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Report

Changes in Life Expectancy of Respiratory Diseases from Attaining Daily $PM_{2.5}$ Standard in China: A Nationwide Observational Study

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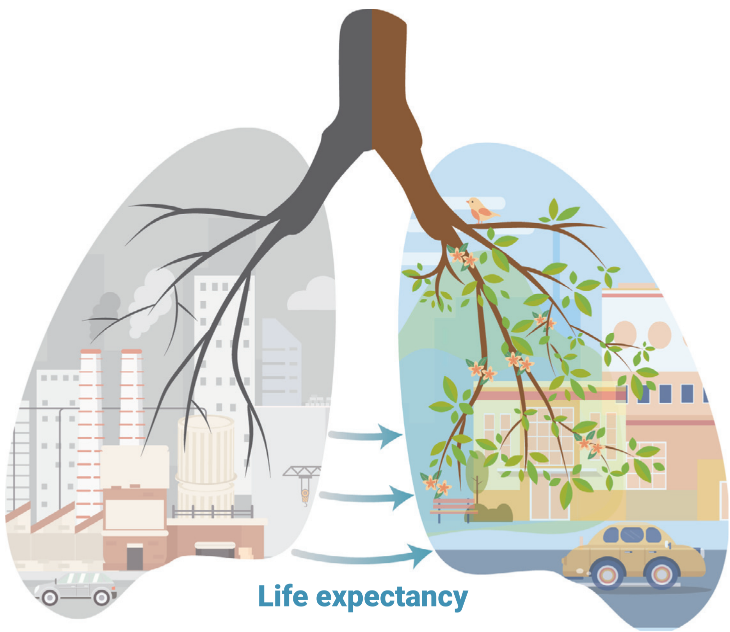
GRAPHICAL ABSTRACT



PUBLIC SUMMARY

- This is a nationwide time-series study in 96 Chinese cities
- $PM_{2.5}$ level was associated with increased risk of respiratory death
- $PM_{2.5}$ level was associated with increased years of life lost of respiratory death
- Daily $PM_{2.5}$ reduction might lead to longer life expectancy from respiratory death

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Although exposure to air pollution increases the risk of premature mortality and years of life lost (YLL), the effects of daily air quality improvement to the life expectancy of respiratory diseases remained unclear. We applied a generalized additive model (GAM) to assess the associations between daily $PM_{2.5}$ exposure and YLL from respiratory diseases in 96 Chinese cities during 2013–2016. We further estimated the avoidable YLL, potential gains in life expectancy, and the attributable fraction by assuming daily $PM_{2.5}$ concentration decrease to the air quality standards of China and World Health Organization. Regional and national results were generated by random-effects meta-analysis. A total of 861,494 total respiratory diseases and 586,962 chronic obstructive pulmonary disease (COPD) caused death from 96 Chinese cities were recorded during study period. Each 10 $\mu g/m^3$ increase of $PM_{2.5}$ in 3-day moving average (lag02) was associated with 0.16 (95% CI: 0.08, 0.24) years increment in life expectancy from total respiratory diseases. The highest effect was observed in Southwest region with 0.42 (95% CI: 0.22, 0.62) years increase in life expectancy. By attaining the WHO's Air Quality Guidelines, we estimated that an average of 782.09 (95% CI: 438.29, 1125.89) YLLs caused by total respiratory death in each city could be avoided, which corresponded to 1.15% (95% CI: 0.67%, 1.64%) of the overall YLLs, and 0.12 (95% CI: 0.07, 0.17) years increment in life expectancy. The results of COPD were generally consistent with total respiratory diseases. Our findings indicate that reduction in daily $PM_{2.5}$ concentrations might lead to longer life expectancy from respiratory death.

KEYWORDS: **FINE PARTICULATES; YEARS OF LIFE LOST; RESPIRATORY DISEASES; CHRONIC OBSTRUCTIVE PULMONARY DISEASE; CHINA**

INTRODUCTION

In the past decade, China has been experiencing serious ambient air pollution mainly due to industrial emission, transportation, and energy use.[1] Fine particulate matter ($PM_{2.5}$) constitutes the predominant ambient air pollutant and is considered as an important risk factor to human health.[1–3] Exposure to $PM_{2.5}$ has been associated with a variety of adverse health effects and disease burden.[4–7]

The respiratory system is directly exposed to its surrounding environment, which makes it more susceptible to the adverse effects of $PM_{2.5}$.[8,9] Increasing evidence supported that $PM_{2.5}$ exposure was closely associated with the increased risk of premature mortality from respiratory diseases.[10–13] One large-scale epidemiological study in China reported that each 10 $\mu g/m^3$ increase in 2-day moving average level of $PM_{2.5}$ was associated with 0.29% increment in respiratory mortality.[14] Moreover, a few recent studies used years of life lost (YLL), a complementary index of mortality count, to evaluate the disease burden caused by $PM_{2.5}$ exposure.[15–17] Significant associations between higher $PM_{2.5}$ exposure and corresponding increment in YLL caused by chronic obstructive pulmonary disease (COPD) were found in a Chinese study.[16]

Considering the well-established links between $PM_{2.5}$ and premature mortality and YLL caused by respiratory diseases, it is reasonable to hypothesize that the improvement of air quality might lead to an increment in the life expectancy.[18–20] However, only several studies have estimated the effects of air pollution improvement on life expectancy, and mainly focused on the long-term $PM_{2.5}$ exposure and overall mortality.[14,21] On the other hand, the effects of short-term air pollution exposure reduction on life expectancy due to respiratory diseases have not been investigated yet.

We thus conducted this nationwide analysis with three specific objectives: (1) to estimate the associations of daily $PM_{2.5}$ and YLLs caused by respiratory diseases in mainland China; (2) to evaluate the avoidable YLLs by assuming that $PM_{2.5}$ has decreased to the WHO's Air Quality Guidelines (25 $\mu g/m^3$) and Chinese National Ambient Air Quality Standard (75 $\mu g/m^3$); and (3) to further estimate the life expectancy gains and attributable fraction (AF) by averaging the avoidable YLL on overall mortality count and YLL. Findings from this study will enhance our understanding of the health effect of $PM_{2.5}$ exposure through providing the information of how longer people can live by reducing air pollution.

RESULTS

Descriptive Statistics

Table 1 summarizes the respiratory mortality and environmental factors in the 96 Chinese cities during 2013–2016. A total of 861,494 respiratory deaths were observed, of which, 586,962 cases were caused by COPD, and 497,686 cases were male individuals. On average, 8.2 deaths and 82.9 YLL per day were recorded for total respiratory diseases, and 6.1 deaths and 55.8 years of life lost per day were recorded for COPD.

Table S2 presents the correlation coefficients among air pollutants and meteorological factors. Overall, $PM_{2.5}$ was positively correlated with O_3, SO_2, and NO_2, and negatively correlated with temperature and relative humidity. The absolute correlation coefficients ranged from 0.04 to 0.47.

Effects of Daily $PM_{2.5}$ Exposure on Mortality Count and YLL

We checked the distribution of YLLs before applying city-specific analyses. The YLLs in the study cities were generally normally distributed (Figure S2). Figure 1 presents the associations between each 10 $\mu g/m^3$ increment in $PM_{2.5}$ at different lag days and YLL or mortality count caused by total respiratory diseases. Each 10 $\mu g/m^3$ increment in $PM_{2.5}$ at 3-day lag (lag02) was associated with 0.16 (95% CI: 0.08, 0.24) year increase in YLL and 0.26% (95% CI: 0.15%, 0.37%) increase in mortality count due to respiratory diseases, and with 0.10 (95% CI: 0.05, 0.15) years increase in YLL and 0.28% (95% CI: 0.15%, 0.41%) increase in mortality count due to COPD at the national level (Table S3).

In the region-specific analyses, differential associations at lag02 were observed between daily $PM_{2.5}$ and YLL or mortality count (Table S3). We found relatively higher associations for total respiratory diseases in

Table 1. Summary Statistics of Daily Respiratory Deaths, YLLs, Air Pollutants and Meteorological Factors

	Range	Mean (SD)	Median (IQR)
Average daily death, n			
Total respiratory diseases	1.0–152.0	8.2 (8.9)	6.0 (3.0–11.0)
COPD	1.0–134.0	6.1 (7.5)	4.0 (2.0–8.0)
Male	0.0–95.0	4.8 (5.4)	3.0 (2.0–6.0)
Female	0.0–62.0	3.5 (4.0)	2.0 (1.0–5.0)
Average daily YLL, years			
Total respiratory diseases	2.4–1560.6	82.9 (89.7)	58.3 (27.6–108.7)
COPD	2.4–1346.2	55.8 (70.4)	36.7 (17.5–69.2)
Male	0.0–914.3	49.3 (57.9)	33.1 (13.8–65.8)
Female	0.0–653.9	33.6 (40.0)	21.3 (7.6–45.4)
Average $PM_{2.5}$ concentration, $\mu g/m^3$			
East (n = 31)	4.0–985.2	73.8 (71.4)	53.9 (33.4–87.7)
South (n = 8)	3.6–577.5	51.6 (51.9)	38.1 (23.3–62.0)
Southwest (n = 8)	5.1–523.4	51.0 (48.1)	35.4 (20.8–65.0)
North (n = 8)	3.7–797.1	86.8 (84.6)	59.8 (34.5–103.4)
Northeast (n = 14)	4.8–878.8	60.6 (56.9)	44.2 (26.6–878.8)
Northwest (n = 12)	5.2–599.4	56.6 (52.6)	42.2 (26.9–67.9)
Central (n = 15)	7.1–745.5	78.3 (70.3)	58.9 (36.9–98.7)
National (n = 96)	3.6–985.2	67.6 (66.1)	47.3 (29.1–77.4)
Average co-pollutant concentrations, $\mu g/m^3$			
SO_2	3.0–909.0	48.7 (74.6)	23.1 (13.1–45.8)
NO_2	3.0–289.6	35.8 (19.6)	32.1 (21.6–45.8)
O_3	2.0–588.0	85.2 (60.5)	56.1(36.2–82.3)
Average meteorological factors			
Mean temperature, °C	−26.4–36.5	15.0 (10.6)	16.8 (7.6–23.5)
Relative humidity, %	5.0–100.0	66.9 (18.7)	70.0 (55.0–81.0)

Abbreviations: IQR = interquartile range; NO_2 = nitrogen dioxide; O_3 = ozone; $PM_{2.5}$ = particulate matter with an aerodynamic diameter less than or equal to 2.5 μm; SO_2 = sulfur dioxide; YLL = years of life lost.

Southwest region, each 10 $\mu g/m^3$ increment of $PM_{2.5}$ was associated with an increase of 0.42 (95% CI: 0.22, 0.62) years in YLL. And relatively lower effects for total respiratory diseases were observed in the East region with 0.23 (95% CI: 0.11, 0.36) years increase in YLL and 0.30% (95% CI: 0.14%, 0.46%) increase in mortality count. No significant associations were found in Central, North, Northeast, and South regions. These associations of COPD were generally consistent with total respiratory diseases (Table S3).

In the gender-specific analyses, relatively stronger effects of $PM_{2.5}$ on mortality count of total respiratory diseases and COPD were found among female individuals. Each 10 $\mu g/m^3$ increment of $PM_{2.5}$ at lag02 was associated with 0.35% (95% CI: 0.22%, 0.48%) increase in total respiratory mortality count for female individuals, and 0.13% (95% CI: 0.02%, 0.24%) increase for male individuals (Table S4). Each 10 $\mu g/m^3$ increment of $PM_{2.5}$ at lag02 was associated with 0.17% (95% CI: 0.03%, 0.31%) and 0.37% (95% CI: 0.26%, 0.48%) increases in COPD mortality count for male and female individuals, respectively (Table S5).

Avoidable YLLs and Potential Gains in Life Expectancy by Attaining Daily $PM_{2.5}$ Standard

Table 2 shows the avoidable YLLs of respiratory diseases by using the Chinese and World Health Organization's (WHO's) standard of $PM_{2.5}$ as the references. For total respiratory diseases, we estimated that the mean avoidable YLL was 17.06 (95% CI: 2.67, 31.45) years using the Chinese national ambient air quality standard (NAAQS), and this number could rise to 782.09 (95% CI: 438.29, 1125.89) years by adopting WHO's Air Quality Guideline (AQG) as the reference. For COPD, the average avoidable YLL was 0.88 (95% CI: −0.29, 2.06) years using Chinese standard and was 389.04 (95% CI: 191.78, 586.30) years using WHO's AQG. Differential results were observed across different regions. The Southwest region possessed the largest avoidable YLLs, with 2247.44 (95% CI: 816.00, 3678.88) years for total respiratory diseases and 1383.14 (95% CI: −504.57, 3270.85) years for COPD when adopting the WHO's AQG.

Potential gains in life expectancy and the AF were further analyzed (Tables 3 and 4). For total respiratory diseases, 0.02 (95% CI: 0.01, 0.03) and 0.12 (95% CI: 0.07, 0.17) years of life expectancy could be gained if $PM_{2.5}$ attained the Chinese standard and WHO's AQG, respectively; the estimated YLL attributable to daily $PM_{2.5}$ exposure was 0.19% (95% CI: 0.09%, 0.28%) using the Chinese standard and 1.15% (95% CI: 0.67%, 1.64%) using WHO's AQG. For COPD, 0.02 (95% CI: 0.01, 0.03) and 0.10 (95% CI: 0.05, 0.15) years in life expectancy could be gained if $PM_{2.5}$ decreased to the Chinese standard and WHO's AQG, respectively; the AF was 0.20% (95% CI: 0.08%, 0.32%) using Chinese standard and 1.10% (95% CI: 0.55%, 1.64%) using WHO's AQG.

The associations between $PM_{2.5}$ and life expectancy lost from respiratory death varied across the seven regions and different genders. The largest effect was observed in the Southwest region. If $PM_{2.5}$ attained the WHO's AQG, 0.25 (95% CI: 0.16, 0.34) years for COPD and 0.23 (95% CI: 0.14, 0.32) years for total respiratory diseases in life expectancy could be gained, respectively. The AF of YLL due to total respiratory diseases was 0.96% (95% CI: 0.42%, 1.49%) for male individuals and 1.30% (95% CI: 0.72%, 1.88%) for female individuals if $PM_{2.5}$ decreased to the WHO's AQG.

Sensitivity Analyses

The results remained generally consistent in the sensitivity analyses. When we included NO_2 (SO_2 or O_3) in the model, each 10 $\mu g/m^3$ increment in $PM_{2.5}$ at lag02 was associated with 0.27 (95% CI: 0.10, 0.44), 0.29 (95% CI: 0.20, 0.37), and 0.23 (95% CI: 0.11, 0.35) years increases in YLL due to total respiratory diseases in the East region, respectively (Table S6). We also got comparable results by changing the degrees of freedom for temperature (Table S7). Moreover, another additional sensitivity analysis was performed by adding the calendar year to further adjust for long-term trend (Table S8). Each 10 $\mu g/m^3$ increment in $PM_{2.5}$ concentration at lag02 was associated with 0.11 (95% CI: 0.05, 0.17) years increase in life expectancy due to total respiratory diseases in the East region.

DISCUSSION

This is a large-scale time-series study to investigate the effects of daily air pollution exposure on life expectancy lost due to respiratory mortality. Based on nationwide data covering 96 Chinese cities, we demonstrated daily $PM_{2.5}$ was significantly associated with increased mortality count and YLL caused by respiratory diseases. In addition, we observed that population might gain longer life expectancy by attaining air quality standards of daily $PM_{2.5}$.

Compared with daily mortality count, YLL is a more informative indicator to assess the disease burden of air pollution exposure by taking account the number of deaths, age structure, and population size.[22] In our previous study, each 10 $\mu g/m^3$ increase in $PM_{2.5}$ was associated with 0.43 years of life expectancy loss of nonaccidental deaths at the national level.[23] In the present study, we mainly focused on the outcome of respiratory mortality and observed the coefficient was 0.16 years at the national level. Compared with our previous study, the mortality data in this study were obtained from Cause of Death Reporting System (CDRS), which was more comprehensive to represent the whole city, whereas the disease surveillance points covered only a few counties or districts in each city. Moreover, we standardized YLL

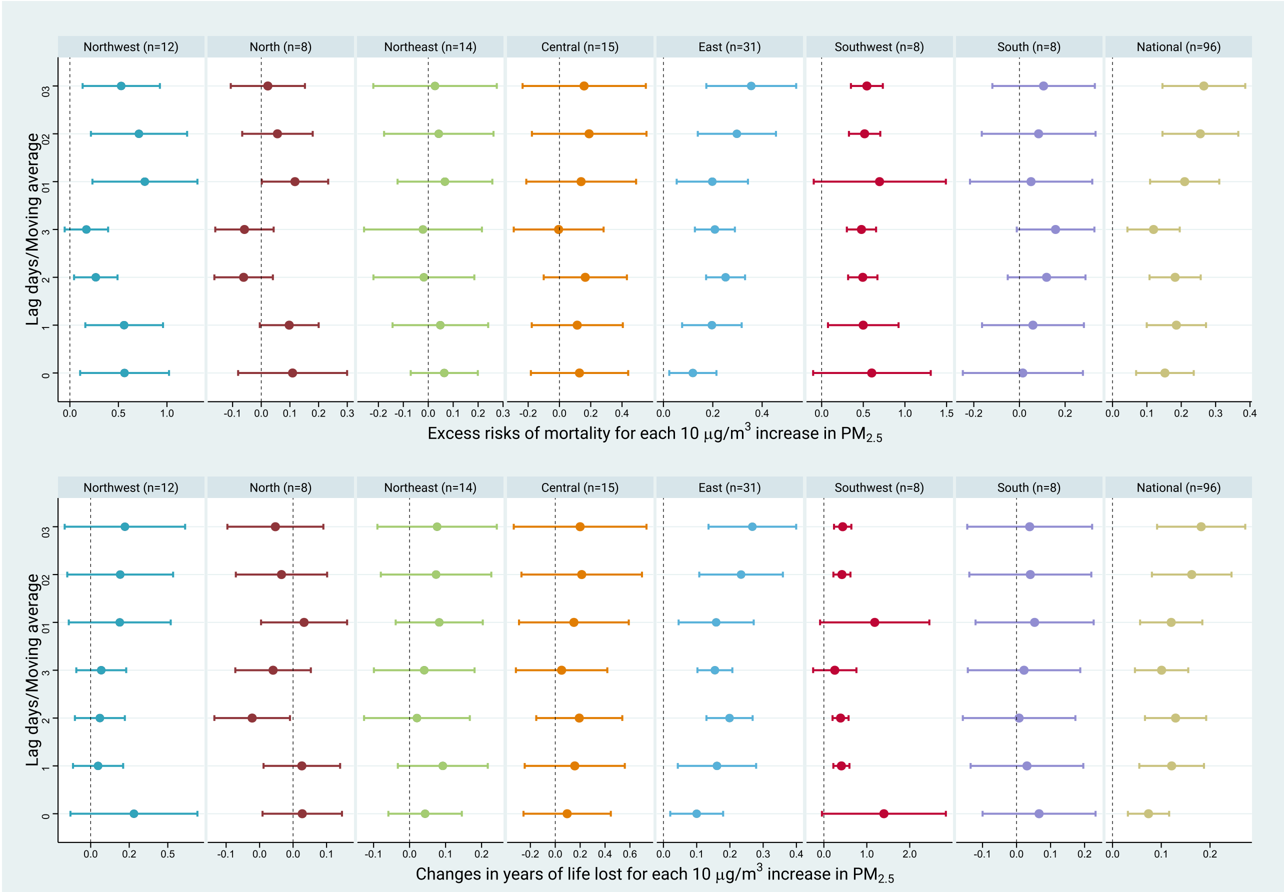

Figure 1. Regression Coefficients of Daily Years of Life Lost or Mortality Count due to Respiratory Diseases Associated with $PM_{2.5}$ at Different Lag Days during 2013–2016

and avoidable YLL by the population of each city before generating the regional and national results of $PM_{2.5}$-YLL association and avoidable YLL in this study.

A few previous studies also used YLL to evaluate the adverse health effects of air pollution.[15,24,25] One Chinese study in Nanjing reported that an IQR (66.3 $\mu g/m^3$) increase in the two-day PM_{10} concentration was associated with 20.5 years increase in YLL from 2009 to 2013.[17] Another study conducted in Beijing demonstrated that an interquartile range (IQR) (94 $\mu g/m^3$) increment in $PM_{2.5}$ at lag01 was associated with 15.8 years increase in YLL during 2004–2008.[15] In the present study, we did not observe significant associations between $PM_{2.5}$ exposure and increment of YLL in Beijing. The difference in study period, methods for estimating $PM_{2.5}$ exposure, and analytical methods might be possible reasons of the differential findings. Moreover, some important covariates associated with YLL were unavailable in this study, which might be another reason.

We further evaluated the avoidable YLLs and beneficial effects in life expectancy by assuming that air pollution met the standards/guidelines set by the Chinese government and WHO. We estimated 0.08 years in life expectancy of respiratory diseases could be gained if the daily $PM_{2.5}$ concentration reduced to the WHO's AQG (25 $\mu g/m^3$). A few studies have reported the effects of long-term (annual) air pollution exposure on life expectancy.[19,26] This study, based on the short-term associations (daily timescale), reported a generally consistent result. One study conducted in the United States estimated each 10 $\mu g/m^3$ decline in yearly $PM_{2.5}$ exposure was associated with an increase of 0.35 years of life expectancy.[21] Another study showed that an increase of 2 $\mu g/m^3$ in the annual $PM_{2.5}$ was associated with 0.64 years of loss in life expectancy in certain areas of Spain.[27]

Regional heterogeneity was observed in the present study. The largest effect was observed in Southwest region of China, which implied the greatest disease burden of $PM_{2.5}$ in this region. However, the average daily $PM_{2.5}$ level in the Southwest region was the lowest among the seven regions. The city heterogeneity of the health effect caused by $PM_{2.5}$ exposure in previous studies might be driven by the differences in population or chemical compositions of $PM_{2.5}$.[28–30] The emission sources of ambient $PM_{2.5}$ in the Southwest region were more related to biomass combustion, which might be one potential reason of its high toxicity. Besides, nonsignificant associations were found in the North and Northeast regions, where $PM_{2.5}$ concentrations were at relatively high level. The potential reason for the differential findings in different regions merits further investigations.

The effects of $PM_{2.5}$ on the daily mortality count were stronger among female than male individuals, which was consistent with the findings in a few other studies.[15,31,32] Zeng et al.[31] found that inhalable particulate matter in Tianjin had a significantly greater impact among female individuals (0.59 vs. 0.26 years). A study in the United States showed hospital risk of respiratory diseases for same-day $PM_{2.5}$ exposure was higher for women than men.[33] $PM_{2.5}$ has been shown to deposit in the alveolar region of the lung, then could activate a range of pathophysiological signaling.[34] The difference in physiological structure between male and female individuals, such as the size of airway diameter, genetic factors, and hormonal level, might be the different effects of air pollution on different population.[35,36] However, there were no significant differences of $PM_{2.5}$ on YLL among genders.

Several limitations should be considered in this study. First, the ecological study design was difficult for causal inference, and potential confounders at the individual level could not be controlled, such as household

Table 2. The Avoidable Years of Life Lost of Total Respiratory Diseases and COPD by Improving $PM_{2.5}$ at lag02 to the Chinese and WHO's Standards during 2013–2016

	Chinese Standard (75 μg/m³)		WHO's AQG (25 μg/m³)	
	Respiratory Diseases	**COPD**	**Respiratory Diseases**	**COPD**
Gender				
Male	**3.40 (0.87, 5.92)**	0.78 (−0.48, 2.03)	**386.60 (148.78, 624.42)**	**174.48 (32.08, 316.88)**
Female	0.91 (−0.57, 2.39)	0.06 (−0.68, 0.79)	**324.67 (150.22, 499.13)**	**188.83 (98.32, 279.35)**
Region				
East (n = 31)	**3.86 (1.33, 6.38)**	0.80 (−0.37, 1.98)	**1146.47 (538.75, 1754.19)**	**765.90 (366.91, 1164.89)**
South (n = 8)	32.60 (−18.12, 83.32)	−8.09 (−28.30, 12.12)	174.63 (−564.72, 913.97)	98.04 (−291.31, 487.39)
Southwest (n = 8)	**46.61 (13.58, 79.64)**	222.04 (−144.18, 588.26)	**2247.44 (816.00, 3678.88)**	**1383.14 (-504.57, 3270.85)**
North (n = 8)	19.45 (−178.92, 217.82)	14.67 (−73.88, 103.22)	9.83 (−627.76, 647.42)	139.91 (−166.99, 446.80)
Northeast (n = 14)	39.64 (−58.99, 138.27)	6.12 (−56.33, 68.56)	234.69 (−406.04, 875.42)	55.44 (−293.84, 404.71)
Northwest (n = 12)	77.61 (−64.87, 220.10)	43.93 (−11.97, 99.82)	1049.32 (−85.11, 2183.75)	**883.04 (236.38, 1529.69)**
Central (n = 15)	440.20 (−647.18, 1527.58)	224.80 (−755.53, 1205.14)	1240.75 (−1630.24, 4111.73)	508.05 (−2110.51, 3126.61)
National (n = 96)	**17.06 (2.67, 31.45)**	0.88 (−0.29, 2.06)	**782.09 (438.29, 1125.89)**	**389.04 (191.78, 586.30)**

Note: The Chinese national ambient air quality standard of daily $PM_{2.5}$ was 75 μg/m³; the WHO's AQG of daily $PM_{2.5}$ was 25 μg/m³; bold typeface indicates statistically significant ($p < 0.05$).
Abbreviations: AF = attributable fraction; AQG = ambient Air Quality guidelines; COPD = chronic obstructive pulmonary disease; WHO = World Health Organization; YLL = years of life lost.

income, smoking, diet, occupational pollution exposure, and physical activities. Second, exposure misclassification was possible, as we used the average air pollution concentration at the city level to present the exposures. Besides, only the concentrations of $PM_{2.5}$ were analyzed in this study; future studies should consider the chemical components and oxidative toxicity of $PM_{2.5}$. Third, we mainly analyzed total respiratory diseases and COPD mortality in this study, because the number of other respiratory diseases was relatively small. Fourth, we used GAM with a Gaussian link to examine the associations between $PM_{2.5}$ and YLL in each city. The model might not fit well as the normal distribution of YLLs did not perfectly exist in all the studied cities, especially a few small cities. However, we only have six cities with the population smaller than one million, such effects on the regional or national findings might be minimal. Lastly, the representativeness of some regions was affected, because the small number of cities in these regions.

Our findings have several important implications for environmental management and public health. We demonstrated that the life expectancy of those with respiratory diseases could be prolonged by attaining the ambient air pollution standards, which provided some new scientific basis for the policy makers to formulate a stricter air quality standard. Secondly, differential

Table 3. The Estimated Potential Gains in Life Expectancy of Total Respiratory Diseases and COPD if $PM_{2.5}$ (lag02) Attaining the Chinese or WHO's Standards during 2013–2016

	Chinese Standard (75 μg/m³)		WHO's AQG (25 μg/m³)	
	Respiratory Diseases	**COPD**	**Respiratory Diseases**	**COPD**
Gender				
Male	**0.003 (0.001, 0.006)**	**0.0006 (0.0001, 0.0012)**	**0.10 (0.04, 0.16)**	**0.08 (0.03, 0.14)**
Female	0.0007 (−0.0001, 0.0016)	**0.0002 (−0.0006, 0.0009)**	**0.13 (0.07, 0.18)**	**0.12 (0.07, 0.18)**
Region				
East (n = 31)	**0.03 (0.01, 0.05)**	**0.03 (0.01, 0.05)**	**0.15 (0.08, 0.22)**	**0.14 (0.08, 0.20)**
South (n = 8)	0.01 (−0.001, 0.01)	−0.002 (−0.007, 0.003)	0.02 (−0.06, 0.09)	0.02 (−0.07, 0.11)
Southwest (n = 8)	**0.004 (0.001, 0.007)**	**0.005 (0.003, 0.008)**	**0.23 (0.14, 0.32)**	**0.25 (0.16, 0.34)**
North (n = 8)	0.01 (−0.04, 0.06)	0.01 (−0.03, 0.05)	0.03 (−0.10, 0.17)	0.06 (−0.05, 0.17)
Northeast (n = 14)	0.02 (−0.01, 0.04)	0.001 (−0.028, 0.031)	0.06 (−0.04, 0.17)	0.02 (−0.10, 0.15)
Northwest (n = 12)	0.01 (−0.01, 0.04)	0.01 (−0.003, 0.03)	0.15 (−0.02, 0.33)	**0.20 (0.04, 0.36)**
Central (n = 15)	0.04 (−0.05, 0.12)	0.02 (−0.07, 0.11)	0.10 (−0.13, 0.33)	0.03 (−0.22, 0.27)
National (n = 96)	**0.02 (0.01, 0.03)**	**0.02 (0.01, 0.03)**	**0.12 (0.07, 0.17)**	**0.10 (0.05, 0.15)**

Note: The Chinese national ambient air quality standard of daily $PM_{2.5}$ was 75 μg/m³; the WHO's AQG of daily $PM_{2.5}$ was 25 μg/m³; bold typeface indicates statistically significant ($p < 0.05$).
Abbreviations: AQG = ambient air quality guidelines; PGLE = potential gains in life expectancy; WHO = World Health Organization.

Table 4. The Attributable Fraction of YLL due to Total Respiratory Diseases and COPD if $PM_{2.5}$ (lag02) Attaining the Chinese or WHO's Standards during 2013–2016

	Chinese Standard (75 $\mu g/m^3$)		WHO's AQG (25 $\mu g/m^3$)	
	Respiratory Diseases, %	**COPD, %**	**Respiratory Diseases, %**	**COPD, %**
Gender				
Male	**0.020 (0.004, 0.035)**	**0.007 (0.001, 0.013)**	**0.96 (0.42, 1.49)**	**0.88 (0.27, 1.49)**
Female	0.007 (−0.001, 0.016)	0.01 (−0.01, 0.03)	**1.30 (0.72, 1.88)**	**1.40 (0.80, 1.99)**
Region				
East (n = 31)	**0.34 (0.12, 0.55)**	**0.38 (0.16, 0.60)**	**1.66 (0.92, 2.40)**	**1.67 (1.03, 2.31)**
South (n = 8)	0.06 (−0.01, 0.13)	−0.02 (−0.08, 0.03)	0.18 (−0.57, 0.93)	0.26 (−0.79, 1.31)
Southwest (n = 8)	**0.04 (0.01, 0.06)**	**0.05 (0.03, 0.07)**	**2.13 (1.26, 2.99)**	**2.53 (1.64, 3.43)**
North (n = 8)	0.11 (−0.32, 0.55)	0.13 (−0.29, 0.55)	0.30 (−1.02, 1.61)	0.70 (−0.57, 1.97)
Northeast (n = 14)	0.16 (−0.06, 0.38)	0.02 (−0.26, 0.30)	0.53 (−0.40, 1.46)	0.25 (−0.90, 1.40)
Northwest (n = 12)	0.10 (−0.09, 0.28)	0.14 (−0.02, 0.30)	1.32 (−0.12, 2.77)	**1.82 (0.35, 3.29)**
Central (n = 15)	0.37 (−0.46, 1.19)	0.19 (−0.76, 1.14)	1.02 (−1.22, 3.26)	0.30 (−2.29, 2.88)
National (n = 96)	**0.19 (0.09, 0.28)**	**0.20 (0.08, 0.32)**	**1.15 (0.67, 1.64)**	**1.10 (0.55, 1.64)**

Note: The Chinese national ambient air quality standard of daily $PM_{2.5}$ was 75 $\mu g/m^3$; the WHO's AQG of daily $PM_{2.5}$ was 25 $\mu g/m^3$; bold typeface indicates statistically significant ($p < 0.05$).

Abbreviations: AF = attributable fraction; AQG = Ambient Air Quality guidelines; WHO = World Health Organization; YLL = years of life lost.

findings in different regions of China suggested the air quality control should not only focus on the concentration of particle matters but also its toxicity and chemical components.

This nationwide study in China demonstrates that daily exposure of ambient $PM_{2.5}$ is associated with increased YLL due to respiratory diseases. Improvement of daily $PM_{2.5}$ level might contribute to longer life expectancy of respiratory diseases. Findings in this study provide important epidemiological evidence for formulating air pollution prevention policy in China.

MATERIALS AND METHODS

Mortality and YLL of Respiratory Diseases

We obtained the daily mortality data from the Chinese CDRS during January 2013 to December 2016. This system is operated by the National Center for Chronic and Noncommunicable Disease Control and Prevention under the direction of the Chinese Center for Disease Control and Prevention (China CDC). Daily mortality data from this system have been widely used in previous studies.[37–39] A total of 100 Chinese cities were initially obtained, among which, 96 cities were included in the following analyses based on these criteria: (1) the availability of daily respiratory death counts and air pollution data, (2) the daily mortality counts did not have large fluctuations during our study period, (3) there were no adjustments to the cities' administrative area. The 96 cities were further divided into seven regions based on the geographic distribution: East (n = 31), South (n = 8), Southwest (n = 8), North (n = 8), Northeast (n = 14), Northwest (n = 12), and Central (n = 15) (Figure 2).

The causes of death were defined according to the International Classification of Diseases, 10th revision. We focused on the death caused by total respiratory diseases (codes J00-J99) and COPD (codes J41-J44). In this study, total respiratory diseases included chronic respiratory diseases and acute respiratory diseases.

Chinese national life table was used to calculate the daily YLL. We matched sex and age to the life table to calculate the YLL for each death.[15] Daily YLLs of each city were computed by summing the YLL of all deaths on that day. The Chinese national life table from 2013 to 2016 is shown in Table S1.

Ethical Approval

This study was approved by the Ethics Committee of Sun Yat-sen University School of Public Health (No. 2019149). No individual information was contained in this study.

Air Pollution and Meteorological Data

Daily $PM_{2.5}$, sulfur dioxide (SO_2), nitrogen dioxide (NO_2), and ozone (O_3) concentrations during the study period were collected from the National Air Quality Real-time Publishing Platform. Air pollutant data in this platform were from state administered air monitoring stations, which monitored the daily concentration of each air pollutant using the standardized methods. Briefly, the concentrations of $PM_{2.5}$, NO_2, SO_2, and O_3 were measured by beta ray attenuation method, UV photometry method, chemiluminescence, and UV fluorescence, respectively.[3] During the study period, fewer than 3% of observation days had missing air pollutants in each city, and they were imputed by a linear interpolation method using the "na.approx" function in the "zoo" package.

Daily meteorological data (including temperature and relative humidity) of the 96 cities were obtained from the China National Meteorological Data Sharing Service System (http://data.cma.cn).

Statistical Analyses

Descriptive analyses were performed for the key variables including daily air pollutants, daily meteorological factors, daily mortality, and YLLs due to respiratory diseases in the 96 cities from 2013 to 2016. The correlations between meteorological factors and air pollutants were examined by using the Spearman rank correlation test.

The associations between daily $PM_{2.5}$ exposure and YLL from respiratory diseases were estimated by Bayesian hierarchical models. Similar approach has been recently introduced in our previous studies focused on all-cause and stroke-cause mortality.[23,40] The analytical process is shown in Figure S1.

At the first stage, we calculated city-specific associations between daily $PM_{2.5}$ and YLL or mortality count by applying GAM with a Gaussian link or a quasi-Poisson link. The normality of YLL data was graphically examined by histogram plot for each city. In the main models, daily mean $PM_{2.5}$ was the independent variable and daily YLL or mortality count in each city was the dependent variable. Both day of the week (DOW) and public holidays (PH) were adjusted as categorical variables in the analyses. Temperature, relative humidity, and long-term and seasonal trends were controlled by the penalized smoothing splines function.[41,42] The degrees of freedom being applied in the models were selected based on previous studies.[41,43] We used the df of 6 per year for temporal trends, the df of 6 for temperature and the df of 3 for relative humidity to adjust for the potential nonlinear relationships. The formula can be specified as:

$$YLL = \alpha + \beta * PM_{2.5} + \beta_1 * DOW + \beta_2 * PH + s\,(t, df = 6/year) + s\,(temperature, df = 6) + s\,(humidity, df = 3)$$

Considering the delayed effects, we explored the associations between YLL and $PM_{2.5}$ in different lag day and multiday lags: the current day (lag0), the previous day (lag1), the previous 2 days (lag2), the previous 3 days (lag3), moving average of current and previous 1 day (lag01), 2 days (lag02), 3 days (lag03).

At the second stage, city-specific avoidable YLLs were estimated by assuming that the $PM_{2.5}$ concentrations have declined to the standards/guidelines. The reference concentrations of daily $PM_{2.5}$ were the Chinese NAAQS (75 $\mu g/m^3$) and WHO's AQG (25 $\mu g/m^3$). The potential gains in life expectancy (PGLE) and AF of YLL by reducing the concentration of $PM_{2.5}$ were further calculated by the following formula:

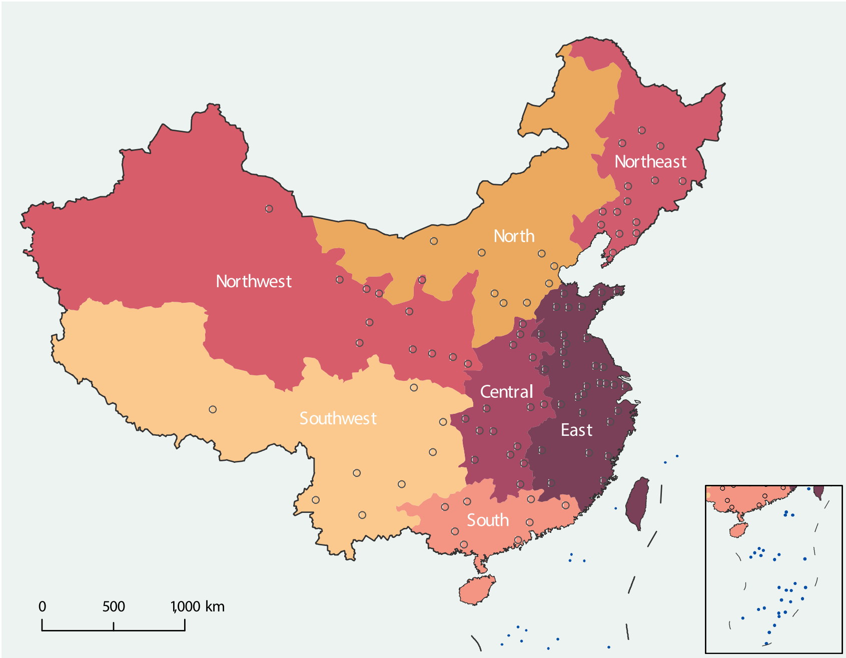

Figure 2. Locations of the 96 Study Cities in Mainland China The locations of the 96 cities were indicated by small black circle. The seven regions were shown in different colors.

$$AF = \frac{Avoidable\ YLLs}{Overall\ YLLs}$$

$$PGLE = \frac{Avoidable\ YLLs}{Overall\ mortality\ count}$$

where avoidable YLL is the sum of the estimated YLL that could be prevented if $PM_{2.5}$ decrease to the reference concentrations; overall YLL is the sum of YLL for respiratory deaths; PGLE is the PGLE for each respiratory death; overall mortality count is the total death number due to respiratory diseases.

At the third stage, we generated the regional and national results of $PM_{2.5}$-YLL association, $PM_{2.5}$-mortality association, avoidable YLL, PGLE, and AF by conducting a random-effects meta-analysis. This approach has been widely used in examining both statistical error within-city and heterogeneity between-city in multisite epidemiological studies.[15,44] We calculated the national and regional results of $PM_{2.5}$-mortality association, potential life expectancy gains, and AF of the 96 cities. Considering the large variation in the population across the cities, which could affect the comparability of the $PM_{2.5}$-YLL association, before generating the regional and national results of $PM_{2.5}$-YLL association and avoidable YLL, we standardized the $PM_{2.5}$-YLL association and avoidable YLL by the population (per 5 million) of each city.

Sensitivity Analyses

We conducted three sensitivity analyses to examine the robustness of the effects between daily $PM_{2.5}$ and YLLs in our study. Firstly, we performed the two-pollutant models to analyze these effects by adjusting for SO_2 (NO_2 or O_3), individually. Secondly, we used different degrees of freedom (5–7) for mean temperature in the main model. Thirdly, we added the calendar year in our main model to adjust for long-term effects.

R software (version 3.6.1) was used to perform all the statistical analyses with the "mgcv" package for GAM models and the "metafor" package for meta-analyses. Two-sided tests with p value <0.05 was considered as statistically significant.

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AUTHOR CONTRIBUTIONS

LW and HL take full responsibility for the content of the manuscript, including data and analysis. YY, HL, JQ, and LW contributed to study design, project administration, methodology, data analysis and writing original draft; ZR, JL, and YL contributed to methodology, data analysis and visualization; PY, SZ, and RL contributed to methodology and revising the original draft. All authors have approved the final version of the manuscript to be submitted.

DECLARATION OF INTERESTS

The authors declare no competing interests.

SUPPLEMENTAL INFORMATION

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