

Burden of disease attributed to ambient PM_{2.5} and PM₁₀ exposure in 190 cities in China

Kamal Jyoti Maji¹ · Mohit Arora² · Anil Kumar Dikshit¹

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Abstract Particulate air pollution is becoming a serious public health concern in urban cities of China. Association of disability-adjusted life years (DALYs) and economic loss with air pollution-related health effects demand quantitative analysis for correctional measures in air quality. This study applies an epidemiology-based exposure–response function to obtain the quantitative estimate of health impact of particulate matter PM_{2.5} and PM₁₀ across 190 cities of China during years 2014–2015. The annual average concentration of PM_{2.5} and PM₁₀ is $57 \pm 18 \mu\text{g}/\text{m}^3$ (ranging from 18 to $119 \mu\text{g}/\text{m}^3$) and $97.7 \pm 34.2 \mu\text{g}/\text{m}^3$ (ranging from 33.5 to $252.8 \mu\text{g}/\text{m}^3$), respectively. Based on the present study, the total estimated annual premature mortality due to PM_{2.5} is 722,370 [95% confidence interval (CI) = 322,716–987,519], 79% of which accounts for adult cerebrovascular disease (stroke) and ischemic heart disease (IHD). The premature mortality in megacities is very high, such as Chongqing (25,162/year), Beijing (19,702/year), Shanghai (19,617/year), Tianjin (13,726/year), and Chengdu (12,356/year). PM₁₀ pollution has caused 1,491,774 (95% CI = 972,770–1,960,303) premature deaths (age >30) in China. Further, 3,614,064 cases of chronic

bronchitis (CB); 13,759,894 cases of asthma attack among all ages; 191,709 COPD-related hospital admission (HA) cases; 499,048 respiratory-related HA; 357,816 cerebrovascular HA; and 308,129 cardiovascular-related HA due to PM₁₀ pollution have been estimated during 2014–2015. Chongqing, Beijing, Baoding, Tianjin, and Shijiazhuang are the top five contributors to pollution-related mortality, accounting for 3.10, 2.71, 2.49, 2.20, and 2.02%, respectively, of the total deaths caused by PM₁₀ pollution. The total DALYs associated with PM_{2.5} and PM₁₀ pollution in China is 7.2 and 20.66 million in 2014–2015, and mortality and chronic bronchitis shared about 93.3% of the total DALYs for PM₁₀. During this period, the economic cost of health impact due to PM₁₀ is approximately US\$304,122 million, which accounts for about 2.94% of China's gross domestic product (GDP). Megacities are expected to contribute relatively more to the total costs. The present methodology could be used as a tool to help policy makers and pollution control board authorities, to further analyze costs and benefits of air pollution management programs in China.

Keywords Particulate matter (PM_{2.5} and PM₁₀) · Premature mortality · Health endpoints · Disability-adjusted life years · Economic cost

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✉ Kamal Jyoti Maji
kamaljm@iitb.ac.in; kjmaji@gmail.com

¹ Center for Environmental Science and Engineering (CESE), Indian Institute of Technology Bombay, Mumbai, Maharashtra 400076, India

² Engineering Product Development Pillar, Singapore University of Technology and Design, 8 Somapah Road, Singapore, Singapore

Introduction

The acute and chronic health impacts of short- and long-term exposures to particulate matter are well-established in the literature (Zanobetti et al. 2008; Pope et al. 1995, 2004, 2011; Anenberg et al. 2011; Cesaroni et al. 2014; Beelen et al. 2014; Hamra et al. 2014; Korek et al. 2015; Brauer et al. 2012, 2015; Brunekreef and Holgate 2002; Shi et al. 2016). Epidemiological cohort studies show that these health impacts rely on long-term

ambient (both household and outdoor) particulate matter (PM) concentrations, and the associated risk factors vary from country to country (Pope and Dockery 2006; Kan and Gu 2011; Cao et al. 2011; Zhou et al. 2014; Zhang et al. 2011; Shang et al. 2013). Under the Global Burden of Disease (GBD) project of the World Health Organization (WHO), air pollution has been considered as a high-priority area. The WHO estimates that air pollution is responsible for 6.7% of all deaths and 7.6% of disability-adjusted life years (DALYs) globally (Lim et al. 2012; WHO 2014, 2016a). Air pollution poses the fourth highest risk factor for premature mortality in the world (IHME 2016). Eighty-five percent of the world population lives in areas where WHO air quality guidelines are exceeded (IHME 2016). Global population-weighted mean PM_{2.5} has increased by 20.4% in South Asia, Southeast Asia, and China from 1990 to 2013 (Lim et al. 2012). The Organization for Economic Cooperation and Development (OECD) recently published a report on the economic consequences of outdoor air pollution. The report shows that the PM_{2.5} could cause 6 to 9 million premature deaths a year by 2060 with 1% of global GDP—around US\$ 2.6 trillion annual cost (OECD 2016). Rapid industrial development and urbanization has greatly changed the economic landscape of China, making it one of the fastest growing economies in the world (IMF 2016; Ellis and Roberts 2016). However, this growth also have a real cost to its environment and public health. In the last 20 years, urban population has increased from 30 to 54% and will reach close to 1 billion (or 70% of the total population) by 2030 (WB 2016a; NCE 2013). In 2010, China's urban residents were responsible for about 7 tons of CO₂ emissions per capita (tCO₂/capita) energy-related CO₂ emissions (Wang et al. 2012; Ohshita et al. 2015). Power generation, transportation, agricultural straw burning, and open burning are the major sources of outdoor air pollution in China (IHME 2016). With severe air pollution and associated negative health outcomes, this environmental challenge has added significant burden to the health system and economy (WB and SEPA 2007; Matus et al. 2012; Li et al. 2016).

The GBD assessments study showed 1.2 million premature deaths and loss of 25 million DALYs due to outdoor air pollution in 2010 and making air pollution the fourth leading cause of deaths in China (IHME 2013; HEI 2013; Brauer et al. 2015). According to the recent GBD study for the year 2013, globally, about 5.5 million premature deaths were due to household and outdoor air pollution, and 55% of those deaths occurred in China and India. The total premature deaths due to PM in China were 0.91 million (95% CI = 0.82–0.99 million) and years lost due to disability (YLDs) and DALYs were 0.55 million and 18.20 million, respectively (IHME 2016, Salomon et al. 2015). In total, premature death due to PM; ischemic heart disease (IHD); chronic obstructive pulmonary disease (COPD); stroke, lower respiratory infection (LRI); and cancer (tracheal, bronchus, and lung) were responsible for 15.25, 9.96, 21.01, 2.31, and 5.97%, respectively (IHME

2016). Other studies observed that about 1.22 and 1.28 million premature death cases occurred due to outdoor air pollution and corresponding economic cost was 741.02 and 1246.7 billion in 2005 and 2010 (OECD 2014). Lelieveld et al. (2013, 2015) estimated that the premature mortality due to PM_{2.5} in China increased from 1 million in 2005 to 1.36 million in 2010.

Study in the Yangtze River Delta region highlighted that the short-term premature deaths caused by PM_{2.5} were 13,162 (95% CI = 10,761–15,554), while the economic loss is 22.1 billion Chinese Yuan (95% CI = 18.1–26.1) (Wang et al. 2015). Different city-level studies accounting for health risk assessment attributed to PM_{2.5} and PM₁₀ pollution have been carried out in China (Zheng et al. 2015; Zhang et al. 2007, 2008; Matus et al. 2012; Tang et al. 2014; Du and Li 2015; Jiang et al. 2015; Zhao et al. 2013; Lu et al. 2016). The city-level studies help pollution control authorities in policy development and air quality control at regional scale.

In this study, the DALYs and economic cost have been estimated based on the long-term mortality and morbidity attributed to PM_{2.5} and PM₁₀ pollution in 190 cities of China during 2014–2015. PM_{2.5} and PM₁₀ concentrations have been sourced from Zhang and Cao (2015) and Zhang et al. (2016a) for 190 air pollution-priority cities. Concentrations were measured during a 1-year (2014–2015) time through continuous monitoring at nearly 950 monitoring stations across 190 cities of China.

Methods

In the present case study, 190 Chinese cities have been selected for quantitative health impacts estimation. According to a recent WHO report (WHO 2016b), 18 of these cities are listed among 100 cities with the worst air pollution levels in the world for the year 2014. The air pollution problem has compounded with 22 cities of china in 100 most populated cities of the world (World Atlas 2016). These 190 cities are home to 869.70 million Chinese population.

PM concentration data

Ambient air contaminants consist of a complex mixture of different pollutants like particulate matter (PM), sulfur dioxide, nitrogen dioxide, carbon monoxide, ozone, polyaromatic hydrocarbon and black carbon. The pollutants are correlated to each other and associated with synergistic effect on human health (WHO 2003; Mauderly and Samet 2009; Konishi et al. 2014). The over counting problem occurs when health effects of multiple pollutants are aggregated (Johns et al. 2012). Consistent with most previous studies conducted in USA, Europe, and China, PM is selected as the indicator of all air pollution because PM shows the most significant adverse health effects among the pollutants

(Brunekreef and Holgate 2002; Pope and Dockery 2006; Qian et al. 2016; Zhou et al. 2014).

PM_{2.5} is a better exposure predictor than PM₁₀ for health risk assessments (Cifuentes et al. 2000), but PM₁₀ has also been used in this study, as morbidity is mostly related to PM₁₀ (Matus et al. 2012).

The annual average PM_{2.5} and PM₁₀ concentrations (µg/m³) from April 2014 to April 2015 have been used in this study for all 190 cities. It was calculated by average level of all monitoring stations in each city, monitored by the Ministry of Environmental Protection of China (Zhang and Cao 2015). Population and age distribution data have been taken from Census data of National Bureau of Statistics of China (Zhang and Cao 2015; NBSC 2016).

Health outcomes

The health endpoints have been selected in this study based on availability of the following parameters: (i) the health outcome due to PM_{2.5} and PM₁₀ pollution, and the corresponding relative risk (RR) or exposure–response (E-R) coefficient (ERC), (ii) the baseline incidence rate (BIR) of each health outcome, (iii) DALYs value of each health outcome, and (iv) economic cost per case of health effects.

After considerable literature review, five types of premature mortality attributed to PM_{2.5} pollution, mortality, and 18 different morbidities attributed to PM₁₀ pollution have been studied. People of all ages (children and adults) have been considered in this study.

The long-term cohort study in China for PM_{2.5} is not yet available. Therefore, the relationship between PM_{2.5} and RR, which are organized in bins from global burden of disease study 2010 (<http://ghdx.healthdata.org/record/global-burden-disease-study-2010-gbd-2010-ambient-air-pollution-risk-model-1990-2010>) has been used to calculate RR over China for causes of premature mortality in adults (>25 years): ischemic heart disease (IHD), cerebrovascular disease (stroke, CEV), chronic obstructive pulmonary disease (COPD), and lung cancer (LC). In addition, the RR for acute lower respiratory infections (ALRI) has also been calculated for infants (<5 years). Regarding BIR due to PM_{2.5}, regional cause-specific mortality value has been estimated (WHO 2012, 2015, 2016c) followed by calculation of IHD, CEV, COPD, LC, and ALRI in China.

For quantitative estimation of mortality and morbidity due to PM₁₀ pollution, ERC has been used in this study. ERC and BIR of each health endpoint have been summarized in Table 1.

The BIR of premature death among adults (i.e., age >30 years) attributed to PM₁₀ is measured as number of

Table 1 Exposure–response coefficients of PM₁₀ (per 1 µg/m³) and incidence rates (per person) of health endpoints

| Health outcome | ERC (mean and 95% CI) | Frequency | Reference |
|---|---------------------------------|-----------|--|
| 1 Total mortality >30 | 0.0043 (0.0026–0.0061) | 0.01013 | Künzli et al. (2000); Tang et al. (2014)) |
| 2 Chronic bronchitis (all ages) | 0.0045 (0.00127–0.00773) | 0.01390 | Zhang et al. (2008); Tang et al. (2014) |
| 3 RADs (adults ≥20) | 0.0094 (0.0079–0.0109) | 3 | Kan and Chen (2004) |
| 4 Asthma attack (children <15) | 0.0044 (0.0027–0.0062) | 0.0693 | Kan and Chen (2004); Zhang et al. (2008) |
| 5 Asthma attack (adults ≥15) | 0.0039 (0.0019–0.0059) | 0.0561 | Kan and Chen (2004); Zhang et al. (2008) |
| 6 Emergency room visits | 2.91E-05 (2.18E-05–3.82E-05) | 1 | ExternE (2005) |
| 7 Acute bronchitis all ages | 0.0055 (0.00189–0.00911) | 0.0372 | Kan and Chen (2004); Zhang et al. (2008) |
| 8 COPD | 2.7E-06 (1.16E-06–2.93E-06) | 1 | ExternE (2005) |
| 9 Respiratory HA | 7.03E-06 (3.83E-06–1.03E-05) | 1 | ExternE (2005); Nam et al. (2010); Matus et al. (2012) |
| 10 Cerebrovascular HA | 5.04E-06 (3.88E-07–9.69E-06) | 1 | ExternE (2005); Nam et al. (2010); Matus et al. (2012) |
| 11 Cardiovascular HA | 4.34E-06 (2.17E-06–6.51E-06) | 1 | ExternE (2005); Nam et al. (2010); Matus et al. (2012) |
| 12 Cough children | 0.133 (0.023–0.243) | 1 | ExternE (2005); Nam et al. (2010); Matus et al. (2012) |
| 13 Cough adult | 0.168 (0.0291–0.307) | 1 | ExternE (2005); Nam et al. (2010); Matus et al. (2012) |
| 14 Respiratory symptoms days (children) | 0.186 (0.092–0.277) | 1 | ExternE (2005); Nam et al. (2010); Matus et al. (2012) |
| 15 Respiratory symptoms days (adults) | 0.13 (0.015–0.243) | 1 | ExternE (2005); Nam et al. (2010); Matus et al. (2012) |
| 16 Lower respiratory symptoms (wheeze) (children <15) | 0.186 (0.092–0.277) | 1 | ExternE (2005); Nam et al. (2010); Matus et al. (2012) |
| 17 Lower respiratory symptoms (wheeze) (adults ≥15) | 0.13 (0.015–0.243) | 1 | ExternE (2005); Nam et al. (2010); Matus et al. (2012) |
| 18 Bronchodilator usage children | 0.078 (0.006–0.15) | 1 | ExternE (2005); Nam et al. (2010); Matus et al. (2012) |
| 19 Bronchodilator usage adults | 0.163 (0.0125–0.313) | 1 | ExternE (2005); Nam et al. (2010); Matus et al. (2012) |

ExternE (2005) refer to Bickel and Friedrich (2005)

deaths before reaching average life expectancy, and the reported number is 1013 per 10⁵ people (WHO 2000).

Assessment of health effects

The excess number of health outcomes due to PM has been estimated by using (1) RR or ERC (which can also be calculated from RR value), (2) BIR of health endpoints, (3) change in ambient air concentration, and (4) exposed population. The health effect of PM depends upon a functional form of the relationship. If the functional form of ERC is log-linear, excess number of cases can be calculated by using a health impact function as given in Eq. (1) (Lelieveld et al. 2013; Pascal et al. 2013; Voorhees et al. 2014; Apte et al. 2015; Maji et al. 2016).

$$\Delta E_{\text{mor}} = \left[\frac{(RR-1)}{RR} \right] \times I_r \times E_{\text{pop}} \quad (1)$$

where ΔE_{mor} is the excess number of mortality or morbidity in a year due to PM, RR is relative risk, I_r is the BIR, and E_{pop} is the exposed population.

The ERC (β) describes the increased risk of a population associated with a certain health response when exposed to PM. The ERC can be derived from established epidemiological cohort studies and that defines the relationship between the change in PM concentration and RR of health impacts, and is given by the following expression:

$$RR = \exp \left[\beta (C_a - C_0) \right] \quad (2)$$

where C_a is the annual average ambient PM concentration, and C_0 is the threshold level.

Based on US cohort studies, the estimated total long-term mortality risk RR is 1.043 for every 10 $\mu\text{g}/\text{m}^3$ increase of PM₁₀, giving rise to an ERC of 0.0043. The 95% CI is also reported as 0.0026–0.0061 (Künzli et al. 2000). But systematic review of Chinese studies of exposure to PM₁₀ pollution and daily mortality shown the ERC value is 0.0032 (95% CI = 0.0028–0.0035) (Shang et al. 2013).

For premature mortality estimation due to PM_{2.5}, the direct RR value is used (<http://ghdx.healthdata.org/record/global-burden-disease-study-2010-gbd-2010-ambient-air-pollution-risk-model-1990-2010>), and ERC value (Table 1) is used for mortality and morbidity estimation due to PM₁₀ in this study.

The World Health Organization (WHO)-recommended annual average threshold concentration (C_0) of PM₁₀ (20 $\mu\text{g}/\text{m}^3$) has been selected as a primary standard in this study (WHO 2005). The threshold concentration 5.8 $\mu\text{g}/\text{m}^3$ has been used for PM_{2.5}-related mortality in the present study (Zheng et al. 2015; Evans et al. 2013; Burnett et al. 2014). E_{pop} can be the entire population or subgroups like children or elderly persons according to the targeted population and related health impacts.

Estimation of DALYs

One DALY represents the loss of the equivalent of 1 year of healthy life. Globally, 60% of DALYs are due to premature mortality (WHO, 2004). The DALYs value for each health outcome has been adopted from the World Bank (WB) (Lvovsky et al. 2000) and Zhang et al. (2006) study. For premature death due to air pollution, 10 DALYs are attributed to each death. DALYs per 10,000 cases of various health endpoints are presented in Table 2.

Economic costs of health effects

The value of a statistical life (VSL) represents an individual's willingness-to pay (WTP) for a marginal reduction in the risk of death. Cost of illness (COI) method was also employed for some morbidity endpoints, which measures the total COI including hospital admission cost, medical cost, and day loss. In 2008, VSL in China was US\$83,574.6 (Zhang et al. 2008). A benefit transfer approach (BTA) is used in this study because a detailed survey of economic costs of various health endpoints from air pollution was not available for China (Matus et al. 2012). Morbidity endpoints value are adjusted with the European valuation table presented in Bickel and Friedrich (2005), by using the average GDP per capita difference between China and European Union (EU) (WB 2016b). The C_{morb} is calculated through BTA by the following equation:

$C_{\text{morb(China)}} = C_{\text{morb(EU)}} \times (\text{PCI}_{\text{China}}/\text{PCI}_{\text{EU}})$; where $C_{\text{morb(China)}}$ and $C_{\text{morb(EU)}}$ are the morbidity treatment cost in China and EU country, while $\text{PCI}_{\text{China}}$ and PCI_{EU} represent the per capita income in China and EU. e is the elastic coefficient of WTP and is assumed to be 1.0 (Zhang et al. 2008). Mortality and morbidity cost are converted to constant price year 2014 US\$ using:

$E_{\text{cost(2014)}} = E_{\text{cost(yt)}} \times (1 + \% \Delta P + \% \Delta Y)^k$; where $E_{\text{cost(2014)}}$ and $E_{\text{cost(yt)}}$ are the economic cost of mortality and morbidity in year 2014 and any year yt . $\% \Delta P$ and $\% \Delta Y$ are percentage change in real GDP per capita growth and the percentage increase in consumer price in real from year yt to 2014 (WB 2016c, d). k is an income elasticity to the power of 0.8 (OECD 2014). Unit value of various health points have been summarized in Table 3.

Results and discussion

This study analyzes PM_{2.5} and PM₁₀ concentration data, collected from the newest air quality monitoring network of the Ministry of Environmental Protection of China in 190 major cities during April 2014 to April 2015 (Fig. 1a) (Zhang and Cao 2015). The annual average concentration of PM_{2.5} is $57 \pm 18 \mu\text{g}/\text{m}^3$ (ranging from 18 to 119 $\mu\text{g}/\text{m}^3$), which has severely exceeded the new national ambient air quality

Table 2 Values of DALYs per 10,000 cases of health endpoints due to air pollution

| Health endpoints | DALYs per 10,000 cases | Reference |
|---------------------------------|------------------------|--|
| Mortality | 100,000 | Lvovsky et al. (2000); Zhang et al. (2006) |
| Chronic bronchitis | 12,037 | Lvovsky et al. (2000); Zhang et al. (2006) |
| Restricted activity days (RADs) | 3 | Lvovsky et al. (2000) |
| Asthma | 4 | Lvovsky et al. (2000); Zhang et al. (2006) |
| Acute bronchitis | 4 | Zhang et al. (2006) |
| Emergency room visit | 3 | Lvovsky et al. (2000) |
| Respiratory hospital admissions | 264 | Lvovsky et al. (2000); Zhang et al. (2006) |
| Other hospital admissions | 264 | Lvovsky et al. (2000); Zhang et al. (2006) |
| Cough day | 3 | Lvovsky et al. (2000) |
| Symptom day | 3 | Lvovsky et al. (2000) |
| Lower respiratory symptoms | 3 | Lvovsky et al. (2000) |
| Respiratory medication use | 3 | Zhang et al. (2006) |

standard (NAAQS) (35 $\mu\text{g}/\text{m}^3$) of China and WHO air quality guideline (10 $\mu\text{g}/\text{m}^3$). $\text{PM}_{2.5}$ concentration is generally lower in the coastal than the inland regions and is higher in the cities located in the north region than those in the south regions. According to the new NAAQS, as many as 167 cities cannot meet the standard, accounting for 88% of the total number of cities. Top five cities having high $\text{PM}_{2.5}$ concentration are Baoding (119 $\mu\text{g}/\text{m}^3$), Xingtai (110 $\mu\text{g}/\text{m}^3$), Shijiazhuang (101 $\mu\text{g}/\text{m}^3$), Handan (100 $\mu\text{g}/\text{m}^3$), and Dezhou (98 $\mu\text{g}/\text{m}^3$).

The annual average concentration of PM_{10} is $97.7 \pm 34.2 \mu\text{g}/\text{m}^3$ (ranging from 33.5 to 252.8 ($\mu\text{g}/\text{m}^3$)). Out of 190 cities, 149 cities are exceeding the new NAAQS (70 $\mu\text{g}/\text{m}^3$) of China and except that all cities are exceeding WHO air quality guideline (20 $\mu\text{g}/\text{m}^3$) for PM_{10} . Top five cities having high PM_{10}

concentration are Korla (252.8 $\mu\text{g}/\text{m}^3$), Baoding (203.8 $\mu\text{g}/\text{m}^3$), Xingtai (195.9 $\mu\text{g}/\text{m}^3$), Hengshui (181 $\mu\text{g}/\text{m}^3$), and Handan (174.8 $\mu\text{g}/\text{m}^3$). $\text{PM}_{2.5}$ and PM_{10} ratio is 0.60 ± 0.09 (range from 0.91 to 0.28) (Fig. 1b).

Premature mortality due to $\text{PM}_{2.5}$:

Long-term exposure to $\text{PM}_{2.5}$ is associated with increased mortality in adult (>25 years) from stroke (CEV), IHD, COPD, and LC, and it is also associated with increased incidence of acute ALRI in infants (<5 years).

Based on the health impact function (Eq. 1), premature mortality by stroke, IHD, COPD, LC, and ALRI has been calculated along with the corresponding uncertainties (95%

Table 3 Unit value (per case) for various health endpoints in China

| Health endpoints | Cost per cases (US\$) | Approach | Data source |
|---------------------------------|-----------------------|----------|---------------------|
| Mortality | 139,967.2 | WTP | Zhang et al. (2008) |
| Chronic bronchitis | 7126.9 | WTP | Zhang et al. (2008) |
| Restricted activity days (RADs) | 10.0 | WTP | Matus et al. (2012) |
| Asthma | 5.9 | WTP | Zhang et al. (2008) |
| Acute bronchitis | 8.4 | WTP | Zhang et al. (2008) |
| Emergency room visit | 99.0 | WTP | Matus et al. (2012) |
| COPD hospital admission | 2472.6 | COI | Hughes (2012) |
| Respiratory HA | 842.1 | COI | Zhang et al. (2008) |
| Cerebrovascular HA | 1222.8 | WTP | Matus et al. (2012) |
| Cardiovascular HA | 1717.5 | COI | Zhang et al. (2008) |
| Cough day | 2.6 | WTP | Matus et al. (2012) |
| Symptom day | 2.6 | WTP | Matus et al. (2012) |
| Lower respiratory symptoms | 56.0 | WTP | Matus et al. (2012) |
| Respiratory medication use | 3.8 | WTP | ExternE (2005) |

ExternE (2005) refer to Bickel and Friedrich (2005)

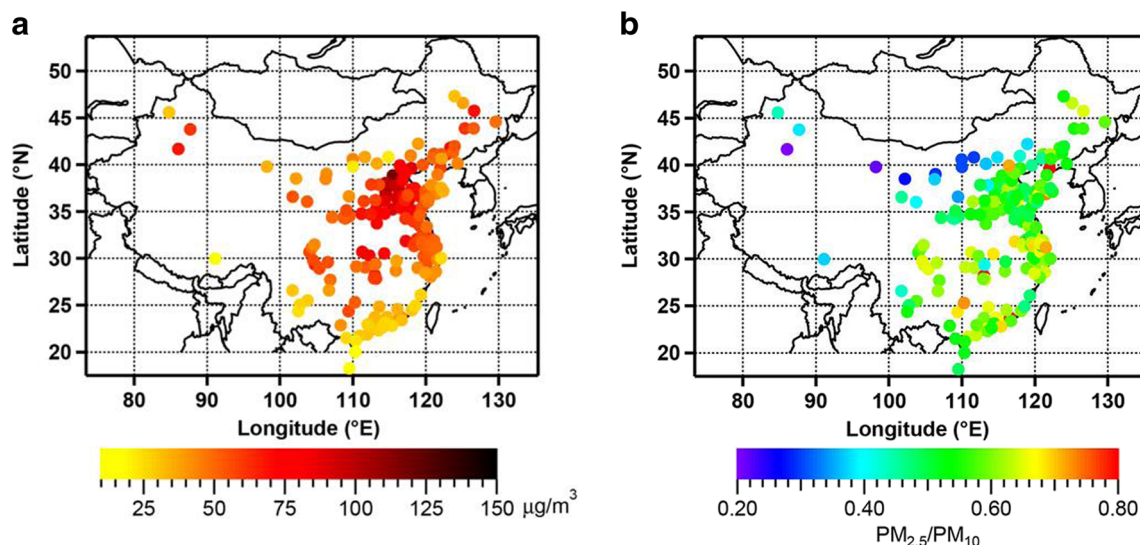


Fig. 1 **a** The averaged $PM_{2.5}$ concentrations ($\mu\text{g}/\text{m}^3$) and **b** the averaged $PM_{2.5}/PM_{10}$ ratio of the 190 cities of China, during the year of 2014–2015 (Zhang and Cao 2015)

CI) of the mortality for all 190 cities. Table 4 illustrates total estimated annual premature mortality due to $PM_{2.5}$. Total premature mortality is estimated to be 722,370 (95% CI = 322,716–987,519), among which adult stroke accounts for 400,064 (95% CI = 139,079–507,681) and IHD accounts for 169,251 deaths (95% CI = 117,670–262,874). These two causes form about 79% of $PM_{2.5}$ -attributable mortalities for all five causes. Megacities (population ≥ 10 million) in China suffer with serious health problems. Their premature mortality are comparatively very high, such as for Chongqing 25,162 (95% CI = 10,919–34,477); Beijing 19,702 (95% CI = 9216–26,287); Shanghai 19,617 (95% CI = 8625–27,154); Tianjin 13,726 (95% CI = 6421–18,314); and Chengdu 12,356 (95% CI = 5526–16,858). Premature death due to $PM_{2.5}$ is calculated based on integrated exposure risk function (IER) which estimates slightly higher value than other methods like non-linear power law (NLP) function (Chowdhury and Dey 2016).

For 2014–2015, average per capita mortality (per 10,000 person-years), for all ages in China, is 8.3 (95% CI = 3.7–

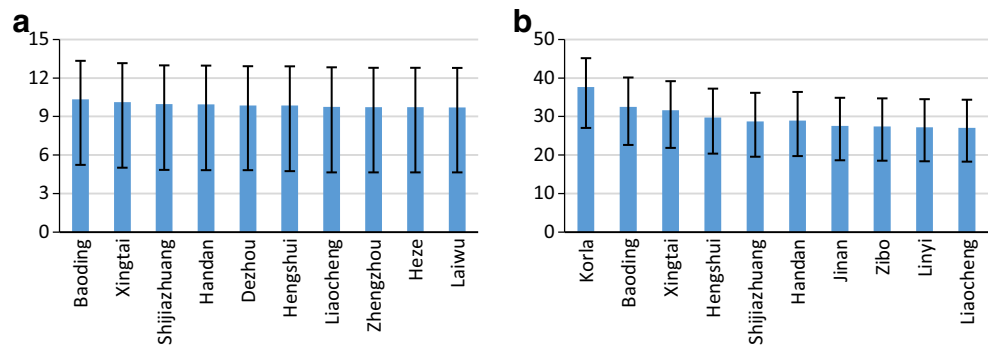
11.4). The per capita mortality for all ages attributable to $PM_{2.5}$ by stroke is 4.6 (95% CI = 1.6–5.8) per 10,000 person-years and IHD is 1.9 (95% CI = 1.4–3.0) per 10,000 person-years. This is higher than other diseases. Cities with high per capita mortalities are Baoding [10.3 (95% CI = 5.2–13.3)], Xingtai [10.1 (95% CI = 5.0–13.2)], and Shijiazhuang [10.0 (95% CI = 4.8–13.0)]. The cities with higher per capita mortality (>9.50) are shown in Fig. 2a. Per capita mortality in Beijing and Shanghai, the most important cities of China, are 9.3 (95% CI = 4.4–12.5) and 8.1 (95% CI = 3.6–11.2), respectively.

In previous studies, the per capita mortality (per 10,000 person-years) among all ages due to $PM_{2.5}$ in China was 9.2 (Apte et al. 2015) and 9.0 in 2013 (Ottery 2015). Institute for Health Metrics and Evaluation (IHME) estimated the global premature mortality attributable to $PM_{2.5}$ in 2013. According to the study of IHME (2016), the per capita mortality was about 6.6 in China. In 2010, average per capita mortality was 9.05 and it will reach 13.74 in

Table 4 Premature mortality attribute to $PM_{2.5}$ pollution in China in 2014–2015

| Country/ city | Mortality (mean and 95% CI) | | | | | |
|------------------|------------------------------|------------------------------|----------------------------|---------------------------|---------------------|------------------------------|
| | Stroke | IHD | COPD | LC | ALRI | Total mortality |
| China | 400,064 (139,079–507,681) | 169,251 (117,670–262,874) | 82,456 (41,068–119,120) | 67,452 (22,739–93,893) | 3147 (2160–3952) | 722,370 (322,716–987,519) |
| Chongqing | 14,120 (4682–17,838) | 5838 (4027–9183) | 2800 (1387–4071) | 2295 (747–3247) | 109 (76–138) | 25,162 (10,919–34,477) |
| Beijing | 10,716 (3973–13,067) | 4517 (3143–7162) | 2411 (1297–3315) | 1964 (739–2624) | 95 (64–118) | 19,702 (9216–26,287) |
| Shanghai | 11,079 (3815–14,267) | 4579 (3170–7154) | 2133 (1037–3141) | 1744 (546–2489) | 82 (56–103) | 19,617 (8625–27,154) |
| Tianjin | 7465 (2768–9104) | 3147 (2189–4990) | 1680 (904–2310) | 1368 (515–1828) | 66 (45–82) | 13,726 (6421–18,314) |
| Chengdu | 6896 (2367–8650) | 2862 (2004–4514) | 1391 (722–2027) | 1153 (396–1599) | 55 (37–69) | 12,356 (5526–16,858) |

Fig. 2 Ten cities in China having high per capita mortality attributable to **a** PM_{2.5} and **b** PM₁₀, during the year of 2014–2015



2030 (OECD 2016). Lelieveld et al. (2013) calculated premature mortality due to PM_{2.5} and found that the per capita mortality (per 10,000 person-years) for all ages is 8.4 in Shanghai, 11.8 in Beijing, and 12.2 in Tianjin. According

to the other study, the estimated per capita mortality for all ages is about 10.8 (Anenberg et al. 2011 and 15.0 (Zheng et al. 2015) in Beijing and 13.7 in Shijiazhuang in 2013 (Ottery 2015).

Table 5 Estimated number of cases attribute to PM₁₀ pollution and associated DALYs and economic costs in China in 2014–2015

| Health endpoints | Attributable number of case (mean and 95% CI) | DALYs (mean and 95% CI) | Economic cost (in million US\$) (mean and 95% CI) |
|--|--|------------------------------------|--|
| Mortality (adult ≥30 years) | 1,491,774 (972,770–1,960,303) | 14,917,742 (9,727,696–19,603,025) | 2.09E + 05 (1.36E + 05–2.74E + 06) |
| Chronic bronchitis (all ages) | 3,614,064 (1,179,845–5,427,952) | 4,350,249 (1420179–6,533,626) | 2.58E + 04 (8.41E + 03–3.87E + 04) |
| RADs (adults ≥20) | 1,012,819,480 (902,581,430–1,109,872,256) | 303,846 (270,774–332,962) | 1.01E + 4 (9.02E + 3–1.11E + 04) |
| Asthma attack (children) | 2,938,280 (1,944,122–3,835,954) | 1175 (778–1534) | 1.72E + 01 (1.14E + 01–2.25E + 01) |
| Asthma attack (adults) | 10,821,614 (5,769,177–15,026,801) | 4329 (2308–6011) | 6.34E + 01 (3.38E + 01–8.81E + 01) |
| Acute bronchitis (all ages) | 11,327,028 (4,565,271–16,216,393) | 3398 (1370–4865) | 1.12E + 03 (4.52E + 02–1.61E + 03) |
| Emergency room visits | 2,063,550 (1,546,437–2,707,658) | 825 (619–1083) | 1.73E + 01 (1.29E + 01–2.27E + 01) |
| COPD | 191,709 (82,370–208,037) | 5061 (2175–5492) | 4.74E + 02 (2.04E + 02–5.14E + 02) |
| Respiratory HA | 499,048 (271,927–731,064) | 13,175 (7179–19,300) | 4.20E + 02 (2.29E + 02–6.16E + 02) |
| Cerebrovascular HA | 357,816 (27,552–687,788) | 9446 (727–18,158) | 4.38E + 02 (3.37E + 01–8.41E + 02) |
| Cardiovascular HA | 308,129 (154,081–462,146) | 8135 (4068–12,201) | 5.29E + 02 (2.65E + 02–7.94E + 02) |
| Cough (children) | 144,133,413 (115,399,533–144,405,620) | 43,240 (34,620–43,322) | 3.72E + 02 (2.98E + 02–3.73E + 02) |
| Cough (adult) | 724,790,598 (623,102,590–725,261,097) | 217,437 (186,931–217,578) | 1.87E + 03 (1.61E + 03–1.87E + 03) |
| Respiratory symptoms days (children) | 144,361,137 (143,218,386–144,412,964) | 43,308 (42,966–43,324) | 3.73E + 02 (3.70E + 02–3.73E + 02) |
| Respiratory symptoms days (adults) | 723,693,526 (483,968,867–725,208,967) | 217,108 (145,191–217,563) | 1.87E + 03 (1.25E + 03–1.87E + 03) |
| Lower respiratory symptoms (wheeze) (children) | 144,361,137 (143,218,386–144,412,964) | 43,308 (42966–43,324) | 8.08E + 03 (8.02E + 03–8.08E + 03) |
| Lower respiratory symptoms (wheeze) (adults) | 723,693,526 (483,968,867–725,208,967) | 217,108 (145,191–217,563) | 4.05E + 04 (2.71E + 04–4.06E + 04) |
| Bronchodilator usage (children) | 142,350,666 (54,014,621–144,252,697) | 42,705 (16,204–43,276) | 5.40E + 02 (2.05E + 02–5.48E + 02) |
| Bronchodilator usage (adults) | 724,713,337 (439,820,972–725,263,123) | 217,414 (131,946–217,579) | 2.75E + 03 (1.67E + 03–2.75E + 03) |
| Total | | 20,659,010 (12,183,885–27,581,784) | 3.04E + 5 (1.95E + 5–3.85E + 5) |

Health effects due to PM₁₀:

Table 1 summarizes E-R coefficients (95% CI) of selected health outcomes due to PM₁₀ and the corresponding incidence rates (per person/year) in the study. Using the E-R functions (β), frequency of health endpoints, threshold concentration (C_0) (as per WHO air quality guidelines, 20 $\mu\text{g}/\text{m}^3$), exposed population (E_p) and exposure concentration (C), the attributable number of cases per year due to PM₁₀ pollution in urban area of China have been calculated, as shown in Table 5.

PM₁₀ pollution has caused 1,491,774 (95% CI = 972,770–1,960,303) premature deaths (age >30) in China. Further, 3,614,064 (95% CI = 1,179,845–5,427,952) cases of chronic bronchitis (CB); 13,759,894 (95% CI = 7,713,300–18,862,755) cases of asthma attack among all ages; 191,709 (95% CI = 82,370–208,037) COPD-related hospital admission (HA) cases; 499,048 (95% CI = 271,927–731,064) respiratory-related HA; 357,816 (95% CI = 27,552–687,788) cerebrovascular HA; 308,129 (95% CI = 154,081–462,146) cardiovascular-related HA; 2,063,550 (95% CI = 1,546,437–2,707,658) emergency room visits for internal medicine; and 11,327,028 (95% CI = 4,565,271–16,216,393) cases of acute bronchitis (AB) due to PM₁₀ pollution have been estimated for Chinese cities in 2014–2015 (Table 5, column 2). The premature deaths due to PM₁₀ based on Chinese cohort study are lower 1,165,328 (1,038,155–1,257,661), due to different ERC value.

As the same β value is selected for all cities, the attributed numbers of mortality or morbidity may be viewed as a function of population and PM₁₀ concentration. The PM₁₀ pollution concentration is likely an important factor in determining the health effects caused by PM. For example, though Harbin, Shenzhen, and Suzhou have similar populations (10.6, 10.6, and 10.5 million, respectively); but the mortality rate in Harbin 19,897 (95% CI = 12,917–26,232) is much higher than in Shenzhen 8886 (95% CI = 5533–12,223) and Suzhou 15,806 (95% CI = 10,101–21,170), because Harbin has a higher PM₁₀ concentration (108.1 $\mu\text{g}/\text{m}^3$). Likewise, Zhengzhou, Weifang, and Wenzhou have very different health endpoint numbers but they have close population values (9.2 million). On the other hand, despite having the same PM₁₀ concentrations (140 $\mu\text{g}/\text{m}^3$), mortality in Anyang [12,245 (95% CI = 8142–15,766)]; Jiaozuo [8393 (95% CI = 5580–10,808)]; and Weifang [22,047 (95% CI = 14,657–28,393)] are very different.

PM₁₀ concentrations in the megacities are often very high, such as in Chongqing (90.5 $\mu\text{g}/\text{m}^3$), Shanghai (73.3 $\mu\text{g}/\text{m}^3$), Beijing (110.2 $\mu\text{g}/\text{m}^3$), Tianjin (129.1 $\mu\text{g}/\text{m}^3$), Harbin (108.1 $\mu\text{g}/\text{m}^3$), Baoding (203.8 $\mu\text{g}/\text{m}^3$), and Shijiazhuang (173.2 $\mu\text{g}/\text{m}^3$). With large populations and high pollutant concentrations, the health effects in megacities account for a large proportion of the total mortality. Chongqing, Beijing, Baoding, Tianjin, and Shijiazhuang are the top five

contributors to pollution-related mortality, accounting for 3.10, 2.71, 2.49, 2.20, and 2.02%, respectively, of the total deaths caused by PM pollution in the 190 cities.

The per capita mortality (per 10,000 person-years) attributable to PM₁₀ pollution, for population having ages >30 on an average is 29.19 (95% CI = 19.03–38.36) and all ages on an average is 17.2 (95% CI = 11.2–22.5) in China for year 2014–2015. The cities with a high per capita mortality (per 10,000 person-years) are Korla [37.6 (95% CI = 27.0–45.1)], Baoding [32.5 (95% CI = 22.6–40.1)], and Xingtai [31.6 (95% CI = 21.8–39.2)]. The cities with a higher per capita mortality (>27.1) are shown in Fig. 2b. The per capita mortality in Beijing, Tianjin, Shanghai, and Taiyuan are 19.1 (95% CI = 12.4–25.2), 22.3 (95% CI = 14.7–28.9), 12.2 (95% CI = 7.7–16.5), and 20.4 (95% CI = 13.3–26.6), respectively.

The past studies have shown that the per capita mortality (per 10,000 person-years) due to PM₁₀ was 25.16 (95% CI = 18.11–30.77) in Beijing in 2004 (C 149 $\mu\text{g}/\text{m}^3$; C_0 70 $\mu\text{g}/\text{m}^3$) (Zhang et al. 2007); 13.88 in Tianjin in 2004 (C 111 $\mu\text{g}/\text{m}^3$; C_0 40 $\mu\text{g}/\text{m}^3$) (Zhang et al. 2008); 14.11 (95% CI = 8.70–19.51) in Shanghai in 2001 (C 100 $\mu\text{g}/\text{m}^3$; C_0 50 $\mu\text{g}/\text{m}^3$) (Kan and Chen 2004); and 9.34 in Taiyuan in 2010 (C 89 $\mu\text{g}/\text{m}^3$; C_0 40 $\mu\text{g}/\text{m}^3$) (Tang et al. 2014).

DALYs due to PM_{2.5} and PM₁₀

The DALYs approach is a robust methodological framework with a firm theoretical base (Ostro 2004). For measurement of impact of air pollution on public health, DALYs scores advantage by making direct comparison with the overall impact of disease, irrespective of cities as well as diseases.

Using the value of DALYs per 10,000 excess number of cases (Table 2) and quantitative health effects for PM_{2.5} and PM₁₀, the corresponding annual DALYs over the period 2014–2015 in 190 cities in China have been estimated. The total DALYs (except for the mortality ALRI in infants, ages <5) associated with PM_{2.5} pollution in China is 7.2 million (95% CI = 3.2–9.8 million) in 2014–2015 (Fig. 1). Chongqing, Beijing, Shanghai, Tianjin, and Chengdu cities are the major contributor to PM_{2.5}-related DALYs in China, accounting for 3.5, 2.7, 2.7, 1.9, and 1.7%, respectively.

Total DALYs associated with PM₁₀ pollution in 190 cities in China in 2014–2015 is 20.66 million (95% CI = 12.18–27.58 million) (Table 5, column 3). Among all health outcomes, mortality and CB predominated, and shared about 93.3% of the total DALYs (Fig. 2).

Economic cost of health impacts due to PM₁₀

Table 3 shows the cost (per cases) for various health impacts in China. These values are much lower than the European and American values (Yang et al. 2016; OECD 2014; WB and SEPA 2007). The difference may be attributed to different

economic background levels. Using the estimated excess number of premature mortality, the economic cost of health impacts of PM_{2.5} pollution in China in 2014–2015 has been calculated to be US\$10,111 million (95% CI = US\$4517–13,823 million).

From Tables 3 and 5 (column 2), the total economic cost of health impact attribute to PM₁₀ pollution has been calculated (Table 5, column 4). During this period, the economic cost of health impact in China has been estimated to be approximately US\$304,122 million (95% CI = 195,331–385,123 million). Among the health effect endpoints, premature death accounted for US\$208,799 (95% CI = 136,156–274,378) million, approximately 68.66% of the total cost. Chronic bronchitis has also made significant contribution to economic costs at an estimated 25,757 (95% CI = US\$8409–38,685) million, which is around 8.47% of the total costs. Moreover, the cost of restricted activity days (RADs) is similarly higher, even though asthma and bronchodilator usage contributed minimum in the total cost.

In the previous study, it has been shown that premature mortality dominated the value of the total economic costs—82.90% in Shanghai in 2001 (Kan and Chen 2004), 87.23% in Beijing in 2004 (Zhang et al. 2007), 88.4% in 111 Chinese cities in 2004 (Zhang et al. 2008), 90% in China in 2010 (OECD 2014), and 67.19% in pearl river delta region in China (Huang et al. 2012).

The total gross domestic product (GDP) losses have been estimated for a parallel comparison. China’s GDP was US\$10,354.83 billion in 2014–2015 (WB 2016e). Estimations in this study show that the economic damage to human health from PM₁₀ accounts for 2.94% (95% CI = 1.89–3.72) of the China’s GDP. Although China’s GDP maintained high growth rate, the PM₁₀ pollution-related economic cost cannot be ignored.

In the previous study, GDP loss due to PM₁₀ pollution was 4.3% in Shijiazhuang (Peng et al. 2002), 6.55% in Beijing (Beijing’s GDP) (Zhang et al. 2007), and 1.35% in Pearl River delta region in China (regional GDP) (Huang et al. 2012). Lu et al. (2016) estimate that the overall short-term all-cause mortality due to NO₂, O₃, and PM₁₀ in Pearl River Delta region in 2013 was 13,217 to 22,800, and corresponding total economic loss was US\$14,768 to 25,305 million, equivalent to 1.4–2.3% of the local GDP.

The World Bank studies estimated that damage to human health from air pollution in China was around 4.6 and 3.8% of GDP levels in 1995 and 2003 (WB 1997; WB and SEPA 2007). Matus et al. (2012) estimated that damage to human health from air pollution (PM₁₀ and ozone) in China was around 8.7, 6.9, and 5.9% of GDP in the years 1995, 2000, and 2005, respectively. Hou et al. (2012) estimated the health-related economic losses that China suffered in 2009 due to the presence of PM₁₀. The results show that China suffered a health-related economic loss due to PM₁₀ of US\$106.5 billion, or 2.1% of China’s GDP, for the year 2009.

The economic cost of health impact due to PM₁₀ mainly depends on exposed population, pollution concentration, number of health outcome parameter considered in studies, and mortality cost (VSL). In this study, some health impacts, for example, minor-restricted activity days and work loss day among adult, upper respiratory tract infection, mortality from acute exposure, and congestive heart failure among elders (age >65) which are related with PM₁₀ pollution, have not been considered. These factors could have led to miscalculation of actual results.

In the assessment of human health impacts, the selection of threshold concentration C_0 greatly impacts the results. In this study, WHO-recommended annual average PM₁₀ standard (20 mg/m³) was used as the C_0 . Chinese NAAQS (70 µg/m³) and no threshold (0 µg/m³) level has also been used for the assessment of health endpoints attributed to PM₁₀ pollution in China, whether in physical and economic terms are listed in Table 6.

Using CNAAQs as C_0 , the number of premature mortality in China is 662,310 (95% CI = 421,623–891,505) and number of chronic bronchitis cases is 1,608,959 (95% CI = 501,363–2,519,879). Total DALYs associated with PM₁₀ pollution is 9.48 million (95% CI = 5.35–12.93 million). Total economic cost associated with PM₁₀ pollution is estimated to be US\$151,136 million (95% CI = 89,317–192,960), which is about 1.46% of GDP in China.

At zero thresholds level ($C_0 = 0$ µg/m³) the premature mortality attributed to PM₁₀ in China is quite high: 1,795,448 (95% CI = 1,185,797–2,329,732) and the number of chronic bronchitis cases is 4,343,477 (95% CI = 1,453,444–6,382,071). Total DALYs is 24.64 million

Table 6 Excess mortality, total DALYs, and total economic cost (in million US\$) using various PM₁₀ threshold levels

| Threshold concentration | Excess mortality | Total DALYs (in million) | total economic cost (in million US\$) |
|---|---------------------------------|--------------------------|---------------------------------------|
| China national ambient air quality standard (70 µg/m ³) | 662,310 (421,623–891,505) | 9.48 (5.35–12.93) | 151,136 (89,317–192,960) |
| No threshold (0 µg/m ³) | 1,795,448 (1,185,797–2,329,732) | 24.64 (14.77–32.49) | 354,274 (233,109–446,309) |

(95% CI = 14.77–32.49 million). And the total economic cost is 354,274 million (95% CI = 233,109–446,309) which is about 3.42% of China's GDP.

In 2030, the Chinese population is estimated to be 1392 million. Demographics of such a population would be 4.1% infants (<5 years), 72.9% adults of >25 years, and 66.9% adults of >30 years, respectively (<http://www.euromonitor.com/china-in-2030-the-future-demographic/report>).

A crucial presumption of this point is that if average $PM_{2.5}$ and PM_{10} levels in year 2030 remains at 31 and 60 $\mu\text{g}/\text{m}^3$ across 190 Chinese cities, then $PM_{2.5}$ and PM_{10} levels have to decline by 46 and 39%, merely to hold the premature mortality attributable to $PM_{2.5}$ and PM_{10} constant at year 2014–2015 levels. Xie et al. (2016) estimated that without $PM_{2.5}$ pollution control policy, China will experiences US\$25.2 billion in health expenditure (2.00% of GDP) from $PM_{2.5}$ pollution in 2030.

Conclusions

Particulate air pollution is responsible for significant health impacts in Chinese cities. This study analyses PM pollution concentrations during year 2014–2015 for 190 Chinese cities. Using $PM_{2.5}$ and PM_{10} pollution data and the E-R function of different health endpoints, the quantitative health impacts of air pollution have been estimated. Total premature mortality attribute to $PM_{2.5}$ and PM_{10} are 722,370 and 1,491,774, and total DALYs are 7.2 and 20.66 million, respectively. The total economic cost attributed to PM_{10} pollution is accounting for about 2.94% of China's GDP.

A new wave of pollution control initiatives is needed to stem the current crippling levels of air pollution. At present, proper air quality management is required to reduce air pollution urgently and effectively, especially for PM_{10} and $PM_{2.5}$ pollutants. Urban $PM_{2.5}$ originates mainly from sources such as traffic-related emissions, road/soil dust, biomass burning, and agriculture activities as well as regional transported aerosols, but source specific quantification still remains a bigger scientific challenge (Zhang et al. 2015a, b; Guo et al. 2014; Huang et al. 2012). But it was found that coal and coal-related industrial processes account for 50–60% of $PM_{2.5}$ in cities of China. China is the world's largest consumer of coal for its energy and is responsible for around half the world's coal consumption. Coal has also been cited as responsible for 60% of the air pollution health impacts in China (Greenpeace 2015). In 2013, particulate matter emissions from 150 coal burning power plants were responsible for 0.37 million premature deaths and it will reach 0.99 to 1.3 million in 2030 unless even more ambitious targets are introduced (IHME 2016). The DALYs due to health impact of coal electricity generation in China was

about 3.2 million in 2007 (Zhang et al. 2007). The major problem is also the number of old vehicles which is about 7.8% of vehicles on China's roads that do not meet the minimum NAAQS (Duggan 2014).

As most Chinese cities fail air quality standards in 2015, China's Ministry of Environment Protection announced some policies to improve air quality in cities; such as (1) Beijing has closed 2500 small polluting firms in 2016 to combat pollution. The capital plans to reduce coal consumption by 0.5 million tons in 2016 and close all coal-fired boilers throughout the city by 2020. (2) The Chinese government has announced plans to scrap up to 6 million vehicles that do not meet emission standards in a bid to reduce the country's air pollution problems (Duggan 2014; Amusing Planet 2015). On the other hand, fuel and vehicular emission control technologies need to be improved. The government must invest in developing more public transport systems. Road dust is a major problem in Chinese cities, which contributes to about 30 to 60% of total PM_{10} (Feng et al. 2010; Kong et al. 2014), toxic polycyclic aromatic hydrocarbons, heavy metals, and black carbon abundant in road dust in high amount (Li et al. 2016; Kong et al. 2012; Han et al. 2009).

Guo et al. (2010) shows that the total economic cost of health impacts due to air pollution contributed from transport in Beijing in 2008 was US\$298 million, which was 0.58% of annual Beijing GDP in 2008. (3) Agricultural straw burning is a major source of air pollution and has many adverse environmental and ecological impact (Zhang et al. 2016b; Lyu et al. 2015; NASA 2012). Agricultural burning removes about one fourth of total crop straw in China and emits about 1.6–2.2 and 0.5–0.14 billion kg of $PM_{2.5}$ and black carbon. Agricultural burning accounts for up to half of the total PM_{10} concentrations in the major burning regions during harvesting periods (Shi et al. 2014). At present, the open burning of crop straw is prohibited in China. A budget of 0.75 billion RMB yuan from the central government has been invested to support the crop straw overall utilization project (UNEP 2015). (4) China bans the approval of new conventional coal-fired power plants and want to increase the share of non-fossil fuels in its energy mix to 20% in the year 2030 (Climate Nexus 2016; Greenpeace 2013).

Current study shows the importance of evaluation and assessment of health impacts of air quality on local scale to protect environment and economic balance. This study is based on the assumption that the entire population of Chinese cities is exposed to the average concentration levels of all air quality monitoring stations in a city. To achieve finer resolution in calculating number and economic value of air pollution-related deaths and illnesses, use of Benefits Mapping and Analysis Program (BenMAP) would be ideal for future studies.

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