



Article

# An Assessment of Annual Mortality Attributable to Ambient PM<sub>2.5</sub> in Bangkok, Thailand

Nathaniel R. Fold <sup>1,2</sup>, Mary R. Allison <sup>1,2</sup>, Berkley C. Wood <sup>1,2</sup>, Pham T. B. Thao <sup>2,\*</sup>,  
Sebastien Bonnet <sup>2</sup>, Savitri Garivait <sup>2</sup>, Richard Kamens <sup>1</sup> and Sitthipong Pengjan <sup>2</sup>

<sup>1</sup> Institute for the Environment, University of North Carolina at Chapel Hill, Chapel Hill, NC 27599, USA; nrfold@gmail.com (N.R.F.); mary.allison27@gmail.com (M.R.A.); berkleyw@live.unc.edu (B.C.W.); richkamens@gmail.com (R.K.)

<sup>2</sup> The Joint Graduate School of Energy and Environment (JGSEE), King Mongkut's University of Technology Thonburi, 126 Pracha Uthit Road, Bangmod, Thungkru, Bangkok 10140, Thailand; sebastien@jgsee.kmutt.ac.th (S.B.); savitri\_g@jgsee.kmutt.ac.th (S.G.); sitthipong.ma@hotmail.com (S.P.)

\* Correspondence: pham.tha@kmutt.ac.th or ptbthao@gmail.com; Tel.: +66-24708309-10 (ext. 4138)

Received: 14 July 2020; Accepted: 29 September 2020; Published: 6 October 2020



**Abstract:** Multiple studies indicate that PM<sub>2.5</sub> is the most deleterious air pollutant for which there are ambient air quality standards. Daily concentrations of PM<sub>2.5</sub> in Bangkok, Thailand, continuously exceed the World Health Organization (WHO) and the Thai National Ambient Air Quality Standards (NAAQSS). Bangkok has only recently begun to measure concentrations of PM<sub>2.5</sub>. To overcome this paucity of data, daily PM<sub>2.5</sub>/PM<sub>10</sub> ratios were generated over the period 2012–2018 to interpolate missing values. Concentration-response coefficients ( $\beta$  values) for PM<sub>2.5</sub> versus non-accidental, cardiopulmonary, and lung cancer mortalities were derived from the literature. Values were also estimated and were found to be comparable to those reported in the literature for a Chinese population, but considerably lower than those reported in the literature from the United States. These findings strongly suggest that specific regional  $\beta$  values should be used to accurately quantify the number of premature deaths attributable to PM<sub>2.5</sub> in Asian populations. Health burden analysis using the Environmental Benefits Mapping and Analysis Program (BenMAP) showed that PM<sub>2.5</sub> concentration in Bangkok contributes to 4240 non-accidental, 1317 cardiopulmonary, and 370 lung cancer mortalities annually. Further analysis showed that the attainment of PM<sub>2.5</sub> levels to the NAAQSS and WHO guideline would reduce annual premature mortality in Bangkok by 33% and 75%, respectively.

**Keywords:** daily PM<sub>2.5</sub>/PM<sub>10</sub> ratios; concentration-response coefficients; health burden; health benefit; Bangkok

## 1. Introduction

Globally, it is estimated that fine particles with aerodynamic diameters equal to or less than 2.5  $\mu\text{m}$  (PM<sub>2.5</sub>) are responsible for approximately 3 to 9 million excess annual deaths [1–7]. It is thus not surprising that PM<sub>2.5</sub> is considered one of the most dangerous pollutants [8]. Fine particles have the ability to enter the smallest airways and alveoli within the lungs, and ultrafine particles can subsequently diffuse into the bloodstream [9]. PM<sub>2.5</sub> has been found to cause respiratory disease, specifically acute lower respiratory infection and chronic obstructive pulmonary disease, cardiovascular disease, specifically ischemic heart disease, cerebrovascular disease and stroke, and lung cancer [8–12].

Megacities around the world are rapidly expanding. This is particularly the case in Asian countries, where population growth is driving the need for continuous urbanization. Bangkok, the capital city of Thailand with a growing population of about 6 million inhabitants, [13] is on the cusp of emerging as the world's next megacity. It is indeed witnessing major infrastructure development, which accounts for the

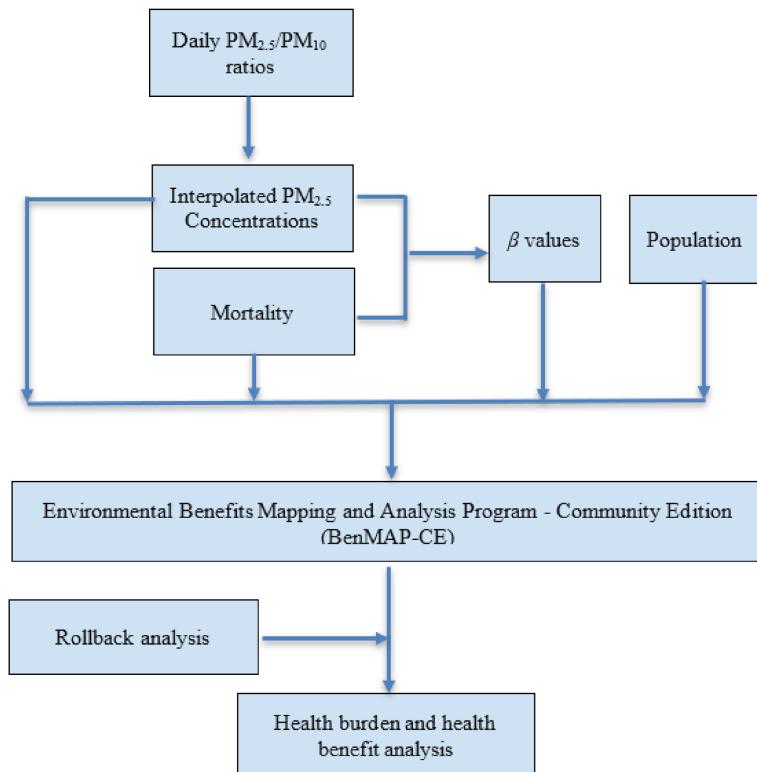
majority of the country's urbanization [14]. When one includes greater Bangkok, which extends beyond the formal Bangkok governmental boundary, there are more than 10 million people. Such expansion is associated with a number of environmental challenges, with air pollution becoming a notorious issue. In recent years, there have been increasing concerns over the situation of air quality in Bangkok. Pollution has risen to harmful levels resulting in unsafe concentrations of PM<sub>2.5</sub>, particularly during the dry season, as indicated by the Thai Pollution Control Department. Increased PM<sub>2.5</sub> concentrations have been linked to consequential impacts that cause premature deaths [13,15]. Since 2012, pollution levels of PM<sub>2.5</sub> have been monitored at various ambient air pollution stations around the country. However, the number of such stations is still limited compared to that of PM<sub>10</sub>. In 2015, only 12 stations were equipped to monitor PM<sub>2.5</sub>, 3 of which were located within the formal boundary of Bangkok. In 2018, the number of PM<sub>2.5</sub> monitoring stations in Bangkok had increased to 19, thus providing better coverage of PM<sub>2.5</sub> levels in the city. During 2016–2019, according to the 2018 Thailand State of Pollution Report, the 24-h NAAQSs standard of 50 µg/m<sup>3</sup> was exceeded approximately 50 days per year. Maximum daily concentrations above 100 µg/m<sup>3</sup> were observed during the dry season (November to April).

Health impacts related to unsafe air quality have been the subject of many studies, and focus on correlating particulate matter concentrations and premature mortality as well as related economic losses [8,12,14–30]. Some of these studies were performed using Thai populations [27–30]. Vichit-Vadakan et al. [27], in 2008, under the Public Health and Air Pollution program in Asia (PAPA), reported on the mortality impact of particle exposures with aerodynamic diameters equal to or less than 10 µm (PM<sub>10</sub>). They observed a 1.3% increase in mortality risk per 10 µg/m<sup>3</sup> increase in PM<sub>10</sub>. This is higher than for similar exposures in some Western cities, as reported by Schwartz [23]. Wong et al. [29] investigated the excess risks associated with sulfur dioxide (SO<sub>2</sub>), ozone (O<sub>3</sub>), and PM<sub>10</sub> also under the PAPA project for three main causes of mortality: non-accidental, cardiovascular disease, and respiratory disease. This study included Bangkok and three cities in China: Hong Kong, Shanghai, and Wuhan. The excess risks identified for Bangkok were found to be 2–5 times higher than those identified for China [29]. Another study by Guo et al. [30], in 2014, focused on assessing the excess risks associated with NO<sub>x</sub>, SO<sub>2</sub>, O<sub>3</sub>, and PM<sub>10</sub> on mortality, including non-accidental, cardiovascular disease, and respiratory disease for 18 provinces in Thailand. They confirmed that air pollutants had significant short-term impacts on non-accidental mortality, and the effect was higher during the winter, compared to the rainy season. The study also highlighted that O<sub>3</sub> is related to cardiovascular mortality, while PM<sub>10</sub> is significantly related to respiratory mortality [30]. In the United States of America, Fann et al. [31] used the U.S. Environmental Protection Agency's Environmental Benefits Mapping and Analysis Program (BenMAP) to investigate the health burden and benefits of PM<sub>2.5</sub>. However, to this day, the effects of PM<sub>2.5</sub> on mortality in Thailand, specifically in Bangkok, have not been well-documented.

This study investigates annual mortality associated with PM<sub>2.5</sub> in Bangkok based on available air quality monitoring data. There are currently no such studies with PM<sub>2.5</sub>. The specific objectives are (1) generate missing PM<sub>2.5</sub> data by interpolation applied to existing PM<sub>2.5</sub> and PM<sub>10</sub> data to determine daily PM<sub>2.5</sub>/PM<sub>10</sub> ratios, (2) investigate the association of PM<sub>2.5</sub> with meteorological parameters, (3) identify relative risks and resulting concentration-response coefficients ( $\beta$  values) for all-cause, cardiopulmonary, and lung cancer mortalities, and (4) determine the annual mortality attributable to PM<sub>2.5</sub> pollution utilizing BenMAP-CE.

## 2. Methodology

The specific steps to quantify mortality attributable to PM<sub>2.5</sub> in Bangkok are illustrated in Figure 1. It begins with daily PM<sub>2.5</sub>/PM<sub>10</sub> ratios, interpretation of PM<sub>2.5</sub> values, and ends with a health benefits analysis.

**Figure 1.** Workflow of the study procedure.

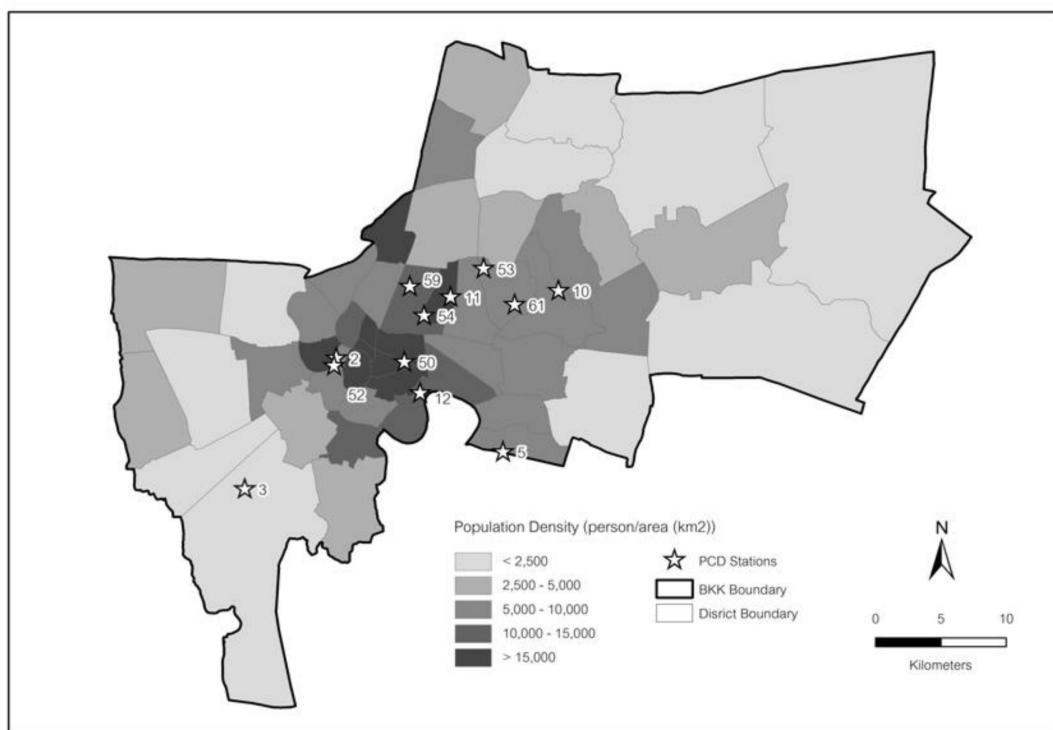
### 2.1. Estimation of Daily PM<sub>2.5</sub>/PM<sub>10</sub> Ratios and PM<sub>2.5</sub> Interpolation

As seen in Figure 2, fixed-site monitoring stations are clustered around Bangkok, especially in the central part of the city. Figure 2 additionally provides the associated sub-district population density nearby to each monitoring station. PM<sub>2.5</sub> was measured by the Beta Ray attenuation method, following the United States Environmental Protection Agency (USEPA) reference method. In 2008, the USEPA designated this method as a federal equivalent method for measuring PM<sub>2.5</sub> according to the US Federal register, 73 FR 22362, EQPM-0308-170 method. The equipment is from two main manufacturers, i.e., MetOne and Thermo. For the former, PM<sub>2.5</sub> concentrations were recorded on an hourly basis. For the latter, PM<sub>2.5</sub> concentrations were recorded every 10–15 min, and hourly average concentrations were calculated accordingly. Information on PM<sub>2.5</sub> monitoring data and associated statistical values are presented in Table 1. We focused on data from 2012 to 2018 because all available monitoring stations collected data during these years.

**Table 1.** Descriptive statistics of PM<sub>2.5</sub> measurements in Bangkok during 2012–2018.

Year	No. of Station	Missing Data (%)	Statistical Values ( $\mu\text{g}/\text{m}^3$ )	
			Mean ( $\pm\text{SD}$ )	Q1, Q3, and IQR
2012	1	90.3	33.7 ( $\pm 14.0$ )	24.2, 38.5, and 14.3
2013	1	92.0	35.5 ( $\pm 17.7$ )	22.5, 41.3, and 18.9
2014	2	88.5	30.6 ( $\pm 16.1$ )	20.7, 39.4, and 18.8
2015	3	73.2	28.1 ( $\pm 15.4$ )	17.5, 35.8, and 18.4
2016	5	61.4	27.7 ( $\pm 14.8$ )	16.8, 34.3, and 17.5
2017	6	46.4	26.1 ( $\pm 14.2$ )	15.6, 33.5, and 17.9
2018	10	22.5	27.2 ( $\pm 15.3$ )	16.6, 33.7, and 17.0

SD: Standard deviation; Q1, Q3: First and third quartiles; IQR: Interquartile range.



**Figure 2.** Population density and air quality monitoring stations over the study domain (stations include 59—PhayaThai; 02—ThonBuri; 03—Bangkhuntien; 05—Bang Na; 61—WangThonglang; 10—BangKapi; 11—DinDaeng; 12—Yannawa; 50—PathumWan; 52—ThonBuri; 53—LatPhrao; 54—DinDaeng).

During the years observed, the average PM<sub>2.5</sub> concentration was 27.9 ( $\pm 16.8$ )  $\mu\text{g}/\text{m}^3$  with maximum and minimum values of 170.7  $\mu\text{g}/\text{m}^3$  and 2.15  $\mu\text{g}/\text{m}^3$ , respectively. The median concentration for PM<sub>2.5</sub> was 24.0  $\mu\text{g}/\text{m}^3$  with first and third quartiles of 16.9  $\mu\text{g}/\text{m}^3$  and 35.0  $\mu\text{g}/\text{m}^3$ , respectively (interquartile range (IQR) = 18.0  $\mu\text{g}/\text{m}^3$ ). As the quality of data varied between stations, the inclusion of specific data was based on the following criteria. A station's PM<sub>2.5</sub> data were accepted only if it contained at least 70% of the daily PM<sub>2.5</sub> values in the original data. Daily means were only included if a station had at least 17 hourly PM<sub>2.5</sub> measurements for each day. PM<sub>2.5</sub> values were estimated from the average ratio of all available PM<sub>10</sub> and PM<sub>2.5</sub> values from other stations for that day. According to the USEPA, the PM<sub>2.5</sub>/PM<sub>10</sub> ratio should fall between a range of 0.50–0.65 and must be applied to data from the same year [32]. Previous studies used a fixed annual PM<sub>2.5</sub>/PM<sub>10</sub> ratio [33–35].

## 2.2. Estimation of Correlation between PM<sub>2.5</sub> and Meteorological Conditions

Each ambient air quality station from the Pollution Control Department also measured a set of meteorological variables, including wind speed, wind direction, relative humidity, temperature, and rainfall, from 2012 to 2018. Wind direction and wind speed at each monitoring station were sampled 10 m above the ground with a 2-dimensional (2D) potentiometer wind vane and cup propeller for respective measurements. Temperature and relative humidity were measured 2 m above the ground using a multistage solid-state thermistor and a thin-film polymer capacitor for respective measurements. Rainfall was measured three meters above the ground with a tipping bucket. The equipment is from two main manufacturers, i.e., Met One and Thermo. Data were continuously recorded at an hourly frequency.

Meteorological variables had a seasonal influence on PM<sub>2.5</sub> concentrations. Seasonality was defined for each month based on the weather conditions in a given month. Table 2 depicts the monthly averages of meteorological occurrences and associated PM<sub>2.5</sub> concentrations. The dry/cool season was associated with lower temperatures and reduced cumulative rainfall (averages of 28 °C and 36 mm), as

compared to the rest of the year. The hot season was associated with elevated temperatures (average of 30 °C) and was higher than the rest of the year. The rainy season was characterized by high levels of cumulative precipitation, averaging 225 mm during each month involved. June had characteristics of both the rainy and hot season, with an average temperature of 30 °C and rainfall of 197 mm. It was, therefore, assigned a mixed season classification of "Hot and Rainy".

**Table 2.** Seasonal variance in meteorological indicators and PM<sub>2.5</sub> concentrations in Bangkok.

Season	Month	Average PM <sub>2.5</sub> ( $\mu\text{g}/\text{m}^3$ )	Average % Relative Humidity	Average Wind Direction (°)	Average Temperature (°C)	Average Wind Speed (m/s)	Monthly Cumulative Rainfall (mm)
Dry, Cool	January	40.8	62.0	165	27.7	1.1	40.9
Dry, Cool	February	39.1	62.7	169	28.9	1.1	14.3
Hot	March	31.0	66.7	185	30.2	1.2	47.0
Hot	April	26.7	65.5	186	31.1	1.1	72.6
Hot	May	17.9	67.2	194	31.0	1.1	132.2
Hot, Rainy	June	18.0	69.4	210	30.0	1.1	197.4
Rainy	July	18.1	70.8	219	29.3	1.1	151.3
Rainy	August	17.4	71.3	220	29.2	1.1	185.2
Rainy	September	18.2	74.7	212	28.7	0.9	314.6
Rainy	October	26.6	73.6	171	28.7	0.8	277.6
Dry, Cool	November	28.8	66.0	156	29.1	0.9	70.9
Dry, Cool	December	39.8	58.6	154	28.0	1.0	20.5

### 2.3. Mortality Data in Bangkok

Individual mortality records, including data on the location of death, age, sex, and primary causes of death from 2007–2016, were obtained from the Thailand Ministry of Public Health for the entire Bangkok metropolis area. There were approximately 460,000 non-accidental deaths during this time. The mean age was identified to be 64 ( $\pm 20$ ) years with a median age of 69 years, and first and third quartiles of 53 years and 79 years, respectively (IQR = 26 years). More men died during this period representing 59.3% of the total number of deaths. All deaths in the data set were classified as all-cause non-accidental, with cardiopulmonary disease and lung cancer contributing 15.7% and 3.2% of the mortalities, respectively. Mortality data in Bangkok are recorded by the Ministry of Public Health in the civil registration database. They are certified based on the death certificates. According to this information, it was assumed that the subjects registered in Bangkok had also lived and died in Bangkok. Each mortality datum was assigned a code classifying the cause of death according to the International Classification of Diseases, Tenth Revision (ICD-10) [36]. Previous epidemiological studies in China [10], India [8], and the United States of America [12,14,25,26] showed associations between PM<sub>2.5</sub> concentration and cause-specific mortalities. Specifically, concordance was noted between PM<sub>2.5</sub> pollution and cardiopulmonary diseases (ICD-10: I10-I15, I20-I52, I60-I70), and lung cancer (ICD-10: C33-C34, D022-D024). Here we also examined the mortality causes of cardiopulmonary disease and lung cancer, and these were coupled with all-cause (non-accidental) mortality (ICD: A00-R99) as a baseline reference. Mortality data were limited to an age range of 30–99 years since specific concentration-response variables from previous studies [10,25] focused on this age range. The age range 30–99 years accounts for 94.6% of the total number of deaths during 2007–2016, with approximately 440,000 deaths. It comprised 54.2% males and 45.8% females. For the age range 30–99 years, the mean age was 67 ( $\pm 15$ ) years with a median of 70 years, and first and third quartiles of 56 years and 80 years, respectively (IQR = 24 years). Regarding cardiopulmonary mortality, ages in the range 30–99 years represented 96.3% of the total number of deaths in this category; the range 0–30 years accounted for the remaining 3.7%. For lung cancer mortality, the age range 30–99 years represented 98.4% of the total number of deaths in this category; the age range 0–30 years accounted for the remaining 1.6%. As a significant proportion of the mortalities observed in this study were attributable to the age range 30–99 years, the focus of the investigations of this study was on this age range. We determined a daily sum of each specific mortality category according to each ICD-10 mortality code, then determined each

category's incidence rate by dividing the number of deaths in each specific ICD-10 category by the total population during the same year.

#### 2.4. Health Impact Assessment Using BenMAP

BenMAP-CE, a Geographic Information System (GIS)-based tool that estimates health impacts resulting from air pollution, was used to determine the links between PM<sub>2.5</sub> concentrations and mortality. BenMAP-CE utilizes a health impact function that incorporates monitored air-quality data, population data, baseline incidence rates, and an effect estimate to calculate health impacts [15,37].

Relative risk (RR) is a ratio that compares, in this case, the mortality of a PM<sub>2.5</sub> exposed group (at some PM<sub>2.5</sub>) to the mortality of a group with no PM<sub>2.5</sub> exposure. The slope of the natural log of RR versus PM<sub>2.5</sub> is called  $\beta$ , or the concentration-response (C-R) coefficient, and it is frequently used across different studies to compare the strength of the relative risk for a similar change in PM<sub>2.5</sub> exposure ( $\Delta\text{PM}_{2.5}$ ).  $\beta$  can also be calculated from  $\beta = \frac{\ln(RR)}{\Delta\text{PM}_{2.5}}$ . A  $\Delta\text{PM}_{2.5}$  of 10  $\mu\text{g}/\text{m}^3$  is often used, but  $\Delta\text{PM}_{2.5}$  can be used to estimate the reduction in mortality from an ambient value to some target or standard. In BenMAP-CE,  $\beta$  is used to calculate the change in the incidence rate, as a function of  $\Delta\text{PM}_{2.5}$  as per Equation (1):

$$\Delta Y = Y_0 (1 - e^{-\beta \Delta\text{PM}_{2.5}}) * pop \quad (1)$$

where

$\Delta Y$  is the change in incidence rate;

$Y_0$  is the baseline incidence rate of the health effects;

$\beta$  is the C-R coefficient;

$pop$  is the exposed population, and

$\Delta\text{PM}_{2.5}$  is the change in PM<sub>2.5</sub> concentration to some target or health standard value.

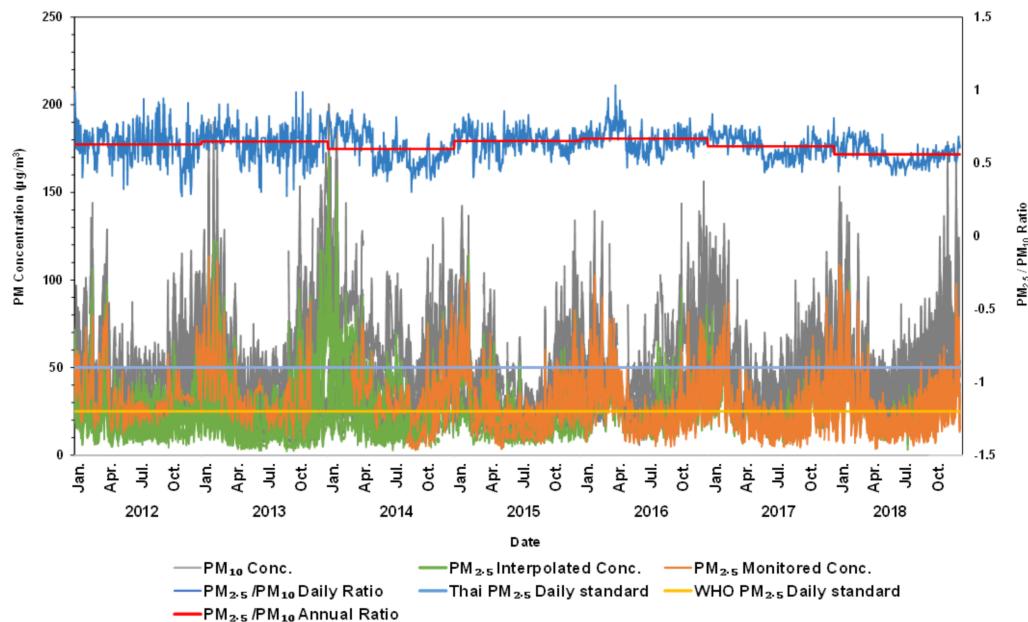
The year 2016 was selected for the health burden and benefit analysis based on the completeness of data collected for that year. Baseline mortality data were obtained from the Ministry of Health and population data from the National Statistic Office. Concentration-response coefficients were derived as described above based on RR values retrieved from the literature. Estimates were also determined for Bangkok, as detailed in Section 3.3. The  $\beta$  values thereby obtained were used as input into Ben-MAP to assess the annual mortality endpoints considered in this study.

### 3. Results and Discussion

#### 3.1. PM<sub>2.5</sub> Interpolation

Figure 3 shows the original available PM<sub>2.5</sub> and PM<sub>10</sub> data from 2012 to 2018, as well as annual ratios and daily ratios. The graph shows gap-filled data (PM<sub>2.5</sub> interpolated in green) compared to non-gap filled data (PM<sub>2.5</sub> original in orange). Further, the Thai and WHO PM<sub>2.5</sub> air quality standards of 50  $\mu\text{g}/\text{m}^3$  and 25  $\mu\text{g}/\text{m}^3$ , respectively, are denoted in Figure 3 to indicate days when air quality exceeded each set standard. PM<sub>2.5</sub> data had a diminished density of data points during the first three years, which then increased through 2018. The above described daily ratio approach permitted the interpolation of more than 8000 PM<sub>2.5</sub> values from all stations that were not previously available. The PM<sub>2.5</sub>/PM<sub>10</sub> relationship was determined by generating a linear plot of PM<sub>10</sub> as the independent variable and PM<sub>2.5</sub> as the dependent variable, with PM<sub>2.5</sub>/PM<sub>10</sub> as the slope of the line. Ten-fold cross-validation was run on the data utilizing a 90–10 model where 90% of the data were trained, and the residual 10% was tested using a generated PM<sub>2.5</sub>/PM<sub>10</sub> ratio from the trained data. Cross-validation was carried out over 10 iterations, and the root-mean-squared error (RMSE) and coefficient of determination ( $R^2$ ) were averaged over the trials. When using the annual PM<sub>2.5</sub>/PM<sub>10</sub> ratio to interpolate PM<sub>2.5</sub> values, an accompanying  $R^2$  value of 0.634 ( $\pm 0.042$ ) and an RMSE of 15.137 ( $\pm 2.51$ )  $\mu\text{g}/\text{m}^3$  were observed. In contrast, the daily ratio was proven to be significantly more accurate

at predicting interpolated values with an averaged  $R^2$  value of 0.866 ( $\pm 0.018$ ) and an RMSE of 3.607 ( $\pm 0.891$ )  $\mu\text{g}/\text{m}^3$ . Data enhancement from the daily ratio allowed for more accurate predictions of  $\text{PM}_{2.5}$  concentrations, which further strengthened the relationships between variables analyzed in this study.



**Figure 3.** Daily average  $\text{PM}_{2.5}$  and  $\text{PM}_{10}$  concentrations, and  $\text{PM}_{2.5}/\text{PM}_{10}$  ratios during 2012–2018.

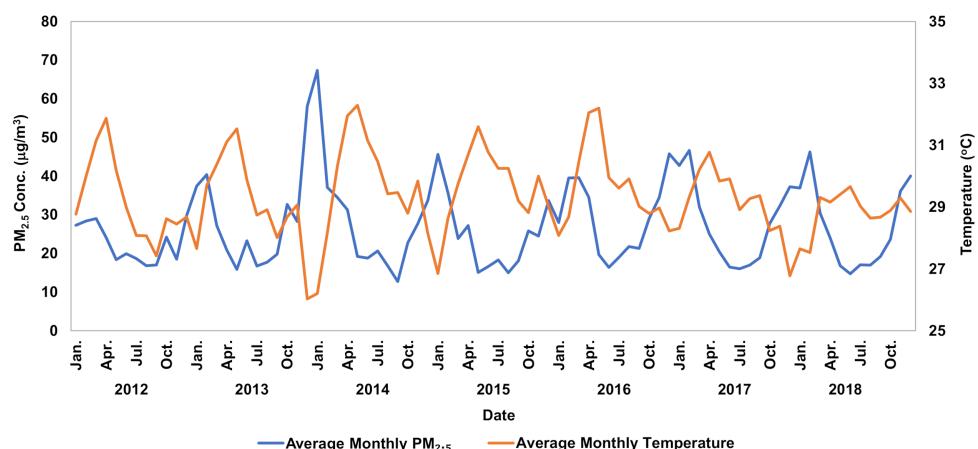
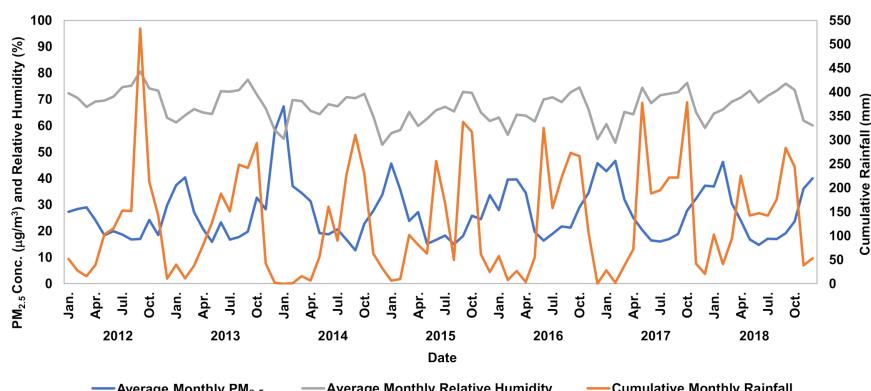
During the dry and cool months,  $\text{PM}_{2.5}$  concentration was high, and the annual ratio underestimated  $\text{PM}_{2.5}$  levels. However, during the rainy season, there were diminished concentrations of  $\text{PM}_{2.5}$ , and the annual ratio overestimated  $\text{PM}_{2.5}$  values. Employing the daily ratio in place of the annual ratio permitted us to generate more accurate data, which improved mortality estimates using BenMAP-CE.

### 3.2. Correlation between $\text{PM}_{2.5}$ and Meteorological Conditions

Observed correlations between particulate matter and meteorological factors showed a negative linear correlation between all meteorological variables and particulate matter. Relative humidity, temperature, and cumulative rainfall showed the strongest correlations with changes in pollutant concentrations, with Pearson correlation coefficients of  $-0.451$ ,  $-0.240$ , and  $-0.201$ , respectively (Table 3).  $\text{PM}_{2.5}$  concentrations had an inverse relationship with changes in temperature and relative humidity (Figures 4 and 5). Although the temperature in Bangkok varied less than  $10^\circ\text{C}$  (mostly between  $25$  and  $30^\circ\text{C}$ ) during the period observed, it was evident that as temperature increased,  $\text{PM}_{2.5}$  concentrations decreased and vice-versa. This trend was attributed to decreased mixing height from temperature inversions created by a change in temperature. These inversions trapped pollution and restricted vertical mixing, making pollution stagnant, thus increasing  $\text{PM}_{2.5}$  concentrations [38,39]. Increased rainfall reduced  $\text{PM}_{2.5}$  concentration through wet deposition by washing out the particles from the atmosphere [40]. Stagnation was perpetuated by lower wind speeds, although a decrease in wind speed did not cause an immediate increase in  $\text{PM}_{2.5}$  concentration because there was a brief lag period in which  $\text{PM}_{2.5}$  concentrations would build up. This lag became more significant throughout the study as stagnation in the atmosphere increased; overall, wind speed decreased by 31% from 2012 to 2018. Future climate is expected to become more stagnant, exacerbating air pollution and subsequent health problems [41,42]. The daily ratio accounted for the above meteorological occurrences and better depicted the daily fluctuations in  $\text{PM}_{2.5}$  concentration.

**Table 3.** Pearson correlations coefficient between particulate matter and meteorological factors.

Factors	PM <sub>2.5</sub>	PM <sub>10</sub>	Relative Humidity	Wind Direction	Temperature	Wind Speed	Rain
PM <sub>2.5</sub>	1.000						
PM <sub>10</sub>	0.944	1.000					
Relative Humidity	-0.451	-0.462	1.000				
Wind Direction	-0.353	-0.370	0.221	1.000			
Temperature	-0.240	-0.255	-0.170	0.291	1.000		
Wind Speed	-0.208	-0.295	-0.174	0.153	0.218	1.000	
Daily Rainfall	-0.201	-0.201	0.485	0.032	-0.261	-0.215	1.000

**Figure 4.** Monthly variation of PM<sub>2.5</sub> concentrations and temperatures during 2012–2018.**Figure 5.** Monthly variation of PM<sub>2.5</sub> concentrations and relative humidity with cumulative monthly rainfall during 2012–2018.

### 3.3. Health Benefit Analysis

In this study, we initially compared the US and Chinese values in BenMap, which represent different western and eastern global populations. These values were obtained by including other mortality risk factors such as sex, education, smoking, lifestyle, socioeconomic status, obesity, etc. As seen in Table 4, the Chinese  $\beta$  values [10] were much lower than the ones used for the United States [25]. The increment rollback function on Ben-MAP was applied to determine the impact of a 10  $\mu\text{g}/\text{m}^3$  rollback in PM<sub>2.5</sub> for the year 2016 (Table 4). This function reduced all PM<sub>2.5</sub> observations by the same increment. A 10  $\mu\text{g}/\text{m}^3$  rollback in Bangkok PM<sub>2.5</sub> concentration utilizing the estimated Bangkok  $\beta$  values resulted in a 1.5%, 3.1%, and 4.1% decrease in annual mortality for non-accidental, cardiopulmonary disease, and lung cancer, respectively.

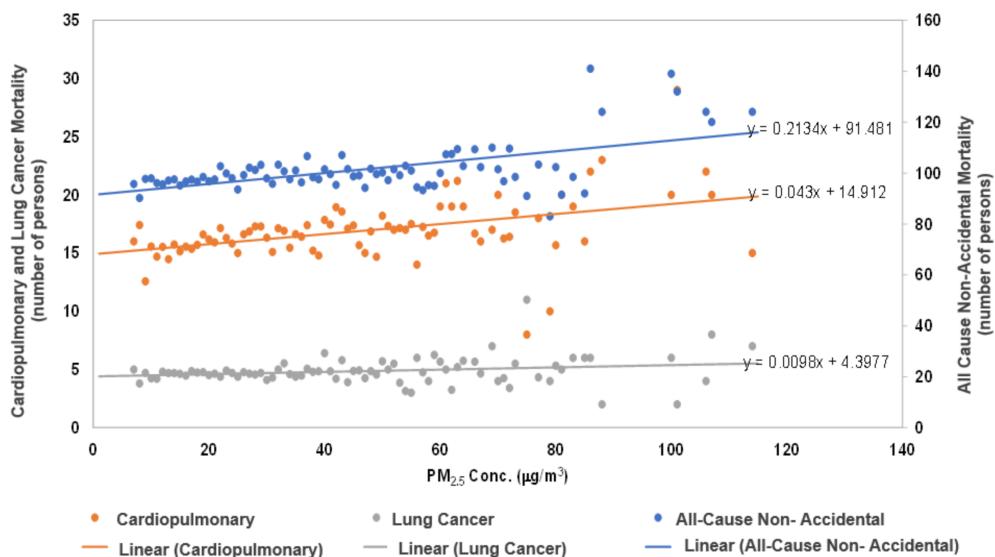
**Table 4.** Avoided deaths in Bangkok from a  $10 \mu\text{g}/\text{m}^3$  rollback of  $\text{PM}_{2.5}$  in the year 2016.

Health Endpoints	United States <sup>a</sup>		China <sup>b</sup>	
	$\beta$ Values (Standard Deviation)	Avoided Mortality	$\beta$ Values (Standard Deviation)	Avoided Mortality
Mortality, All-cause non-accidental	0.00583 ( $\pm 0.00096$ )	2772	0.000896 ( $\pm 0.000538$ )	374
Mortality, cardiopulmonary	0.0122 ( $\pm 0.00135$ )	1686	0.002547 ( $\pm 0.006250$ )	316
Mortality, lung cancer	0.0131 ( $\pm 0.00379$ )	291	0.00334 ( $\pm 0.001758$ )	67

<sup>a</sup>: Pope et al. [25]; <sup>b</sup>: Cao et al. [10].

Differences in the number of avoided deaths in Bangkok were observed depending on the  $\beta$  values used. The number of avoided deaths in Bangkok, calculated from the Chinese  $\beta$  values [10], were found to be seven- (non-accidental), five- (cardiopulmonary), and four-times (lung cancer) lower when using  $\beta$  values reported in the literature for the United States [25].

It is also possible to obtain simple RR values from the Bangkok population directly, by plotting Bangkok mortality data versus Bangkok  $\text{PM}_{2.5}$ . Average daily mortality was computed for every  $1 \mu\text{g}/\text{m}^3$  increase in  $\text{PM}_{2.5}$  over the range of concentrations observed. This produced trends, as shown in Figure 6. Specific relations were observed between  $\text{PM}_{2.5}$  concentrations and all non-accidental mortality, cardiopulmonary diseases, and lung cancer. The incorporation of interpolated  $\text{PM}_{2.5}$  concentrations allowed for improvement in the  $R^2$  significance for all the relationships between particulate matter and cause of death in this study, which provided strengthened conclusions. Initial  $R^2$  values between  $\text{PM}_{2.5}$  and all-cause non-accidental, cardiopulmonary, and lung cancer mortality classifications were 0.324, 0.184, and 0.098, respectively. Following the adjustment of  $\text{PM}_{2.5}$  data through interpolation, these values increased to 0.554, 0.364, and 0.162.



**Figure 6.** Relationship between All-Cause Non-Accidental, Cardiopulmonary, and Lung Cancer Mortalities and  $\text{PM}_{2.5}$  concentrations in Bangkok.

From the ratio of the mortality response on the y-axis and the y-intercept (unexposed  $\text{PM}_{2.5}$  mortality) in Figure 6, it was possible to compute RR values for a given  $\Delta\text{PM}_{2.5}$ . These values were then utilized to yield  $\beta$  values and estimates of mortality attributable to a given  $\text{PM}_{2.5}$  exposure. The authors are aware that although this approach is rudimentary and does not include other RR mortality factors, as per the Chinese and United States studies, it is very interesting that  $\beta$  values (standard deviations in

(parentheses) obtained in this manner ( $0.001743 (\pm 0.0007458)$ ,  $0.002284 (\pm 0.003878)$ ,  $0.003134 (\pm 0.002754)$ ), for all-cause non-accidental, cardiopulmonary, and lung cancer mortality, were more similar with those determined from the Chinese population by Cao et al. [10]. Through generating our own  $\beta$  values, we were able to compare the associated population health risks from air pollution to other concentration-response values determined in studies from other countries.

These results suggest that populations in Bangkok and China tended to be more similarly affected by the same  $PM_{2.5}$  exposures, and were different from the US population. This observation is consistent with the study by Newell (2017) [43], which found regional differences in impacts on cardiorespiratory mortality and morbidity are observed for the same increase in particulate matter concentration. Populations in different regions of the world have a myriad of different traits (i.e., physiology, risk factors, lifestyle, etc.), which, apparently, influence their susceptibility and mortality response to  $PM_{2.5}$  exposures.

As reported in Table 5, anthropogenic  $PM_{2.5}$  levels above the background concentration of  $2.15 \mu g/m^3$  in Bangkok using  $\beta$  values determined in this study, resulted in 4240 non-accidental mortalities, 1317 cardiopulmonary deaths, and 370 lung cancer mortalities. In comparison to meeting the Thailand annual standard of  $25 \mu g/m^3$ , meeting the WHO annual guideline of  $10 \mu g/m^3$  would result in a significant reduction in premature mortality. While meeting the Thai annual standard is a goal that the Thai government is working towards, it is notable that this standard does not represent a  $PM_{2.5}$  level that is completely safe. Meeting the more stringent WHO annual standard is estimated to have a three-fold number of avoided non-accidental deaths. Meeting the Thai annual standard of  $PM_{2.5}$  would enable a 25% reduction in premature mortality, whereas meeting the WHO annual guideline would contribute a 71% reduction in premature mortality each year.

**Table 5.** Health burden and avoided deaths in 2016 due to rollbacks to the Thai National Ambient Air Quality Standards (NAAQS) and the World Health Organization (WHO) guidelines.

Health Endpoint	Health Burden	Thailand Standard $25 \mu g/m^3$	WHO Guideline $10 \mu g/m^3$
	Deaths * (95% CI)	Avoided Deaths * (95% CI)	Avoided Deaths * (95% CI)
Mortality, non-accidental	4240 (1219–6938)	1393 (593–2691)	3159 (893–5248)
Mortality, cardiopulmonary	1317 (1065–1551)	360 (284–434)	959 (769–1140)
Mortality, lung cancer	370 (175–530)	102 (45–156)	270 (125–397)

\* Specific for age 30–99.

### 3.4. Uncertainty of the Analysis

BenMAP-CE required many data inputs. With each input, a layer of uncertainty is added that rests on the quality of the data. Mortality data had general limitations regarding the specificity of the district in which the mortality occurred. Because of this, the calculated incidence rates were generalized to the entire Bangkok province, as opposed to specific districts within the province. Of the available data, there were long periods in which  $PM_{2.5}$  values were not recorded. This was especially obvious between 2012 and 2014 when most monitoring stations only collected  $PM_{10}$  data. Missing  $PM_{2.5}$  concentration values were estimated using a daily  $PM_{2.5}/PM_{10}$  ratio, which allowed for a continuous data set of  $PM_{2.5}$ . For the BenMAP analysis,  $PM_{2.5}$  monitoring data from five monitoring stations in the year 2016 were used in accordance with the criteria of quality set out in this study. These five stations are located in central Bangkok and are not evenly dispersed. The Voronoi Neighbor Averaging (VNA) algorithm is an innate function of BenMAP-CE that was used to remediate the lack of  $PM_{2.5}$  monitoring stations in all 50 districts of the city. To determine the non-anthropogenic background concentrations of  $PM_{2.5}$ , we used the lowest value recorded ( $2.15 \mu g/m^3$ ) from the 11  $PM_{2.5}$  monitoring stations in Bangkok over 2012–2018. This procedure was followed because, to our knowledge, there is no established background concentration of  $PM_{2.5}$  in Bangkok. In regards to the health impact function, a key factor is the  $\beta$  value. Ideally, estimates of C-R coefficients should take into account other mortality covariates that could help

provide additional insights into estimated Thai  $\beta$  values, such as male/female, BMI (body mass index), smoking/nonsmoking, alcohol intake, hypertension, educational level, individual socioeconomic status, other health conditions, medications, behaviors, etc. These well-known mortality determinants are missing in this analysis. Additional studies are needed to reduce their uncertainty.

#### 4. Conclusions and Recommendations

This study used an innovative method for interpolating PM<sub>2.5</sub> data based on seasonality and daily concentration changes in PM<sub>2.5</sub> and PM<sub>10</sub>. Interpolating data points from this daily ratio, instead of annual ratios allowed for more accurate predictions of missing PM<sub>2.5</sub> concentrations. With regard to human health, this study is the first health-related study linking annual mortality and PM<sub>2.5</sub> in Bangkok. The results showed that by decreasing the annual PM<sub>2.5</sub> concentration in Bangkok to the Thai NAAQS and WHO air quality standards, a consequential reduction of 1393 and 3159 in premature mortality attributable to unsafe PM<sub>2.5</sub> levels can be achieved. Our results show that populations in Bangkok and China are more similarly affected by the same PM<sub>2.5</sub> exposures than the population of the United States, and strongly suggest that regional  $\beta$  values be used in estimating PM<sub>2.5</sub> mortality impacts.

Further studies should focus on investigating how PM<sub>2.5</sub> may affect population health on episodic bases. In this study, meteorological information specific to Bangkok was gathered and investigated, and correlation analysis provided a rudimentary understanding of the potential of meteorological variables in assessing the concentration of PM<sub>2.5</sub>. This should be further investigated in future studies. Future epidemiological cohort studies should be carried out to determine concentration-response  $\beta$  values specific to Bangkok to more accurately quantify and model the relationship between PM<sub>2.5</sub> levels and mortality. It is also very desirable to determine if these  $\beta$  values can be applied to non-Bangkok Thai populations.

**Author Contributions:** Conceptualization, S.G., P.T.B.T., R.K. and S.B.; Methodology, P.T.B.T., R.K., S.B. and S.G.; Software, P.T.B.T., N.R.F., M.R.A. and B.C.W.; Validation, P.T.B.T., R.K., S.B. and S.G.; Formal Analysis, N.R.F., M.R.A. and B.C.W.; Investigation, N.R.F., M.R.A. and B.C.W.; Data Curation, N.R.F., M.R.A., B.C.W. and S.P.; Writing—Original Draft Preparation, N.R.F., M.R.A. and B.C.W.; Writing—Review and Editing, P.T.B.T., R.K., S.B., N.R.F., M.R.A., B.C.W., S.P. and S.G.; Visualization, P.T.B.T., N.R.F., M.R.A., B.C.W. and S.P.; Supervision, R.K., S.G., P.T.B.T. and S.B.; Project Administration, S.G., R.K., P.T.B.T. and S.P.; Funding Acquisition, S.G. and R.K. All authors have read and agreed to the published version of the manuscript.

**Funding:** This research received no external funding

**Acknowledgments:** This work was financially supported by the Joint Graduate School of Energy and Environment, Centre of Excellence on Energy Technology and Environment at King Mongkut's University of Technology Thonburi, Bangkok, Thailand, through the Exchange Program of the University of North Carolina Project and Development of Thailand's Air Pollutants and Greenhouse Gases (GHGs) Emission Inventory and Projection for use in Air Quality Models Project. In addition, the authors would like to thank Orachorn Kamnoet for her assistance with the GIS work involved in this study.

**Conflicts of Interest:** The authors declare no conflict of interest.

#### References

1. World Health Organisation Ambient (Outdoor) Air Quality and Health. Available online: <https://www.who.int/news-room/fact-sheets/detail/ambient-> (accessed on 23 June 2019).
2. Cohen, A.J.; Brauer, M.; Burnett, R.; Anderson, H.R.; Frostad, J.; Estep, K.; Balakrishnan, K.; Brunekreef, B.; Morawska, L.; Pope, C.A., III; et al. Estimates and 25-year trends of the global burden of disease attributable to ambient air pollution: An analysis of data from the Global Burden of Diseases Study 2015. *Lancet* **2017**, *6736*, 1–12. [[CrossRef](#)]
3. Xing, Y.-F.; Xu, Y.-H.; Shi, M.-H.; Lian, Y.-X. The impact of PM<sub>2.5</sub> on the human respiratory system. *J. Thorac. Dis.* **2016**, *8*, E69–E74. [[CrossRef](#)] [[PubMed](#)]
4. Kloog, I.; Ridgway, B.; Koutrakis, P.; Coull, B.; Schwartz, J. Long- and short-term exposure to PM<sub>2.5</sub> and mortality. *Epidemiology* **2013**, *24*. [[CrossRef](#)] [[PubMed](#)]
5. Krzyzanowski, M.; Künzli, N.; Gutschmidt, K.; Pope, A.; Romieu, I.; Samet, J.M.; Smith, K. The global burden of disease due to outdoor air pollution. *J. Toxicol. Environ. Health Part A* **2005**, *68*, 1301–1307. [[CrossRef](#)]

6. Afshin, A.; Abate, K.H.; Cristiana, A.; Abbastabar, H. Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks for 195 countries and territories, 1990–2017: A systematic analysis for the Global Burden of Disease. *Lancet* **2018**, *392*, 1923–1924. [[CrossRef](#)]
7. Burnett, R.; Chen, H.; Szyszkowicz, M.; Fann, N.; Hubbell, B.; Pope, C.; Apte, J.; Brauer, M.; Cohen, A.; Weichenthal, S.; et al. Global estimates of mortality associated with long-term exposure to outdoor fine particulate matter. *Proc. Natl. Acad. Sci. USA* **2018**, *115*, 9592–9597. [[CrossRef](#)]
8. Limaye, V.S.; Schöpp, W.; Amann, M. Applying integrated exposure-response functions to PM 2.5 pollution in India. *Int. J. Environ. Res. Public Health* **2019**, *16*. [[CrossRef](#)]
9. Du, Y.; Xu, X.; Chu, M.; Guo, Y.; Wang, J. Air particulate matter and cardiovascular disease: The epidemiological, biomedical and clinical evidence. *J. Thorac. Dis.* **2016**, *8*, E8–E19. [[CrossRef](#)]
10. Cao, J.; Yang, C.; Li, J.; Chen, R.; Chen, B.; Gu, D.; Kan, H. Association between long-term exposure to outdoor air pollution and mortality in China: A cohort study. *J. Hazard. Mater.* **2011**, *186*, 1594–1600. [[CrossRef](#)]
11. Simkhovich, B.Z.; Kleinman, M.T.; Kloner, R.A. Air pollution and cardiovascular injury: Epidemiology, toxicology, and mechanisms. *J. Am. Coll. Cardiol.* **2008**, *52*, 719–726. [[CrossRef](#)]
12. Krewski, D.; Pope, C.A.; Thurston, G.D.; Thun, M.J. *Extended Follow-Up and Spatial Analysis of the American Cancer Society Study Linking Particulate Air Pollution and Mortality*; HEI Research Report 140; Health Effects Institute: Boston, MA, USA, 2009.
13. National Statistical Office Thailand. *Executive Summary: The 2010 Population and Housing Census*; National Statistical Office Thailand: Bangkok, Thailand, 2010.
14. Sarnat, J.A.; Schwartz, J.; Suh, H.H.; Samet, J.M.; Dominici, F.; Zeger, S.L. Fine particulate air pollution and mortality in 20 U.S. Cities. *N. Engl. J. Med.* **2001**, *344*, 1253–1254. [[CrossRef](#)] [[PubMed](#)]
15. Chen, L.; Shi, M.; Gao, S.; Li, S.; Mao, J.; Zhang, H.; Sun, Y.; Bai, Z.; Wang, Z. Assessment of population exposure to PM2.5 for mortality in China and its public health benefit based on BenMAP. *Environ. Pollut.* **2017**, *221*, 311–317. [[CrossRef](#)] [[PubMed](#)]
16. Qu, Z.; Wang, X.; Li, F.; Li, Y.; Chen, X.; Chen, M. PM2.5-related health economic benefits evaluation based on air improvement action plan in Wuhan city, middle China. *Int. J. Environ. Res. Public Health* **2020**, *17*. [[CrossRef](#)]
17. Ngo, T.H.; Tsai, P.C.; Ueng, Y.F.; Chi, K.H. Cytotoxicity assessment of PM2.5 collected from specific anthropogenic activities in Taiwan. *Int. J. Environ. Res. Public Health* **2019**, *16*. [[CrossRef](#)] [[PubMed](#)]
18. Zhang, X.; Hu, H. Combining data from multiple sources to evaluate spatial variations in the economic costs of PM2.5-related health conditions in the Beijing–Tianjin–Hebei region. *Int. J. Environ. Res. Public Health* **2019**, *16*. [[CrossRef](#)] [[PubMed](#)]
19. Piscitelli, P.; Valenzano, B.; Rizzo, E.; Maggiotto, G.; Rivezzi, M.; Corcione, F.E.; Miani, A. Air pollution and estimated health costs related to road transportations of goods in Italy: A first healthcare burden assessment. *Int. J. Environ. Res. Public Health* **2019**, *16*. [[CrossRef](#)] [[PubMed](#)]
20. Huang, R.; Hu, Y.; Russell, A.G.; Mulholland, J.A.; Odman, M.T. The impacts of prescribed fire on PM2.5 air quality and human health: Application to asthma-related emergency room visits in Georgia, USA. *Int. J. Environ. Res. Public Health* **2019**, *16*. [[CrossRef](#)]
21. Yu, G.; Wang, F.; Hu, J.; Liao, Y.; Liu, X. Value assessment of health losses caused by PM2.5 in Changsha city, China. *Int. J. Environ. Res. Public Health* **2019**, *16*, 2063. [[CrossRef](#)]
22. Kihal-Talantikite, W.; Legendre, P.; Le Nouveau, P.; Deguen, S. Premature adult death and equity impact of a reduction of NO<sub>2</sub>, PM10, and PM2.5 levels in Paris—A health impact assessment study conducted at the census block level. *Int. J. Environ. Res. Public Health* **2019**, *16*. [[CrossRef](#)]
23. Schwartz, J. The effects of particulate air pollution on daily deaths: A multi-city case crossover analysis. *Occup. Environ. Med.* **2004**, *61*, 956–961. [[CrossRef](#)] [[PubMed](#)]
24. Vajanapoom, N.; Shy, C.M.; Neas, L.M.; Loomis, D. Associations of particulate matter and daily mortality in Bangkok, Thailand. *Southeast Asian J. Trop. Med. Public Health* **2002**, *33*, 389–399. [[PubMed](#)]
25. Pope, C.A.; Burnett, R.T.; Thun, M.J.; Calle, E.E.; Krewski, D.; Ito, K.; Thurston, G.D. Lung cancer, cardiopulmonary mortality, and long-term exposure to fine particulate air pollution. *J. Am. Med. Assoc.* **2002**, *287*, 1132–1141. [[CrossRef](#)] [[PubMed](#)]
26. Schwartz, J.; Dockery, D.W.; Neas, L.M. Is daily mortality associated specifically with fine particles? *J. Air Waste Manag. Assoc.* **1996**, *46*, 927–939. [[CrossRef](#)]

27. Vichit-Vadakan, N.; Vajanapoom, N.; Ostro, B. The Public Health and Air Pollution in Asia (PAPA) Project: Estimating the mortality effects of particulate matter in Bangkok, Thailand. *Environ. Health Perspect.* **2008**, *116*, 1179–1182. [CrossRef] [PubMed]
28. Vichit-Vadakan, N.; Vajanapoom, N. Health impact from air pollution in Thailand: Current and future challenges. *Environ. Health Perspect.* **2011**, *119*, 2–5. [CrossRef]
29. Wong, C.M.; Vichit-Vadakan, N.; Kan, H.; Qian, Z. Public Health and Air Pollution in Asia (PAPA): A multicity study of short-term effects of air pollution on mortality. *Environ. Health Perspect.* **2008**, *116*, 1195–1202. [CrossRef] [PubMed]
30. Guo, Y.; Li, S.; Tawatsupa, B.; Punnasiri, K.; Jaakkola, J.J.K.; Williams, G. The association between air pollution and mortality in Thailand. *Sci. Rep.* **2014**, *4*, 5509. [CrossRef]
31. Fann, N.; Baker, K.R.; Fulcher, C.M. Characterizing the PM2.5-related health benefits of emission reductions for 17 industrial, area and mobile emission sectors across the U.S. *Environ. Int.* **2012**, *49*, 141–151. [CrossRef]
32. US EPA. *Review of the National Ambient Air Quality Standards for Particulate Matter: Policy Assessment of Scientific and Technical Information*; Environmental Protection Agency: Research Triangle Park, NC, USA, 1996.
33. Chuersuwan, N.; Nimrat, S.; Lekphet, S.; Kerdkumraij, T. Levels and major sources of PM2.5 and PM10 in Bangkok Metropolitan Region. *Environ. Int.* **2008**, *34*, 671–677. [CrossRef]
34. Vichit-Vadakan, N.; Ostro, B.D.; Chestnut, L.G.; Mills, D.M.; Aekplakorn, W.; Wangwongwatana, S.; Panich, N. Air pollution and respiratory symptoms: Results from three panel studies in Bangkok, Thailand. *Environ. Health Perspect.* **2001**, *109*, 381–387. [CrossRef]
35. Pinichka, C.; Makka, N.; Sukkumnoed, D.; Chariyalertsak, S.; Inchai, P.; Bundhamcharoen, K. Burden of disease attributed to ambient air pollution in Thailand: A GIS-based approach. *PLoS ONE* **2017**, *12*, e0189909. [CrossRef] [PubMed]
36. WHO International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10). Available online: <https://icd.who.int/browse10/2016/en#> (accessed on 10 July 2019).
37. US EPA. Environmental Benefits Mapping and Analysis Program—Community Edition User’s Manual; 2017. Available online: [https://www.epa.gov/sites/production/files/2015-04/documents/benmap-ce\\_user\\_manual\\_march\\_2015.pdf](https://www.epa.gov/sites/production/files/2015-04/documents/benmap-ce_user_manual_march_2015.pdf) (accessed on 1 June 2019).
38. Nodzu, M.I.; Ogino, S.Y.; Tachibana, Y.; Yamanaka, M.D. Climatological description of seasonal variations in lower-tropospheric temperature inversion layers over the Indochina Peninsula. *J. Clim.* **2006**, *19*, 3307–3319. [CrossRef]
39. Al-Hemoud, A.; Al-Sudairawi, M.; Al-Rashidi, M.; Behbehani, W.; Al-Khayat, A. Temperature inversion and mixing height: Critical indicators for air pollution in hot arid climate. *Nat. Hazards* **2019**, *97*, 139–155. [CrossRef]
40. Kwak, H.Y.; Ko, J.; Lee, S.; Joh, C.H. Identifying the correlation between rainfall, traffic flow performance and air pollution concentration in Seoul using a path analysis. *Transp. Res. Procedia* **2017**, *25*, 3552–3563. [CrossRef]
41. Jacob, D.J.; Winner, D.A. Effect of climate change on air quality. *Atmos. Environ.* **2009**, *43*, 51–63. [CrossRef]
42. Lambert, S.J.; Fyfe, J.C. Changes in winter cyclone frequencies and strengths simulated in enhanced greenhouse warming experiments: Results from the models participating in the IPCC diagnostic exercise. *Clim. Dyn.* **2006**, *26*, 713–728. [CrossRef]
43. Newell, K.; Kartsonaki, C.; Lam, K.B.H.; Kurmi, O.P. Cardiorespiratory health effects of particulate ambient air pollution exposure in low-income and middle-income countries: A systematic review and meta-analysis. *Lancet Planet. Health* **2017**, *1*, e360–e367. [CrossRef]



© 2020 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<http://creativecommons.org/licenses/by/4.0/>).