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Air pollution and lung cancer incidence in China: Who are faced with a greater effect?



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ABSTRACT

Background: Whether socioeconomic indicators modify the relationship between air pollution exposure and health outcomes remains uncertain, especially in developing countries.

Objective: This work aims to examine modification effects of socioeconomic indicators on the association between PM2.5 and annual incidence rate of lung cancer for males in China.

Methods: We performed a nationwide analysis in 295 counties (districts) from 2006 to 2014. Using multivariable linear regression models controlling for weather conditions and socioeconomic indicators, we examined modification effects in the stratified and combined datasets according to the tertile and binary divisions of socioeconomic indicators. We also extensively investigated whether the roles of socioeconomic modifications were sensitive to the further adjustment of demographic factors, health and behaviour covariates, household solid fuel consumption, the different operationalization of socioeconomic indicators and PM2.5 exposure with single and moving average lags.

Results: We found a stronger relationship between PM2.5 and incidence rate of male lung cancer in urban areas, in the lower economic or lower education counties (districts). If PM2.5 changes by $10 \,\mu\text{g/m}^3$, then the shift in incidence rate relative to its mean was significantly higher by 3.97% (95% CI: 2.18%, 4.96%, p = 0.000) in urban than in rural areas. With regard to economic status, if PM2.5 changes by $10 \,\mu\text{g/m}^3$, then the change in incidence rate relative to its mean was significantly lower by 0.99% (95% CI: -2.18%, 0.20%, p = 0.071) and 1.39% (95% CI: -2.78%, 0.00%, p = 0.037) in the middle and high economic groups than in the low economic group, respectively. The change in incidence rate relative to its mean was significantly lower by 1.98% (95% CI: -3.18%, -0.79%, p = 0.001) and 2.78% (95% CI: -4.17%, -1.39%, p = 0.000) in the middle and high education groups compared with the low education group, respectively, if PM2.5 changes by $10 \,\mu\text{g/m}^3$. We found no robust modification effects of employment rate and urbanisation growth rate.

Conclusion: Male residents in urban areas, in the lower economic or lower education counties are faced with a greater effect of PM2.5 on the incidence rate of lung cancer in China. The findings emphasize the need for public health intervention and urban planning initiatives targeting the urban–rural, educational or economic disparities in health associated with air pollution exposure. Future prediction on air pollution-induced health effects should consider such socioeconomic disparities, especially for the dominant urban–rural disparity in China.

1. Introduction

The increasing severity of air pollution in Chinese cities has become a global concern. Air pollution exacerbates the health disparity amongst socioeconomic groups because it causes greater suffering amongst the poor who are more exposed and may be socioeconomically susceptible

to air pollution (Sacks et al., 2010; Fuller et al., 2017). In addition to the extensive examination of differential exposure (Evans and Kantrowitz, 2002; Havard et al., 2009; Bell and Ebisu, 2012; Huang et al., 2019), an in-depth understanding of socioeconomic modifying roles on air pollution-induced health effects is also essential in informing policymaking to attenuate health inequality. Consequently, a consensus is growing

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regarding the need to understand whether socioeconomic factors modify the association between air pollution exposure and health outcomes. However, research on this issue is still in its infancy in China.

The relationship between air pollution exposure and health outcomes can be theoretically modified by socioeconomic positions through differences in material resources, biological factors and psychological stress. Limited material resources, such as access to medical care and fresh food, give rise to the decreased intake of polyunsaturated fatty acids and vitamins (Romieu et al., 1998; Kan et al., 2008). Biological factors, such as advanced age, are usually associated with increasing diseases, such as diabetes, which reduces heart rate variability (Gold et al., 2000) and increases inflammatory symptoms in the blood (Peters et al., 2001). In the psychological aspect, groups in low socioeconomic positions usually suffer from high psychological stress (Wright and Steinbach, 2001; Clougherty et al., 2014). Acute stress can exert its single or synergistic effects on the fight-or-flight response, whilst chronic stress can affect the immune function and inflammatory response, which has been summarized in a review paper (Clougherty and Kubzansky, 2009).

The hypothesis that residents with a low socioeconomic position are faced with a greater effect of air pollution exposure on health outcome is debated. Although studies that measure socioeconomic position using an individually defined unit tend to support this hypothesis, findings from research that gauges socioeconomic position using a spatially defined unit are inconsistent. The different findings between these two levels' examinations could partly be a function of measurement of socioeconomic position, model specification, including variable control, and data availability (Pickett and Pearl, 2001; Fuller et al., 2017). In addition, the difference in findings might come from the various mechanisms of the two-level factors' effects. In other words, the mechanism of the manner by which socioeconomic factors affect the associations between air pollution and health outcomes might differ between the individual- and area-level measurements (Fuller et al., 2017). The area-level socioeconomic context might exert its effects on health through deprivation situation in an area, accessibility of public goods and social support (Krieger et al., 1993; Duncan et al., 1998; Morland et al., 2002; O'Neill et al., 2003). Both individual- and arealevel factors (including socioeconomic indicators) can exert their effects on individual health and health outcomes' association with environmental exposure (Dragano et al., 2009; Bravo et al., 2016). However, these multilevel studies suggested that the findings on the two-level (individual and area) examinations of the same socioeconomic indicator are sometimes inconsistent (Hicken et al., 2013; Chi et al., 2016; Hicken et al., 2016; Fuller et al., 2017). Area-level variables, as the supplement of individual-level studies, might capture unmeasured individual-level variation in health outcome or unobserved mechanisms of socioeconomic effects at the individual level (Geronimus et al., 1996; Pickett and Pearl, 2001). Studies using a spatially defined unit also bear their strengths on large population sample sizes and broad area coverage. The spatially defined unit examination, together with studies using an individually defined unit, would contribute to an in-depth understanding and the robust examinations of socioeconomic modification roles. Despite the additional examinations of socioeconomic modification effects at the individual level, such effects at the area level

Here, we mainly review findings that examine socioeconomic modification effects using spatially defined units. Amongst these studies, socioeconomic position is usually measured in geographical units with fine resolution of the census tract/block/neighbourhood (Wong et al., 2008; Chiusolo et al., 2011; McGuinn et al., 2016) and coarse resolution of the city or county (Samet et al., 2000; O'Neill et al., 2004). Several studies found that areas with low socioeconomic position are statistically associated with large health effects of air pollution exposure. Socioeconomic factors with statistical significance mainly include income (Richardson et al., 2013), educational level (Jerrett et al., 2004; Ostro et al., 2005; Chen et al., 2012; Chen et al., 2017),

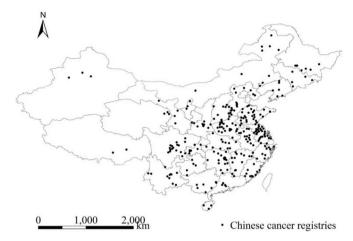
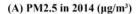


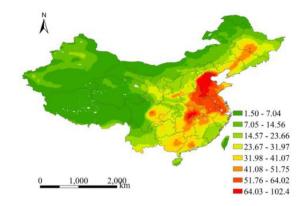
Fig. 1. Locations of the 295 Chinese cancer registries.

employment (Jerrett et al., 2004; Yin et al., 2017) and composite socioeconomic index (Wong et al., 2008; Chi et al., 2016). In particular, a study from Hong Kong using time-series analysis suggested that non-accidental, cardiovascular and respiratory mortality was strongly associated with exposure to NO2 and SO2 in communities with a high social deprivation index (Wong et al., 2008). A nationwide study in China extending the analysis unit to the city level indicated the negative association between PM10 exposure and cause-specific mortality and found that the percentage of workers in the construction industry statistically and negatively modified the dose–response relationship (Yin et al., 2017). In a study using a coarse geographic unit of the subnational regions in Europe, the authors suggested that low-income regions were more susceptible to the health effects of PM10 (Richardson et al., 2013)

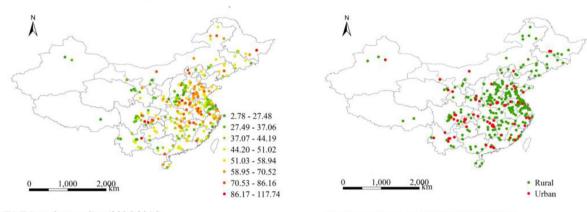
Several studies found no socioeconomic modification effects. McGuinn et al. (2016) noted in their study with a total of 5679 participants that block-level educational attainment and median home value insignificantly modify the association between the annual PM2.5 exposure and the coronary artery disease index. In a time-series study in 20 American cities extending the analysis unit to a large geographic scale, Samet et al. (2000) found that the association between daily cause-specific mortality rate and PM10 exposure was insignificantly affected by the city-wide socioeconomic indicators of education and income. Schwartz (2000) found that the health effect from airborne particle exposure was unmodified by socioeconomic indicators, such as unemployment rate and percentage of college degrees, measured at the city level by examining the effect of airborne particles on daily deaths in 10 US cities. A few studies reported results, contrary to the hypothesis of socioeconomic modifications. In a study using a time-stratified case-crossover analysis in São Paulo, Brazil, Bravo et al. (2016) found that districts with unknown SES characteristics suffer from a high relative risk of cardiovascular mortality with exposure to SO2, O3, CO and NO2 compared with low SES districts. The same authors likewise reported that cardiovascular mortality risk is usually higher in the communities at medium and high socioeconomic positions compared with those at a low socioeconomic position (Bravo et al., 2016). Despite the increasing interest in examining socioeconomic modification effects, whether socioeconomic positions modify the relationship between air pollution exposure and health outcome remains uncertain. Studies using large population samples across geographical units are rather limited, especially at the city (or district) level.

To fill the aforementioned gaps, we performed a nationwide study for examining the potential modifying roles of socioeconomic indicators on the association between PM2.5 exposure and annual incidence rates of male lung cancer using health outcome data collected from 295 cancer registries in China from 2006 to 2014. The present study is an extension of our previous work that has indicated the significant effects

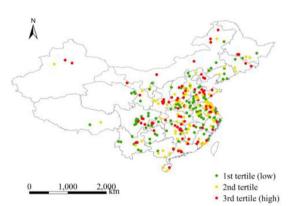




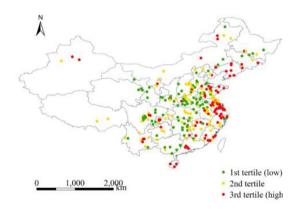
(B) Incidence case of male lung cancer per 100,000 people in 2014 (C) Urban-rural division (2006-2014)



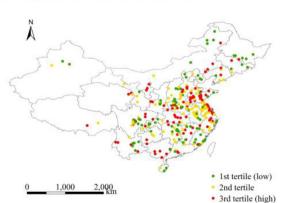
(D) Education tertiles (2006-2014)



(E) Economic status tertiles (2006-2014)



(F) Employment rate tertiles (2006-2014)



(G) Urbanization growth rate tertiles (2006-2014)

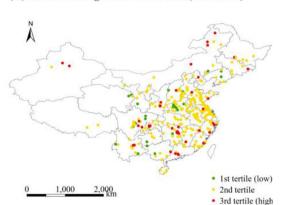


Fig. 2. Spatial distributions of PM2.5 in 2014, incidence rate of male lung cancer in 2014 and socioeconomic modifiers between 2006 and 2014.

38.00

36.00

High

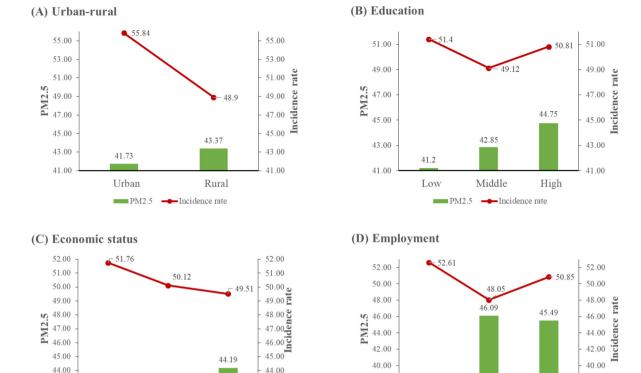


Fig. 3. Descriptive statistics of PM2.5 and the incidence rate of lung cancer for each socioeconomic stratum.

43.00

42.00

High

38.00

36.00

36.67

Low

of PM 2.5 exposure (Guo et al., 2019). We evaluated the modification effects in the stratified and combined datasets according to the tertile and binary division of socioeconomic indicators using multivariable linear regression model controlling for weather conditions and socioeconomic indicators. Moreover, we extensively investigated whether the socioeconomic modifying roles were sensitive to the further adjustment of demographic factors, health and behaviour covariates, household solid fuel consumption, the different operationalization of socioeconomic indicators and PM2.5 exposure with single and moving average lags.

42.32

Middle

■ PM2.5 Incidence rate

2. Materials and methods

43.00

42.00

42.32

Low

2.1. Study area

The study examined the modification effects in 295 cancer registries in China. This work included 222 counties (i.e. rural registries) and 73 districts (i.e. urban registries). The 295 county-level registries were selected primarily because of the collection of the most available nationwide data on lung cancer incidence for males from 2006 to 2014. These cancer registries are dispersed over 31 of 34 provinces, autonomous regions and municipalities in China (Fig. 1) and cover a population of approximately 190.21 million in 2014.

2.2. Data collection

2.2.1. Air pollution

The variable of air pollution is the annual mean PM2.5 concentration in each county (or district). Despite the multi-contaminant air pollution in China (Han et al., 2018b), PM2.5 pollution is highly prominent, which has received significant scholarly and government attention. Meanwhile, Volume 109 of International Agency for Research

on Cancer Monographs on the Evaluation of Carcinogenic Risks to Humans has identified outdoor PM2.5 is as a Group I carcinogenic factor to lung cancer; biologically, exposure to outdoor air pollution, including PM2.5, increases cancer risks in humans through the elevations in genetic damage, such as cytogenetic abnormalities, altered gene expression and mutations occurring in somatic and germ cells (Loomis et al., 2013; International Agency for Research on Cancer, 2016c). Empirically, suggestive evidence from China and Western countries revealed that PM2.5 has detrimental effects on lung cancer outcomes (Hamra et al., 2014; Guo et al., 2016; Han et al., 2017; Guo et al., 2019). Hence, we select PM2.5 as the variable of air pollution in the present study.

Middle

PM2.5 Incidence rate

PM2.5 data were collected from the dataset of Global Annual PM2.5 Grids from MODIS, MISR and SeaWiFS Aerosol Optical Depth (AOD) with GWR, v1 (1998-2016), released by the Socioeconomic Data and Applications Center, NASA (http://beta.sedac.ciesin.columbia.edu/ data/set/sdei-global-annual-gwr-pm2-5-modis-misr-seawifs-aod). this dataset, AOD was retrieved on the basis of multiple satellite inthe NASA Moderate Resolution Spectroradiometer, Multi-angle Imaging Spectroradiometer and Sea-Viewing Wide Field-of-View Sensor. A GEOS-Chem chemical transport model was employed to link the retrieved AOD to near-surface PM2.5 concentrations, thus producing the data of annual time series of PM2.5 concentration with approximately 1 km * 1 km resolution from 1998 to 2016 (Van Donkelaar et al., 2016; van Donkelaar et al., 2018). Because of the residual PM2.5 bias in the initial satellite-derived values, the geographically weighted regression model and ground-based measurements were further used to adjust for such bias. Van Donkelaar et al. (2016) reported that high consistency is evident between the satellitederived ground-level PM2.5 data and monitored measurements with $R^2 = 0.81$. To date, this dataset has been widely used in PM2.5-related research (Peng et al., 2016; Lavigne et al., 2017; Han et al., 2018a,

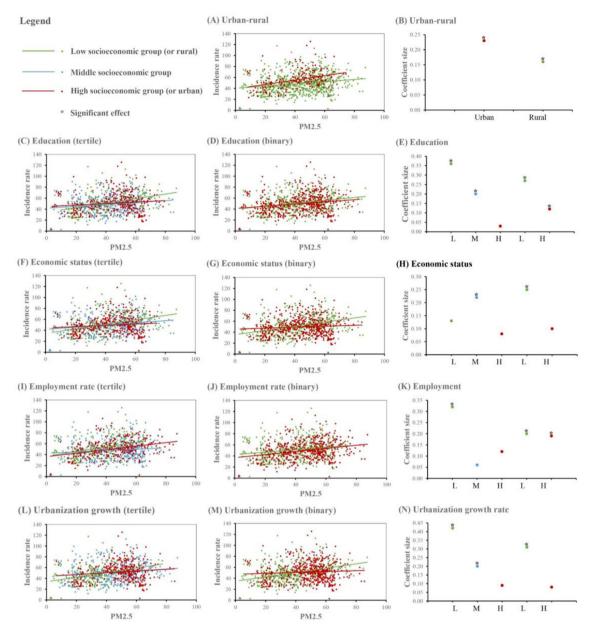


Fig. 4. Stratified analysis of PM2.5 effects in the tertile and binary divisions of socioeconomic factors.

2018b; Wang et al., 2018; Li et al., 2018; Gui et al., 2019). Fig. 2(A) showed the spatial distribution of PM2.5 concentration in 2014.

2.2.2. Health outcome

The variable of health outcome is the annual age-standardised incidence rate of male trachea, bronchus and lung cancer (i.e. the incidence rate of male lung cancer will be discussed in the following parts). This variable is defined as the number of incidents of male lung cancer per 100,000 people per year in a given county (district), which is age-standardised using Segi's world population. Hence, the original health outcome data used in present study have excluded the effects of age and sex on health outcome. The 2017 China Cancer Registry Annual Report (He and Chen, 2018) indicated that the incidence rate of lung cancer for males is 50.07 per 100,000 people, which is more than twofold higher than 23.60 per 100,000 people for females, thereby attracting our focus on the vulnerable group of males. Hence, the incidence rate of lung cancer for males was selected as the variable of health outcome in our current work.

Data on the incidence rate of male lung cancer (C33-C34) from

2006 to 2014 were extracted from the 2009–2017 China Cancer Registry annual report in terms of the International Classification of Diseases (ICD) version 10 (ICD-10). These reports were annually released by the Chinese Cancer Registry of the National Cancer Centre, led by the Disease Prevention and Control Bureau, Ministry of Health, China. The Cancer Registry was established to provide timely information on the number and rate of cancer incidence and mortality, which is considerably comprehensive and representative at the national scale. The 2017 annual report released the data of specific cancer incidence and mortality for 339 cancer registries in 2014; it covered 31 of 34 provinces, autonomous regions and municipalities and a population of > 288 million in China (He and Chen, 2018). Fig. 2(B) presents the spatial distribution of the incidence rate of lung cancer for males in 2014.

2.2.3. Socioeconomic indicators

Our socioeconomic data, including demographic factors, for each county (or district) from 2006 to 2014 mainly come from five data sources, namely, the China County (City) Economic Statistical

Table 1Modification effects of urban-rural division.

	Mean incidence rate = 50.38	
	β	95% CI
PM2.5	2.58% ***	(0.79%, 4.37%)
Log	0.10	(-0.10, 0.29)
Lat	1.24 ***	(0.68, 1.81)
Year 2007	3.82	(-5.66, 13.29)
Year 2008	6.03	(-3.37, 15.42)
Year 2009	5.34	(-2.92, 13.59)
Year 2010	6.83 *	(-0.81, 14.47)
Year 2011	10.31 ***	(2.73, 17.90)
Year 2012	11.66 ***	(4.04, 19.28)
Year 2013	10.28 ***	(2.91, 17.66)
Year 2014	9.99 ***	(2.66, 17.32)
Precipitation	1.10 ***	(0.65, 1.54)
Temperature	1.13 ***	(0.54, 1.72)
Finance	0.00	(0.00, 0.00)
Avg_Edu	-1.66 **	(-3.36, 0.04)
Employment	-19.79 **	(-39.06, -0.52)
Construction	-0.08	(-0.62, 0.45)
Manufacture	-0.25 ***	(-0.42, -0.08)
Population	0.04 **	(0.00, 0.07)
PM2.5*Urban	3.97% ***	(2.18%, 4.96%)

^{*} for p < 0.1, ** for p < 0.05 and *** for p < 0.01. With a $10 \,\mu\text{g/m}^3$ change in PM2.5, the change in incidence rate relative to its mean = $(10 \,\text{*coefficient}$ for PM2.5 or its interaction terms)/mean incidence rate.

Yearbook, China Statistical Yearbook for Regional Economy, Tabulation of the 2010 Population Census of the People's Republic of China, Report on the Work of the Government and Statistical Communique on National Economic and Social Development. Socioeconomic indicators include finance per capita, education level (i.e. average education years), employment rate, percentage of construction workers, percentage of manufacturing workers, population size and urban–rural dummy. Demographic factors include marital status (the percentage of males married) and percentage of ethnic minorities. Finance per capita and education level characterise the economic and education situation-induced differences, respectively, in

Table 3Modification effects of economic status (i.e. finance per capita).

	Binary divisio	n	Tertile divisi	on
	Mean incidence rate = 50.38		Mean incidence rate = 50.38	
	β	95% CI	β	95% CI
PM2.5	4.17% ***	(2.38%, 5.95%)	4.37% ***	(2.38%, 6.15%)
Log	0.16 *	(-0.03, 0.36)	0.14	(-0.06, 0.34)
Lat	1.25 **	(0.69, 1.81)	1.21 ***	(0.65, 1.78)
Year 2007	4.20	(-5.21, 13.6)	4.03	(-5.43, 13.49)
Year 2008	6.10	(-3.22, 15.42)	6.13	(-3.24, 15.50)
Year 2009	5.45	(-2.74, 13.63)	5.54	(-2.69, 13.77)
Year 2010	6.91 **	(-0.66, 14.47)	6.89 ***	(-0.71, 14.50)
Year 2011	10.44 ***	(2.98, 17.90)	10.41 ***	(2.91, 17.91)
Year 2012	11.60 ***	(4.16, 19.03)	11.65 ***	(4.17, 19.12)
Year 2013	10.23 ***	(2.96, 17.51)	10.26 ***	(2.95, 17.58)
Year 2014	9.92 ***	(2.70, 17.14)	9.92 ***	(2.66, 17.19)
Precipitation	1.15 ***	(0.71, 1.60)	1.16 ***	(0.71, 1.60)
Temperature	1.08 ***	(0.50, 1.66)	1.05 ***	(0.46, 1.64)
Edu_avg	-1.09	(-2.84, 0.66)	-1.29	(-3.08, 0.51)
Employment	- 22.90 **	(-41.95, -3.85)	-21.56 **	(-40.76, -2.37)
Construction	0.07	(-0.47, 0.62)	-0.04	(-0.58, 0.51)
Manufacture	-0.16 **	(-0.33, 0.01)	-0.20 **	(-0.38, -0.03)
Population	0.03 **	(0.00, 0.07)	0.03 *	(-0.01, 0.06)
Urban-rural	7.39 ***	(4.03, 10.74)	7.63 ***	(4.22, 11.03)
PM2.5*Fin2	-1.98% ***	(-3.18%,	-0.99% **	(-2.18%,
		-0.99%)		0.20%)
PM2.5*Fin3			-1.39% **	(-2.78%, 0.00%)

^{*} for p < 0.1, ** for p < 0.05 and *** for p < 0.01. With a $10 \,\mu\text{g/m}^3$ change in PM2.5, the change in incidence rate relative to its mean = $(10 \,\text{*coefficient}$ for PM2.5 or its interaction terms)/mean incidence rate.

the incidence rate of male lung cancer across counties (or districts). Employment rate, percentage of construction workers, and percentage of manufacturing workers differentiate the situation of occupation. Population size and urban–rural dummy represent the comprehensive measures of socioeconomic disparity in health outcome. The spatial distribution of socioeconomic modifiers was shown in Fig. 2(C–G).

 Table 2

 Modification effects of educational level (i.e. average education years).

	Binary division Mean incidence rate = 50.38		Tertile division	
			Mean incidence rate = 50.38	
	β	95% CI	β	95% CI
PM2.5	4.96% ***	(3.18%, 6.95%)	5.36% ***	(3.37%, 7.34%)
Log	0.13	(-0.06, 0.32)	0.14	(-0.06, 0.33)
Lat	1.13 ***	(0.58, 1.68)	1.12 ***	(0.56, 1.68)
Year 2007	3.88	(-5.48, 13.25)	4.20	(-5.22, 13.61)
Year 2008	6.11	(-3.17, 15.39)	6.16	(-3.17, 15.49)
Year 2009	4.88	(-3.27, 13.04)	5.25	(-2.95, 13.45)
Year 2010	6.08	(-1.47, 13.63)	6.42 *	(-1.17, 14.02)
Year 2011	9.44 **	(1.94, 16.95)	9.66 ***	(2.11, 17.21)
Year 2012	10.74 ***	(3.20, 18.28)	11.02 ***	(3.44, 18.6)
Year 2013	9.38 **	(2.08, 16.67)	9.72 ***	(2.39, 17.06)
Year 2014	8.92 **	(1.66, 16.18)	9.29 ***	(2.00, 16.59)
Precipitation	1.09 ***	(0.64, 1.53)	1.06 ***	(0.61, 1.51)
Temperature	1.02 ***	(0.44, 1.60)	1.01 ***	(0.42, 1.59)
Finance	0.00	(0.00, 0.00)	0.00	(0.00, 0.00)
Employment	-17.09 **	(-33.36, -0.83)	-18.48 **	(-35.23, -1.72)
Construction	-0.13	(-0.66, 0.39)	0.06	(-0.48, 0.60)
Manufacturing	-0.26 ***	(-0.42, -0.09)	-0.26 ***	(-0.43, -0.10)
Population	0.02	(-0.01, 0.06)	0.03	(-0.01, 0.06)
Urban-rural	8.71 ***	(5.62, 11.81	8.08 ***	(4.94, 11.21)
PM2.5*Education2	-2.58% ***	(-3.57%, -1.59%)	-1.98% ***	(-3.18%, -0.79%)
PM2.5*Education3			-2.78% ***	(-4.17%, -1.39%)

^{*} for p < 0.1, ** for p < 0.05 and *** for p < 0.01. With a $10\,\mu\text{g/m}^3$ change in PM2.5, the change in incidence rate relative to its mean = (10*coefficient for PM2.5 or its interaction terms)/mean incidence rate.

Table 4 Modification effects of employment rate.

	Binary division	Binary division			
	Mean incidence rate = 50.38		Mean incidence rate = 50.38		
	β	95% CI	β	95% CI	
PM2.5	3.18% ***	(1.39%, 5.16%)	5.16% ***	(2.98%, 7.34%)	
Log	0.13	(-0.07, 0.32)	0.13	(-0.06, 0.33)	
Lat	1.27 ***	(0.71, 1.84)	1.24 ***	(0.68, 1.80)	
Year 2007	3.85	(-5.65, 13.35)	4.01	(-5.35, 13.38)	
Year 2008	5.95	(-3.47, 15.36)	6.18	(-3.10, 15.47)	
Year 2009	5.16	(-3.10, 13.43)	5.34	(-2.81, 13.49)	
Year 2010	6.65 *	(-1.00, 14.31)	6.79 **	(-0.76, 14.33)	
Year 2011	10.08 ***	(2.48, 17.69)	10.20 ***	(2.70, 17.69)	
Year 2012	11.25 ***	(3.62, 18.89)	11.63 ***	(4.11, 19.16)	
Year 2013	10.05 ***	(2.65, 17.44)	10.31 ***	(3.02, 17.60)	
Year 2014	9.62 ***	(2.27, 16.97)	9.92 ***	(2.67, 17.16)	
Precipitation	1.23 ***	(0.78, 1.67)	1.16 ***	(0.71, 1.60)	
Temperature	1.09 ***	(0.50, 1.67)	1.05 ***	(0.47, 1.63)	
Finance	0.00	(0.00, 0.00)	0.00	(0.00, 0.00)	
Edu_avg	-0.86	(-2.37, 0.66)	-1.92 **	(-3.49, -0.35)	
Construction	-0.06	(-0.60, 0.47)	0.18	(-0.36, 0.72)	
Manufacturing	-0.31 ***	(-0.48, -0.15)	-0.28 ***	(-0.44, -0.11)	
Population	0.03	(-0.01, 0.06)	0.04 **	(0.01, 0.07)	
Urban-rural	9.16 ***	(5.83, 12.48)	8.92 ***	(5.61, 12.24)	
PM2.5*Employment2	0.00%	(-0.99%, 0.99%)	-3.18% ***	(-4.57%, -1.79%)	
PM2.5*Employment3			-0.99%	(-2.58%, 0.40%)	

^{*} for p < 0.1, ** for p < 0.05 and *** for p < 0.01. With a $10\,\mu\text{g/m}^3$ change in PM2.5, the change in incidence rate relative to its mean = (10*coefficient for PM2.5 or its interaction terms)/mean incidence rate.

Table 5Modification effects of urbanisation trajectory (i.e. urbanisation growth rate).

	Binary division Mean incidence rate = 50.38		Tertile division	
			Mean incidence rate = 50.38	
	β	95% CI	β	95% CI
PM2.5	4.57% ***	(2.58%, 6.55%)	4.37% ***	(1.98%, 6.75%)
Log	0.14	(-0.06, 0.33)	0.13	(-0.07, 0.33)
Lat	1.24 ***	(0.68, 1.81)	1.23 ***	(0.67, 1.80)
Year 2007	4.03	(-5.43, 13.48)	3.83	(-5.65, 13.31)
Year 2008	6.18	(-3.19, 15.55)	6.07	(-3.33, 15.46)
Year 2009	5.70	(-2.54, 13.93)	5.35	(-2.91, 13.61)
Year 2010	6.92 **	(-0.70, 14.54)	6.68 *	(-0.98, 14.33)
Year 2011	10.32 ***	(2.75, 17.89)	10.11 ***	(2.51, 17.71)
Year 2012	11.68 ***	(4.07, 19.28)	11.45 ***	(3.81, 19.1)
Year 2013	10.24 ***	(2.88, 17.60)	10.08 ***	(2.69, 17.47)
Year 2014	9.88 ***	(2.56, 17.19)	9.74 ***	(2.38, 17.09)
Precipitation	1.10 ***	(0.65, 1.55)	1.14 ***	(0.68, 1.59)
Temperature	1.10 ***	(0.52, 1.69)	1.07 ***	(0.48, 1.66)
Finance	0.00	(0.00, 0.00)	0.00	(0.00, 0.00)
Edu_avg	-1.60 **	(-3.34, 0.14)	-1.75 **	(-3.50, -0.01)
Employment	-20.76 **	(-39.88, -1.63)	-21.49 **	(-40.72, -2.26)
Construction	-0.04	(-0.58, 0.50)	-0.10	(-0.64, 0.45)
Manufacturing	-0.22 ***	(-0.40, -0.05)	-0.25 ***	(-0.42, -0.07)
Population	0.03	(-0.01, 0.06)	0.03 **	(0.00, 0.07)
Urban-rural	9.02 ***	(5.63, 12.40)	8.75 ***	(5.33, 12.18)
PM2.5*Urb-growth2	-1.39% **	(-2.38%, -0.20%)	-0.40%	(-1.79%, 0.99%)
PM2.5*Urb-growth3			-0.99%	(-2.58%, 0.79%)

^{*} for p < 0.1, ** for p < 0.05 and *** for p < 0.01. With a 10 μ g/m³ change in PM2.5, the change in incidence rate relative to its mean = (10*coefficient for PM2.5 or its interaction terms)/mean incidence rate.

2.2.4. Weather condition, location and time covariates

The variables of annual mean temperature and precipitation were selected to control weather conditions. We collected the weather data from the UDel_AirT_Precip dataset version V4.01, released by the Earth System Research Laboratory at National Oceanic and Atmospheric Administration (NOAA), USA (https://www.esrl.noaa.gov/psd/data/gridded/data.UDel AirT Precip.html). This dataset was mainly drawn from the Global Historical Climatology Network (GHCN2) and Legates

and Willmott's station records of monthly and annual mean air temperature and total precipitation; it provided the data of monthly time series of surface air temperature and precipitation with approximately 50 km*50 km resolution from 1990 to 2014 (Willmott and Matsuura, 2001). To date, the UDel_AirT_Precip dataset has been widely used to characterise climate patterns and estimate climate effects (Gang et al., 2014; Barrett and Hameed, 2017).

Similar to many studies (Almond et al., 2009; Ebenstein et al.,

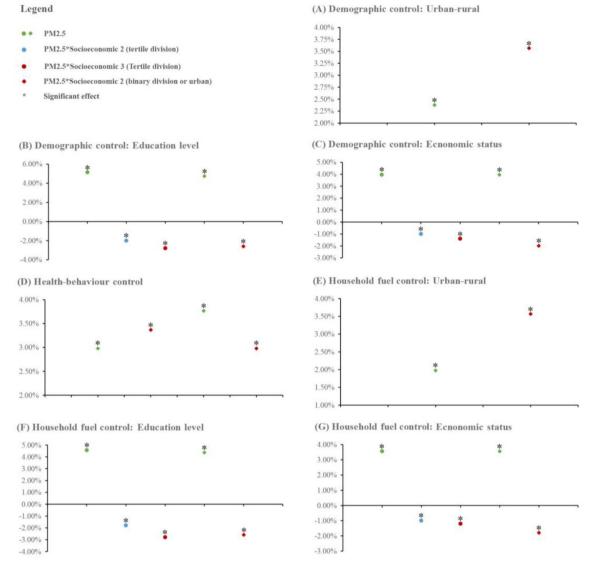


Fig. 5. Sensitive analysis with further control of demographic factors, health-behaviour covariates or household solid-fuel consumption.

2017), we added the degrees of longitude and latitude and a dummy variable for year to control time and location, respectively.

2.2.5. Health and behaviour covariates

The health and behaviour data were drawn from the 2015 China Health and Retirement Longitudinal Study (CHARLS) wave4, published by the National School of Development of Peking University (http://charls.pku.edu.cn/en/page/data/2015-charls-wave4). CHARLS is a high-quality nationally representative survey of Chinese residents with ages 45 or older, which aims to assess the socioeconomic and health conditions of Chinese residents. CHARLS wave4 included approximately 12,400 households and 23,000 individuals, which covered 28 of 34 provinces, autonomous regions and municipalities in China. We extracted and calculated the health and behaviour covariates of smoking, number of cigarettes smoked per day, alcohol consumption, hypertension and diabetes on the basis of the module of health status and functioning within CHARLS survey.

2.3. Statistical analysis

Data were stratified in terms of the tertile division of socioeconomic factors. The additional two interaction terms between air pollution and socioeconomic dummy variable were then constructed and added to the

combined model. We further stratified data into two socioeconomic categories instead of the commonly used two or three division of socioeconomic factors in most studies (Zeka et al., 2006; Dragano et al., 2009; Ostro et al., 2014) to examine the socioeconomic modifying roles in a robust way. An additional interaction between air pollution and socioeconomic dummy variable was incorporated into the combined model.

A multivariable linear regression model was employed to perform the analyses in the stratified and combined models. In the stratified model, we included the annual mean concurrent PM2.5 concentration, time and location factors, weather conditions, including temperature and precipitation, socioeconomic factors of finance per capita, education level (i.e. average education years), employment rate, percentage of construction workers, percentage of manufacturing workers, population size and urban-rural dummy variable. Such model specifications are used to not only mitigate the effects of unmeasured or unobserved county-specific covariates but also address the effects of time and location. The stratified data were then combined, and the interaction term(s) were further added to construct our combined model. We excluded the modifier dummy variable to our combined model due to its high correlation not only with PM2.5 but also with its interaction term. We examined the modification effects of five socioeconomic factors, namely, urban-rural division, finance per capita, education level,

Table 6Sensitive analysis of demographic control: urban–rural division.

	Mean incidence rate = 50.38		
	β	95% CI	
PM2.5	2.38% ***	(0.60%, 4.37%)	
Log	0.10	(-0.10, 0.29)	
Lat	1.21***	(0.64, 1.78)	
Year 2007	3.87	(-5.60, 13.34)	
Year 2008	6.05	(-3.33, 15.44)	
Year 2009	5.22	(-3.03, 13.47)	
Year 2010	6.71*	(-0.93, 14.34)	
Year 2011	10.09***	(2.51, 17.68)	
Year 2012	11.38***	(3.76, 19.00)	
Year 2013	10.07***	(2.70, 17.44)	
Year 2014	9.73***	(2.40, 17.07)	
Precipitation	1.10***	(0.65, 1.54)	
Temperature	1.06***	(0.47, 1.65)	
Finance	0.00	(0.00, 0.00)	
Avg_Edu	-1.59**	(-3.30, 0.13)	
Employment	-14.17	(-34.44, 6.10)	
Construction	-0.04	(-0.58, 0.50)	
Manufacture	-0.24***	(-0.41, -0.07)	
Population	0.03*	(-0.01, 0.06)	
PM2.5*Urban	3.57% ***	(1.98%, 4.96%)	
Marital status	-15.02	(-43.13, 13.09)	
Ethnic Minorities	-0.06*	(-0.13, 0.01)	

^{*} for p < 0.1, ** for p < 0.05 and *** for p < 0.01. With a $10 \,\mu\text{g/m}^3$ change in PM2.5, the change in incidence rate relative to its mean = $(10 \,\text{*coefficient}$ for PM2.5 or its interaction terms)/mean incidence rate.

employment rate and urbanisation trajectory (i.e. urbanisation growth rate).

Five types of sensitivity analysis were performed. First, we examined whether the modifying roles of socioeconomic factors were robust to the control of demographic factors. Suggestive evidence revealed that sex, age, race and marital status are the dominant demographic factors showing their subgroups' disparity in lung cancer outcome (Pope III et al., 2002; Lipsett et al., 2011; Jerrett et al., 2013).

Marital status and ethnic minorities were selected as the further demographic controls because health outcome at the present study is age-standardised incidence rate of lung cancer for males. Second, we tested whether the modification effects were sensitive to the control of health and behaviour covariates. Smoking, number of cigarettes smoked per day and alcohol consumption were selected, which has significant effects on lung cancer outcomes (International Agency for Research on Cancer (Volume 83 and 44), 2016a, 2016b; Hamra et al., 2014). We restricted our samples to those that are located in the targeted cities of CHARLS survey, leaving approximately half of the original samples for the robust analysis. Since the location information is available at the prefectural city level, we attributed the same health and behaviour information to districts/counties that are located in the same prefectural city.

Third, we examined whether the modification effects were robust to the control of household solid fuel consumption. Since the statistical data of household solid fuel consumption at the county level is not available, we employed the data of black carbon emissions from the residential and commercial sectors as a proxy. This monthly, 10-km grid-based emission data was derived from a unique global black carbon (BC) emission inventory (2006-2014) (Wang et al., 2014a, 2014b), released by Peking University (http://inventory.pku.edu.cn/ download/download.html). Fourth, socioeconomic factors with significant modification effects were further tested through their different operationalization (e.g., percentage of people having senior degree or above to further proxy educational attainment). Fifth, we investigated whether the significant modifying effects of socioeconomic factors were robust to PM2.5 exposure with different lag structures, namely, singlelag (lag1-lag8) and moving-average lag (lag01-lag08). All sensitivity analyses were performed using multivariable linear regression models.

3. Results

3.1. Descriptive statistics

Fig. 3 provides the summary statistics of PM2.5 and the incidence

Table 7Sensitive analysis of demographic control: education level (i.e. average education years).

	Binary division		Tertile division	
	Mean incidence rate = 50.38		Mean incidence rate = 5	0.38
	β	95% CI	β	95% CI
PM2.5	4.76% ***	(2.98%, 6.75%)	5.16% ***	(3.18%, 7.15%)
Log	0.12	(-0.08, 0.32)	0.13	(-0.07, 0.33)
Lat	1.09***	(0.53, 1.65)	1.08***	(0.52, 1.64)
Year 2007	3.91	(-5.45, 13.28)	4.23	(-5.18, 13.65)
Year 2008	6.09	(-3.2, 15.37)	6.15	(-3.18, 15.48)
Year 2009	4.79	(-3.37, 12.95)	5.14	(-3.06, 13.34)
Year 2010	6.01	(-1.54, 13.56)	6.33*	(-1.26, 13.93)
Year 2011	9.27**	(1.76, 16.77)	9.47**	(1.92, 17.02)
Year 2012	10.51***	(2.97, 18.06)	10.77***	(3.19, 18.35)
Year 2013	9.21**	(1.91, 16.51)	9.53***	(2.20, 16.87)
Year 2014	8.72**	(1.46, 15.99)	9.08**	(1.78, 16.38)
Precipitation	1.08***	(0.63, 1.52)	1.05***	(0.61, 1.50)
Temperature	0.96***	(0.38, 1.55)	0.95***	(0.36, 1.54)
Finance	0.00	(0.00, 0.00)	0.00	(0.00, 0.00)
Employment	-14.64*	(-32.28, 3.01)	-15.13*	(-33.25, 2.99)
Construction	-0.12	(-0.65, 0.41)	79.00	(-0.46, 0.62)
Manufacturing	-0.26***	(-0.43, -0.09)	-0.26***	(-0.43, -0.09)
Population	0.02	(-0.02, 0.05)	0.02	(-0.01, 0.06)
Urban-rural	8.56***	(5.44, 11.68)	7.89***	(4.74, 11.05)
PM2.5*Education2	-2.58% ***	(-3.57%, -1.59%)	-1.98% ***	(-2.98%, -0.79%)
PM2.5*Education3			-2.78% ***	(-3.97%, -1.39%)
Marital status	-3.86	(-31.86, 24.15)	-0.06	(-0.13, 0.01)
Ethnic Minorities	-0.05	(-0.12, 0.02)	-7.57	(-35.60, 20.47)

^{*} for p < 0.1, ** for p < 0.05 and *** for p < 0.01. With a $10\,\mu\text{g/m}^3$ change in PM2.5, the change in incidence rate relative to its mean = (10*coefficient for PM2.5 or its interaction terms)/mean incidence rate.

Table 8Sensitive analysis of demographic control: economic status (i.e. finance per capita).

	Binary divisio	n	Tertile divisi	ion
	Mean inciden	Mean incidence rate = 50.38		nce rate = 50.38
	β	95% CI	β	95% CI
PM2.5	3.97% ***	(2.18%, 5.76%)	3.97% ***	(2.18%, 5.95%)
Log	0.16	(-0.04, 0.35)	0.14	(-0.06, 0.33)
Lat	1.22***	(0.65, 1.78)	1.19***	(0.62, 1.76)
Year 2007	4.23	(-5.18, 13.63)	4.06	(-5.40, 13.52)
Year 2008	6.10	(-3.22, 15.42)	6.14	(-3.23, 15.52)
Year 2009	5.37	(-2.81, 13.56)	5.46	(-2.78, 13.69)
Year 2010	6.86**	(-0.71, 14.42)	6.84**	(-0.77, 14.44)
Year 2011	10.32***	(2.86, 17.78)	10.29***	(2.79, 17.8)
Year 2012	11.44***	(4.01, 18.88)	11.50***	(4.02, 18.98)
Year 2013	10.11***	(2.84, 17.39)	10.15***	(2.83, 17.47)
Year 2014	9.78***	(2.55, 17.00)	9.79***	(2.52, 17.05)
Precipitation	1.14***	(0.70, 1.59)	1.15***	(0.70, 1.60)
Temperature	1.03***	(0.45, 1.62)	1.00***	(0.41, 1.59)
Edu_avg	-1.00	(-2.77, 0.78)	-1.24	(-3.06, 0.58)
Employment	-19.17**	(-39.29, 0.95)	-17.56*	(-37.83, 2.70)
Construction	0.09	(-0.45, 0.64)	-0.01	(-0.56, 0.53)
Manufacture	-0.16**	(-0.34, 0.10)	-0.20**	(-0.39, -0.02)
Population	0.03	(-0.01, 0.06)	0.02	(-0.01, 0.06)
Urban-rural	7.15***	(3.78, 10.52)	7.42***	(4.01, 10.84)
PM2.5*Fin2	-1.98% ***	(-2.98%, -0.99%)	-0.99% *	(-2.18%, 0.20%)
PM2.5*Fin3		•	-1.39% **	(-2.78%, 0.00%)
Marital status	-7.90	(-36.15, 20.35)	-10.02	(-39.03, 19.00)
Ethnic Minorities	-0.05	(-0.12, 0.02)	-0.05	(-0.12, 0.02)

^{*} for p<0.1, ** for p<0.05 and *** for p<0.01. With a $10\,\mu g/m^3$ change in PM2.5, the change in incidence rate relative to its mean = $(10^*\text{coefficient}$ for PM2.5 or its interaction terms)/mean incidence rate.

rate of male lung cancer for each socioeconomic stratum. The incidence rate was 55.84 per 100,000 people (95% CI: 53.52, 58.16) in urban areas, which is considerably higher than 48.90 per 100,000 people (95% CI: 47.71, 50.10) in rural areas. By contrast, the pattern of PM2.5 level between these two types of areas reversed, showing the low PM2.5 level in urban areas (Fig. 3(A)). With regard to education level, the low education group exposed to the lowest PM2.5 concentration exhibited the highest incidence rate, whereas the high education group demonstrated higher incidence rate and PM2.5 level compared with the middle education group (Fig. 3(B)). A decreasing trend of incidence rates across three economic groups was observed with the increase of the economic status, declining from 51.76 per 100,000 people (95% CI: 49.68, 53.84) in the low economic group to 49.51 per 100,000 people (95% CI, 47.87, 51.14) in the high economic group (Fig. 3(C)). For employment, the low employment group was exposed to the lowest PM2.5 level but exhibited the highest incidence rate; compared with the high employment group, there was a higher PM2.5 level but a lower incidence rate in the middle employment group (Fig. 3(D)).

3.2. Modification effects

Fig. 4(A–B) and Table 1 present the results of modifying role of urban-rural division on the association between PM2.5 on the incidence rate of male lung cancer. A significant difference was detected in the PM2.5 effects between urban and rural areas. The stratified dataset plotted in Fig. 4(A) demonstrated that a higher effect of PM2.5 was

detected in urban compared with rural areas in the unadjusted model; the PM2.5 effects were significant in urban and rural groups in the fully adjusted model, with a higher effect in the former group (Fig. 4(B)). In the combined estimation, the change in incidence rate relative to its mean was significantly higher by 3.97% (95% CI: 2.18%, 4.96%, p=0.000) in urban than in rural areas, with a $10\,\mu\text{g/m}^3$ change in PM2.5 (Table 1).

The modification effect of education level was shown in Fig. 4(C-E) and Table 2. In general, education level significantly and negatively modifies the effects of PM2.5 on the incidence rate of male lung cancer. Fig. 4(C–D) plotted the incidence rate versus PM2.5 concentration for each stratum in education's tertile and binary divisions, respectively. In the stratified dataset of tertile division, a significant effect of PM2.5 was detected in the low and middle education groups but not in the high education group (Fig. 2(E)). In the combined dataset, if PM2.5 changes by $10 \,\mu\text{g/m}^3$, then the change in incidence rate relative to its mean was significantly lower by 1.98% (95% CI: -3.18%, -0.79%, p = 0.001) and 2.78% (95% CI: -4.17%, -1.39%, p = 0.000) in the middle and high education groups compared with the low education group, respectively (Table 2). With regard to the binary division, we observed the significant effects of not only PM2.5 in the low and high education groups in the stratified analysis (Fig. 2(E)) but also interaction between PM2.5 and education dummy variable in the combined dataset (= -2.58%, 95% CI: -3.57%, -1.59%, p = 0.000).

Fig. 4 and Table 3 present the modification effect of economic status (i.e. finance per capita). Economic status was negatively correlated with the association between PM2.5 and incidence rate of male lung cancer. We observed a decreased effect of PM2.5 in either the tertile or binary division plotted in Fig. 4(F-G), respectively, with the increase of economic status. With regard to the stratified dataset according to the tertile division, the effect of PM2.5 on the incidence rate of male lung cancer was significant in the middle economic group but not in the low and high economic groups (Fig. 4(H)). In the combined dataset, if PM2.5 changed by $10 \,\mu \text{g/m}^3$, then the change in incidence rate relative to its mean was significantly lower by 0.99% (95% CI: -2.18%, 0.20%, p = 0.071) and 1.39% (95% CI: -2.78%, 0.00%, p = 0.037) in the middle and high economic groups compared with the low economic group, respectively (Table 3). A similar pattern of results was observed for the situation of binary division (Table 3). Specifically, the interaction between PM2.5 and economic dummy variable was significantly associated with the incidence rate of male lung cancer (= -1.98%, 95% CI: -3.18%, -0.99%, p = 0.000).

The modification effect of employment rate was presented in Fig. 4(I-K) and Table 4. No significant difference was detected in PM2.5 effects. The incidence rate against PM2.5 concentration for each stratum in employment rate's tertile and binary divisions was plotted in Fig. 4(I-J), respectively. With regard to the tertile division in the combined dataset, despite the significantly higher PM2.5 effect in the middle employment group than in the low employment group, no such a significant higher effect was observed in the high employment group (Table 4). The effect of interaction was also insignificant for the binary division situation.

Fig. 4(L–N) and Table 5 show the modification effect of urbanisation trajectory (i.e. urbanisation growth rate). The urbanisation trajectory was insignificantly correlated with the association between PM2.5 and incidence rates of male lung cancer. We observed the decreased effect of PM2.5 on incidence rates with the increased urbanisation growth rate, which was plotted in Fig. 4(L–M). With regard to the stratified dataset according to the tertile division, significant effects of PM2.5 were detected in the low and middle growth rate group but not in the high growth rate group (Fig. 4(N)). The effect size increasingly decreased with an increase of growth rate level. A similar pattern of results was observed for the situation of stratified dataset according to the binary division. However, no significant effects of interaction terms in the combined dataset were detected in the tertile division, although the interaction between PM2.5 and the dummy variable was significant in

Table 9Sensitive analysis of health and behaviour control: urban-rural division.

	Mean incidence rate = 50.38 Without health-behaviour control			
			Health-behaviour control	
	β	95% CI	β	95% CI
PM2.5	2.98% **	(0.40%, 5.56%)	3.77% ***	(1.19%, 6.35%)
Log	-0.23	(-0.59, 0.13)	0.17	(-0.22, 0.56)
Lat	2.20***	(1.31, 3.09)	2.35***	(1.48, 3.22)
Year 2007	4.38	(-7.55, 16.31)	4.93	(-6.53, 16.39)
Year 2008	5.71	(-6.20, 17.63)	7.12	(-4.33, 18.57)
Year 2009	5.81	(-4.95, 16.56)	6.72	(-3.62, 17.06)
Year 2010	11.84**	(1.89, 21.79)	11.96**	(2.40, 21.53)
Year 2011	13.78***	(3.93, 23.63)	13.68***	(4.21, 23.14)
Year 2012	13.45***	(3.54, 23.35)	13.98***	(4.47, 23.50)
Year 2013	13.61***	(4.05, 23.16)	13.38***	(4.20, 22.55)
Year 2014	11.82**	(2.32, 21.32)	11.74**	(2.62, 20.87)
Precipitation	1.79***	(1.13, 2.45)	1.59***	(0.94, 2.23)
Temperature	1.56***	(0.75, 2.38)	1.84***	(1.04, 2.64)
Finance	0.00	(0.00, 0.00)	0.00	(0.00, 0.00)
Avg_Edu	1.70	(-0.63, 4.02)	2.24**	(-0.02, 4.49)
Employment	6.84	(-19.58, 33.25)	20.12	(-5.67, 45.91)
Construction	-0.02	(-0.76, 0.72)	-0.13	(-0.85, 0.60)
Manufacture	-0.03	(-0.25, 0.20)	-0.10	(-0.32, 0.13)
Population	0.01	(-0.04, 0.05)	0.00	(-0.04, 0.04)
PM2.5*Urban	3.37% ***	(1.19%, 5.36%)	2.98% ***	(0.99%, 4.96%)
Smoking			32.68 ***	(20.26, 45.10)
Smoking strength			0.33 ***	(0.08, 0.59)
Drinking			36.24 ***	(12.95, 59.53)

^{*} for p < 0.1, ** for p < 0.05 and *** for p < 0.01. With a $10\,\mu\text{g/m}^3$ change in PM2.5, the change in incidence rate relative to its mean = (10*coefficient for PM2.5 or its interaction terms)/mean incidence rate.

Table 10
Sensitive analysis of household fuel control: urban-rural division.

	Mean incidence rate =	= 50.38
	β	95% CI
PM2.5	1.98%**	(0.00%, 3.77%)
Log	0.12	(-0.08, 0.31)
Lat	1.22***	(0.66, 1.78)
Year 2007	4.12	(-5.28, 13.53)
Year 2008	6.45	(-2.87, 15.78)
Year 2009	5.81	(-2.38, 14.00)
Year 2010	7.26**	(-0.33, 14.84)
Year 2011	10.67***	(3.14, 18.21)
Year 2012	11.87***	(4.30, 19.43)
Year 2013	10.81***	(3.49, 18.14)
Year 2014	10.17***	(2.89, 17.45)
Precipitation	1.26***	(0.81, 1.71)
Temperature	1.08***	(0.50, 1.66)
Finance	0.00	(0.00, 0.00)
Avg_Edu	-1.98**	(-3.68, -0.28)
Employment	-17.80***	(-36.96, 1.36)
Construction	-0.01	(-0.55, 0.52)
Manufacture	-0.24***	(-0.40, -0.08)
Population	0.04**	(0.01, 0.07)
PM2.5*Urban	3.57%***	(2.18%, 5.16%)
Black carbon	0.10***	(0.05, 0.15)

^{*} for p < 0.1, ** for p < 0.05 and *** for p < 0.01. With a $10 \,\mu\text{g/m}^3$ change in PM2.5, the change in incidence rate relative to its mean = $(10 \,\text{*coefficient}$ for PM2.5 or its interaction terms)/mean incidence rate.

the binary division (Table 5).

3.3. Sensitivity analysis

Fig. 5(A–C) and Tables 6–8 show the first sensitive analysis with the further demographic control. Findings of the significant modification effects were still insensitive to this control. With the demographic adjustment, PM2.5 and its interaction with the dummy of urban–rural

division were still significantly associated with the incidence rate of male lung cancer (Fig. 5(A), Table 6). A similar pattern of results was observed for the indicators of economic status and education level in the situation of their binary and tertile divisions (Fig. 5(B–C), Tables 7–8).

The significant modifying effect by urban–rural division was robust to the adjustment of health and behaviour covariates. Specifically, significant effects of PM2.5 and its interaction with the urban–rural dummy were observed for the situation of no adjustment; when adjusting for the covariates of smoking rate, smoking strength and drinking, PM2.5 and its interaction with urban–rural dummy still kept their significant effects (Fig. 5(D), Table 9).

Fig. 5(E–G) and Tables 10–12 show the sensitive analysis with the further household solid-fuel consumption control. Findings of significant modification effects by urban-rural division, education level and economic status were still robust to this control. Specifically, with further adjustment, the black carbon emission from residential and commercial sectors (as a proxy of household solid-fuel consumption) was significantly associated with the incidence rate of male lung cancer; PM2.5 and its interaction with the dummy of urban–rural division still kept their significances. (Fig. 5(E), Table 10). A similar pattern of results was observed for the indicators of economic status and education level in the situation of their binary and tertile divisions (Fig. 5(F–G), Tables 11–12).

Table 13 presents our robust test using the percentage of people having a senior degree or above to further proxy the education level. The lower educational level was still significantly correlated with a stronger association between PM2.5 and incidence rate of male lung cancer. In the combined dataset of tertile division, the change in incidence rate relative to its mean per $10\,\mu\text{g/m}^3$ change in PM2.5 was significantly lower by 1.79% (95% CI: -2.78%, -0.60%, p=0.005) and 2.58% (95% CI: -3.97%, -1.19%, p=0.000) in the middle and high education groups compared with the low education group, respectively (Table 13). With regard to the binary division, a significant difference was observed in PM2.5 effects between the low and high education groups (= -1.39%, 95% CI: -2.38%, -0.40%, p=0.009).

Table 11Sensitive analysis of household fuel control: education level (i.e. average education years).

	Binary division	on	Tertile division	on
	Mean incidence rate = 50.38		Mean incidence rate = 50.38	
	β	95% CI	β	95% CI
PM2.5	4.37%***	(2.58%, 6.35%)	4.57%***	(2.58%, 6.75%)
Log	0.15	(-0.04, 0.34)	0.16	(-0.04, 0.35)
Lat	1.09***	(0.54, 1.65)	1.08***	(0.53, 1.64)
Year 2007	4.16	(-5.15,	4.50	(-4.87,
		13.48)		13.87)
Year 2008	6.50	(-2.74,	6.56	(-2.73,
		15.73)		15.84)
Year 2009	5.34	(-2.78,	5.64	(-2.52,
		13.46)		13.81)
Year 2010	6.58*	(-0.94,	6.87**	(-0.69,
		14.09)		14.43)
Year 2011	9.88**	(2.41, 17.34)	10.05***	(2.54, 17.57)
Year 2012	11.04***	(3.54, 18.54)	11.29***	(3.75, 18.83)
Year 2013	9.96***	(2.70, 17.22)	10.26***	(2.96, 17.56)
Year 2014	9.21***	(1.99, 16.43)	9.56***	(2.30, 16.82)
Precipitation	1.22***	(0.77, 1.66)	1.20***	(0.74, 1.65)
Temperature	0.97***	(0.39, 1.55)	0.95***	(0.37, 1.54)
Finance	0.00	(0.00, 0.00)	0.00	(0.00, 0.00)
Employment	-0.01**	(-0.03, 0.00)	-0.02**	(-0.03, 0.05)
Construction	-0.06	(-0.58, 0.47)	0.11	(-0.43, 0.65)
Manufacturing	-0.25***	(-0.41,	-0.26***	(-0.42,
		-0.09)		-0.09)
Population	0.02	(-0.01, 0.06)	0.03*	(0.00, 0.06)
Urban-rural	8.23***	(5.14, 11.32)	7.70***	(4.57, 10.83)
PM2.5*Education2	-2.58%***	(-3.57%,	-1.79%***	(-2.98%,
		-1.59%)		-0.60%)
PM2.5*Education3			-2.78%***	(-3.97%,
				-1.39%)
Black carbon	0.09***	(0.04, 0.14)	0.09***	(0.04, 0.14)

^{*} for p < 0.1, ** for p < 0.05 and *** for p < 0.01. With a $10 \,\mu\text{g/m}^3$ change in PM2.5, the change in incidence rate relative to its mean = $(10 \,\text{*coefficient}$ for PM2.5 or its interaction terms)/mean incidence rate.

The modifying roles of significant socioeconomic factors were robust to PM2.5 exposure with different lag structures. With regard to the PM2.5 single or moving-average lags (i.e. lag 1 to lag 8 and lag 01 to lag 08), the PM2.5 effects on the incidence rate of male lung cancer were significant and positive. Fig. 6(A) presented that the PM2.5 effects were still significantly higher in urban than in rural areas. Similarly, Fig. 6(B–G) indicated that the lower education level (operationalised by the average education years and percentage of people having a senior degree above) or lower economic status was still associated with a stronger relationship between PM2.5 and incidence rate of male lung cancer for the situations of tertile and binary divisions.

4. Discussion

An in-depth understanding of socioeconomic indicators modifying the relationship between air pollution and health outcome is essential to attenuate health inequality. However, whether socioeconomic indicators modify the effects of air pollution on health outcomes remains uncertain. Most studies performed the examination using an individually defined unit, whereas those using large population samples across geographical units are rather limited, especially at the city or district level.

To our knowledge, this is the first nationwide county-level study that systematically examined the socioeconomic modification effects on the association between air pollution and lung cancer incidence in China. Our findings contributed to the literature on socioeconomic modification effects through the examination in a developing setting where air pollution is severe. The relationship between PM2.5 and

Table 12
Sensitive analysis of household fuel control: economic status (i.e. finance per capita)

	Binary division	Binary division		sion		
	Mean incidence rate = 50.38		Mean incide	Mean incidence rate = 50.38		
	β	95% CI	β	95% CI		
PM2.5	3.57%***	(1.59%, 5.36%)	3.57%***	(1.59%, 5.56%)		
Log	0.17*	(-0.02, 0.37)	0.15	(-0.04, 0.35)		
Lat	1.23***	(0.67, 1.79)	1.19***	(0.63, 1.75)		
Year 2007	4.42	(-4.95, 13.78)	4.28	(-5.13, 13.69)		
Year 2008	6.46	(-2.83, 15.74)	6.51	(-2.82, 15.83)		
Year 2009	5.88	(-2.28, 14.03)	5.98	(-2.21, 14.17)		
Year 2010	7.36**	(-0.18, 14.90)	7.38**	(-0.19, 14.95)		
Year 2011	10.88***	(3.45, 18.31)	10.90***	(3.43, 18.37)		
Year 2012	11.96***	(4.56, 19.37)	12.05***	(4.60, 19.49)		
Year 2013	10.80***	(3.54, 18.05)	10.88***	(3.59, 18.17)		
Year 2014	10.23***	(3.03, 17.43)	10.27***	(3.04, 17.50)		
Precipitation	1.27***	(0.82, 1.72)	1.29***	(0.84, 1.74)		
Temperature	1.05***	(0.47, 1.63)	1.01***	(0.43, 1.59)		
Edu_avg	-1.31	(-3.06, 0.44)	-1.55*	(-3.34, 0.23)		
Employment	-0.02**	(-0.04, -0.00)	-0.02**	(-0.04, -0.00)		
Construction	0.11	(-0.43, 0.65)	0.01	(-0.53, 0.56)		
Manufacture	-0.16**	(-0.33, 0.00)	-0.21**	(-0.39, -0.03)		
Population	0.03**	(0.00, 0.07)	0.03**	(0.00, 0.06)		
Urban-rural	7.16***	(3.81, 10.50)	7.36***	(3.97, 10.74)		
PM2.5*Fin2	-1.79%***	(-2.98%,	-0.99%*	(-2.18%,		
		-0.79%)		0.20%)		
PM2.5*Fin3			-1.19%*	(-2.58%,		
				0.20%)		
Black carbon	0.08***	(0.03, 0.13)	0.09***	(0.04, 0.14)		

^{*} for p < 0.1, ** for p < 0.05 and *** for p < 0.01. With a $10 \,\mu\text{g/m}^3$ change in PM2.5, the change in incidence rate relative to its mean = $(10 \,\text{*coefficient}$ for PM2.5 or its interaction terms)/mean incidence rate.

incidence rate of male lung cancer was stronger in urban areas, in the lower economic or lower educational counties. We found no robust modification effects of employment rate or urbanisation trajectory.

We found that PM2.5 might exert high effect on the incidence rates of male lung cancer in urban areas. This result might seem unexpected. However, our findings were consistent with previous studies. A recent nationwide study of 708 counties in US using health data from Medicare National Claims History files (2002–2006) suggested that the relationship between PM2.5 exposure and cardiovascular hospitalisations was stronger in urban than nonurban counties (Bravo et al., 2016). Similarly, a recent Chinese study also indicated a greater effect of air pollution on lung cancer incidence amongst urban than rural inhabitants (Zhou et al., 2017). Two health-related mechanisms might be responsible for our unexpected findings. One potential explanation might come from a difference in primary sources of domestic fuel between urban and rural areas in China. Domestic fuel in rural China is dominated by biomass fuel, whilst the primary source of domestic fuel in urban areas is solid fuel. A recent Chinese study published in PNAS suggested that the decrease in household solid-fuel consumption is mostly responsible for the reduced integrated exposure (i.e. ambient and indoor) to PM2.5 pollution in China (Zhao et al., 2018). Hence, the high consumption of solid fuel in urban areas might enable urban residents to have a high exposure to PM2.5 pollution, thus leading to a high effect in the urban group. Another Chinese study predicted that smoking and solid fuel use will be responsible for 75% of death caused by lung cancer in China if they remain unchanged between 2003 and 2033 (Lin et al., 2008). Therefore, the difference in solid fuel consumption might be responsible for the urban-rural gaps in health effects.

The second explanation for the differential urban–rural effects might be due to a difference in smoking status. Several studies (Vena, 1982; Wong et al., 2007) indicated that the effects of air pollution on lung cancer and cardio-respiratory diseases are greater in smokers

Table 13Sensitive analysis of education level operationalised by the percentage of people having a senior degree or above.

	Binary division Mean incidence rate = 50.38		Tertile division Mean incidence rate = 50.38	
	β	95% CI	β	95% CI
PM2.5	4.17% ***	(2.18%, 6.15%)	5.16% ***	(3.18%, 7.15%)
Log	0.14	(-0.05, 0.34)	0.14	(-0.06, 0.33)
Lat	1.10 ***	(0.54, 1.66)	1.09 ***	(0.53, 1.65)
Year 2007	3.92	(-5.54, 13.39)	4.12	(-5.31, 13.55)
Year 2008	6.16	(-3.22, 15.54)	6.25	(-3.10, 15.59)
Year 2009	5.15	(-3.09, 13.4)	5.26	(-2.95, 13.47)
Year 2010	6.66 *	(-0.97, 14.29)	6.63 *	(-0.97, 14.23)
Year 2011	10.11 ***	(2.53, 17.69)	10.08 ***	(2.52, 17.63)
Year 2012	11.40 ***	(3.78, 19.02)	11.30 ***	(3.71, 18.89)
Year 2013	10.17 ***	(2.81, 17.54)	10.01 ***	(2.66, 17.35)
Year 2014	9.74 ***	(2.41, 17.07)	9.50 **	(2.20, 16.81)
Precipitation	1.12 ***	(0.67, 1.57)	1.16 ***	(0.71, 1.61)
Temperature	0.96 ***	(0.37, 1.55)	0.89 ***	(0.30, 1.48)
Finance	0.00	(0.00, 0.00)	0.00	(0.00, 0.00)
Employment	-13.18	(-29.57, 3.21)	-15.54 **	(-31.99, 0.90)
Construction	-0.02	(-0.55, 0.52)	0.02	(-0.51, 0.56)
Manufacturing	-0.27 ***	(-0.43, -0.10)	-0.20 **	(-0.38, -0.03)
Population	0.03	(-0.01, 0.06)	0.03 *	(0.00, 0.06)
Urban-rural	7.74 ***	(4.63, 10.86)	8.33 ***	(5.17, 11.50)
PM2.5*Education2	-1.39% ***	(-2.38%, -0.40%)	-1.79% ***	(-2.78%, -0.60%)
PM2.5*Education3			-2.58% ***	(-3.97%, -1.19%)

^{*} for p < 0.1, ** for p < 0.05 and *** for p < 0.01. With a $10 \,\mu\text{g/m}^3$ change in PM2.5, the change in incidence rate relative to its mean = (10*coefficient for PM2.5 or its interaction terms)/mean incidence rate.

compared with non-smokers. On the one hand, the intergenerational increase in cigarette smoking by Chinese young men was larger in urban than rural areas (Chen et al., 2015). Correspondingly, in Chinese males, the smoking-induced proportional excess mortality risks between 1995 and 2010 nationwide prospective cohort studies were 1.32 (95% CI: 1.24–1.41) and 1.65 (95% CI: 1.53–1.79) in urban areas, which is higher than 1.13 (95% CI: 1.09–1.17) and 1.22 (95% CI: 1.16–1.29) in rural areas, respectively (Chen et al., 2015). One the other hand, the passive smoking in non-smokers has significant adverse effects on human health, such as chronic obstructive pulmonary disease (Menezes and Hallal, 2007). Consequently, a higher male smoking rate in urban areas might further cause greater health burdens for non-smokers in urban than rural areas. These two mechanisms might synthetically lead to a higher effect of PM2.5 exposure on the incidence rate of male lung cancer in urban than rural areas.

We found that the low economic status was significantly related to a great association between PM2.5 exposure and incidence rate of male lung cancer. The pathways of the manner by which economic status or income level modify the effects of air pollution on health outcomes remain obscured. But as indicated in the introduction, socioeconomic status, including economic status, can exert its modification effects through differences in material resources, biological factors and psychological stress (Gold et al., 2000; Kan et al., 2008; Clougherty et al., 2014). With regard to the empirical findings, actually, the modifying role of economic status is debated. Several studies found high health effects in the low economic or low income groups (Dragano et al., 2009; Ostro et al., 2014), whereas other research suggested either no significant modification effects (Rosenlund et al., 2009; Chi et al., 2016) or high health effects in the high-income groups (Hicken et al., 2013). Findings in the present study were consistent with the former. A potential explanation for the modifying role of economic status in China may be a difference in avoidance behaviour against air pollution. On the one hand, people in the high economic cities are apt to search for and further use anti-PM2.5 air filters than those in the low economic cities (Liu et al., 2018). On the other hand, people in the high economic cities are likely equipped with high sensitivity of activity to air pollution (Sun et al., 2017; Yan et al., 2018) or high flexibility in activity

substitution (Ferreira and Moro, 2013). Both avoidance behaviours would alleviate the health effects, partly as a result of the reduction in air pollution exposure.

We found that education level modified the effects of PM2.5 on the incidence rates of male lung cancer. Fundamental questions about whether and how education level modifies the relationship between air pollution and health outcome still remain. Several studies found the significant modification effects (Zeka et al., 2006; Ostro et al., 2008; Bravo et al., 2016), whilst other research suggested the insignificant modification effects (Ostro et al., 2014; Stafoggia et al., 2014). Findings from the present study were consistent with the former. In particular, a short-term time series study conducted in urban areas of 16 Chinese cities indicated that low education residents are faced with a high effect of PM10 exposure on daily mortality (Chen et al., 2012). A potential explanation for the modifying role of education may be the differential awareness of air pollution effects on health outcomes. People with high education levels are likely to have high awareness of the health effects induced by air pollution. Furthermore, people attaining a high education level are likely to engage in jobs with low exposure to air pollution, thus decreasing the effects of PM2.5 on health outcomes.

Our findings could have far-reaching policy implications. The present study indicated that a greater relationship between PM2.5 and incidence rates of male lung cancer exists in urban areas, in the lower economic or lower education levels. These findings help identify directions for developing environmental and social policies that are tailored for different population groups and locations. A public health policy that aims at decreasing air pollution-induced health effects should target the three aspects, namely, air pollution regulation, social policy development and urban planning practices. One the one hand, air pollution control could lower the adverse effects of air pollution. On the other hand, developing appropriate social policy or practicing rational urban planning could reduce the additional effects of interaction between air pollution and socioeconomic status on health outcomes. Social policy, such as general education on air pollution-induced health effects and the corresponding protective measures, could be offered to locations with lower education levels. In urban planning practices, with regard to the layout of public service facility, especially for the planning



Fig. 6. Sensitive analysis of socioeconomic modifications to PM2.5 with both single and moving-average lags.

of health services and resources, priority could be given to the low economic counties to improve access to emergent medical and health assistance

Several limitations and uncertainties regarding our findings should be acknowledged. First, with regard to the sensitive analysis of PM2.5 effects adjusted by health and behaviour covariates, we attributed the same health-related covariates to districts/counties that are located in the same prefectural city, which might ignore the behaviour variation between these districts/counties. Second, similar to ecological studies, inevitable errors in exposure measurement were detected in our study because air pollution variation and the pattern of daily human activity could affect actual human exposure (Yoo et al., 2015; Park and Kwan, 2017). Third, the use of several time-invariant socioeconomic factors that were extracted from 2010 population census neglected the effects of socioeconomic mobility, which might bias our examination (Kreiner et al., 2018). Certain limitations should be addressed if data is available in the future.

5. Conclusions

Urban areas or counties with high percentages of low economic or low educational male residents have high risks of PM2.5-induced lung cancer incidence in China. Policymakers in public health and urban planning should develop area-specific strategies, such as alleviating the urban–rural gaps in access to high-quality medical resources in the planning of health service and resources, to reduce the socioeconomic gaps in health effects. Future prediction on health effects of air pollution exposure should consider socioeconomic disparities in lung cancer risks, especially for the urban–rural gaps, which is a major phenomenon in China.

Declaration of Competing Interest

All authors declared no conflicts of interests.

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