and the incidence rate of male lung cancer was still positive; moreover, the mediation effect of PM<sub>2.5</sub> on the association of the incidence rate of male lung cancer with urban–rural division was still significant (Fig. 5(A)). A similar pattern of results could be observed for the mortality rate (Fig. 5(B)). Apart from the significant effect of urban–rural division on exposure to PM<sub>2.5</sub>, for example, there was a significant difference in mortality rates by urban–rural division, which is related to differential PM<sub>2.5</sub> exposures (Fig. 5(B)).

## Discussions

It is of great significance to determine factors potentially explaining socioeconomic disparities in human health. Despite the potential role of exposure to air pollution, it remains unknown whether exposure to air pollution mediates the relationship between socioeconomic status and health outcome. To remedy this issue, the present study examined whether there is a mediation effect of exposure

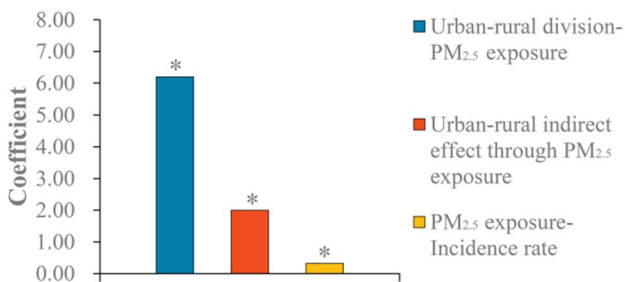
to PM<sub>2.5</sub> (the prominent air pollutant in China) on the association of lung cancer disease with urban–rural division in China.

We found that exposure to PM<sub>2.5</sub> significantly varies between urban and rural areas. This finding is consistent with those of prior studies. For example, taking 35 prefecture-level cities of China as research area, Han et al. (2020) suggested that PM<sub>2.5</sub> air pollution is much more severe in urban than in rural areas, especially in summer. Similarly, Lin et al. (2012) reported considerable urban–rural variation in air pollution concentrations in North China. Urban–rural disparity observed in the present study is a dominant phenomenon in China and can also be found in the indicated effects of environmental elements such as air pollution and temperature (Guo et al. 2015; Hu et al. 2019a, b; Li et al. 2020) as well as smoking behaviors (Chen et al. 2015a, b). We found that there are significant associations of incidence (mortality) rate of male lung cancer with urban–rural division and exposure to PM<sub>2.5</sub>. These two findings are in line with those of studies investigating urban–rural disparity in human health (Cohen and Pope 3rd 1995; Dikshit et al. 2012; He and Chen 2018; International Agency for Research on Cancer (Volume 168) 2019) as well as the effects of air pollution (Pope and Dockery 2006; Chen et al. 2017;

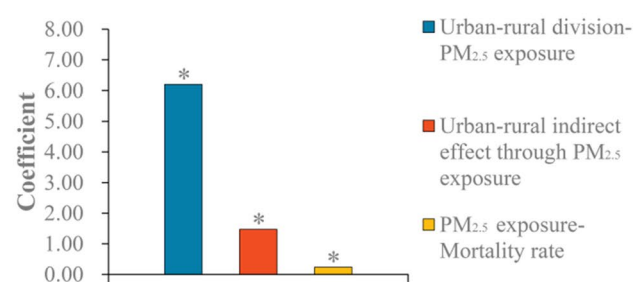
(A) PM<sub>2.5</sub> exposure with different lags (for incidence rate)(B) PM<sub>2.5</sub> exposure with different lags (for mortality rate)**Fig. 4** Sensitivity analysis of mediation effect by PM<sub>2.5</sub> to PM<sub>2.5</sub> exposures with different lag structures

\* Significant effect

(A) Additional air pollutant control (for incidence)



(B) Additional air pollutant control (for mortality)

**Fig. 5** Sensitivity analysis of mediation effect by PM<sub>2.5</sub> to the adjustment of additional air pollutant

International Agency for Research on Cancer (Volume 168) (2016).

We found the mediation effect of exposure to PM<sub>2.5</sub> on the association between urban–rural division and the incidence (mortality) rate of male lung cancer in China. It is usually argued that the difference in air pollution exposures across socioeconomic groups can partly explain socioeconomic disparities in human health. The mediation role of exposure to air pollution observed in the present study is consistent with those of some prior studies. In particular, Schulz et al.

(2020) reported that exposure to ambient PM<sub>2.5</sub> significantly mediates the association between race-based residential segregation and all-cause mortality at the level of census tract in the Detroit Metropolitan Area of United States. Using data collected from the nationally representative survey (i.e., Indagine Multiscopo sulle Famiglie), Franzini and Giannoni (2010) indicated that differential exposures to ambient air pollution are responsible for the difference in self-reported health statuses across socioeconomic groups at regional level of Italy. A similar pattern of results can be

observed in relevant studies investigating the contribution of air pollution exposure to health disparities across racial groups (Woodruff et al. 2003; Benmarhnia et al. 2017; Song et al. 2020). Findings from the present study highlight that apart from smoking behaviors which are known as the most prominent risks of lung cancer (Chen et al. 2015a, b), the difference in exposures to air pollution between urban and rural areas may also contribute to the great urban–rural difference in lung cancer diseases in China.

There are several strengths and policy implications in the present study. Firstly, to our knowledge, this is one of the earliest attempts to investigate the potential role of PM<sub>2.5</sub> exposures to uncover urban–rural disparities in lung cancer diseases in China. Understanding socioeconomic (and racial) disparities in health outcomes requires a great emphasis on the discovery of contributors. Many studies focus on the determinants of such disparities from the perspectives of health and behavior factors (Basu et al. 2015; Rasmussen-Torvik et al. 2016), social factors (Kondo et al. 2008; Lorch and Enlow 2016) and access to or quality of health care (Bosworth et al. 2006). Instead, the present study provides insight into the determinants of urban–rural disparities in lung cancer diseases from the perspective of air pollution, which complements the knowledge on the mechanisms linking socioeconomic statuses to health outcomes in the literature. Secondly, we investigate the mediation effect of air pollution exposure in a setting (China) where urban–rural disparity is much more dominant, instead of racial issue popular in most prior studies (Woodruff et al. 2003; Hackbarth et al. 2011; Song et al. 2020). Thirdly, air pollution as a potential mediator identified in the present study not only provides a well understanding of the high burden of lung cancer diseases in urban than in rural areas in China, but also provides the potential to alleviate urban–rural disparities in lung cancer diseases in the same country through the control and management of air pollution (especially the prominent PM<sub>2.5</sub> air pollution in urban areas).

Several limitations and future research should be discussed. Firstly, ecological design of the present study which is similar to those of most prior ecological studies (Woodruff et al. 2003; Hackbarth et al. 2011; Schulz et al. 2020), suffers from inevitable problems such as estimate errors in PM<sub>2.5</sub> exposures as well as ecological fallacy. Like many studies (Hackbarth et al. 2011; Guo et al. 2015), the mean concentration of PM<sub>2.5</sub> aggregated at the geographic unit is used as the surrogate of exposure to PM<sub>2.5</sub> in the present study. Such operationalization of exposure to PM<sub>2.5</sub> does not consider variations in individual mobility and air pollution concentrations (i.e., the two key determinants of the estimate of air pollution exposure), which therefore may produce misclassification errors in exposure estimates (Yoo et al. 2015; Shafran-Nathan et al. 2018; Guo et al. 2020a, b) as well as ecological fallacy (Schwartz 1994). However, ecological

studies (e.g. the present study) also have their strengths in broad area coverage as well as large sample (population) size. Cross-sectional ecological studies combined with studies using longitudinal individual-level data, would contribute to a more robust and scientific determination of air pollution mediation effect.

Secondly, the operationalization which uses smoking data at city level to test whether the mediation role of exposure to PM<sub>2.5</sub> is sensitive to the control of smoking factors, may ignore the variation in smoking situations across counties/districts belonging to the same city. If data on smoking covariates at county (district) level are available in the future, such limitation should be well addressed to warrant the findings of the mediation effect by air pollution exposure. Thirdly, like many previous studies examining the concurrent or longer time effect of air pollution (Garshick et al. 2012; Guo et al. 2015; Chung et al. 2021), the 6-year lag adopted to test the robustness of PM<sub>2.5</sub> mediation effect to PM<sub>2.5</sub> exposures with different lag structures (i.e., single- and moving-average lags) is likely to be insufficient to take the long latency of lung cancer development into account. This limitation should be fully considered, if air pollution data prior to 2000 and earlier are available in future work. Fourthly, pathways linking socioeconomic factors to human health have not been well understood from the perspectives of environmental elements such as temperature, soundscape and access and accessibility to public facilities (Hong et al. 2021). Future studies, especially epidemiological research, can target these issues to facilitate the understanding of socioeconomic disparities in human health.

## Conclusions

Exposure to PM<sub>2.5</sub> mediates the association between urban–rural division and the incidence (mortality) rate of male lung cancer in China. That is, the difference in PM<sub>2.5</sub> air pollutions between urban and rural areas may be partly responsible for urban–rural disparity in male lung cancer diseases in China. Intervention strategies relevant to air pollution management and control should be well developed to reduce such great disparity.

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**Data availability** The datasets analyzed during the current study available from the corresponding author on reasonable request.

## Declarations

**Ethics approval and consent to participate** Not applicable.

**Consent for publication** Not applicable.

**Competing interests** The authors declare no competing interests.

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