From INSTITUTE OF ENVIRONMENTAL MEDICINE
Karolinska Institutet, Stockholm, Sweden

# USE OF NOVEL STATISTICAL METHODS IN ASSESSING PARTICULATE AIR POLLUTION AND EVALUATING ITS ASSOCIATION WITH MORTALITY IN CHINA

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Stockholm 2018

Published by Karolinska Institutet.
Printed by E-Print AB, 2018

ISBN 978-91-7831-050-0

# Use of novel statistical methods in assessing particulate air pollution and evaluating its association with mortality in China

THESIS FOR DOCTORAL DEGREE (Ph.D.)

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To my beloved family

致我深爱的家人

# ABSTRACT

Particle matter (PM) has been associated with numerous adverse health effects including cardiovascular disease, chronic obstructive pulmonary disease and lung cancer in experimental studies and observation studies. The close and quantitative relationship between exposure to high concentrations of coarse particles ($PM_{10}$) and fine particles ($PM_{2.5}$) and increased mortality and morbidity in human has been confirmed in many epidemiology studies. The increases in urbanization and road motor vehicle use in China have raised concerns about the health effects of exposure to PM pollution from traffic emissions.

In Study I, we obtained hourly $PM_{2.5}$ concentrations at 35 air quality monitoring (AQM) stations in Beijing between 2013 and 2014, and daily meteorological data and geographic information during the same time period. Based on the $PM_{2.5}$ concentrations from different AQM station types, a two-stage method comprising a dispersion model and a generalized additive mixed model (GAMM) was developed to estimate the traffic and non-traffic contributions to daily $PM_{2.5}$ concentrations separately. The method provides a new solution for ecological and epidemiological studies to estimate the road traffic contribution to $PM_{2.5}$ concentrations when there is limited vehicle and emission profiles' data.

In Study II, we used causes of death registry and daily AQM data from eight districts in Beijing between 2009 and 2010 to demonstrate an application of Bayesian model averaging (BMA) method and provide a novel modelling technique to assess the association between $PM_{10}$ concentration and respiratory mortality. The BMA method within GAMM frame gave slightly but noticeable wider confidence intervals (CIs) for the single-pollutant model and the principal components based model, which indicates that BMA may provide a useful tool for modelling uncertainty in time-series studies when evaluating the effect of air pollution on fatal health outcomes.

In Study III, we evaluated the effects of $PM_{2.5}$ concentrations on non-accidental mortality as well as their interactions with extreme weather conditions and weather types in Shanghai between 2012 and 2014. A fully Bayesian generalized additive model (GAM) was set up to link the mortality with $PM_{2.5}$ and weather conditions. We found that the effects of $PM_{2.5}$ on non-accidental mortality differed under specific weather conditions.

In Study IV, we compared the estimates from frequentist GAM and Bayesian GAM with simulated data. We also examined the sensitivity of Bayesian GAM to choices both of the priors and of the true parameter. The frequentist GAM and Bayesian GAM showed similar means and variances of the parameters of interest. However, the estimates from Bayesian GAM show relatively more fluctuation, which to some extent reflects the uncertainty inherent in Bayesian estimation.

In conclusion, PM pollution poses great threat to human health in China. Road traffic is one of the major sources of PM pollution, and our two-stage model is a useful tool to proportionate its contribution to PM pollution in large cities such as Beijing where daily meteorological and

traffic data are available. Given the statistically significant interactions between $PM_{2.5}$ and weather, and climate and pollution challenges, adequate policies and public health actions are needed, taking into account the interrelationship between the two hazardous exposures. Although computationally intensive, Bayesian approaches would be better solutions to avoid potentially over-confident inferences in traditional frequentist methods. With the increasing computing power of computers and statistical packages available, fully Bayesian methods for decision making may become more widely applied in the future.

# LIST OF SCIENTIFIC PAPERS

This thesis is based on the following papers, which will be referred to in the text by their Roman numbers (I-IV). * Equal contribution.

I. **Fang X**, Li R*, Xu Q, Bottai M, Fang F, Cao Y. A Two-Stage Method to Estimate the Contribution of Road Traffic to $PM_{2.5}$ Concentrations in Beijing, China. *Int J Environ Res Public Health. 2016 Jan 13;13(1).*

II. **Fang X**, Li R, Kan H, Bottai M, Fang F, Cao Y. Bayesian Model Averaging Method for Evaluating Associations between Air Pollution and Respiratory Mortality: A Time-series Study. *BMJ Open. 2016 Aug 16;6(8):e011487.*

III. **Fang X**, Fang B*, Wang C, Xia T, Bottai M, Fang F, Cao Y. Relationship between Fine Particulate Matter, Weather Condition and Daily Non-accidental Mortality in Shanghai, China: A Bayesian Approach. *PLoS One. 2017 Nov 9;12(11):e0187933.*

IV. **Fang X**, Fang B, Wang C, Xia T, Bottai M, Fang F, Cao Y. Comparison of Frequentist and Bayesian Generalized Additive Models for Assessing the Association between Daily $PM_{2.5}$ and Respiratory Mortality: A Simulated Time Series Analysis. *Manuscript submitted*.

# RELATED PUBLICATIONS

(not included in this thesis; * equal contribution)

I. Ren M, **Fang X***, Li M, Sun S, Pei L, Xu Q, Ye X, Cao Y. Concentration-Response Relationship between $PM_{2.5}$ and Daily Respiratory Deaths in China: A Systematic Review and Meta-regression Analysis of Time-Series Studies. *Biomed Res Int. 2017;2017:5806185.*

II. Luo K, Li R, Li W, Wang Z, Ma X, Zhang R, **Fang X**, Wu Z, Cao Y, Xu Q. Acute Effects of Nitrogen Dioxide on Cardiovascular Mortality in Beijing: An Exploration of Spatial Heterogeneity and the District-specific Predictors. *Sci Rep. 2016 Dec 2;6:38328.*

# CONTENTS

# LIST OF ABBREVIATIONS

The following abbreviations have been used in this thesis.

| | |
|---|---|
| AIC | Akaike Information Criterion |
| AQI | Air Quality Index |
| AQM | Air Quality Monitoring |
| ARMS | Adaptive Rejection Metropolis Sampling |
| BIC | Bayesian Information Criterion |
| BLUE | Best Linear Unbiased Estimation |
| BMA | Bayesian Model Averaging |
| CBD | Central Business District |
| CCM | Coupled Chemistry-Meteorology |
| CDR | Causes of Death Registry |
| CI | Confidence Interval |
| CMAQ | Community Multiscale Air Quality |
| CMB | Chemical Mass Balance |
| CO | Carbon Monoxide |
| COPD | Chronic Obstructive Pulmonary Disease |
| COPREM | Constrained Physical Receptor Model |
| CrI | Credible Interval |
| *df* | Degrees of Freedom |
| DOW | Day of Week |
| EC | Elemental Carbon |
| EPA | Environmental Protection Agency |
| ER | Excess Risk |
| ESS | Effective Sample Sizes |
| EU | European Union |
| EU-27 | European Union 2007 enlargement of the European Union |
| GAM | Generalized Additive Model |
| GAMM | Generalized Additive Mixed Model |
| GIS | Geographic Information System |

| | |
|---|---|
| GLM | Generalized Linear Model |
| GLMM | Generalized Linear Mixed Model |
| HYSPLIT | Hybrid Single-particle Lagrangian Integrated Trajectory |
| lag01 | Two-day moving average of current day and the previous day |
| ICD | International Classification of Disease |
| IL-8 | Interleukin 8 |
| IQR | Interquartile Range |
| LOESS | Locally Weighted Smoothers |
| LUR | Land Use Regression |
| MCMC | Markov Chain Monte Carlo |
| ME | Multilinear Engine |
| MR | Mortality Rate |
| NA | Not Available |
| $NO_2$ | Nitrogen Dioxide |
| $NO_x$ | Mono-nitrogen Oxides |
| $O_3$ | Ozone |
| OC | Organic Carbon |
| P25 | The 25th percentile |
| P75 | The 75th percentile |
| PC | Principal Component |
| PCA | Principal Component Analysis |
| PM | Particle Matter |
| $PM_{10}$ | Particles with an aerodynamic diameter smaller than 10 µm; Coarse particles |
| $PM_2$ | Particles with an aerodynamic diameter smaller than 2 µm |
| $PM_{2.5}$ | Particles with an aerodynamic diameter smaller than 2.5 µm; Fine particles |
| PMF | Positive Matrix Factorization |
| PPB | Parts Per Billion |
| RR | Relative Risk |

| | |
|---|---|
| SCDC | Shanghai Municipal Center for Disease Control and Prevention |
| SD | Standard Deviation |
| $SO_2$ | Sulfur Dioxide |
| SWT | Synoptic Weather Type |
| UNMIX | A mathematical receptor model developed by U.S. EPA |
| U.S. | The United States |
| V | Variance |
| WCDMP | World Climate Data and Monitoring Programme |
| WHO | World Health Organization |

# 1 INTRODUCTION

At the beginning of 2013, a term '$PM_{2.5}$' suddenly began attracting attention around China. It became the headline in almost every main traditional media and new media in China. Every Chinese began to talk about it, which even started drawing worldwide attention. What is $PM_{2.5}$ and why it suddenly became a daily hot topic in China?

$PM_{2.5}$ refers to atmospheric particulate matters (PM) with an aerodynamic diameter less than 2.5 micrometers (μm), which is about 3% the diameter of a human hair.[1] PM, also called particles or particulates, is a mixture of solid particles and liquid droplets found in the air. These particles come from many different sources with different sizes and can be made up of hundreds chemicals, including acids (such as nitrates and sulfates), organic chemicals, metals, and soil or dust particles. Based on size, PM is often divided into two main groups: the coarse particles that contain larger particles with a size ranging from 2.5 to 10 μm ($PM_{10}$), and fine particles, i.e. $PM_{2.5}$. The particles smaller than 0.1 μm are called ultrafine particles. The larger particles usually contain earth crust materials and fugitive dust from roads and industries. The fine ones contain most of the acidity (hydrogen ion) and mutagenic activity of PM, although in fog some coarse acid droplets are also present. The aerodynamic properties of particles determine how they are transported in air and how they can be removed from it. Both $PM_{10}$ and $PM_{2.5}$ are called inhalable particulates, and have been associated with numerous adverse health effects including cardiovascular disease, chronic obstructive pulmonary disease and lung cancer in experimental studies and observation studies.[2] The close and quantitative relationship between exposure to high concentrations of $PM_{10}$ and $PM_{2.5}$ and increased mortality and morbidity in human has been confirmed in many epidemiology studies. PM may have adverse impacts even at very low concentrations, and the threshold without health damage has not been identified.

Our studies focused on the two largest and most populous cities in China, Beijing and Shanghai, and estimated the contribution of road traffic, a major source of air pollution in China, to daily $PM_{2.5}$ concentrations, and evaluated the association of PM air pollution with daily non-accidental mortality in the two cities. The following research questions were explored in our studies:

1. How to use limited mornitoring data to estimate district-specific contribution of road traffic on $PM_{2.5}$ concentrations?
2. What is the spatiotemporal relationship between daily $PM_{10}$ level and respiratory mortality in Beijing, China?
3. Did $PM_{2.5}$ air pollution and weather condtions affect non-accidental deaths interactively in Shanghai, China?
4. How to better assess the effects of $PM_{2.5}$ air pollution on respiratory mortality in a time-series study?

# 2 BACKGROUND

## 2.1 THE METHODS FOR ESTIMATING THE CONTRIBUTION OF ROAD TRAFFIC TO PARTICULATE MATTER CONCENTRATIONS

Road traffic related pollution is one of the main sources of ambient PM, which includes both exhaust and non-exhaust resources. The emissions of different vehicles such as passenger cars, trucks or busses vary largely in terms of their emission class. Traffic related air pollution has shown negative health impacts according to a growing body of epidemiological evidence.[3] Increases in urbanization and road motor vehicle use in China have raised concerns about the health effects of exposure to pollutants from traffic emissions. Among all air pollutants, $PM_{2.5}$ is on the top of the list due to it posing great public health hazards, including higher risks of respiratory diseases, impaired lung function, asthma attacks, cardiovascular diseases, and potentially also premature death.[3] Despite significant emission reductions in Europe during the last two decades, the road transport remains to be a major source of important pollutants, contributing with 42% to total EU-27 emissions in 2009.[4] By collecting and analyzing aerosol samples of $PM_{2.5}$ both in summer and winter seasons at different traffic, industrial and residential areas in Beijing, a multisite study found that industrial and motor vehicle emissions, together with coal burning, were the major contributors to the air-borne PM pollution.[5] They have immediate impacts on air quality, mainly in urban areas and therefore on human exposed to the road traffic related pollution. However, measurements at regional monitoring stations may be too sparse to reflect the actual concentrations of pollutants related to automobile, bus, and truck traffic to which the surrounding population is exposed. This stresses the need to count on reliable inventories which can describe the sources of such emissions thoroughly. Consequently, these inventories need to be constantly improved and adapted to new methodologies and data as they become available.

### 2.1.1 Field measurement methods

In the last three decades, a significant amount of researches have been conducted to characterize and estimate exhaust emissions from road traffic based on the field measurement methods. These methods evaluate emissions from road vehicles using dynamometers, measurements in tunnels, near roadside measurements, and road simulator tests.[6-11]

#### *2.1.1.1 Tunnel measurements*

In tunnel studies, emission rate of vehicles in the tunnel is measured as the sum of the difference between the pollutant influx and outflux while velocity and concentration are assumed to be the same across the tunnel's cross-section.[12] Therefore, we may calculate the difference in PM concentrations between entrance and exit of a tunnel (Figure 1).[13,14] The distribution of organic compounds between particles and vapor is heavily affected by the high PM concentrations in a road tunnel, and thus may influence the estimate of emission factors for semi-volatile components.[15] Because of the variations in vehicle speed, aerodynamic conditions in the tunnel and the fleet characteristics (i.e. proportion of heavy-duty vehicles and light-duty vehicles), variability in measurements exists in tunnel studies when measuring PM emission on a mixed vehicle fleet.[12,16] We should also notice that vehicles in the tunnel are often driving at a steady speed which does not happen under other road conditions where traffic follows a stop-and-go pattern, which may influence the estimate of emission.[17]

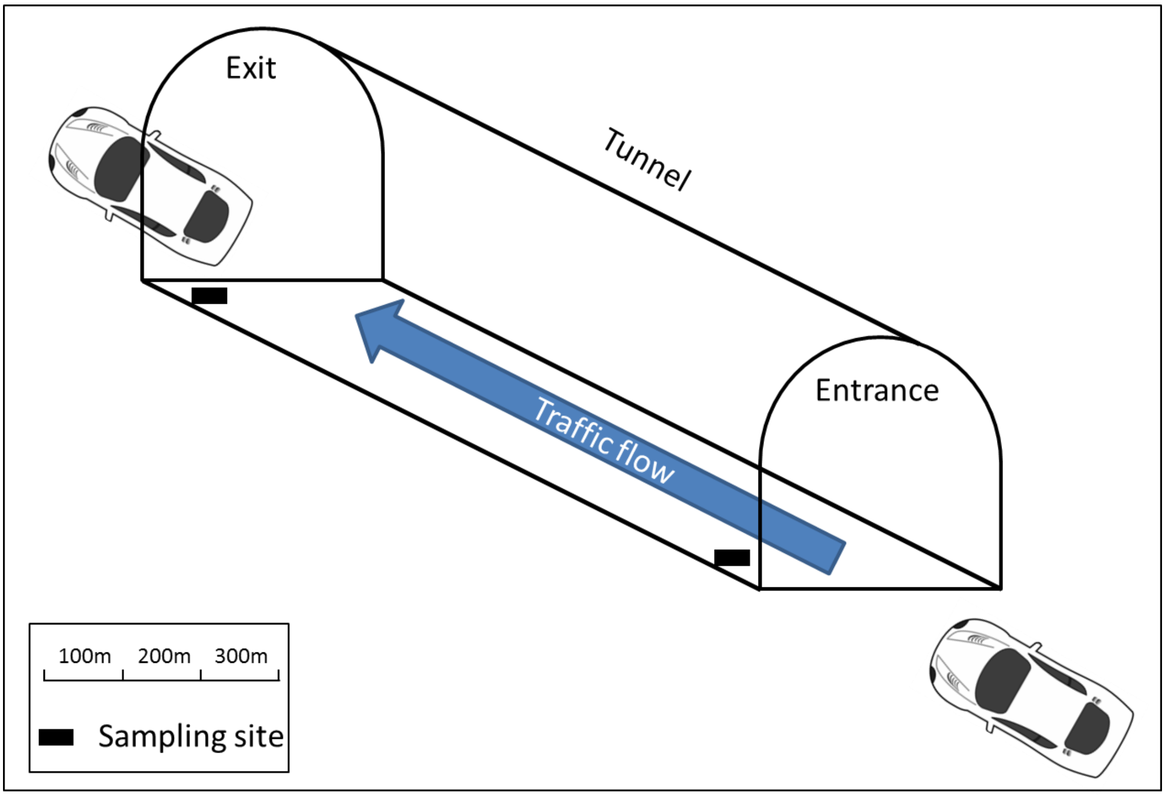



Figure 1. Tunnel method

### *2.1.1.2 Receptor modelling*

Receptor models interpret measurements of physical and chemical properties taken at different times and places to infer the possible sources of excessive concentrations and to quantify the contributions from those sources (Figure 2).[18] A number of receptor models are used for source apportionment including the chemical mass balance (CMB) model [19], statistical models such as principal component analysis (PCA) and positive matrix factorization (PMF) [20], multilinear engine (ME) [21], constrained physical receptor model (COPREM) [22] and UNMIX.[23] Receptor models assume that the relative concentrations of chemical species are preserved between air pollution sources and receptors, and use the principle of mass conservation for apportionment of PM mass to different sources.

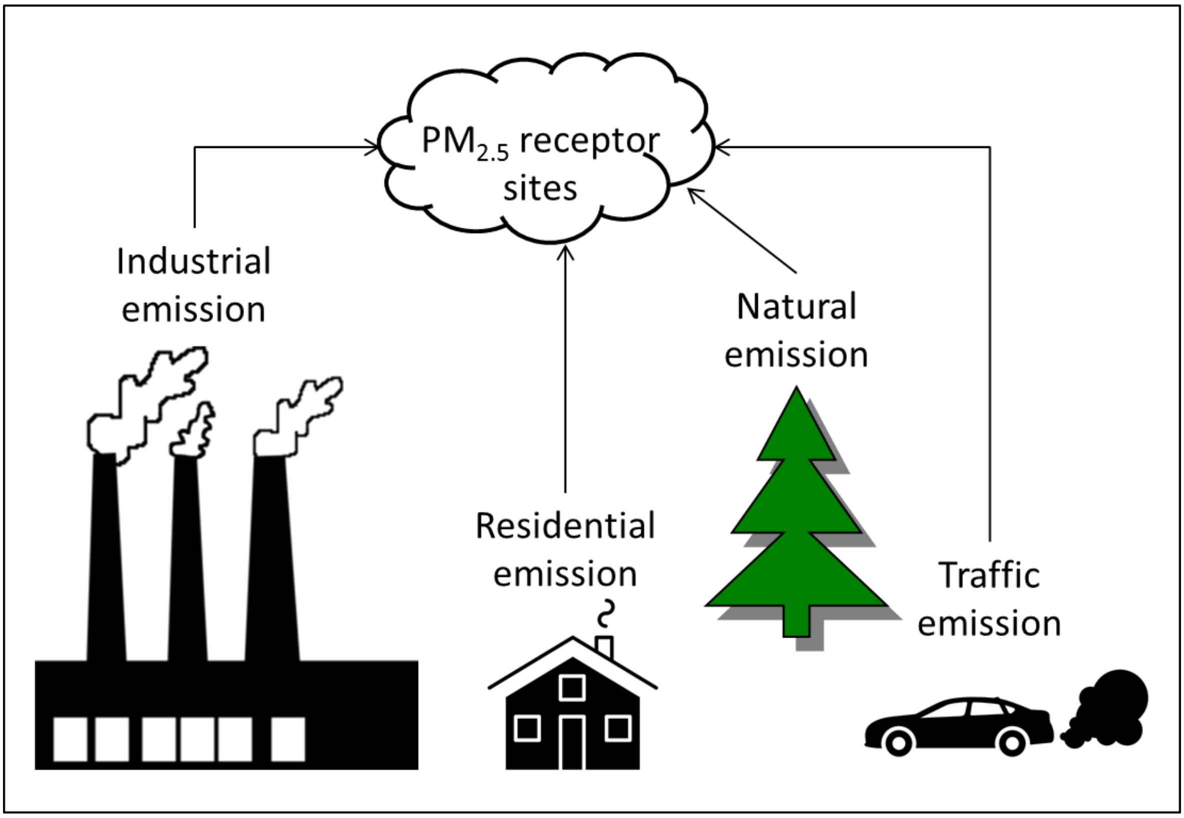



Figure 2. Receptor model

### 2.1.1.3 $NO_x$ as tracer

In the situation where road traffic is the primary source for ambient mono-nitrogen oxides ($NO_x$), we may use regression analysis between particle mass fractions and $NO_x$ to estimate the contributions of the traffic source to ambient PM concentration.[24] The method assumes that the regression intercept in PM at zero $NO_x$ is due to non-traffic sources, with the traffic contribution estimated by difference from the measured mean concentration. However, this method is only useful when traffic is the predominant source for local $NO_x$ concentrations.

### 2.1.1.4 Twin-site studies

Twin-site studies assume that all sources other than traffic (including any local or regional sources) have the same impact at both roadside and background sites, the increment at the roadside site obtained using the equation (1) is used as a local traffic increment estimate [11,25]:

$$\text{Concentration of X}_{traffic} = \text{Concentration of X}_{roadside} - \text{Concentration of X}_{background} \quad (1)$$

The difference in observed concentrations between rural and urban areas provides an estimate (usually) for the urban increment while the difference between roadside concentration and urban background concentration provides an estimate for the traffic increment. Pattern of air circulation is an important determinant of ambient PM concentration at an enclosed street site, therefor results from such studies may be influenced by street geometry.[26]

### 2.1.2 Surrogate models

Although traffic emission is the principal source of intra-urban concentration of PM, the field measurement of motor-vehicle emission may not be feasible for most studies to track vehicles and measure corresponding components of the pollutant mixtures on site.[27] As a result, different surrogates have been used to assess the contribution of road traffic to ambient air pollution. These surrogates allow for relatively easy computation of distances from emissions sources, such as roadways, and for enhanced characterization of land use likely to influence the emission or dispersion of traffic-related pollution. The emergence of remote sensing technologies based on satellite imagery has contributed to a further refinement of the data inputs, although at this time direct estimates of ground-level pollution from remote sensing are generally at scales coarser than estimates obtainable on the ground.[28]

#### *2.1.2.1 Land use regression models*

The land use regression (LUR) models use surrounding land usage and traffic characteristics at a given site to predict pollution concentrations. Regression mapping is the base of the models for assessing traffic-related pollution.[29-31] It uses measured pollution concentration at a location as the dependent variable and land use type within the areas around the location as predictor. When air quality monitoring data and exogenous independent variables are available, LUR can be used to predict pollution surfaces.

The advantage of LUR is accounting for small scale variability in intraurban pollutant concentrations. It requires similar geographic variables (traffic volume, distance to pollutant source), but necessitates sampling data. The ability to differentiate exposure within proximity distances through the use of additional land use variables is an added benefit. Geostatistical models (e.g., kriging) are similar to LUR models with respect to the need for sampling data.[32]

#### *2.1.2.2 Dispersion models*

Dispersion models use data on emissions, meteorological conditions, and topography to estimate ambient air pollution concentrations.[33,34] The models require data on pollution, meteorological conditions, and emission to fulfill model assumptions (Figure 3). Data on background pollution concentrations are usually obtained from monitoring stations near the study area and are used for model calibration.[35] Depending on the type of source, emission data are classified into stationary sources and mobile sources. Traffic emissions are estimated using traffic volume and standard emission factors for different types of vehicles, speeds, and gradients of the road network.[34,36]

Recently, dispersion models have been used in conjunction with geographic information system (GIS), which allows both information from monitoring systems and data concerning the population distribution in the study area to be analyzed together. With additional data on the topography of the study area, local road network, and traffic characteristics, a more realistic representation of the pollution can be formed.[37-41] The obstacles in the implementation of these models are the costly data input and expensive hardware requirements.[42]

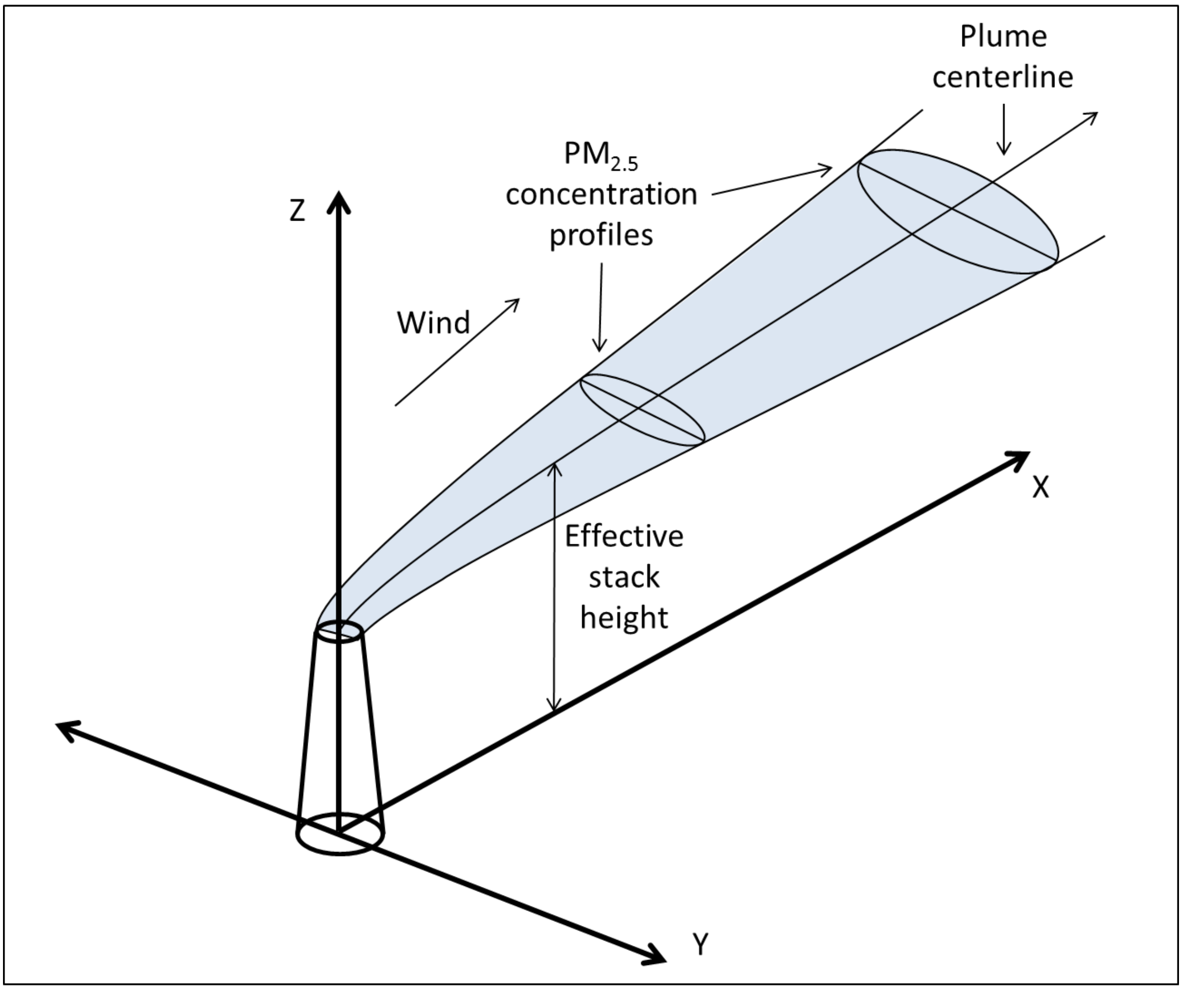



Figure 3. Illustration of $PM_{2.5}$ dispersion plume

#### *2.1.2.3 Interpolation models*

Interpolation models may be deployed where measurements of the target pollutant are available from a set of air quality monitoring (AQM) stations distributed throughout the study area. The method relies on geostatistical techniques. The most common geostatistical technique used in the air pollution field is ‘‘kriging’’.[43] Kriging methods supply the best linear unbiased estimation (BLUE) of the variable’s value at any point in the study area.[44,45] Estimates from interpolation models are usually obtained at the center of a grid, imposed over the study area, so that a continuous surface of pollution concentration can be established, then the concentration of pollutant at sites other than monitored locations are generated.

However, geostatistical interpolation is limited by the requirement of a reasonably dense monitoring network. Government monitoring data come from a sparse network of stations that are likely to be affected by industrial and heavy transportation emission sources. Reliance on government monitoring data may introduce large errors in where few observations are available.[34]

#### 2.1.2.4 Coupled chemistry-meteorology models

It has been well recognized that weather has a profound impact on air quality and atmospheric transport of hazardous materials. Coupled chemistry-meteorology (CCM) models use meteorological and chemical modules together to simulate dynamics of atmospheric pollutants (Figure 4).[46,47] The models provide tighter temporal coupling between meteorology and air quality models as well as feedback from the air quality simulation to the physical processes in the meteorology model. CCM models typically consist of three modules: meteorological module, chemistry transport module, and visualization and analysis module. Some of them were developed by essentially adding atmospheric chemistry, along with source and sink processors, to established meteorology models. In these models, meteorological data are provided to the chemistry modules at every simulation.[48]

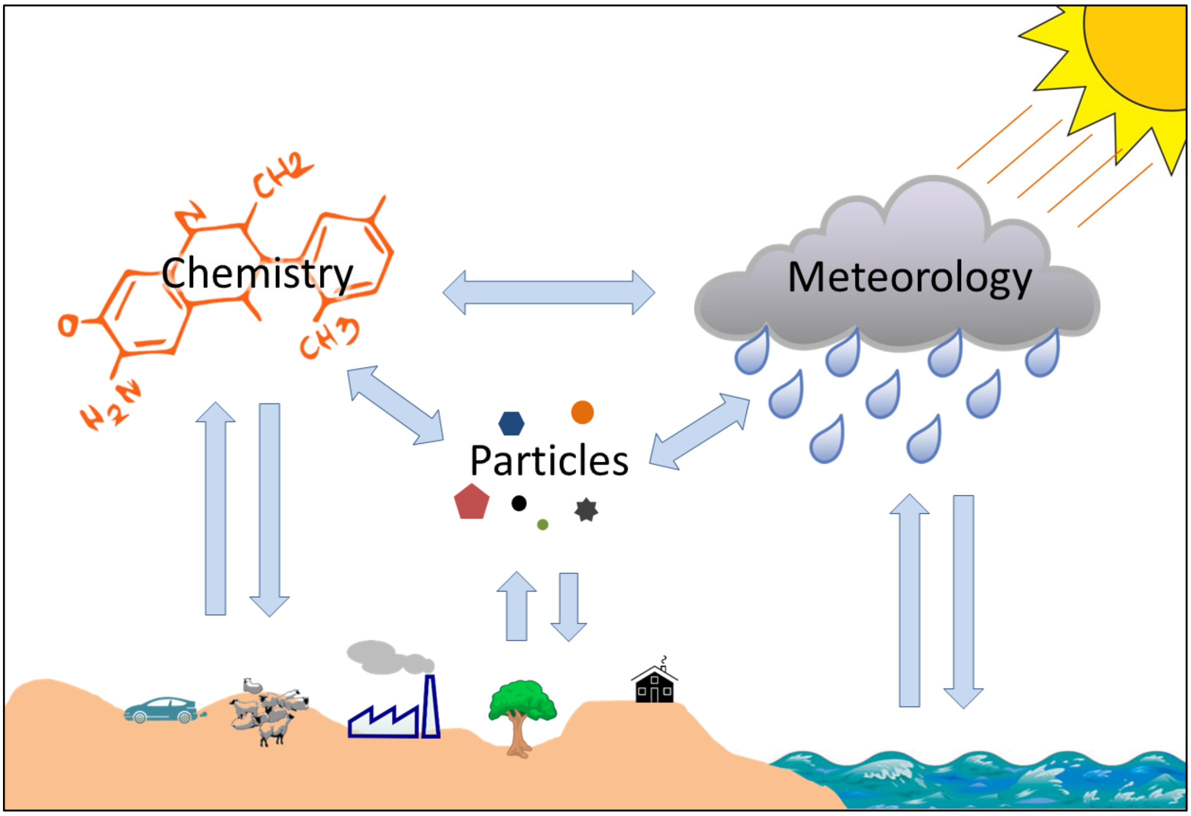



Figure 4. Coupled chemistry-meteorology model

The models are useful for areas that do not have comprehensive observations to define characteristics of the key meteorological fields required for air quality application.[34] A disadvantage of this approach is that air chemistry models often have different requirements for numerical integration such as strict mass conservation, positive definiteness, and greater computational efficiency, which make their use a costly endeavor. Although CCM models have not been widely used for linking air quality to health, they have considerable potential in areas with large populations, where relatively small air pollution risks may exert large burdens of illness and mortality.[34,48]

#### 2.1.2.5 Hybrid Models

The hybrid models combine personal or regional monitoring data with other air pollution exposure measurements. Most studies using hybrid models were conducted in European cities, which used personal monitoring methods in conjunction with fixed outdoor stations.[49-51] Long-term mean exposure to pollutants was assumed to be a function of different components: regional background, urban concentration, and local variation due to traffic. The regional background concentration was estimated by the inverse distance weighting interpolation method with use of data from a national monitoring network.[52] To address the limitations of available monitoring data and the various metrics of exposure, a hybrid approach uses output from both a grid-based chemical transport model and a plume dispersion model to provide contributions from photochemical interactions, long-range (regional) transport, and details attributable to local-scale dispersion.[53]

The modeling approach allows for estimating pollution from mobile vs. stationary sources and background vs. roadways, which provides an opportunity to compare relative contributions of various sources and total. The hybrid models may provide new information regarding exposure to traffic-related air pollutants that is not captured by simpler metrics commonly used in environmental epidemiology studies of traffic-related air pollution.[53] Yet, the difficulty in implementing hybrid models depends on the combination of models being used. When ambient data are unavailable, this method becomes more difficult to implement.[34]

## 2.2 HEALTH EFFECTS OF PARTICULATE MATTER

### 2.2.1 Global health effects of particulate matter

Inhalable PMs, including $PM_{10}$ and $PM_{2.5}$ are small enough to penetrate the thoracic region of the respiratory system. Their effects have been well documented, including:

- respiratory and cardiovascular morbidity, such as aggravation of asthma, respiratory symptoms, and increase in hospital admissions;
- mortality from cardiovascular and respiratory diseases, and from lung cancer.[54]

$PM_{2.5}$ is especially harmful because it can easily enter the alveoli and cross the membrane of lung cells, and eventually accumulates in the respiratory system (Figure 5). It is estimated that 75% of $PM_{2.5}$ particles, and 100% of $PM_2$ particles will reach the alveoli.[55]

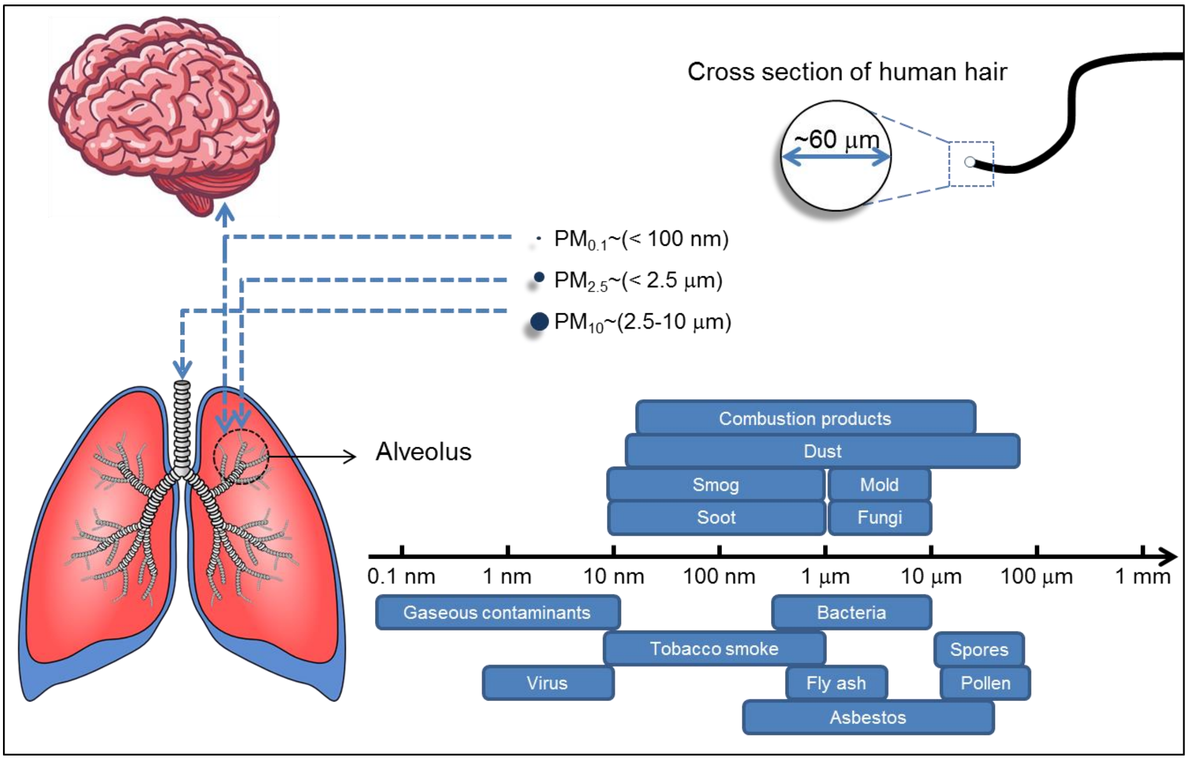



Figure 5. Visualization of air particles comparing with human hair

$PM_{2.5}$ has been one of the major causes of premature mortality in Asia, Europe and America. Concern over the health effects of $PM_{2.5}$ in the ambient environment led the United States (U.S.) Environmental Protection Agency (EPA) to develop the first standard for $PM_{2.5}$ in 1997.[56] Numerous time series studies have showed a considerable association of $PM_{2.5}$ with daily respiratory death counts.[57-62] According to the *Air Quality in Europe – 2015 Report*, about 432,000 premature deaths were attributable to $PM_{2.5}$ exposure in 2012 in 40 European countries.[63] A recent review of seventeen studies showed that the excess risk percentage (ER%) per 10 $\mu g/m^3$ increase of pollutants was 1.5% [95% confidence interval (CI): 0.6% – 2.4%] for $PM_{10}$ and 1.8% (95% CI: 0.5% – 3.1%) for $PM_{2.5}$. The corresponding values per 10 parts per billion (ppb) increment of gaseous pollutants were 2.9% (95% CI: 0.4% – 5.3%) for sulfur dioxide ($SO_2$), 1.7% (95% CI: 0.5% – 2.8%) for ozone ($O_3$), and 1.4% (95% CI: 0.4% – 2.4%) for nitrogen dioxide ($NO_2$). ER% per 1000 ppb increment of carbon monoxide (CO) was 0.9% (95% CI: 0.0% – 1.9%).[64] On a global scale, the estimated premature deaths due to outdoor air pollution, mostly by $PM_{2.5}$, can be as high as 3.3 (95% CI: 1.61 – 4.81) million per year, predominantly in Asia. Emissions from residential energy use such as heating and cooking, prevalent in India and China, have the largest impact on premature mortality, being even more dominant if carbonaceous particles are assumed to be most toxic. Whereas in much of the U.S. and in a few other countries emissions from traffic and power generation are important, in eastern U.S., Europe, Russia and East Asia agricultural emissions make the largest relative contribution to $PM_{2.5}$.[65]

As with all population studies, the conclusions are still open to debate. The arguments include:

- Are the measured $PM_{2.5}$ concentrations accurate?

- Are the confounders such as lifesyle and co-exposure to other pollutants accounted for adequately?
- Do the concentrations measured at a monitoring station actually reflect the individual exposure?

The last point is particularly important since the most epidemiological studies use fixed and limited monitoring stations' data as human exposure.[56]

### 2.2.2 Health effects of particulate matter in China

Due to the rapid urbanization and dramatic increase of energy consumption and motor vehicles in major cities such as Beijing, Shanghai and Guangzhou in China after 1980s, air pollution has become a choking problem. Chinese researchers started conducting $PM_{2.5}$ measurement since early 2000s, much earlier than the first Chinese $PM_{2.5}$ standard promulgated in January 2012.[66]

Beijing, the capital city of China, is suffered from air pollution for decades because of its unique geographic location and manufactory industry. Local governmental authorities have paid the attention to environmental problem for three decades. The monitoring system was built from 1984, and $PM_{2.5}$ became a new monitoring pollutant from 2006. According to the air quality guideline of the World Health Organization (WHO), 24-hour mean of $PM_{2.5}$ concentration < 25 $\mu g/m^3$ or annual mean < 10 $\mu g/m^3$ is considered as no risk.[67] The corresponding standard of the U.S. EPA is 35 $\mu g/m^3$ and 12 $\mu g/m^3$, respectively.[68] However, the U.S. Embassy in Beijing posted that the $PM_{2.5}$ levels were frequently over than 500 $\mu g/m^3$ in 2012, which meant extremely severe pollution. Since October 2012, Beijing government increased its fixed AQM stations from 27 to 35which covered the entire municipal area from the central business district (CBD) to rural industry region. A randomized intervention study of indoor $PM_{2.5}$ filtration conducted in Beijing revealed that the reduction of main components of indoor $PM_{2.5}$ by 42% to 63% resulted in significant reductions on systemic inflammation measured as of interleukin 8 (IL-8) by 58.59% (95% CI: -76.31% – -27.64%) in the senior group and 70.04% (95% CI: -83.05% – -47.05%) in the chronic obstructive pulmonary disease (COPD) patients with adjustments.[69] Another observational study also found a significant association with ambient $PM_{2.5}$ concentration and increased use of asthma-related health services. Every 10 $\mu g/m^3$ increase in $PM_{2.5}$ concentration on the same day was associated with a 0.67% (95% CI: 0.53% – 0.81%), 0.65% (95% CI, 0.51% – 0.80%), and 0.49% (95% CI, 0.35% – -0.64%) increase in total hospital visits, outpatient visits, and emergency room visits, respectively.[70]

Shanghai, one of the biggest financial cities in the world, has been also impacted by heavy road traffic pollution. Hourly $PM_{2.5}$ has been monitored in Shanghai since 2012. Till 2017, there have been approximate 50 monitoring stations in Shanghai. An earlier study has already found that $PM_{2.5}$ was associated with the death rates from all causes and from cardiorespiratory diseases in Shanghai. A 10 $\mu g/m^3$ increase in the two-day moving average of current day and the previous day (lag01) concentration of $PM_{2.5}$ corresponded to 0.36% (95% CI: 0.11% – 0.61%), 0.41% (95% CI 0.01% – 0.82%) and 0.95% (95% CI 0.16% – 1.73%) increase of total, cardiovascular, and respiratory mortality, respectively.[71] Another relative recent study investigated $PM_{2.5}$ constituents and hospital emergency-room visits in Shanghai. During the study period, the mean of daily average $PM_{2.5}$ concentrations in Shanghai was 55 μg/m$^3$. Major contributors to $PM_{2.5}$ mass included organic carbon (OC), elemental carbon (EC), sulfate, nitrate, and ammonium. The researchers found that for a 1-day lag, an interquartile range (IQR) increment in $PM_{2.5}$ mass (36.47 μg/m$^3$) corresponded to 0.57% (95% CI: 0.13% – 1.01%) increase of emergency room visits.[72]

When China Daily reported the worst air quality in Beijing in December 2013, more than 80% of the seventy-four major cities in China could not meet the Chinese national standard for most days in that month.[73] Even though, in a public survey about whether they felt harms environmental pollution, only 6% people across 28 provinces experiencing sever air pollution in China answered “YES”.[74] In a nationwide time-series analysis performed in 272 representative Chinese cities from 2013 to 2015, city-specific effects of $PM_{2.5}$ on daily mortality were estimated using overdispersed generalized additive model. The average of annual-mean $PM_{2.5}$ concentrations of the cities was 56 μg/m$^3$ (ranging from 18 to 127 μg/m$^3$). Each 10 μg/m$^3$ increase in daily $PM_{2.5}$ concentrations (lag 01) was significantly associated with increments of 0.22% in mortality from total non-accidental causes, 0.27% from cardiovascular diseases, 0.39% from hypertension, 0.30% from coronary heart diseases, 0.23% from stroke, 0.29% from respiratory diseases, and 0.38% from chronic obstructive pulmonary disease.

These findings provided key epidemiological evidence for the review of the ambient air quality standards in China. Furthermore, these results have important policy implications as well, making the critical evaluation of the diverse modeling approaches that have been proposed in the literature an important task.

### 2.2.3 Interaction with meteorological factors

Both extreme weather conditions and PM air pollution are well-established risk factors of adverse health outcomes (Figure 6). The PM air pollution shows a clear seasonal trend.[75-78] In China, the air quality is influenced by wind direction and temperature, and seasonal changes in $PM_{2.5}$ and $PM_{10}$ concentrations are striking, which may increase 2 to 3 times in winter in average.[79-81] Dozens of studies showed the exposure to the climate change especially the extreme weather condition increased respiratory morbidity and mortality. There is a wealth of evidence showing that all-cause mortality increases during both cold season and hot wave period.[82-97] There were differences in the spatiotemporal variations of extreme low temperatures for emergency transport during winter in Japan. The nationwide study indicated the overall cumulative relative risk (RR) at the first percentile vs. the minimum morbidity percentile was 1.59 (95% CI: 1.33 – 1.89) for respiratory diseases.[98] The recent statistics from a European country showed the effect of cold temperatures in mortality was presented a 1 – 2-day delay, reaching maximum increased risk of death after 6 – 7 days and lasting up to 20 – 28 days.[99] In China, cold spells significantly increased the risk of deaths due to non-accidental mortality (RR 1.08, 95% CI: 1.06 – 1.11), respiratory disease (RR 1.19, 95% CI: 1.11 – 1.27), and COPD (RR 1.27, 95% CI: 1.16 – 1.38). Heat waves significantly increased the risk of deaths due to non-accidental mortality (RR 1.02, 95% CI: 1.00 – 1.05). Especially, the elderly and the children were more vulnerable to the extreme event.[100]

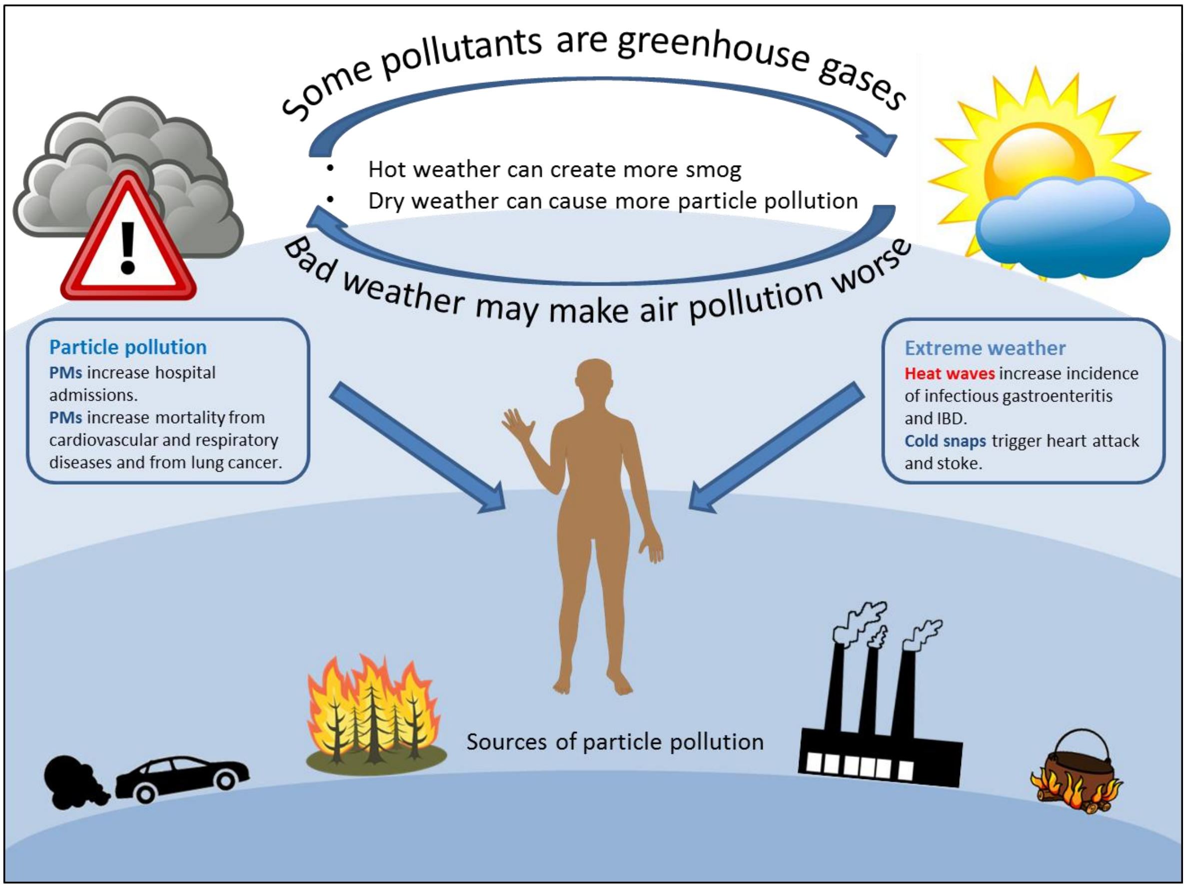



Figure 6. Effects of particle matter pollution and extreme weather on human health

In general, it has been well documented that both PM pollution and meteorological conditions are significantly associated with non-accidental mortality. Therefore, there are concerns that the reported association of PM with mortality might be a mixture of PM and weather conditions. However, few studies have investigated the interaction between meteorological variables and PM concentrations so far. In the thesis, a Bayesian approach within generalized additive model (GAM) framework was deployed to explore the influence of meteorological conditions on the effect of $PM_{2.5}$ on non-accidental mortalities.

## 2.3 BAYESIAN METHOD

### 2.3.1 Bayes' theorem

There are two schools of statistical inference: Bayesian and frequentist. Both approaches allow one to evaluate evidence about competing hypotheses. Compare to the frequentist approach, Bayesian one requires prior distribution and likelihood of observed data.

Bayes' theorem (Figure 7) describes the posterior or conditional probability of a hypothesis ($H$) based on prior knowledge of evidence ($e$) that might be related to the hypothesis. The posterior $p(H|e)$ of $H$ given $e$ is definite as:

$$p(H|e) = \frac{p(H,e)}{p(e)} \tag{2}$$

By manipulating the definition, we may have the equations below:

$$p(H,e) = p(H|e) \cdot p(e), \text{ and } p(e,H) = p(e|H) \cdot p(H) \tag{3}$$

Because of $p(H,e) = p(e,H)$, by rewriting the above equations we get:

$$p(H|e) = \frac{p(e|H) \cdot p(H)}{p(e)} \tag{4}$$

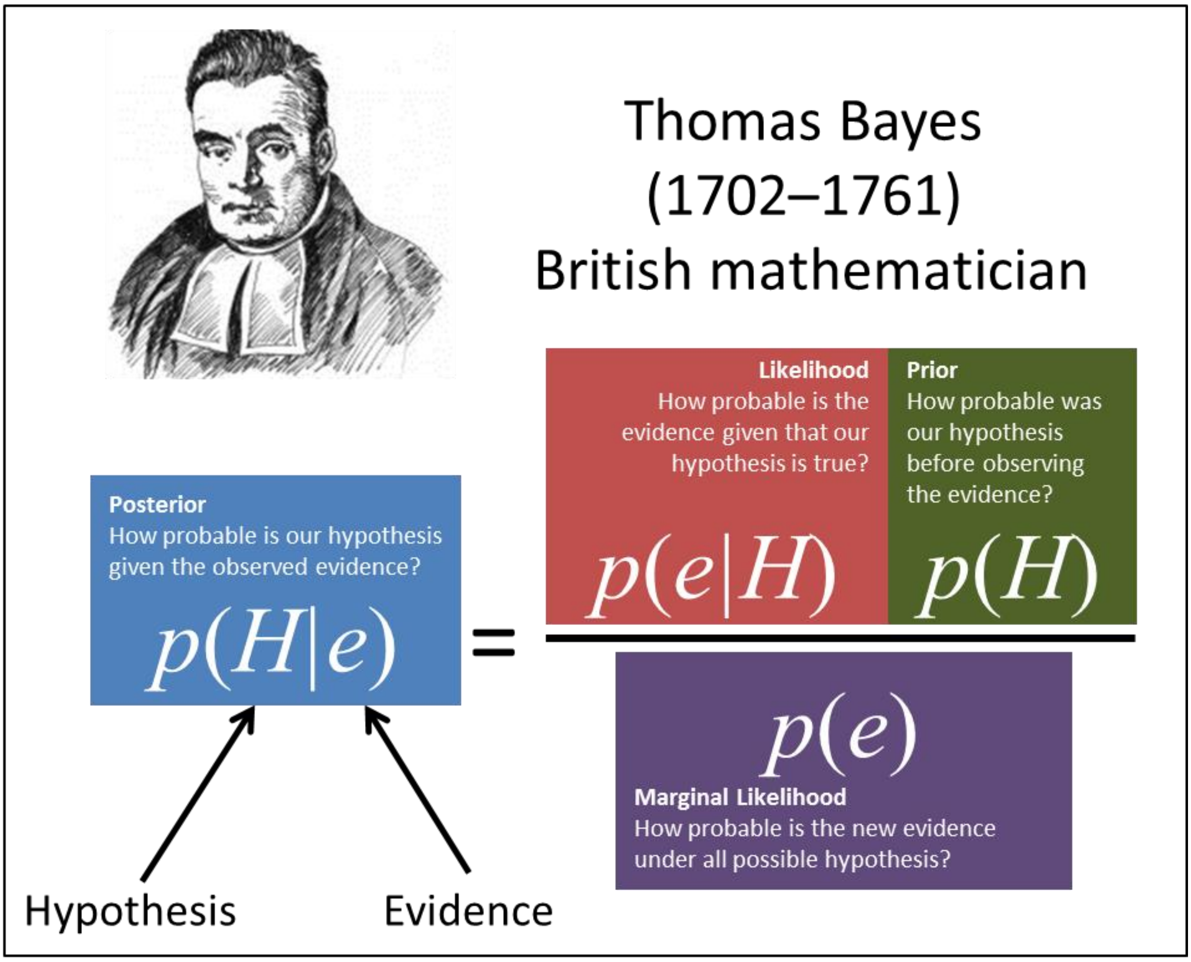



Figure 7. Bayes' theorem

When rewriting the denominator in (4) in terms of $p(e|H)$, we may have:

$$p(H|e) = \frac{p(e|H) \cdot p(H)}{\sum_{H^*} p(e|H^*) \cdot p(H^*)} \tag{5}$$

Equation (5) is the Bayes' rule and lies at the core of Bayesian inference whereas $H^*$in the denominator is a variable that takes on all possible hypotheses.[101]

With Bayes' rule, we may convert the prior distribution with probability of the various parameters to what we really want to know, and shift the attention from the marginal distribution of the parameters and the prior to the posterior or conditional probability of the parameters.

When we obtain a particular dataset $D$ and denote $\theta$ is the parameter that we are interested in, then the posterior can be denoted as $p(\theta|D)$; the likelihood denoted as $p(D|\theta)$, which means the probability of the data might be obtained with the parameter $\theta$ under certain model assumptions; and the prior denoted as $p(\theta)$, which means the credibility of the parameter values without $D$.

The marginal likelihood or the denominator in Bayes' rule can be rewritten for continuous variables using the denotations above as:

$$p(D) = \int \mathrm{d}\theta^* \, p(D|\theta^*)p(\theta^*) \tag{6}$$

where $\theta^*$denotes any possible value of $\theta$.

### 2.3.2 Bayesian model averaging

Bayesian model averaging (BMA) is an application of Bayesian inferential analysis. It has been applied to model selection problems, where one combines estimation and prediction to produce a straightforward model choice criteria and less risky predictions. By averaging over many different competing models, BMA incorporates model uncertainty into the estimation of parameters and prediction. BMA has been applied successfully in many statistical model classes including linear regression, generalized linear models (GLMs), Cox regression models, and discrete graphical models, in all cases improving predictive performance.[102] So the average estimation across a set of models would generate more robust interval estimation, and meanwhile, reduce the type I error.

Suppose in a study, $M_l$ is one of a set of models considered to fit the research question, $\Delta$ is the interested parameter, $D$ is the dataset given, then the BMA-averaged $\Delta$ is the sum of specific model derived $\Delta_l$ weighted by the posterior model probability $p(M_l|D)$ (Figure 8):[102]

$$E(\Delta|D) = \sum_{l=1}^{K} \Delta_l \, p(M_l|D) \tag{7}$$

Although we cannot get the posterior probability $p(M_l|D)$ directly, according to the Bayes' rule, the posterior for a given model $M_k$ is:

$$p(M_k|D) = \frac{p(D|M_k)\cdot p(M_k)}{\sum_{l=1}^{K} p(D|M_l)\cdot p(M_l)} \tag{8}$$

where $p(M_k)$ is the probability that $M_k$ is true and the likelihood $p(D|M_k)$ is given by:

$$p(D|M_k) = \int \mathrm{d}\theta_k \;\, p(D|\theta_k, M_k\,)\, p(\theta_k|M_k) \tag{9}$$

In equation (9), $\theta_k$ is the parameter vector of model $M_k$, $p(\theta_k|M_k)$ is the prior density of $\theta_k$ under model $M_k$, and $p(D|\theta_k, M_k\,)$ is the likelihood. The posterior distribution of $\Delta$ given data $D$ is:

$$p(\Delta|D) = \sum_{l=1}^{K} p(\Delta|M_l, D)\, p(M_l|D) \tag{10}$$

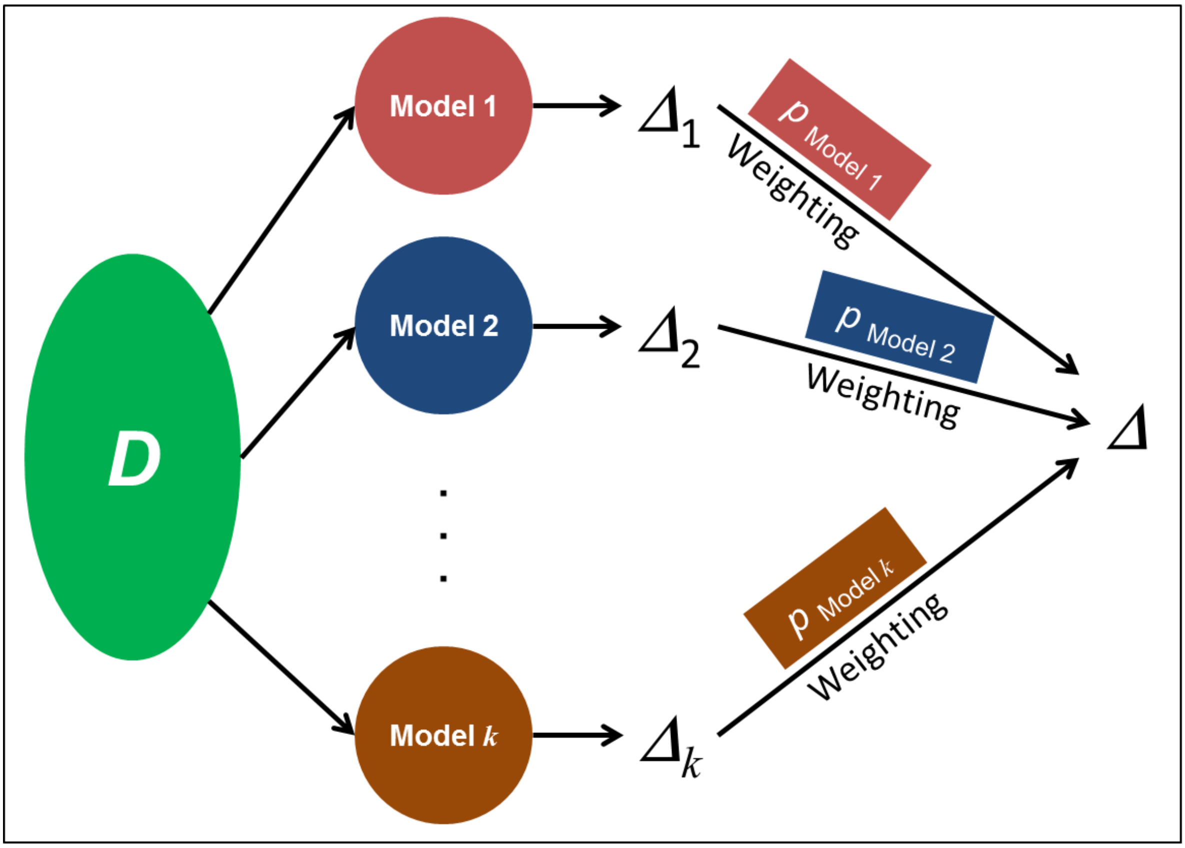



Figure 8. Illustration of Bayesian model averaging

Although there are some computational difficulties, by averaging all potential models, BMA provides better predictive results and less uncertainty. In the thesis, we demonstrated an application of BMA within a generalized additive mixed model (GAMM) frame in a time-series study.

### 2.3.3 Frequentist and Bayesian inferences in air pollution study

Both frequentist and Bayesian approaches are used to evaluate the evidence about competing hypotheses of health effects of air pollution. The Bayesian school uses probabilities for both hypotheses and data given the prior and likelihood of the data. The robustness of its result somehow depends on the subjective prior distribution. However, the frequentist school depends on the likelihood for observed and unobserved data and uses the conditional distribution. It presumes that a certain hypothesis is true and the observed data are sampled from that distribution.[103]

In literatures, GLM with parametric splines (e.g. natural cubic splines)[104] or GAM with nonparametric splines (e.g. smoothing splines or locally weighted smoothers [LOESS])[105] are used to estimate effects associated with exposure to air pollution while accounting for smooth fluctuations in outcomes that confound the estimated effects of pollution. These two similar models sever as different analytic purpose, usually GLM emphasizes on estimation and inference for the parameters of the model while GAM focuses on non-parametrical model for exploring the association between the dependent and independent variables.[106] The conventional algorithm for fitting GAM (hereinafter called frequentist GAM) is the back fitting algorithm and corresponding robust estimation method has also been developed.[107,108] A disadvantage of GAM is that it is difficult to integrate with the estimation of the degree of smoothness of the model terms, so that in practice the user must set these, or select between a modest set of predefined smoothing levels.

During recent decades, Bayes methods enjoyed the popularity due to the computational progress. A class of Markov chain Monte Carlo (MCMC) algorithm became a practical method to estimate the complex random variables instead of direct sampling. A detailed tutorial is given by Hanson and Kruschke.[101,109] A semi-parametric Bayesian approach and a simulation study was displayed by Conley et al.[110] The computationally efficient approaches such as fully Bayesian method thus have been developed in recent years. A fully Bayesian approach for modeling and inference within GAM requires prior assumption for unknown smooth function $S(\cdot)$. Several alternatives have been recently proposed for specifying smoothness prior for continuous covariates or time trends, such as random walk priors or more generally autoregressive priors[111,112], Bayesian P-splines[113], and Bayesian smoothing splines.[114]

Although there are some applications[115-119] of Bayesian GAM analysis in recent years, few of them compared the performance of frequentist and Bayesian GAMs in terms of accuracy and precision. In the thesis, we took advantage of the available citywide data in China including causes of death registry data and daily air quality monitoring data to conduct a simulation study. The study compared the estimates from frequentist and Bayesian methods using simulated data with underlying 'true' parameters based on a genuine time-series study on $PM_{2.5}$ and respiratory deaths in Shanghai.

# 3 AIMS

The overall aim of the studies is to develop a simple method to estimate the contribution of road traffic to $PM_{2.5}$ concentration in metropolises in China, and evaluate the spatiotemporal relationship of PM pollution with non-accidental mortality, by setting up the hybrid models and introducing the Bayes approach.

The specific objectives are as follows:

- Study I: to characterictize geographical profile of $PM_{2.5}$ concentrations in 16 municipal districts in Beijing, China, and develop a hybrid model to estimate the contribution of road traffic to $PM_{2.5}$ concentrations.
- Study II: to evaluate the association between daily $PM_{10}$ concentrations and respiratory mortality in eight municipal districts in Beijing, China using GAMM, and demonstrate the application of BMA method for GAM estimates.
- Study III: to quantify the effects of $PM_{2.5}$ on daily non-accidental mortality in Shanghai, China, and evaluate the interaction between weather conditions and $PM_{2.5}$ concentrations using a fully Bayesian approach within GAM framework.
- Study IV: to compared the performance of frequentist and Bayesian GAMs in terms of accuracy and precision using simulated data with underlying ‘true’ parameters derived from the genuine time-series data in Study III.

# 4 MATERIALS AND METHODS

## 4.1 STUDY DESIGN

All the four studies are time-series study using daily $PM_{2.5}$ or $PM_{10}$ concentrations, meteorological variables, traffic information, and population registry-based non-accidental death data in Beijing or Shanghai, China.

## 4.2 STUDY AREA AND POPULATION

The studies were conducted in the two biggest cities in China: Beijing, the capital city of China (studies I and II), and Shanghai, one of the biggest global financial centers in the southeast of China (studies III and IV).

### 4.2.1 Beijing (studies I and II)

Beijing, located in the northern China plain with a vast land of 16,410 $km^2$, 16 municipal districts and a population of 21.148 million, is surrounded by serval severe contaminated industry cites. However, 92% of the land belongs to the suburban and rural area. The urban area of Beijing covers a small central municipality’s part and spreads out in ring roads. The geographical distribution and demographical information of the 16 districts in Beijing is shown in Figure 9 and Table 1.

In studies I and II, the geographical information was collected by the College of Resources and Environment, University of Chinese Academy of Sciences.

In Study II, 10.38 million permanent residents from 8 municipal districts of Beijing and 9,559 respiratory deaths were included in the study period between Jan 1st, 2009 and Dec 31st, 2010.

### 4.2.2 Shanghai (studies III and IV)

Studies III and VI were conducted in Shanghai, one of the most important financial cities in the world and the largest transport hub in China, located in the Yangtze River Delta and bounded by the East Sea with a population of 24 million in 2014 and 6,340 $km^2$.[120] Due to its location, the whole city land is flat, divided into east and west sections by the Huangpu River. Compare to Beijing, the smog and PM pollution is lower, however it remains a substantial problem by European Union (EU) or U.S. standards.

There are also 16 municipal districts in Shanghai, all with own urban cores. The geographical distribution and demographical information of the districts are shown in Figure 10 and Table 2.

In studies III and IV, 336,379 non-accidental deaths occurred during the study period between January 1st, 2012 and December 31st, 2014 in Shanghai.


Figure 9. Geographical distribution of the 16 municipal districts in Beijing

Table 1. Demographical information of the 16 municipal districts in Beijing[121]

| District | Population (2010) | Area ($km^2$) | Population density (per $km^2$) |
|---|---|---|---|
| Dongcheng | 919,000 | 40.6 | 22,635 |
| Xicheng | 1,243,000 | 46.5 | 26,731 |
| Chaoyang | 3,545,000 | 470.8 | 7,530 |
| Haidian | 3,281,000 | 426.0 | 7,702 |
| Fengtai | 2,112,000 | 304.2 | 6,943 |
| Shijingshan | 616,000 | 89.8 | 6,860 |
| Tongzhou | 1,184,000 | 870.0 | 1,361 |
| Shunyi | 877,000 | 980.0 | 895 |
| Changping | 1,661,000 | 1,430.0 | 1,162 |
| Daxing | 1,365,000 | 1,012.0 | 1,349 |
| Mentougou | 290,000 | 1,331.3 | 218 |
| Fangshan | 945,000 | 1,866.7 | 506 |
| Pinggu | 416,000 | 1,075.0 | 387 |
| Huairou | 373,000 | 2,557.3 | 146 |
| Miyun | 468,000 | 2,335,6 | 200 |
| Yanqing | 317,000 | 1,980.0 | 160 |

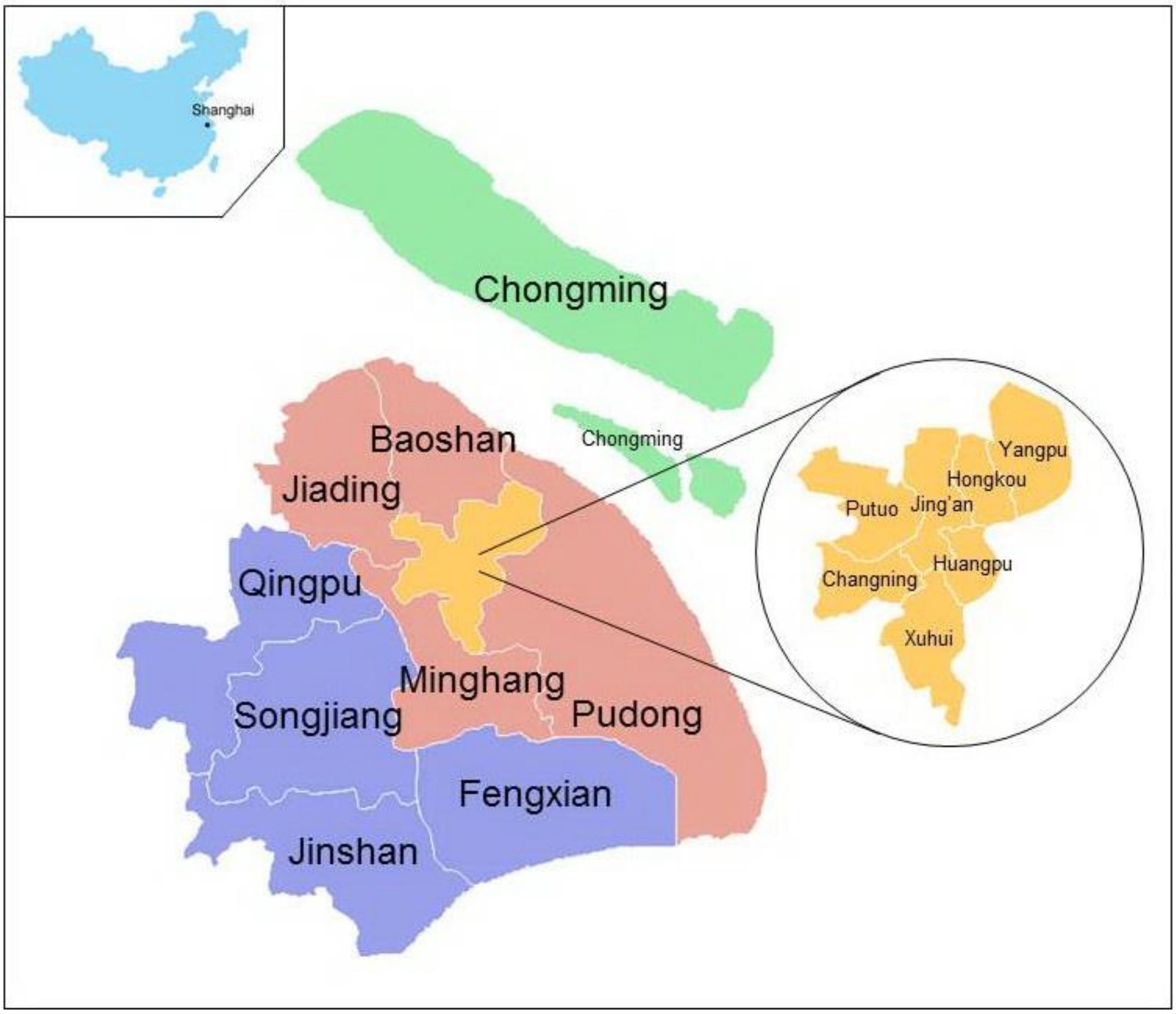



Figure 10. Geographical distribution of the 16 municipal districts in Shanghai

Table 2. Demographical information of the 16 municipal districts in Shanghai[122]

| District | Population (2015) | Area ($km^2$) | Population density (per $km^2$) |
|---|---|---|---|
| Huangpu | 658,600 | 20.46 | 32,190 |
| Xuhui | 1,089,100 | 54.76 | 19,889 |
| Changning | 691,100 | 38.30 | 18,044 |
| Jing'an* | 1,074,000 | 36.88 | 29,121 |
| Putuo | 1,288,000 | 54.83 | 23,491 |
| Hongkou | 809,400 | 23.46 | 34,501 |
| Yangpu | 1,315,200 | 60.73 | 21,657 |
| Minhang | 2,537,900 | 370.75 | 6,845 |
| Baoshan | 2,022,900 | 270.99 | 7,465 |
| Jiading | 1,568,231 | 464.20 | 3,378 |
| Pudong New Area | 5,474,900 | 1,210.41 | 4,523 |
| Jinshang | 798,000 | 586.05 | 1,362 |
| Songjiang | 1,760,200 | 605.64 | 2,906 |
| Qingpu | 1,209,100 | 670.14 | 1,804 |
| Fengxian | 1,159,900 | 687.39 | 1,687 |
| Chongming | 696,400 | 1,185.49 | 587 |

* Combined with Zhabei district on November 4, 2015.

## 4.3 AIR QUALITY AND METEOROLOGICAL DATA

### 4.3.1 Beijing (studies I and II)

Because of the unique location, increasing industrialization, and dramatically increased coal and fossil fuel burning, Beijing has been suffered from environmental problems for a long period. Since October 2012, Beijing has established 35 fixed AQM stations across the entire municipal area (Figure 11). Both hourly ambient air pollution concentrations and air quality indices (AQI) are reported by the AQM stations. Beijing has a monsoon-influenced humid continental climate, with four distinctive seasons, very dry and cold winter, and humid and hot summer. The average temperature high varies from 1.8 °C in January to 30°C in June and July, and the temperature low usually is between -8°C to 22°C.

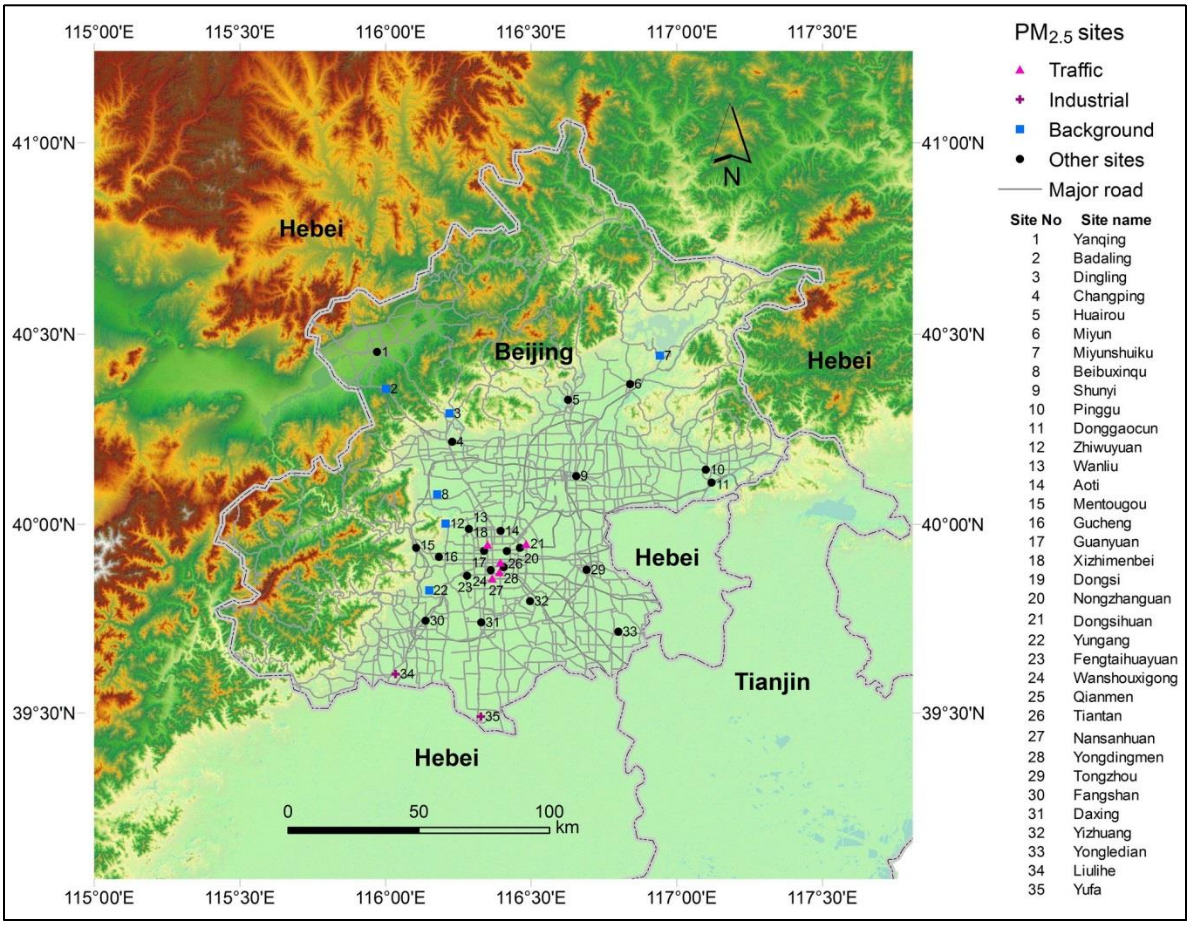



Figure 11. Distribution of 35 air quality monitoring stations in Beijing

In Study I, hourly $PM_{2.5}$ concentrations from the 35 AQM stations during January 1st, 2013 to December 31st, 2014 were collected by the College of Resources and Environment, University of Chinese Academy of Sciences. According to the standard of Ministry of Environmental Protection of China, the AQI measurements are classified into six categories, good, moderate, unhealthy for sensitive group, unhealthy, very unhealthy, and hazardous.[123,124] Daily meteorological data during the same period were obtained from National Meteorological Information Center of China, which included temperature, wind speed, wind direction, barometric pressure, rainfall volume and hours of daylight. In Study II, daily air quality data included the concentrations of $PM_{10}$, nitrogen oxides ($NO_x$) and CO and meteorological conditions were obtained from eight districts having AQM stations in Beijing between January 1st, 2009 and December 31st, 2010. Furthermore, for Study I, five-minute traffic volume and speed data per 30 minutes from eight road conjunctions in core city districts were also collected by University of Chinese Academy of Sciences between January 1st, 2013 and December 31st, 2014. Traffic densities of the AQM stations were calculated using an inverse function of mean road vehicle speed on the main roads.[125]

### 4.3.2 Shanghai (studies III and IV)

In studies III and IV, daily average $PM_{2.5}$ concentrations between January 1st, 2013 and December 31st, 2014 were obtained from the Shanghai Meteorological Bureau. Only the measurements from one AQM station were available during the study period and used for whole Shanghai area. Because $PM_{2.5}$ was not routinely monitored in Shanghai until late 2012, the hourly $PM_{2.5}$ data in 2012 were obtained from the online database published by the AQM station of the U.S. Consulate General in Shanghai, China, which is located in the Xuhui district of Shanghai.[126] The daily average $PM_{2.5}$ concentrations in 2012 were calculated from the hourly concentrations published by the U.S. Consulate General in Shanghai. Recent studies have indicated that $PM_{2.5}$ data from the U.S. embassy and consulates' AQM stations were highly consistent with those reported by local AQM stations.[127,128] Shanghai has a climate with subtropical characteristic, characterized by very humid summer and winter, comparatively dry and pleasant autumn. The average temperature averages around 4.2°C in January and 28°C in July. Daily meteorological data from Jan 1st, 2013 to Dec 31st, 2014 were obtained from Shanghai Meteorological Bureau. Citywide daily meteorological data used in studies III and IV include temperature, relative humidity, barometric pressure, wind speed, precipitation and sunshine time et al. No district-specific data were available in studies III and IV.

## 4.4 MORTALITY DATA

In Study II, the respiratory mortality data between January 1st, 2009 and December 31st, 2010 were obtained from the Causes of Death Registry (CDR) in Beijing. The causes of death were coded according to the 10th version of the International Classification of Disease (ICD-10). Death codes J00-J98 were used to identify deaths due to respiratory diseases.

In studies III and IV, the daily mortality data from Jan 1st, 2012 to Dec 31st, 2014 were obtained from the CDR in Shanghai collected by Shanghai Municipal Center for Disease Control and Prevention (SCDC). Deaths for all non-accidental causes (ICD-10 codes A00-R99) and respiratory diseases (ICD-10 codes J00-J99) were examined. Individual information of age, sex, occupation, education, residential area and smoking rate were also obtained from SCDC and summarized for each 5-year age group.

## 4.5 METHODS FOR CATEGORIZING WEATHER CONDITIONS

To investigate the effects of weather conditions on non-accidental mortality and interaction between weather conditions and $PM_{2.5}$ in studies III and IV, we identified extreme weather conditions and categorized the days into different synoptic types during the study period.

According to *Guidelines on Analysis of Extremes in a Changing Climate in Support of Information Decision for Adaptation of the World Meteorological Organization* (Climate Data and Monitoring, WCDMP-No. 72),[129] one of the methods to get extreme weather is to calculate the number of the days in a year exceeding specific threshold. Day-count indices based on percentile threshold are expression of anomalies related to local climate. These anomalies have fixed rarity, that is, the thresholds are chosen so as to be exceeded at a fixed frequency, often 10 percent. As for the statistical modelling, usually the extreme quantiles were estimated from an extreme value distribution, usually using the "peaks over threshold" mothed or "block maximum" method. We adopted the similar rule to define extreme weather conditions in our study as the daily minimum/maximum temperature, minimum/maximum barometric pressure, average humidity or wind speed lower or higher than the corresponding yearly the 10th percentile or the 90th percentile in the 3-year study period, respectively. The derived eight extreme weather conditions are hot, cold, hyperbaric, hypobaric, humid, dry, windy and windless. Numbers of the days with two or more extreme conditions are shown in Table 3.

Table 3. Numbers of the days with two or more extreme weather conditions

| | Hot n=109 | Cold n=109 | Hyperbaric n=107 | Hypobaric n=105 | Humid n=101 | Dry n=103 | Windy n=100 | Windless n=94 |
|---|---|---|---|---|---|---|---|---|
| Cold | | | | | | | | |
| Hyperbaric | | 60 | | | | | | |
| Hypobaric | 40 | | | | | | | |
| Humid | | | | 13 | | | | |
| Dry | 16 | 18 | 12 | 9 | | | | |
| Windy | 14 | 8 | 7 | 22 | 11 | 6 | | |
| Windless | 4 | 20 | 11 | 8 | 17 | | | |

We also categorized the observed days in studies III and IV into different synoptic weather types (SWTs) as proposed by Kalkstein et al.[130] Our clustering approach offered categories by 15 meteorological parameters, including three barometric pressure measurements, three temperature measurements, two humidity measurements, five wind speed measurements, one precipitation measurement and one time of sunshine measurement. Since there was high inter-correlation within these parameters, we used principal component analysis (PCA) for dimensionality reduction for the variables. As a result, we got six principal components (PCs) that may explain 93% of the variance of the original 15 meteorological parameters, therefore we classified the 1096 days into six SWTs based on six PCs, which are hot dry, warm humid, cold dry, moderate dry, moderate humid and cold humid weather types. Meteorological profiles and $PM_{2.5}$ concentrations of the SWTs are shown in Table 4.

Table 4 Meteorological characteristics and $PM_{2.5}$ concentrations of synoptic weather types

| | Number of days | Pressure (kPa) | Temperature (°C) | Humid (%) | Precipitation (mm) | Wind speed (m/s) | Sunshine (hour) | $PM_{2.5}$ (μg/m$^3$) |
|---|---|---|---|---|---|---|---|---|
| Hot dry | 167 | 100.6±0.4 | 28.4±4.0 | 62.0±10.2 | 1.25±4.55 | 3.41±0.91 | 8.79±2.76 | 41.2±29.3 |
| Warm humid | 214 | 100.8±0.4 | 23.8±3.8 | 79.9±6.9 | 4.11±8.28 | 2.24±0.63 | 2.25±32.77 | 49.5±30.1 |
| Cold dry | 158 | 102.4±0.4 | 8.0±5.1 | 60.8±13.2 | 0.98±3.43 | 2.82±0.94 | 5.45±3.39 | 82.8±50.6 |
| Moderate dry | 225 | 101.7±0.3 | 18.5±3.8 | 66.4±10.8 | 0.32±1.35 | 2.68±0.68 | 6.67±3.30 | 49.0±30.4 |
| Moderate humid | 107 | 101.1±0.6 | 19.1±6.1 | 82.3±8.3 | 17.28±25.26 | 3.83±1.17 | 8.99±1.76 | 40.4±25.1 |
| Cold humid | 225 | 102.5±0.4 | 6.7±3.2 | 72.0±9.6 | 1.81±4.39 | 2.48±0.82 | 3.32±3.36 | 63.5±42.9 |

## 4.6 STATISTICAL METHODS

### 4.6.1 Two-stage method to estimate the contribution of road traffic to fine particle concentrations (Study I)

In Study I, we developed a two-stage method to estimate the road traffic contribution to the daily ambient fine particle ($PM_{2.5}$) concentrations measured in Beijing. Thirty-five AQM stations were categorized into four groups, including six background stations, five traffic stations, two industrial stations and 22 other stations adjusted for the locations, traffic densities and meteorological conditions. Background stations were comparatively located far away from the busy roads, therefore they were less affected by traffic emission and most of pollution variation was accounted for geographic trend, usually heavier in the south part than in the north. In the first stage, regional non-traffic portion of $PM_{2.5}$ in the background stations was fitted by a three-level generalized liner mixed model (GLMM) and the traffic contribution to $PM_{2.5}$ at the background stations was then estimated by a dispersion model:

$$\hat{C}_{p(t)} = [k_1\times C_{p(t-1)} + k_2 \times \frac{1}{\sqrt{D_{ind_p}}} \times C_{ind(t)} \times (\widehat{W}_{ind(t)}/W_{avg})^{k_3} + k_4 \times \frac{1}{\sqrt{D_{traffic_p}}} \times C_{traffic(t)} \times (\widehat{W}_{traffic(t)}/W_{avg})^{k_3}] \times e^{-k_5\times W_{(t)}} \quad (11)$$

where $\hat{C}_{p(t)}$ denotes the expected $PM_{2.5}$ concentration at station $p$ on day $t$; $C_{p(t-1)}$ denotes the observed $PM_{2.5}$ concentration on day $t$-1; $D_{ind_p}$ represents the average distance from station $p$ to industrial stations; $C_{ind(t)}$ denotes the observed $PM_{2.5}$ concentration of industrials stations on day $t$; $D_{traffic_p}$ represents the average distance from station $p$ to traffic stations; $C_{traffic(t)}$ denotes the observed $PM_{2.5}$ concentration of traffic stations on day $t$; $\widehat{W}_{ind(t)}$ denotes the summation of valid flux of wind from industrial stations and $\widehat{W}_{traffic(t)}$ means the summation of valid flux of wind from traffic stations on day $t$; $W_{avg}$ is the average wind speed of the year; $W_{(t)}$ is the maximum wind speed on day $t$; and $k_1,\cdots,k_5$ are the parameters to be estimated.

The dispersion model made the reference to the hybrid single-particle Lagrangian integrated trajectory (HYSPLIT) model used to track the transport corridors that are regarded as a "region of influence" i.e. the five traffic stations and two industrial stations in our study.[131] According to the community multiscale air quality (CMAQ) model, all emissions are assumed to be instantaneously well-mixed and have own lifetime.[132] The model simulated the decay of previous pollutant concentration mixed with newly dispersed pollution making use of $PM_{2.5}$

concentrations of certain station, distance between the stations, wind speed and wind direction. The parameters $k_1,\cdots,k_5$ in the model were estimated by computational method of Levenberg-Marquardt and global minimum algorithm till their convergence in software 1stOpt.[133]

Based on equation (11), the daily traffic contribution to $PM_{2.5}$ at background stations can be calculated as:

$$T_{p(t)}\% = \frac{k_4 \times \frac{1}{\sqrt{D_{traffic_p}}} \times C_{traffic(t)} \times (\frac{\widehat{W}_{traffic(t)}}{W_{avg}})^{k_3} \times e^{-k_5 \times W_{(t)}}}{C_{p(t)}} \times 100\% \quad (12)$$

where $T_{p(t)}\%$ is estimated percentage of daily traffic contribution to total $PM_{2.5}$ concentration at background stations. Meanwhile, the expected daily non-traffic contribution ${NT_{p(t)}}^*$ can be calculated as:

$${NT_{p(t)}}^* = C_{p(t)} \times (1 - T_{p(t)}\%) \quad (13)$$

The second stage is to quantify the non-traffic contribution to $PM_{2.5}$ concentrations at non-background stations. In this stage, a GAMM was established with B-spline as additive smoothing function. The numbers of knots were determined by minimizing Akaike information criterion (AIC). The final selection of the variables was determined by the top-down rule.[134] The final GAMM is:

$$log\left(NT_{p(t)}\right)^* = \beta_0 + \beta_1 \times Y_p + \beta_2 \times Wind_{(t)} + \beta_3 \times Light_{(t)} + \beta_4 \times Rain_{(t)} + \boldsymbol{\beta}_5 \times Max\_wind\_dir_{(t)} + \boldsymbol{\beta}_6 \times DOW_t + S(t, k = 10\ per\ year) + S\left(temperature_{(t)}, k = 5\right) + s\left(humid_{(t)}, k = 5\right) + S\left(atmos_{(t)}, k = 4\right) + \mu \times Z_p \quad (14)$$

where $log\left(NT_{p(t)}\right)^*$ is expected log transformed non-traffic $PM_{2.5}$ concentration; $\beta$s are parameters to be estimated; $S(.)$s are additive smoothing functions which illustrate the effects of day, temperature, humidity and atmospheric pressure on non-traffic concentrations; $Z_p$ is a random intercept for station $p$.

Log transformed non-traffic $PM_{2.5}$ concentrations at non-background station $q$, $log\left(NT_{q(t)}\right)^*$, were then predicted using equation (14). The estimated contribution of road traffic to $PM_{2.5}$ contribution at non-background station $q$, $T_{q(t)}\%$ , was calculated as observed $PM_{2.5}$ concentration deducted by estimated non-traffic $PM_{2.5}$ concentration:

$$T_{q(t)}\% = \frac{C_{q(t)} - e^{\log(NT_{q(t)})^*}}{C_{q(t)}} \times 100 \quad (15)$$

The whole process of the two-stage method is demonstrated in Figure 12.

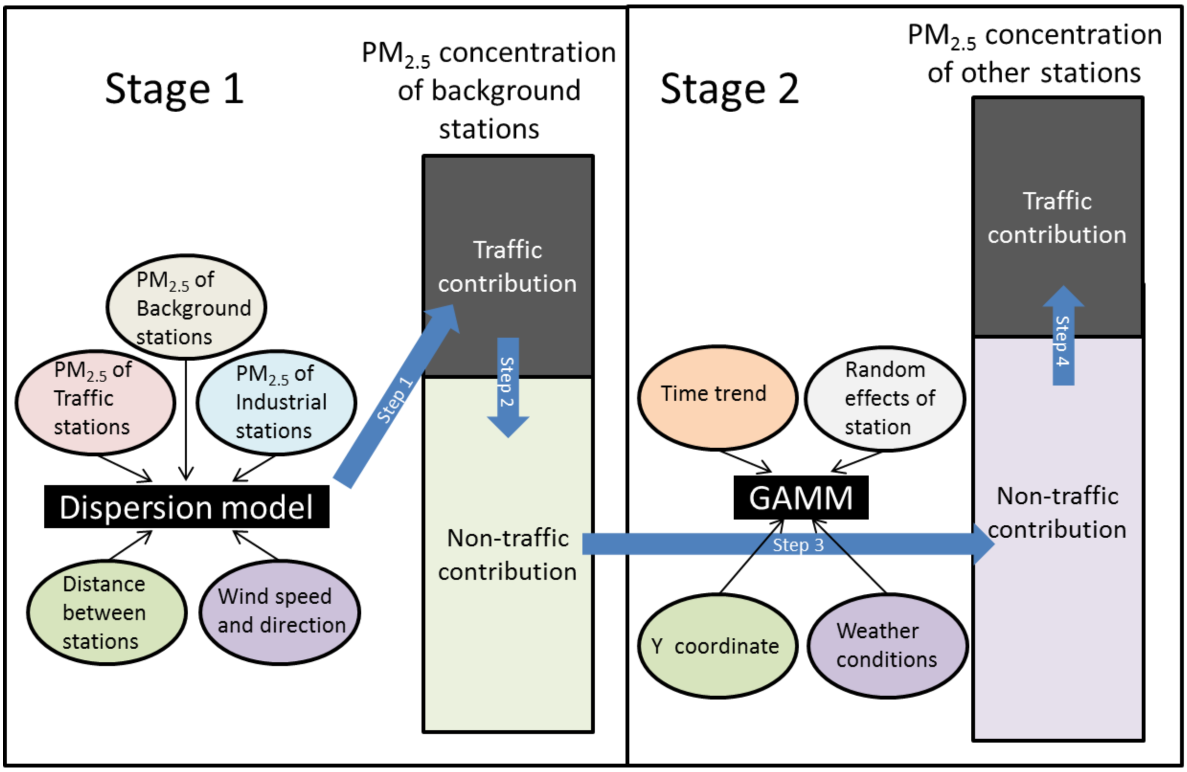



Figure 12. Two-stage method for estimating road traffic contribution to $PM_{2.5}$ concentrations in Beijing, China

### 4.6.2 Bayesian model averaging within the generalized additive mixed model frame (Study II)

In this time-series study, we evaluated the association between daily $PM_{10}$ concentrations and respiratory deaths in eight municipal districts in Beijing using GAMM. The daily deaths due to respiratory diseases subjected to quasi-Poisson distribution. To model the nonlinear relationship with daily deaths, the GAMM used calendar day, temperature and barometric press as nonparametric part and district as random effect. As for the smoothing function, we used natural splines for calendar day, temperature and barometric pressure. The optimal number of knots was selected by AIC. For the parametric part, we included the $PM_{10}$ concentration, humidity, wind speed and day of the week (DOW). The full GAMM can be expressed as:

$$\mathrm{Log}\left(\mathrm{E}\left(y_{i,t}\right)\right) = \beta_0 + \beta_1 \times \mathrm{PM}_{10_{i,t}} + \beta_2 \times \text{Relative Humidity}_t + \beta_3 \times \text{Wind speed}_t + \beta_4 \times \mathrm{DOW}_t + S(\mathrm{Day}_t, n_1/\ \mathrm{year}) + S(\mathrm{Temperature}_t, n_2) + S(\text{Barometric pressure}_t, n_3) + \beta \times \mathrm{District}_i + Z_i\mu + \log(\mathrm{Population}_i) \quad (16)$$

where $E(y_{i,t})$ is the expected number of deaths in district $i$ on the $t$th day, DOW is a dummy variable for day of week, $\mathrm{District}_i$ is a dummy variable for the eight districts and $Z_i$ is a random intercept for districts $i$. $S(.)$s are the smoothing functions realized by natural cubic spline with $n_1$ knots per year to adjust for long-term temporal trend, $n_2$ knots for temperature and $n_3$ knots for barometric pressure.

Since we had very few information about the time trend in mortality, the knots selection would increase the model uncertainty and leading to over-confident inferences, therefore we used BMA method to build up a more robust predictive performance. The BMA estimation as illustrated in equation 7 and Figure 8 essentially is an average of posterior estimations under each model we've considered, weighted by the posterior model probabilities. For Bayesian reference in Study II, we assumed the prior probability of the models followed a uniform distribution:

$$p(M_l) = \frac{1}{K} \tag{17}$$

The likelihood $p(D|M_k)$ in equation (9) can be approximately estimated using Bayesian information criterion (BIC), thus the posterior probability of model *k* could be represented as:[135]

$$p(M_k|D) = \frac{p(M_l)\cdot e^{-0.5\cdot BIC_{M_k}}}{\sum_{l=1}^{K}[p(M_l)\cdot e^{-0.5\cdot BIC_{M_l}}]} \tag{18}$$

To simplify the computation, equation 18 can be rewritten as:

$$\mathrm{pr}(M_k|D) = \frac{e^{-0.5(BIC_{M_k}-\overline{BIC})}}{\sum_{l=1}^{K} e^{-0.5(BIC_{M_l}-\overline{BIC})}} \tag{19}$$

where $\overline{BIC}$ is the average of the BICs for all models. With this key step, the weight in equation 7 can be analytically solved in any mainstream statistical software. We have already given the BMA expectation of the interested parameter $\Delta$ in equation (7), and the corresponding variance is given by:[102]

$$\begin{aligned}
\mathrm{Var}[\Delta|D] &= \textstyle\sum_{l=1}^{K}(\mathrm{Var}[\Delta|D, M_l] + (\Delta_l - E[\Delta|D])^2)p(M_l|D) \\
&= \textstyle\sum_{l=1}^{K}\left(\mathrm{Var}[\Delta|D, M_l] + \left(\Delta_l^2 - 2\Delta_l\cdot E[\Delta|D] + E[\Delta|D]^2\right)\right)p(M_l|D) \\
&= \textstyle\sum_{l=1}^{K}\left(\mathrm{Var}[\Delta|D, M_l] + \left(\Delta_l^2 - 2\Delta_l\cdot E[\Delta|D]\right)\right)p(M_l|D) + E[\Delta|D]^2\sum_{l=1}^{K}p(M_l|D) \\
&= \textstyle\sum_{l=1}^{K}\left(\mathrm{Var}[\Delta|D, M_l] + \Delta_l^2\right)p(M_l|D) - 2E[\Delta|D]\sum_{l=1}^{K}\Delta_l\cdot p(M_l|D) + E[\Delta|D]^2 \\
&= \textstyle\sum_{l=1}^{K}\left(\mathrm{Var}[\Delta|D, M_l] + \Delta_l^2\right)p(M_l|D) - 2E[\Delta|D]\cdot E[\Delta|D] + E[\Delta|D]^2 \\
&= \textstyle\sum_{l=1}^{K}\left(\mathrm{Var}[\Delta|D, M_l] + \Delta_l^2\right)p(M_l|D) - E[\Delta|D]^2
\end{aligned} \tag{20}$$

where $\Delta_l = E[\Delta|D, M_l]$. The 95% Bayesian credible interval (CrI) of $\Delta$ is:

$$E[\Delta|D]\pm 1.96\sqrt{\mathrm{Var}[\Delta|D]} \tag{21}$$

### 4.6.3 Generalized additive model within fully Bayesian frame (Study III)

In study III, we applied the GAM for fitting and inference within a fully Bayesian frame to evaluate the associations of non-accidental mortality with $PM_{2.5}$ concentrations and extreme weather conditions in Shanghai, China. The daily non-accidental deaths in Shanghai followed a Poisson distribution. We set up a model with log form of expected daily death count as dependent variable, and $PM_{2.5}$ concentration, gender, age, job, day of week, and smoking status as independent variables. A smoothing function for calendar day was included to present the seasonal trend of deaths. To investigate the impact of weather on mortality, we generated a set of dummy variables for the extreme weather conditions and SWTs. The interaction between weather variables and $PM_{2.5}$ was also taken into consideration. With regard to knot selection for the smoothing function, according to generalized cross-validation and our simulation study, which indicated that 14 knots were enough to present the temporal trend and capture the underlying true parameter of $PM_{2.5}$, five knots per year was adopted to fit the temporal trend of death. The final GAM linking the mortality with $PM_{2.5}$ and weather conditions is given by:

$$\log\big(E(Y_t)\big) = \beta_0 + \beta_1 \cdot PM_{2.5,t} + \boldsymbol{\beta_2} \cdot \boldsymbol{W}_t + \boldsymbol{\beta_3} \cdot PM_{2.5,t} \times \boldsymbol{W}_t + \beta_4 \cdot Sex + \boldsymbol{\beta_5} \cdot \boldsymbol{Age} + \boldsymbol{\beta_6} \cdot \boldsymbol{Job} + \boldsymbol{\beta_7} \cdot \boldsymbol{DOW}_t + \beta_8 \cdot Smoking + S(t) \tag{22}$$

where $E(Y_t)$ refers to the expected count of deaths on calendar day *t*; $PM_{2.5,t}$ refers to the $PM_{2.5}$ concentration on day *t*; $\boldsymbol{W_t} = (W_1, \cdots, W_j)'$ denotes a vector of the *j* (=5 or 7) dummy variables of the six SWTs or the eight extreme weather conditions on day *t*; $PM_{2.5,t} \times \boldsymbol{W}_t$ denotes the interaction term between $PM_{2.5}$ and $\boldsymbol{W}_t$; *Sex* is a dummy variable of sex; $\boldsymbol{Age}$ denotes a vector of the dummy variables of age groups; $\boldsymbol{Job}$ denotes a vector of the dummy variables of occupations; $\boldsymbol{DOW}_t$ denotes a vector of the dummy variables of day of week; *Smoking* denotes smoking rate; *S*(*t*) is the smoothing function for *t* realized by cubic B-splines.

To benefit from Bayesian approach with as limited influence from the prior distribution as possible, we chose the Jeffreys' distribution as the prior distribution, which does not change much over the region where the likelihood is significant and does not have large values outside that range, i.e. the local uniformity property. Because of this good attribution that is consistent with the prior distribution after several transformation, it is always a practical way of setting a non-informative prior in Bayes model. [136-138]

Depending on the parameterization in equation (22) and daily mortality *Y* follows a Poisson distribution, the likelihood for an observed *Y* given data *X* is given by:

$$L(Y|\boldsymbol{X}, \boldsymbol{\beta}, \boldsymbol{S}) = \prod_{t=1}^{N} \left\{ \frac{e^{-e^{\beta_0 + X_t^T\beta + S(t)}} e^{[\beta_0 + X_t^T\boldsymbol{\beta} + \boldsymbol{S}(t)]Y_t}}{Y_t!} \right\} \tag{23}$$

As a very key step that Bayes model bridges the prior to the posterior, we reallocated the CrI of the parameters value by MCMC simulation method with adaptive rejection sampling algorithm to overcome the integration problem of high dimensional data. We also implemented the adaptive rejection Metropolis sampling (ARMS) algorithms to increase the computational efficiency.[139] Implementation of the ARMS algorithm in our study is based on the code provided by Gilks.[140] To define the convergence of MCMC chain, we set the Gelman-Rubin statistics less than 1.01 as the stop sign.[141,142] Representative of the MCMC chains was evaluated visually using the trace plots,[101] and dependency and efficiency of the chains were evaluated using autocorrelation and effective sample sizes (ESS).[143]

We reported the posterior mean of $\beta_i$ with corresponding CrI$_i$. The definition of posterior mean is:

$$E(\beta_i|\boldsymbol{X}, Y, \boldsymbol{S}) = \int \beta_i \, p(\beta_i|\boldsymbol{X}, Y, \boldsymbol{S}) d\beta_i \tag{24}$$

where $p(\beta_i|\boldsymbol{X}, Y, \boldsymbol{S})$ is posterior probability of $\beta_i$ given the observed $\boldsymbol{X}$ and $Y$. The definition of posterior CrI$_i$ is:

$$p(\beta_i \in \mathrm{CrI}_i|\boldsymbol{X}, Y, \boldsymbol{S}) = \int_{\mathrm{CrI}_i} p(\beta_i|\boldsymbol{X}, Y, \boldsymbol{S}) d\beta_i \tag{25}$$

### 4.6.4 Simulation of time-series data based on quasi-Poisson distribution (Study IV)

The distribution of the observed daily respiratory mortality in Shanghai and the theoretical quasi Poisson distribution with the same mean and an overdispersion index = 1.3 are shown in Figure 13. In the simulation study, the estimates derived from the real world data were used as 'true' parameters. We used the predicted daily deaths $\widehat{Y_t}$ as the mean daily deaths, then simulated daily deaths $Y_t'$ by multiplying $\widehat{Y_t}$ by a random error $e^{\varepsilon}$:

$$Y_t' = \widehat{Y_t} \cdot e^{\varepsilon}, \varepsilon \sim \mathrm{N}(0, \sigma^2) \tag{26}$$

where $\varepsilon$ follows a distribution from exponential family and we applied normal distribution here. The simulation framework ensures that the same concurvity will exist between the simulated mortality and covariates. By changing $\sigma$ we may introduce different 'noise' in mortality to simulate the effects from unobserved confounders. In our simulation, the changing of the $\sigma$ was achieved by multiplying $\hat{\sigma}$, the standard deviation (SD) of logarithmic daily deaths, by a factor $\gamma$, i.e. $\sigma = \gamma\hat{\sigma}$. By selecting different random seeds, we may generate different time-series using random number generator in any statistical software. Figure 14 shows nine simulated time-series of daily respiratory deaths for $\gamma$=0.1, 0.2, …, 0.9. We can see that when $\gamma$ is equal to 0.4 or 0.5 the simulated data are most approximate to the real world data.

In the first simulation, we set $\gamma$=0.5, 0.6, …, 1.0 to generate six sets of simulated respiratory mortality data, where each set included 2,000 time-series. In total, 12,000 time-series datasets were generated. When we run the frequentist GAMs using simulated daily mortality as dependent variable we set the degrees of freedom (*df*) for $S(t)$ from 1 to 20 per year in our models. For each *df* we run the frequentist GAM using 100 simulated time-series.

In the second simulation, we investigated the impact of informative priors rather than non-informative uniform prior on the posterior parameter $\beta_1$ of $PM_{2.5}$. We simulated the time-series of daily respiratory mortality with a fixed $\sigma$ = 0.5$\hat{\sigma}$ and true $\beta_1$ = 0.0049. In our analyses, we used a normal prior for $\beta_1$, and set the varied prior mean $\mu(\beta_1)$ ranging from 0.001 to 0.020 by 0.001, and varied prior variance [$V(\beta_1)$] equal to $\gamma\beta_1$, where $\gamma$=0.5, 0.6, …, 1.0. For each combination of $\mu(\beta_1)$ and $V(\beta_1)$, we did 100 analyses. In total 12,000 simulated time-series datasets were used.

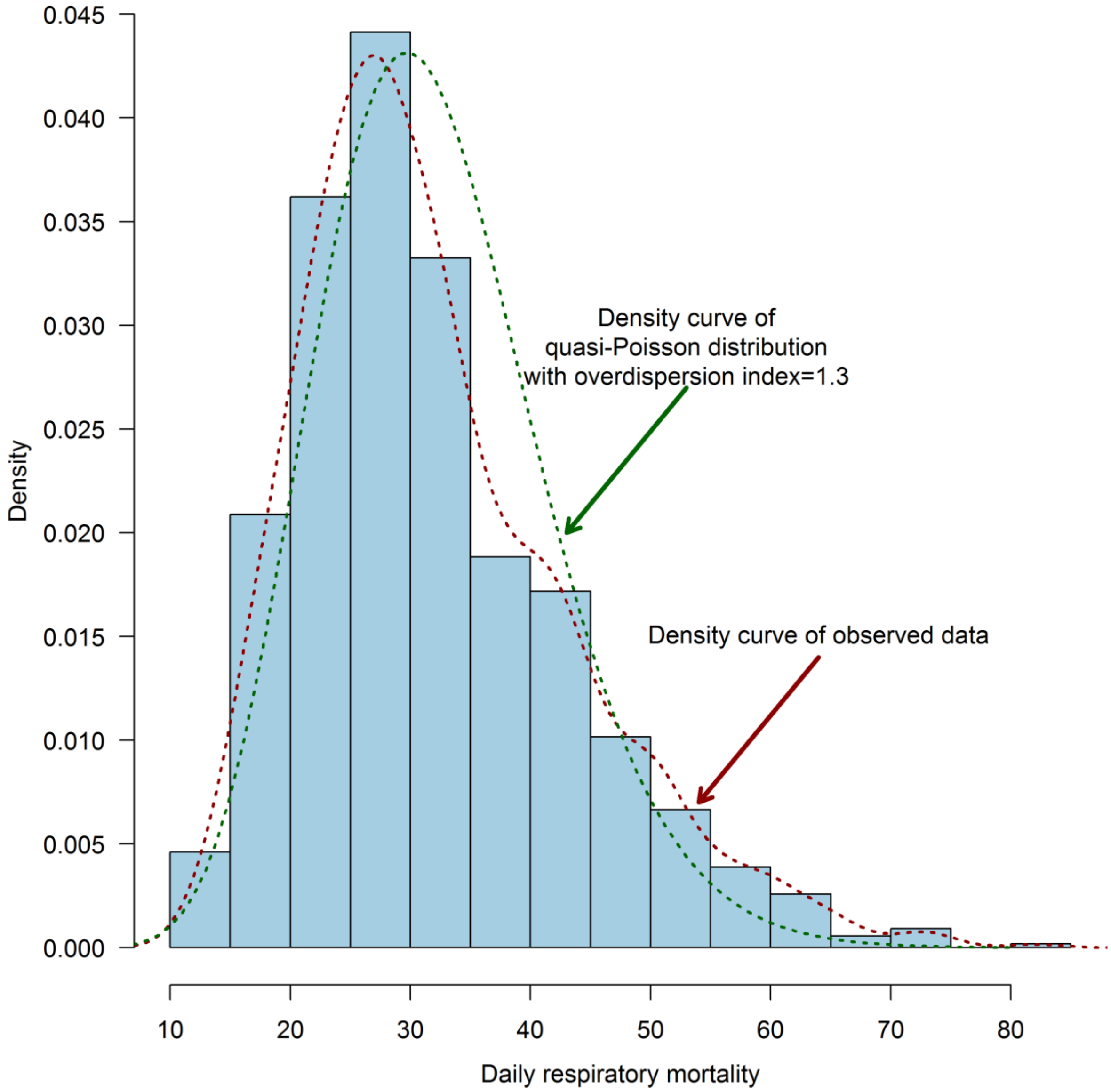



Figure 13. Distribution of the observed daily respiratory deaths in Shanghai and theoretical distribution quasi-Poisson distribution (mean=32, overdispersion index=1.3)

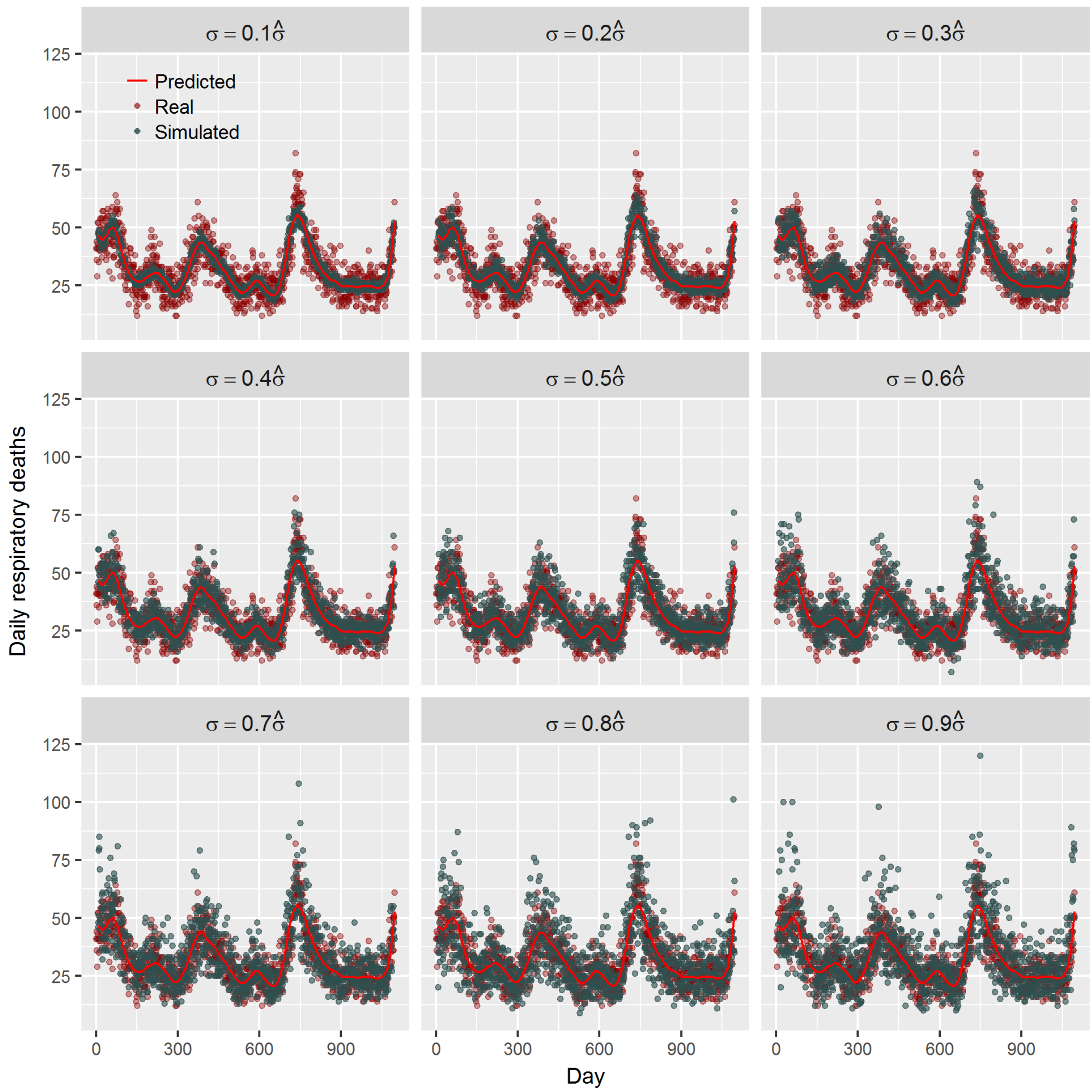



Figure 14. Examples of simulated time-series of daily respiratory deaths with different random noises

### 4.6.5 Comparison of frequentist and Bayesian generalized additive models (Study IV)

We used the distributed lag model instead of a single-day exposure model in Study IV. The basic form of the distributed lag GAM applied in the study may be expressed as:[144]

$$log\big(E(Y_t)\big) = \beta_0 + \beta_l X_{t-l} + S(t) + S(weather) + \boldsymbol{\phi} \cdot \boldsymbol{DOW}_t \qquad (27)$$

where $Y_t$ is count of daily deaths, $\beta_0$ denotes the intercept, $t$ indicates calendar day, $X_t$ are daily concentration of the studied air pollutant, i.e. $PM_{2.5}$ in our study, $l$ is the lag time of the pollution exposure (which is generally restricted to 1 to 7 days for acute effects), $S(\cdot)$ denotes a smooth function of a covariate (calendar day or meteorological variable such as temperature and humidity). $\boldsymbol{\phi}$ is the vector of the regression coefficients associated with vector $\boldsymbol{DOW}_t$ (indicating the 7 days of a week) for the $t$th day. $\beta_l$ is the parameter of our interest describing the change in the logarithm of the average mortality count over population per unit of change in $X_{t-l}$.

We defined the unknown function evaluation $S_j(\cdot)$ as the matrix product of a design matrix $\boldsymbol{\psi}_j$ and a vector of unknown parameters $\boldsymbol{\beta}_j$ with variance parameter $\tau_j^2$, i.e.:[145,146]

$$S_j(\cdot) = \boldsymbol{\psi}_j \boldsymbol{\beta}_j, j = 1, \cdots, p \quad (28)$$

then we obtain the predictor in equation (27) as

$$log\big(E(Y_t)\big) = \beta_0 + \beta_l X_{t-l} + \textstyle\sum_{j=1}^{p} \boldsymbol{\psi}_j \boldsymbol{\beta}_j + \boldsymbol{\phi} \cdot \boldsymbol{DOW} \quad (29)$$

Depending on the above parameterization of the model, the posterior for fully Bayesian inference is given by:

$$p(\beta_0, \beta_l, \boldsymbol{\beta}_1, \cdots, \boldsymbol{\beta}_p, \tau_1^2, \cdots, \tau_p^2, \boldsymbol{\phi} | y) \propto L(y, \beta_0, \beta_l, \boldsymbol{\beta}_1, \cdots, \boldsymbol{\beta}_p, \boldsymbol{\phi}) \textstyle\prod_{j=1}^{p} \big(p(\boldsymbol{\beta}_j | \tau_j^2) p(\tau_j^2)\big) \quad (30)$$

where $L(\cdot)$ denotes the likelihood which is the product of individual likelihood contributions.

In the fully Bayesian approach, parameter estimates are obtained by drawing random samples from the posterior (30) via MCMC simulations techniques. More details about the fully Bayesian inference can be found in Fahrmeir and Lang[111], and Brezger and Lang[147].

## 4.7 STATISTICAL SOFTWARE

All the analyses in the studies were performed in SAS 9.4 M4 (SAS Institute Inc, Cary, North Carolina, U.S.), Stata 14.2 (StataCorp LLC, College Station, Texas, U.S.), and R 3.33 (R Foundation for Statistical Computing, Vienna, Austria).

## 4.8 ETHICAL CONSIDERATIONS

The four studies are observational study and based on Chinese population-based CDRs, which only observed and analyzed information about exposure to risk factors and health outcomes but did not alter the health care services that the participants received, and there was not any conflict between the investigators and grant bodies. The anonymized data files obtained from the Chinese collaborators are stored in the server in the Institute of Environmental Medicine, Karolinska Institutet. Only researchers directly involved in the analysis are authorized to the access. All data had been anonymized when we started to process them for the specific research questions, and the data were analyzed and reported exclusively at group level. Since we only used de-identified aggregated data and have not access to the original Chinese databases, there was no risk that any individual information could be identified. Only statistical findings were and will be published or used in scientific journals and this thesis, and no personal information will be released.

We consulted with the Regional Ethical Review Board in Stockholm (EPN) about the ethical approval issue and got reply that no ethical approval was needed for the studies. For using the

Chinese data, our four studies were approved by the local ethical review boards in Beijing (approval #: 028-2013) and Shanghai (approval #: 2016-8).

# 5 RESULTS

## 5.1 CONTRIBUTION OF ROAD TRAFFIC TO FINE PARTICLE CONCENTRATIONS IN BEIJING (STUDY I)

During 2013 – 2014, the medians of $PM_{2.5}$ concentrations in 35 AQM monitoring stations were 40 – 92 μg/m$^3$ with a total median of 65 μg/m$^3$, the mean of the concentration varied from 63 – 112 μg/m$^3$ with a total average of 90 μg/m$^3$ which was higher than 55.4 μg/m$^3$ reported in the previous study.[148] The detailed $PM_{2.5}$ and meteorological information are listed in tables 5 and 6.

Table 5. $PM_{2.5}$ concentrations and Y coordinates of 35 AQM stations in Beijing, 2013 – 2014

| Stations | $PM_{2.5}$ (μg/m$^3$) | | | | Y coordinate (km) |
|---|---|---|---|---|---|
| | Mean | P25 | Median | P75 | |
| Background stations | | | | | |
| Badaling | 64.8 | 17.0 | 40.0 | 91.0 | 100.47 |
| Beibuxinqu | 86.5 | 24.2 | 62.0 | 122.7 | 69.47 |
| Dingling | 71.2 | 15.0 | 45.0 | 101.0 | 93.12 |
| Miyunshuiku | 63.4 | 13.0 | 40.3 | 91.0 | 109.68 |
| Yungang | 90.0 | 28.0 | 65.0 | 125.0 | 41.32 |
| Zhiwuyuan | 79.7 | 19.0 | 56.0 | 112.7 | 60.91 |
| Traffic stations | | | | | |
| Dongsihuan | 97.5 | 29.0 | 71.0 | 135.0 | 54.82 |
| Nansanhuan | 106.6 | 36.2 | 81.0 | 147.0 | 44.70 |
| Qianmen | 100.0 | 31.0 | 76.6 | 138.8 | 49.45 |
| Xizhimenbei | 92.8 | 29.0 | 68.3 | 127.2 | 54.66 |
| Yongdingmen | 98.0 | 31.0 | 73.0 | 135.1 | 46.62 |
| Industrial stations | | | | | |
| Liulihe | 122.2 | 44.0 | 92.0 | 169.0 | 16.81 |
| Yufa | 109.6 | 38.0 | 79.8 | 148.0 | 4.06 |
| Other stations | | | | | |
| Aoti | 89.8 | 27.0 | 67.0 | 125.0 | 58.61 |
| Changping | 78.0 | 19.0 | 53.0 | 111.0 | 84.81 |
| Daxing | 106.9 | 35.0 | 79.0 | 147.0 | 31.81 |
| Donggaocun | 79.3 | 22.0 | 58.0 | 113.0 | 72.61 |
| Dongsi | 90.4 | 25.2 | 66.5 | 128.0 | 52.71 |
| Fangshan | 101.2 | 33.0 | 75.8 | 140.8 | 32.43 |
| Fengtaihuayuan | 99.7 | 31.0 | 74.1 | 139.0 | 45.53 |
| Guanyuan | 88.4 | 27.0 | 65.5 | 123.4 | 52.82 |
| Gucheng | 90.0 | 28.0 | 67.5 | 125.0 | 51.16 |
| Huairou | 76.1 | 19.0 | 52.9 | 108.0 | 96.85 |
| Mentougou | 79.2 | 22.0 | 55.4 | 111.0 | 53.85 |
| Miyun | 71.9 | 17.5 | 49.0 | 100.0 | 101.39 |
| Nongzhanguan | 91.3 | 26.4 | 66.0 | 126.0 | 53.63 |
| Pinggu | 80.8 | 23.0 | 57.0 | 111.0 | 76.40 |
| Shunyi | 84.8 | 22.0 | 61.0 | 121.0 | 74.58 |
| Tiantan | 89.0 | 27.0 | 66.4 | 125.2 | 48.00 |
| Tongzhou | 105.7 | 33.2 | 79.3 | 144.0 | 47.08 |
| Wanliu | 93.6 | 29.8 | 69.5 | 130.1 | 59.28 |
| Wanshouxigong | 91.2 | 26.0 | 68.0 | 128.0 | 47.13 |
| Yanqing | 72.0 | 20.0 | 49.5 | 102.0 | 111.24 |
| Yizhuang | 105.3 | 34.2 | 78.9 | 144.0 | 37.93 |
| Yongledian | 111.8 | 38.7 | 81.7 | 149.8 | 28.87 |
| Total | 90.0 | 25.2 | 65.0 | 125.5 | 59.13 |

P25: the 25th percentile; P75: the 75th percentile.

Table 6. Meteorological conditions in Beijing, 2013 – 2014

| Meteorological conditions | Mean | P25 | Median | P75 |
|---|---|---|---|---|
| Temperature (°C) | 13.4 | 3.2 | 14.3 | 23.7 |
| Humid (%) | 53 | 38 | 53 | 68 |
| Atmospheric pressure (hPa) | 1012.5 | 1004.2 | 1012.7 | 1021.1 |
| Wind speed (m/s) | 2.1 | 1.5 | 1.9 | 2.5 |
| Hours of light (h) | 6.5 | 2.4 | 7.8 | 9.6 |
| Rain volume (mm) * | 15.6 | - | - | - |

P25: the 25th percentile; P75: the 75th percentile.

* Because 81% of days had no rain, P25, median, and P75 are 0.

Based on a three-level GAM with 15-minute observations nested within hour and hour nested within day, we found a significant linear relationship between Y coordinates and log transformed $PM_{2.5}$ concentrations in AQM stations in Beijing (Figure 15), supporting our assumption that $PM_{2.5}$ concentration followed an exponential decline function on distance.

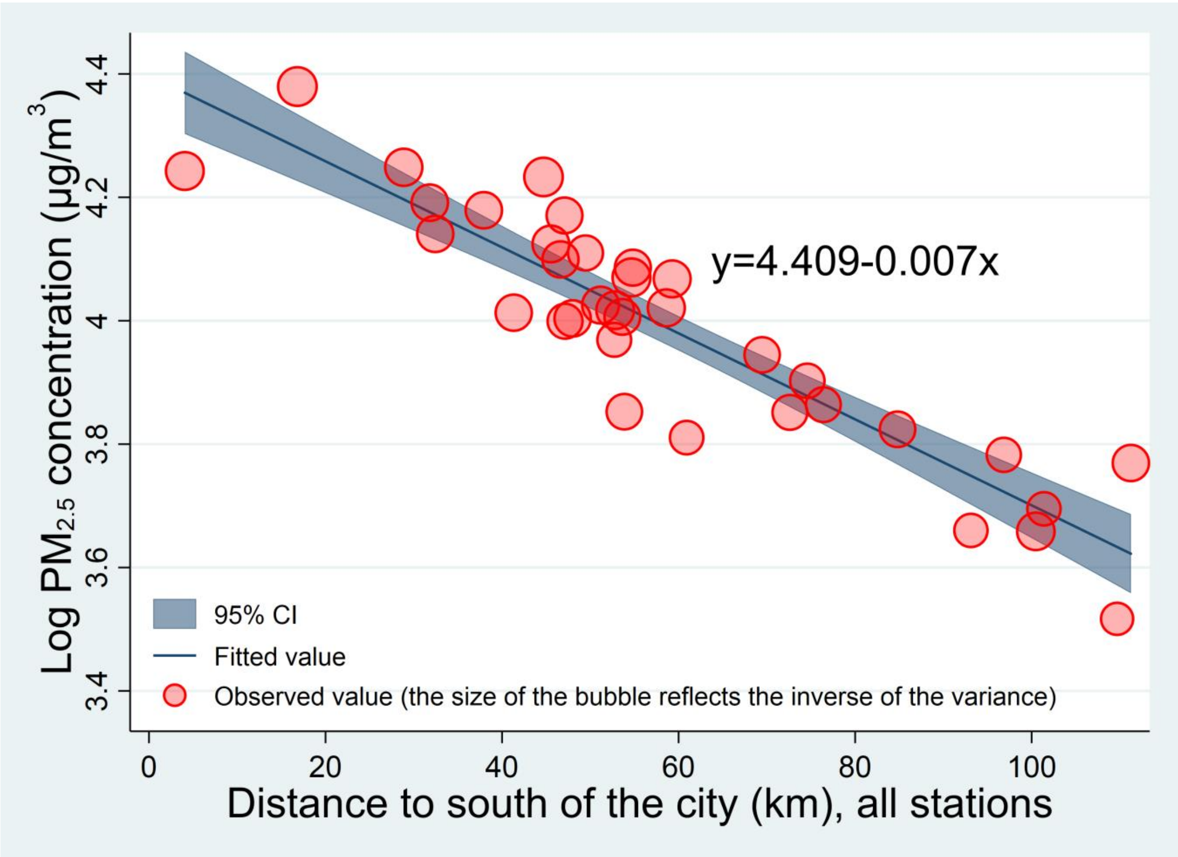



Figure 15. Relationship between Y coordinate (distance to the south of the city) and log transformed $PM_{2.5}$ concentrations at air quality monitoring stations in Beijing

According to the GAM results, $PM_{2.5}$ pollution level increased with the stations getting approaching to the southern industrial area of Beijing, and the north-south location of the stations may account for approximate 80% of the variation in the log transformed $PM_{2.5}$ concentrations.

Moving to the dispersion model, the estimated parameters covered more than 60% of the variation in the background stations, and the rest of the variation could be explained by the

GAMM. The result showed the greater wind speed and rain volume would lead to better pollution dispersion. Hours of sunshine and rain volume were negatively associated with $PM_{2.5}$ concentration. The residuals were examined for a good fitness.

The road traffic contribution to $PM_{2.5}$ concentration of the background stations is shown in Table 7. The contributions ranged from 17.2% in Yungang station to 25.3% in Zhiwuyuan station.

Table 7. Contribution (%) of road traffic to $PM_{2.5}$ concentrations of background stations

| Station | Mean | 95% Confidence Interval |
|---|---|---|
| Badaling | 20.5 | 18.7 – 22.2 |
| Beibuxinqu | 19.6 | 18.1 – 21.1 |
| Dingling | 20.9 | 19.2 – 22.6 |
| Miyunshuiku | 21.8 | 19.5 – 24.1 |
| Yungang | 17.2 | 15.5 – 18.8 |
| Zhiwuyuan | 25.3 | 23.3 – 27.3 |

The absolute and relative contributions of road traffic to $PM_{2.5}$ concentrations of all the stations are shown in Figure 16. The average annual contributions of road traffic to $PM_{2.5}$ concentrations ranged from 17.2% to 37.3% with a mean of 30%. The highest contribution was found in busy road areas, and the contribution in traffic-related stations is about 14% higher than those in rural areas.

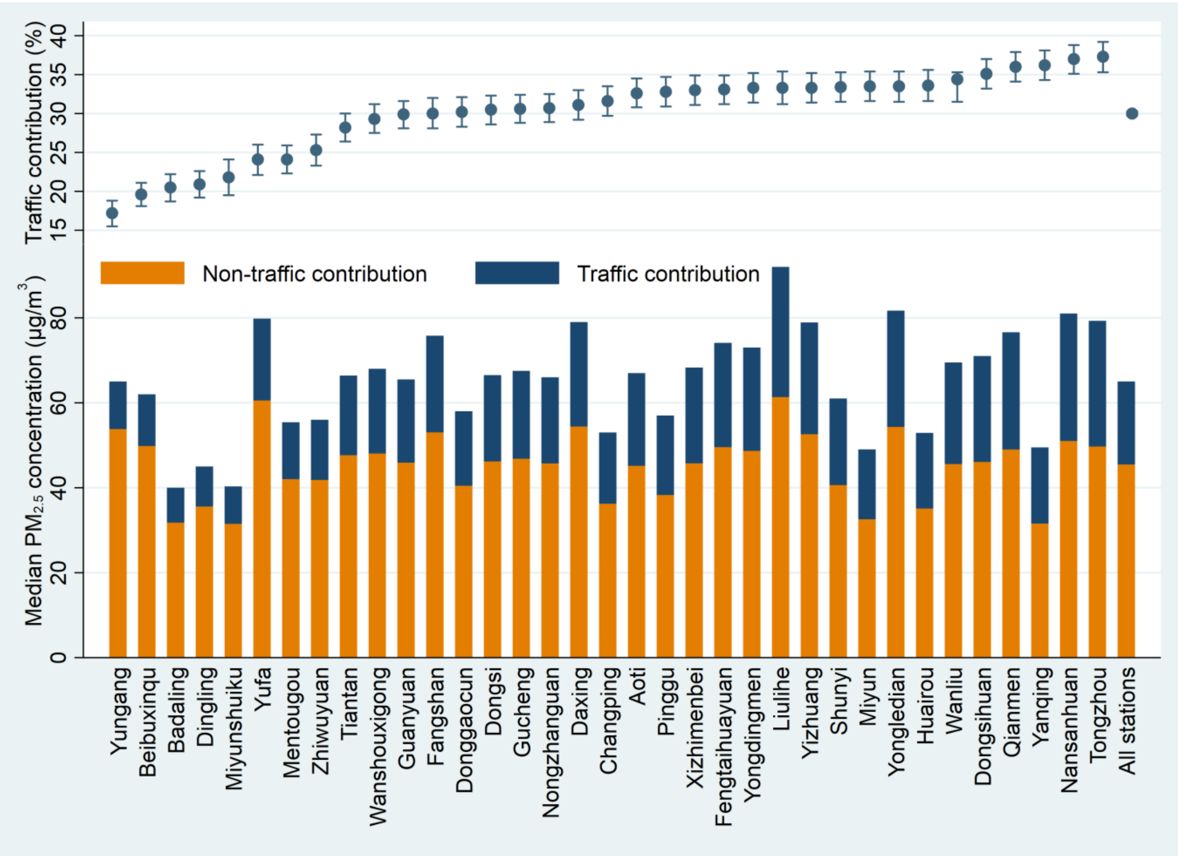



Figure 16. Contributions of road traffic to $PM_{2.5}$ concentrations in Beijing, 2013 – 2014

## 5.2 ASSOCIATION BETWEEN COARSE PARTICLES AND RESPIRATORY MORTALITY IN BEIJING (STUDY II)

Daily respiratory mortality rate (per 100,000 persons) and $PM_{10}$, $NO_x$ and carbon monoxide CO concentrations of the eight studied districts in Beijing are shown in Table 8. During the two-year study period, annual median concentrations for $PM_{10}$, $NO_x$ and CO were 106.0 μg/m$^3$, 61.0 μg/m$^3$ and 1.20 mg/m$^3$, respectively. The annual median concentrations of $PM_{10}$ and $NO_x$ were above the limits of Class II of the National Ambient Air Quality Standards of China (70 μg/m$^3$ for $PM_{10}$ and 50 μg/m$^3$ for $NO_x$), but annual median CO concentration was below the national limit (4 mg/m$^3$).[149]

Table 8. Daily respiratory mortality rate and pollutants' concentrations in the studied districts in Beijing, 2009 – 2010

| Districts | Population (in 1000) | Mortality rate (1/100,000 persons) | | $PM_{10}$ (μg/m$^3$) | | $NO_x$ (μg/m$^3$) | | CO (mg/m$^3$) | |
|---|---|---|---|---|---|---|---|---|---|
| | | Median | P25 – P75 | Median | P25 – P75 | Median | P25 – P75 | Median | P25 – P75 |
| District 1 | 896 | 0.11 | 0 – 0.22 | 94.0 | 57 – 138 | 52.0 | 33 – 78 | 1.20 | 0.8 – 1.7 |
| District 2 | 3,001 | 0.10 | 0.06 – 0.13 | 106.5 | 67 – 151 | 72.0 | 50.5 – 109.5 | 1.30 | 0.85 – 1.9 |
| District 3 | 851 | 0.24 | 0.12 – 0.35 | 110.3 | 73.5 – 159 | 70.5 | 50.5 – 107.5 | 1.38 | 1.0 – 2.1 |
| District 4 | 2,814 | 0.07 | 0.04 – 0.14 | 112.0 | 71 – 154 | 79.0 | 52 – 116 | 1.20 | 0.8 – 2.0 |
| District 5 | 316 | 0.00 | 0 – 0.32 | 82.5 | 49 – 124 | 33.0 | 23 – 53 | 1.00 | 0.6 – 1.4 |
| District 6 | 546 | 0.18 | 0 – 0.18 | 129.0 | 83 – 174 | 60.0 | 44 – 88 | 1.40 | 1.0 – 2.0 |
| District 7 | 736 | 0.00 | 0 – 0.14 | 108.5 | 66 – 154 | 52.0 | 37 – 75 | 0.90 | 0.6 – 1.4 |
| District 8 | 1,218 | 0.25 | 0.08 – 0.33 | 105.5 | 68.5 – 150.5 | 73.0 | 53 – 107.5 | 1.35 | 0.95 – 2.0 |
| Total | 10,378 | 0.11 | 0 – 0.22 | 106.0 | 66 – 150 | 61.0 | 41 – 93 | 1.20 | 0.8 – 1.8 |

P25: the 25th percentile; P75: the 75th percentile

We observed strong linear correlation between temperature and barometric pressure (Figure 17; $r$ = -0.83, $p$ < 0.001). To control for the collinearity, we included temperature, relative humidity and wind speed but not barometric pressure in the regression models.

To account for correlations between $PM_{10}$ and CO and $NO_x$, we introduced PCs derived from PCA into the multi-pollutant models to exclude the impacts of collinearity between the three pollutants. The first two PCs may explain about 94.22% of the variance of the three pollutants (Figure 18) and were included in the GAM. We then transformed the regression coefficients of the PCs back to the regression coefficients of the original pollutants.

We tried different numbers of knots for each smoothing function. The knot combinations with convergence problem or extreme small posterior probability were excluded from analysis. The results indicated that the model with 6, 7, 8 knots per year for calendar day, 5, 6, 7 knots for temperature and 4, 5, 6 knots for the aerometric pressure got the relative large posterior probabilities. We compared the GLMM, optimal GAMM and GAMM+BMA methods for single-pollutant, multi-pollutant and PCA-based multi-pollutant settings. The results are listed in Table 9. The GAMM of a single pollutant model showed a statistical significant association between $PM_{10}$ and respiratory mortality that every IQR increase in $PM_{10}$ would lead to 1.39 (95% CI: -1.08 – 3.93) percent increase in daily respiratory mortality. In addition, the BMA+GAMM gave a relative wider confidence interval (-1.09 – 4.28) in single-pollutant model and (-2.23 – 4.07) in PCA-based model which reflected a noticeable uncertainty originating in the knots selection. In addition, the effects of the first PC in GAMM and GAMM+BMA were statistically significant, potentially indicating a joint effect of $PM_{10}$, $NO_x$ and CO on respiratory mortality.

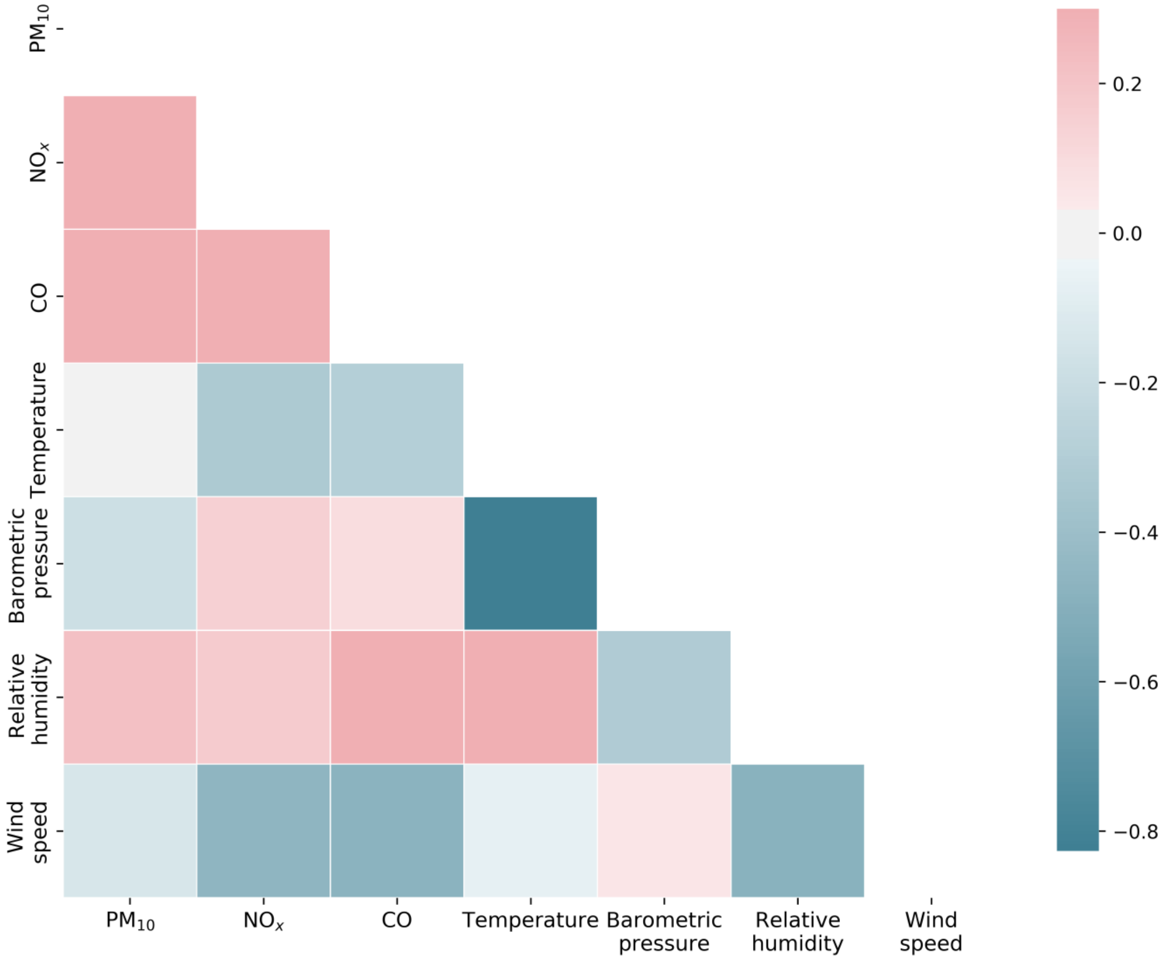
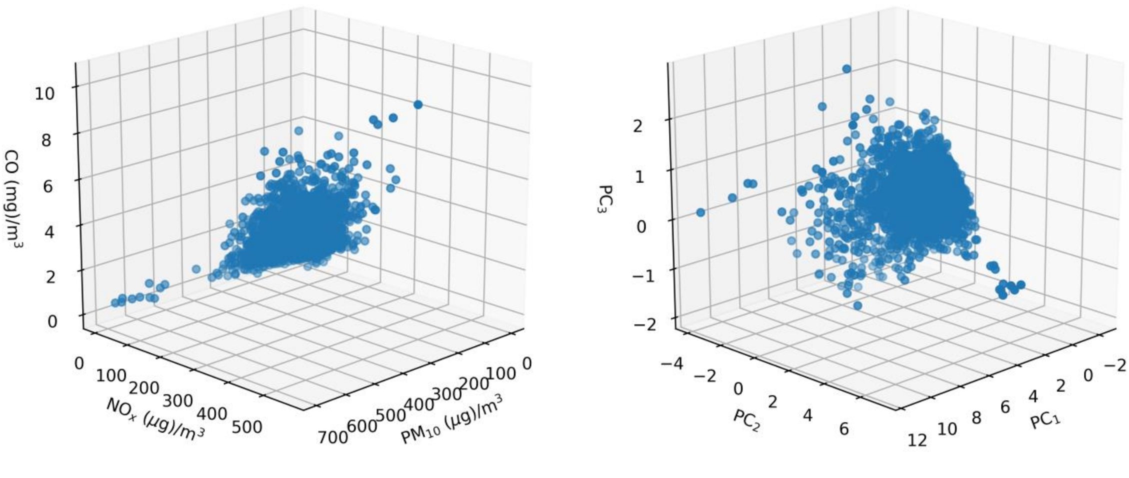



Figure 17. Bivariate Pearson's correlation coefficients between the meteorological variables and the studied air pollutants

Table 9. Percent increase in daily respiratory mortality rate (MR) associated with an IQR increase in $PM_{10}$ concentration from GLMM, optimal GAMM and GAMM+BMA

| Model | Single-pollutant | | Multi-pollutant | | Multi-pollutant (PCA) | |
|---|---|---|---|---|---|---|
| | Percent (%) | 95% CI | Percent (%) | 95% CI | Percent (%) | 95% CI |
| GLMM | 3.07 | 0.91 – 5.27 | 1.94 | -0.80 – 4.75 | 1.47 | -1.17 – 4.17 |
| Optimal GAMM† | 1.39 | -1.08 – 3.93 | 1.83 | -1.11 – 4.83 | 0.88 | -2.03 – 3.88 |
| GAMM+BMA | 1.38 | -1.09 – 4.28 | 1.81 | -1.12 – 4.85 | 0.87 | -2.23 – 4.07 |

GLMM, generalized linear mixed model; GAMM, generalized additive mixed model; GAMM+BMA, generalized additive mixed models with Bayesian model averaging; IQR, interquartile range.




(a) Original pollutants (b) Principal components

Figure 18. Original pollutants and principal components

## 5.3 EFFECTS OF FINE PARTICLES AND EXTREME WEATHER CONDITIONS ON NON-ACCIDENTAL MORTALITY IN SHANGHAI (STUDY III)

In total, 336,379 non-accidental deaths occurred during the study period between January 1st, 2012 and December 31st, 2014 in Shanghai. Average daily deaths were 307. The demographic characteristics of the subjects are shown in Table 10.

Table 10. Demographic characteristics of the non-accident deaths in Shanghai (2012 – 2014)

| | |
|---|---|
| Sex, n (%) | |
| Male | 178,786 (53.15%) |
| Female | 153,593 (46.85%) |
| Age (year), mean±SD | 77.0±12.6 |
| Age distribution, n (%) | |
| 0-14 years | 1,252 (0.37%) |
| 15-39 years | 3,080 (0.92%) |
| 40-64 years | 54,404 (16.17%) |
| 65+ years | 277,643 (82.54%) |
| Education, n (%) | |
| Illiterate | 84,943(25.25%) |
| Preliminary school | 100,194 (29.79%) |
| High school | 118,235 (35.15%) |
| Undergraduate and above | 27,063 (8.05%) |
| NA | 5,944 (1.77%) |
| Occupation, n (%) | |
| Governmental | 2,760 (0.82%) |
| Professional | 28,992 (8.62%) |
| Administrative | 34,431 (11.13%) |
| Business | 32,823 (9.76%) |
| Agriculture and stockbreeding | 77,832 (23.14%) |
| Manufactory | 123,998 (36.86%) |
| Military | 201 (0.06%) |
| Others | 3,185 (0.95%) |
| Preschooler | 1,060 (0.32%) |
| Students | 337 (0.10%) |
| Retired or jobless | 27,760 (8.25%) |
| Smoking rate *, % | |
| Male | 29.71% |
| Female | 0.92% |

* Indirectly standardized rate.

The Elbow method indicates that six clusters are optimal for the K-means cluster analysis (Figure 19). Using the six PCs derived from the PCA, the 1096 days during the study period were categorized into six SWTs. The meteorological characteristics and $PM_{2.5}$ concentrations of the six SWTs in Shanghai between 2012 and 2014 are show in Figure 20.

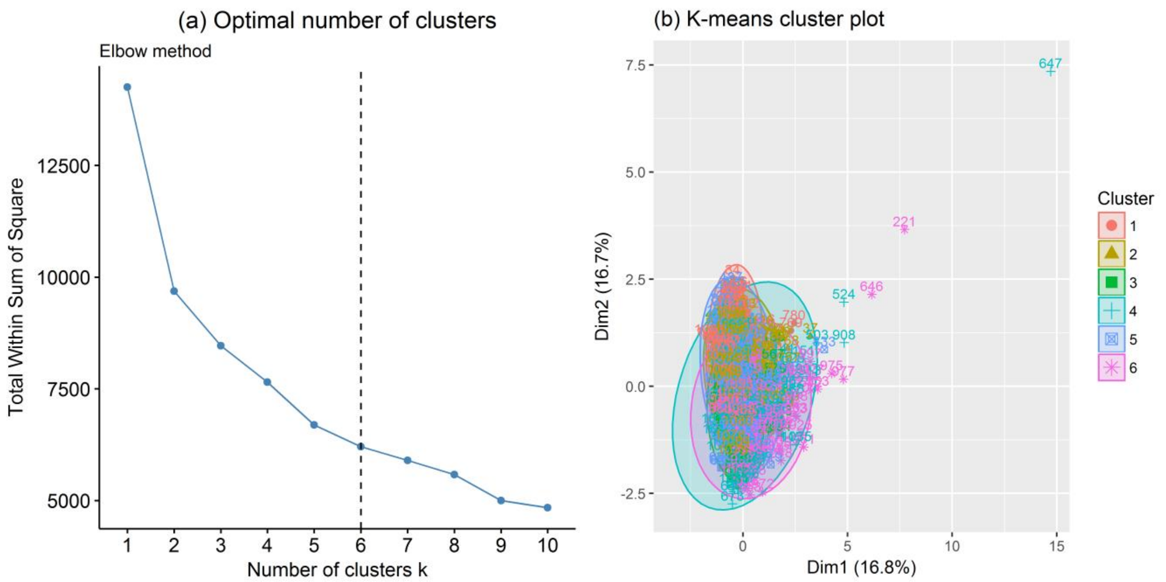



Figure 19. K-means cluster analysis of the 15 meteorological variables

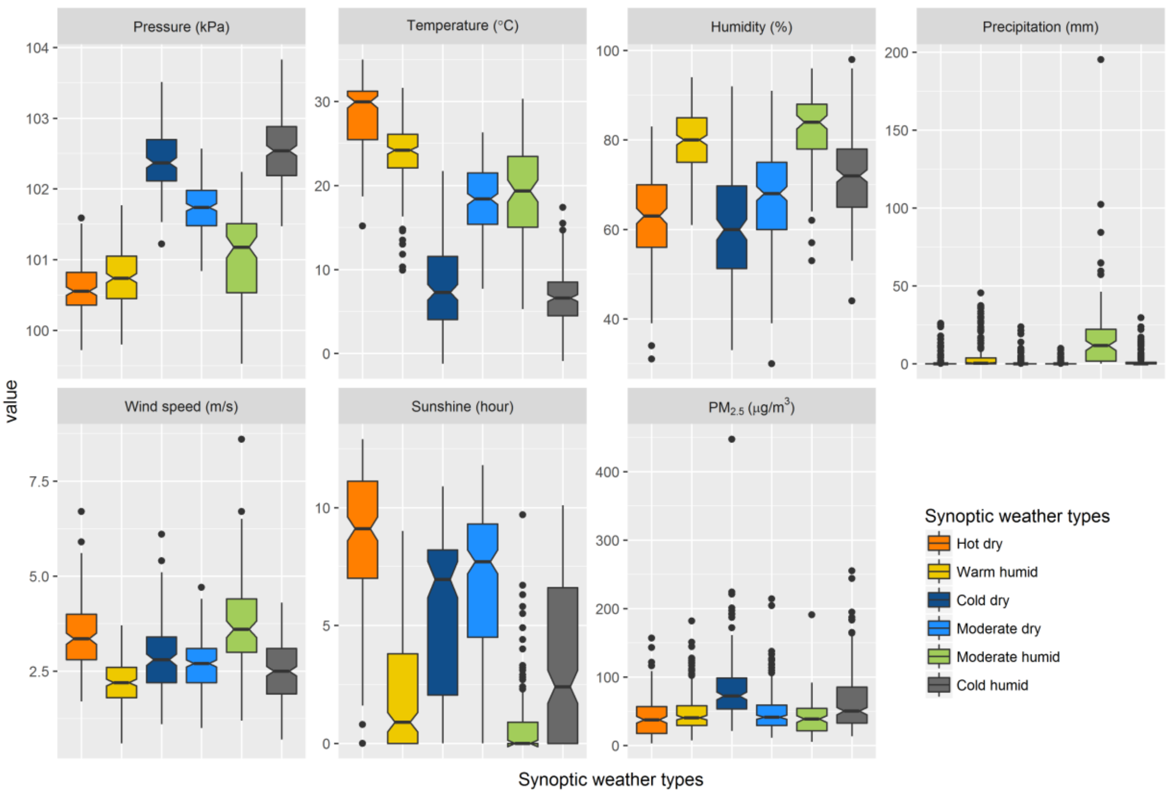



Figure 20. Meteorological characteristics and $PM_{2.5}$ concentrations of the six synoptic weather types in Shanghai, 2012 – 2014

We summarize the effects of extreme weather conditions and $PM_{2.5}$ on non-accidental mortality in Table 11. With no interaction assumption, every 10 μg/m$^3$ increase in $PM_{2.5}$ concentration was associated with 0.31 (95% CrI: 0.22 – 0.40) percent increase in non-accidental mortality. Moreover, hot, hypobaric and windy days were statistical significantly associated with increased mortality as well. However when considering the interaction between $PM_{2.5}$ and extreme weather conditions, every 10 μg/m$^3$ increase in $PM_{2.5}$ concentration was associated with 0.27 (95% CrI: 0.13 – 0.41) percent increase in deaths. The interaction between $PM_{2.5}$ with three types of extreme weather conditions (hot, hypobaric and dry) was significantly and positively associated with mortality.

Table 11. Effects of $PM_{2.5}$, extreme weather conditions and demographic characteristics on non-accidental mortality

| Variables | Percent increase in mortality (95% CrI) | |
|---|---|---|
| | Model without interaction | Model with interaction |
| $PM_{2.5}$ (per 10 μg/m$^3$) | 0.31 (0.22 – 0.40) | 0.27 (0.13 – 0.41) |
| Hot | 6.41 (4.93 – 7.96) | 3.59 (1.22 – 6.13) |
| Cold | 0.87 (-0.41 – 2.07) | 0.02 (-2.36 – 2.68) |
| Hyperbaric | 0.46 (-0.85 – 1.80) | 0.73 (-1.77 – 3.19) |
| Hypobaric | 1.52 (0.19 – 2.87) | -1.55 (-4.05 – 1.05) |
| Humid | 0.73 (-0.48 – 1.98) | 1.41 (-0.36 – 3.19) |
| Dry | -0.75 (-1.91 – 0.50) | -4.80 (-7.76 – -2.07) |
| Windy | 2.58 (1.29 – 3.96) | 3.75 (1.74 – 5.85) |
| Windless | -0.60 (-1.91 – 0.64) | 0.54 (-2.11 – 2.96) |
| Interactions | | |
| $PM_{2.5}$×Hot | | 0.50 (0.08 – 0.95) |
| $PM_{2.5}$×Cold | | 0.12 (-0.17 – 0.40) |
| $PM_{2.5}$×Hyperbaric | | -0.02 (-0.33 – 0.29) |
| $PM_{2.5}$× Hypobaric | | 0.62 (0.16 – 1.14) |
| $PM_{2.5}$×Humid | | -0.12 (-0.36 – 0.10) |
| $PM_{2.5}$×Dry | | 0.59 (0.21 – 1.00) |
| $PM_{2.5}$×Windy | | -0.22 (-0.66 – 0.19) |
| $PM_{2.5}$×Windless | | -0.15 (-0.41 – 0.12) |
| Female | 47.68 (44.55 – 51.00) | 47.60 (44.49 – 50.85) |
| Age | | |
| 0-14 years | -98.81 (-98.87 – -98.75) | -98.81 (-98.88 – -98.74) |
| 15-39 years | -99.32 (-99.34 – -99.30) | -99.32 (-99.34 – -99.29) |
| 40-64 years | -94.43 (-94.51 – -94.33) | -94.42 (-94.52 – -94.34) |
| 65+ years (Ref) | | |
| Occupation | | |
| Governmental | -97.78 (-97.87 – -97.69) | -97.78 (-97.86 – -97.70) |
| Professional | -76.63 (-76.94 – -76.32) | -76.62 (-76.90 – -76.32) |
| Administrative | -69.83 (-70.21 – -69.49) | -69.82 (-70.18 – -69.47) |
| Business | -73.53 (-73.84 – -73.23) | -73.55 (-73.87 – -73.23) |
| Agriculture | -37.26 (-37.84 – -36.71) | -37.25 (-37.77 – -36.69) |
| Manufactory (Ref) | | |
| Military | -99.84 (-99.86 – -99.81) | -99.84 (-99.86 – -99.81) |
| Others | -97.43 (-97.53 – -97.34) | -97.43 (-97.52 – -97.32) |
| Preschool | -99.15 (-99.19 – -99.10) | -99.15 (-99.20 – -99.09) |
| Students | -99.73 (-99.75 – -99.70) | -99.73 (-99.76 – -99.69) |
| Jobless | -77.62 (-77.93 – -77.34) | -77.63 (-77.90 – -77.35) |
| Day of week | | |
| Sunday (Ref) | | |
| Monday | 1.67 (0.45 – 3.00) | 1.73 (0.27 – 3.04) |
| Tuesday | 0.68 (-0.56 – 1.95) | 0.70 (-0.52 – 2.04) |
| Wednesday | 0.93 (-0.33 – 2.24) | 0.89 (-0.35 – 2.11) |
| Thursday | -0.01 (-1.24 – 1.32) | 0.07 (-1.19 – 1.35) |
| Friday | 0.05 (-1.14 – 1.41) | 0.03 (-1.17 – 1.24) |
| Saturday | 0.09 (-1.08 – 1.47) | 0.04 (-1.24 – 1.26) |
| Smoking rate | 2.01 (1.95 – 2.08) | 2.01 (1.95 – 2.08) |

## 5.4 EFFECTS OF FINE PARTICLES AND SYNOPTIC WEATHER TYPES ON NON-ACCIDENTAL MORTALITY IN SHANGHAI (STUDY III)

The effects of $PM_{2.5}$ and the SWTs on non-accidental mortality are shown in Table 12. Without including the interaction term between $PM_{2.5}$ and SWTs, per 10 μg/m$^3$ increase in $PM_{2.5}$ concentration was associated with 0.35 (95% CrI: 0.26 – 0.44) percent increase in mortality. Compared to cold humid SWT, hot dry SWT had the greatest effect followed by moderate humid and warm humid SWTs, while cold dry SWT had the smallest effect.

The effects of SWTs on mortality shown significant changed when including the interactions. The highest effect of SWTs was found in moderate humid SWT (4.37, 95%CI: 1.49 – 7.32) followed by moderate dry SWT (2.78, 95%CI: 0.53 – 5.13). The greatest effect of $PM_{2.5}$ was found in hot dry SWT, followed by warm humid SWT.

Table 12. Effects of $PM_{2.5}$, synoptic weather types and demographic characteristics on non-accidental mortality

| Variable | Percent increase in mortality (95% CrI) | |
|---|---|---|
| | Model without interaction | Model with interaction |
| PM2.5 | 0.35 (0.26 – 0.44) | 0.26 (0.10 – 0.43) |
| Synoptic weather types | | |
| Hot dry | 7.09 (5.18 – 9.14) | 1.51 (-1.42 – 4.52) |
| Warm humid | 2.18 (0.41 – 4.11) | -0.32 (-2.78 – 2.37) |
| Cold dry | -1.98 (-3.15 – -0.85) | -1.84 (-3.83 – 0.23) |
| Moderate dry | 1.94 (0.48 – 3.37) | 2.78 (0.53 – 5.13) |
| Moderate humid | 5.36 (3.61 – 7.08) | 4.37 (1.49 – 7.32) |
| Cold humid (Ref) | | |
| Interactions | | |
| PM2.5×Hot dry | | 1.02 (0.62 – 1.40) |
| PM2.5× Warm humid | | 0.38 (0.05 – 0.70) |
| PM2.5×Cold dry | | 0.00 (-0.23 – 0.23) |
| PM2.5×Moderate dry | | -0.16 (-0.47 – 0.14) |
| PM2.5×Moderate humid | | 0.16 (-0.27 – 0.63) |
| PM2.5×Cold humid (Ref) | | |
| Female | 47.74 (44.6 – 51.20) | 47.57 (43.84 – 50.83) |
| Age | | |
| 0-14 years | -98.81 (-98.88 – -98.74) | -98.81 (-98.88 – -98.74) |
| 15-39 years | -99.32 (-99.34 – -99.29) | -99.32 (-99.34 – -99.30) |
| 40-64 years | -94.43 (-94.51 – -94.34) | -94.42 (-94.52 – -94.34) |
| 65+ years (Ref) | | |
| Occupation | | |
| Governmental | -97.78 (-97.87 – -97.69) | -97.78 (-97.87 – -97.70) |
| Professional | -76.62 (-76.91 – -76.32) | -76.64 (-76.93 – -76.34) |
| Administrative | -69.81 (-70.13 – -69.46) | -69.82 (-70.20 – -69.42) |
| Business | -73.55 (-73.84 – -73.23) | -73.55 (-73.90 – -73.24) |
| Agriculture | -37.24 (-37.81 – -36.64) | -37.25 (-37.79 – -36.69) |
| Manufactory (Ref) | | |
| Military | -99.84 (-99.86 – -99.81) | -99.84 (-99.86 – -99.81) |
| Others | -97.43 (-97.52 – -97.33) | -97.43 (-97.52 – -97.35) |
| Preschool | -99.15 (-99.20 – -99.09) | -99.15 (-99.20 – -99.09) |
| Students | -99.73 (-99.76 – -99.70) | -99.73 (-99.76 – -99.70) |
| Jobless | -77.62 (-77.91 – -77.33) | -77.63 (-77.93 – -77.35) |
| Day of week | | |
| Sunday (Ref) | | |
| Monday | 1.88 (0.63 – 3.24) | 1.91 (0.63 – 3.27) |
| Tuesday | 0.92 (-0.34 – 2.24) | 0.88 (-0.33 – 2.12) |
| Wednesday | 0.95 (-0.39 – 2.20) | 0.98 (-0.30 – 2.17) |
| Thursday | 0.24 (-0.97 – 1.56) | 0.31 (-0.92 – 1.57) |
| Friday | -0.10 (-1.35 – 1.13) | -0.10 (-1.30 – 1.22) |
| Saturday | 0.07 (-1.19 – 1.43) | 0.06 (-1.14 – 1.32) |
| Smoking rate | 2.02 (1.95 – 2.09) | 2.01 (1.94 – 2.09) |

In terms of the smoking effect, the report indicated the mortality risk was almost doubled in the smoking population adjusting for the gender and occupations.

We performed a sensitivity analysis using the estimates from Chen's study[150] as the informative normal prior mean in the Bayesian reference but no detectable changes in the results were found.

## 5.5 SENSITIVITY OF BAYESIAN GENERALIZED ADDITIVE MODEL TO CHOICE OF PRIOR MEAN AND VARIANCE (STUDY IV)

Using the simulation data with a fixed $\sigma = 0.5\hat{\sigma}$ and true $\beta_1 = 0.0049$ based on the real-world data in Shanghai 2012 – 2014, we investigated the impact of informative priors on the posterior $\hat{\beta}_1$ in Bayesian GAM analysis. For Bayesian GAM analyses, we set the varied normal prior mean $\mu(\beta_1)$ ranging from 0.001 to 0.020 by 0.001, and varied prior variance [$V(\beta_1)$] equal to $\gamma\beta_1$, where $\gamma$=0.5, 0.6, …, 1.0. For each combination of $\mu(\beta_1)$ and $V(\beta_1)$, we did 100 Bayesian analyses. To reduce computation task, we set the *df* for splines to 8 per year. The distribution of Bayesian estimates ($\hat{\beta}_1$s) are shown in Figure 21. The mean of $\hat{\beta}_1$s is fluctuated but closely around the true $\beta_1$ for different $\mu(\beta_1)$. These is no noticeable difference among the means of $\hat{\beta}_1$s derived from different $V(\beta_1)$ (Figure 21). The SD of $\hat{\beta}_1$s is not sensitive to the $V(\beta_1)$.

## 5.6 SENSITIVITY OF BAYESIAN GENERALIZED ADDITIVE MODEL TO TRUE PARAMETER (STUDY IV)

In another simulation, we artificially set the $\sigma = 0.5\hat{\sigma}$ and 'true' $\beta_1$ ranged from 0.001 to 0.020 to generate 20 sets of simulated daily respiratory deaths, while kept the other coefficients in equation (29) unchanged. In Bayesian GAM analysis, we used a normal prior for $\beta_1$ with a fixed mean $\mu(\beta_1) = 0.005$ but varied $V(\beta_1) = 0.5, 0.6, \ldots, 1.0$ times of $\mu(\beta_1)$, i.e. 0.0025, 0.003, 0.0035, 0.004, 0.0045 and 0.005. For each combination of $\beta_1$ and $V(\beta_1)$, we did 100 Bayesian GAM analyses. The estimates were shown in Figure 22.

We can see that the mean of the estimated $\hat{\beta}_1$s is only sensitive to the underlying true $\beta_1$ and is almost not affected by the prior $\mu(\beta_1)$ (Figure 22). Because of the small coefficients the difference between means and SDs of the estimated $\hat{\beta}_1$s can only be seen in the fifth or sixth decimal digit.

Regarding the comparison between frequentist GAM and Bayesian GAM, although the Bayesian $\hat{\beta}_1$s appear more fluctuated around the true $\beta_1$, their SDs are comparable to those of their frequentist counterparts.

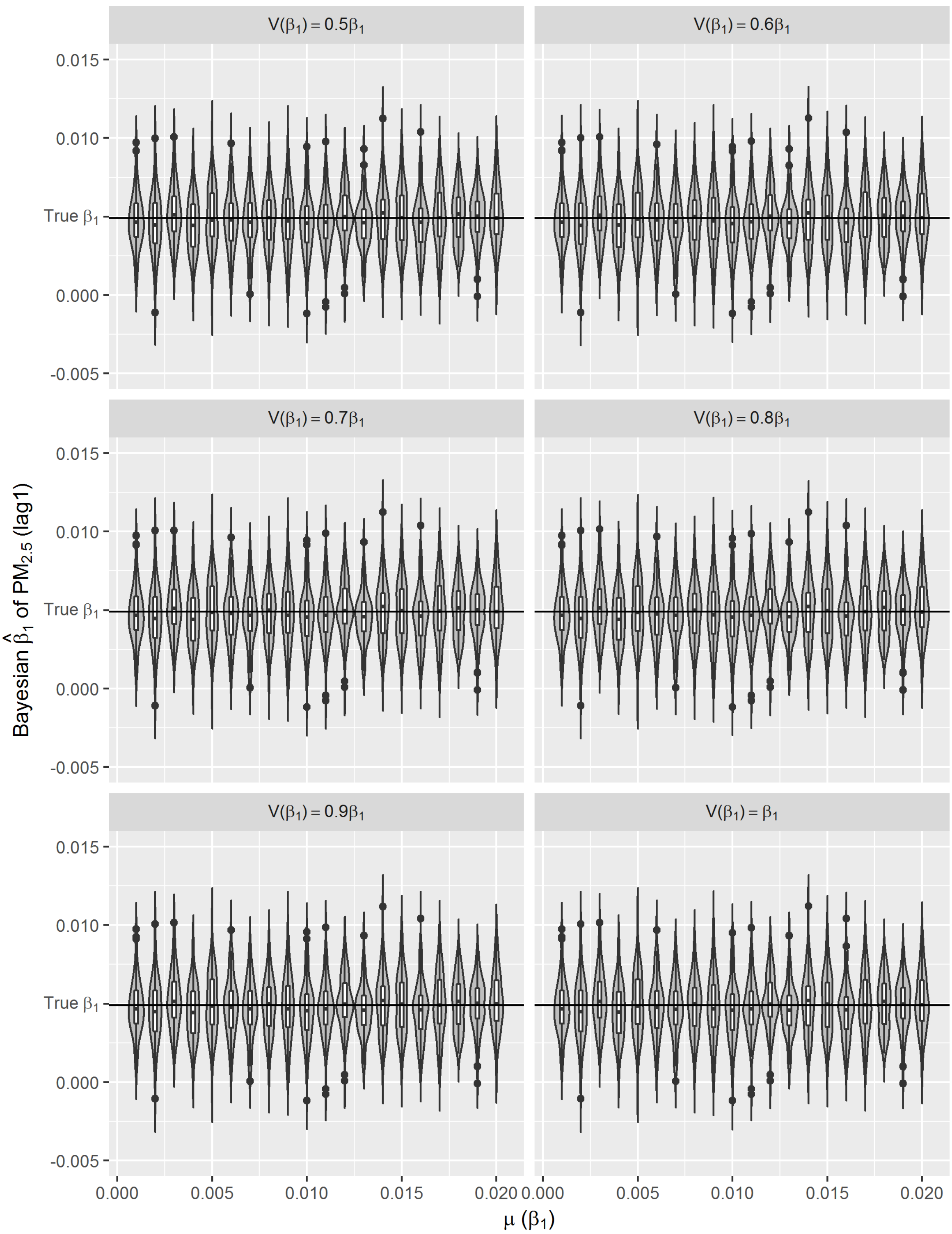



Figure 21. Distributions of Bayesian $\hat{\beta}_1$s from simulated data with $\sigma$=0.5$\hat{\sigma}$, the true $\beta_1$=0.0049; in Bayesian GAM analyses, *df* =8 for *S*(*t*), normal prior with varied μ($\beta_1$)=0.001 to 0.02 by 0.001 and varied V($\beta_1$) equal to $\gamma\beta_1$, where $\gamma$=0.5, 0.6, …, 1.0

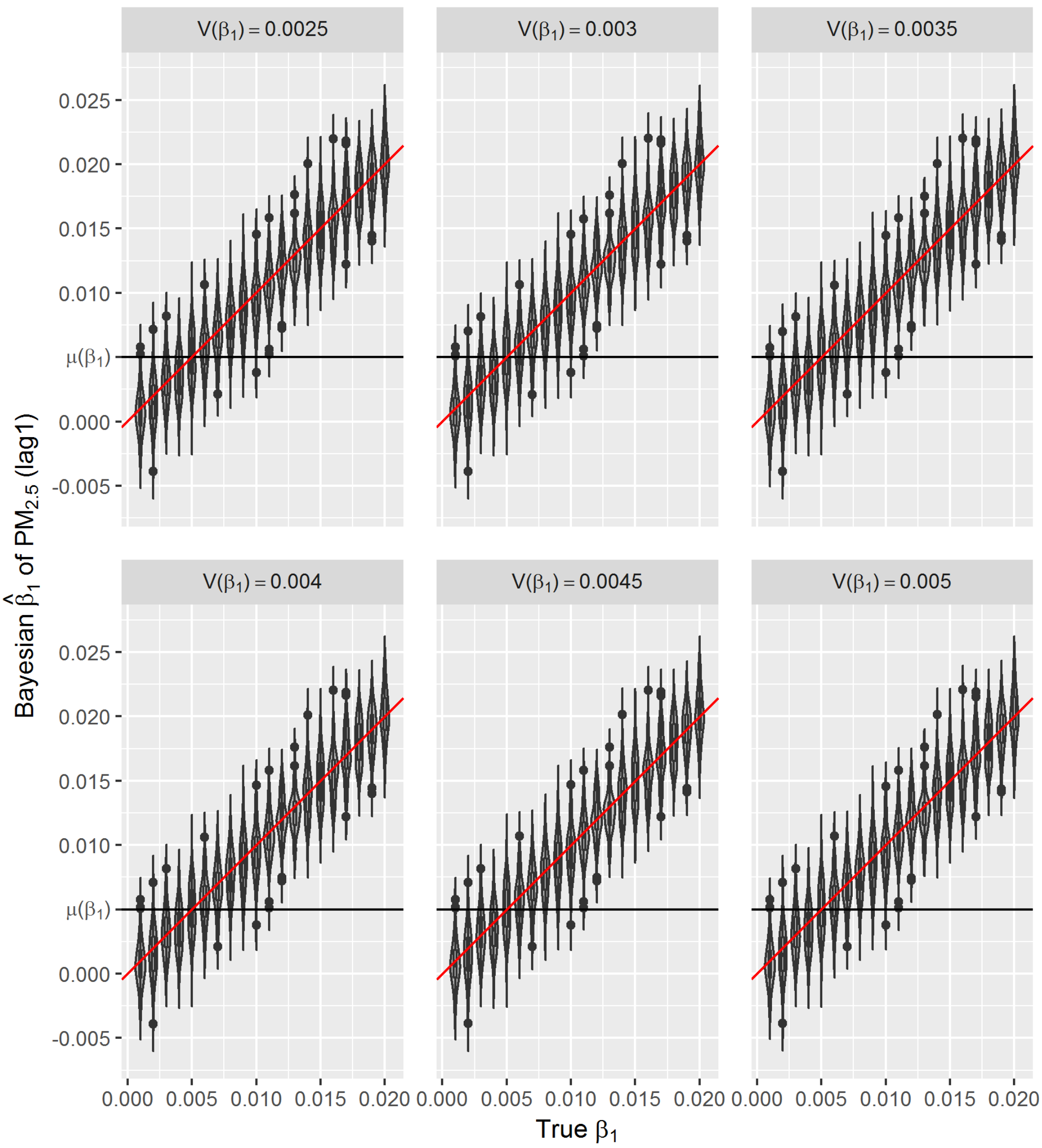



Figure 22: Distributions of Bayesian $\hat{\beta}_1$s from simulated data with $\sigma$=0.5$\hat{\sigma}$, varied true $\beta_1$=0.001 to 0.02 by 0.001; in Bayesian GAM analyses, *df* =8 for *S*(*t*), normal prior with fixed μ($\beta_1$) =0.005 and varied V($\beta_1$) =0.0025, 0.003, 0.0035, 0.004, 0.0045 and 0.005.

# 6 DISCUSSION

## 6.1 MAIN FINDINGS

Road traffic emissions make significant contribution to the $PM_{2.5}$ pollution in Beijing. According to our estimation, about 17.2% – 37.3% of daily $PM_{2.5}$ concentrations were due to road vehicles' emissions. The closer a site is to a busy road the higher contribution of the traffic is, which can also partially explain the spatiotemporal pattern of the road traffic emissions in Beijing. Beijing Municipal Environmental Protection Bureau had also released similar statistic which was between 22% and 30%. The wider range revealed in our study may be due to the longer monitoring period and the increasing fuel burning in recent years. Compared to other results in the literature during different seasons[151-153], the road traffic accounted for 10% – 50% to $PM_{2.5}$ concentrations in the city, and Study I is highly consist with these results.

In studies II, III and IV, we investigated the association between daily PM concentrations and deaths in the two most populous and developed cities in China using GAMM within BAM frame or fully Bayesian GAM. Although there have been some studies looking for the PM impacts on mortality using GAM previously,[57,154] they did not take the inner heterogeneity of covariates or the model uncertainty into account. Adding the random effects and averaging the results of different knot selections, our GAMM+BMA method for single-pollutant gave comparable results, percent increase ranging from 0.87 to 1.38 vs. 1.01 to 2.07.[57,154-157] However, our multi-pollutant models showed smaller effect of $PM_{10}$, which was consistent with previous findings suggesting that the effect of $PM_{10}$ in multi-pollutant models was about 2-3 times smaller [57,157] or slightly reversed.[154]

In the simulation study IV, the results are quite consistent with the previous studies. We found that the fully Bayesian GAM might generate almost as the same accurate estimations as the frequentist GAM did, moreover it might increase the power and include more uncertainty compared to frequentist one.

## 6.2 METHODOLOGY

To estimate the traffic-related pollution, traditionally it largely depends on the detailed compilation of traffic flow volume, traffic emission factor, vehicle speed and type et al during a consistent period. It is hardly practical to conduct such a study citywide. For example, the receptor models and air quality dispersion model[158], source apportionment estimation methods[159] such as CMB[160] or PMF, air mass trajectory analysis, and land regression model are all commonly used to analyze the various pollutant source. In study I, we developed a two-stage method combining the simplified dispersion model with GAMM model since we were lacking of the full compilation of traffic emission data and meteorological data over the whole city. With limited information about vehicle account and emission factors, we took advantage of the geographical location and wind dispersion trajectory to classify the stations, and used numerical calculation algorithm to estimate the parameters for the dispersion model. It is a novel way to model the association between geographical and meteorological data and $PM_{2.5}$ concentrations using fixed AQM stations' data over given time period.

In study II, because the mortality data were available on district level, we added the random effects from districts to take the intra-cluster correlation and inter-cluster heterogeneity into consideration when we evaluated the association between daily $PM_{10}$ concentrations and respiratory mortalities in Beijing. Due to the uncertainty in our GAMM analysis derived from knot selection, we averaged the model coefficients weighted by model posterior probability, given the prior as uniform distribution. The estimates demonstrated wider interval compared to those from the conventional single optimal model method.

In Study III, we made some modification in GAM to control for confounding from meteorological variables. We introduced categorical SWTs rather than put very individual weather variables in the GAM. Although our estimate is higher than the one from another similar study in China[150], it is consist with the result of a U.S. study.[161] Extreme weather does have interactive impact with $PM_{2.5}$ on mortality. We found higher mortality in extreme hot days than cold days. Given the interaction, there were significant interactions between hypobaric and dry weather with $PM_{2.5}$ concentration, this might be duo to hypoxia and excessive dehydration caused by low pressure and humidity, which is more informative than only looking into temperature, humidity or $PM_{2.5}$ concentration.

In Bayesian inference, sometimes subjectivism is a controversial problem due to the prior selection. There is no correct way to choose a prior. In most practice, analyses are performed with non-informative priors. In our study, we selected the Jeffreys' rules as non-informative prior. Kass et al have already pointed out that the problems raised by the research on priors chosen by formal rules are serious and may not be dismissed lightly. When sample sizes are small (relative to the number of parameters being estimated), it is dangerous to put faith in any 'default' solution; but when asymptotics take over, Jeffreys' rules and their variants remain reasonable choices.[137]

In Study IV, we compared frequentist GAM and Bayesian GAM with simulation data. Both methods showed similar mean estimates of the interested parameters. The estimates from frequentist GAM showed relatively less fluctuation, which to some extent reflects the over-confident inferences embedded in this method. Regarding the accuracy and precision of the estimates, both methods gave mean estimates close to the true parameter with comparable variances. It suggests that Bayesian GAM might be an ideal alternative to the conventional frequentist GAM. Our simulation study also indicated that when the underlying parameter was true, the informative normal priors had no noticeable influence on the Bayesian estimate (Figure 21), which was only sensitive to the underlying true parameter (Figure 22). The reason might be the large number of data that we have and the posterior is dominated by the data rather than the prior.

## 6.3 SENSITIVITY AND BIAS

In stage 1 of Study I, we made simulation using different parameters to control for the precision of road traffic contribution and test the sensitivity of the model. The results showed that 20% of the change in parameters would lead to less than 7% deviation in results. In stage 2, we tested the residual of the GAMM model and the results implied that geographical trend was almost regressed by the coordinate variables.

In Study II, we added the wind speed as a linear predictor in GAMM and the results turned out almost the same.

In Study III, we used an informative normal prior mean from Chen's study[150] but we did not found detectable change.

In Study IV, more sensitivity analyses were performed in depth. In general, the Bayesian GAM estimates are not sensitivity to the choice of prior mean and variance but only sensitive to the underlying true parameter.

## 6.4 STRENGTHS

There were very few studies on $PM_{2.5}$ concentration decomposing studies in China during 2012 to 2014, however deep knowledge of the traffic contribution to $PM_{2.5}$ pollution in big cities was in exigent demand for the government. Our Study I made maximum use of the available data to develop a simple model to estimate road traffic related $PM_{2.5}$ concentrations within a wide region quickly and economically as long as there were enough monitoring sites, regular district-specified traffic volume, and citywide meteorological data.

In Bayesian inference, probability represents degree of belief, therefore there is no need to figure out many thresholds to come up with a hypothesis. Unlike the frequentist methods, which provide point estimation or interval estimation for each model parameter, Bayesian methods believe that parameters follow a certain distribution, and simulate a bunch estimates from posterior distribution for each parameter, then report the mean and posterior distribution. Under a probability model, Bayesian methods provide inferences that are conditional on the data, and the results are exact, without reliance on asymptotic approximation, and are more interpretable.

Although in Bayes inference it always comes with a high computational cost, especially in models with a large number of parameters, thanks to the advances in current computer science and statistical software, the computational process has become much more cost effective than two decades before.

We tested the sensitivity to choice of the prior mean and variance, and all the results showed very little changes when we set different $\mu$ and $\sigma$, which indicated the stability of the estimation.

## 6.5 LIMITATIONS

Because of the complex aerodynamic process of pollution dispersion and pollutant source formation, our dispersion model used in Study I may oversight some other factors such as the secondary production of $PM_{2.5}$, the chemical interaction of $PM_{2.5}$ with other pollutants, and/or the dispersion caused by other factors rather than wind. Furthermore, due to the limited available data sources, we only took into account industrial and traffic emissions, whereas combined all other pollution sources as a whole. Besides, the dispersion model in Study I highly depended on the location of the stations that may add extra uncertainty in estimates.

There is a limitation of prior selection in Study III, i.e. although Jeffreys' priors work well for single parameter models, they are not so suitable for multidimensional parameters, and even contribute to a poor convergence sometimes. One better alternative is proposed by Jeffreys himself using a production of the separate priors for $\mu$ and $\sigma$, or selecting reference prior proposed by Berger et al.[162]

In studies II and III, we ignored the lag effects that might lead to some overestimation of the effects of PM pollutants. Besides, in studies III and IV, only citywide $PM_{2.5}$ concentrations were available that on the other hand might underestimate the association of $PM_{2.5}$ with mortality.[163]

In Study IV, although lag effects were considered, we did not impose any structure on the relationship of the coefficients of the lagged $PM_{2.5}$ concentrations with each other. Potential multicollinearity among the lagged independent variables often arises, leading to high variance of the coefficient estimates.

# 7 CONCLUSIONS

PM pollution has already become a severe public concern because it poses great threat to human health. Road traffic is one of the major sources of PM pollution, and our two-stage model demonstrated its proportional contribution in Beijing, China, which would be up to 37% in the busy road, even worse, in view of the increasing traffic volume in the metropolis.

Interactive effects of PM pollutants and weather conditions on non-accidental mortality do exist. Given the global climate change, policy makers should consider the application of the synoptic approach in decision making and prevention activities to ameliorate the adverse effects from air pollution.

Both our time series analysis study and simulation study indicate that fully Bayesian GAM may generate as accurate and precise estimations as conventional frequentist GAM does while reveals potential uncertainty that frequentist GAM could not detect. Bayesian GAM would be a better solution to avoid over-confident inferences potentially seen in a frequentist one. With the increasing computing power of computers and statistical packages available, we may see the increasing application of fully Bayesian methods for decision making.

# 8 FUTURE PERSPECTIVES

Study I helps us to get more understanding of the $PM_{2.5}$ concentrations brought by road traffic and the importance of vehicle control for a city. It largely confirms the assumption that road traffic does play an essential role in air pollution. Our future emphasis will focus on the multilevel data collected to compare both the indirect and direct methods, and develop a more precise way for assessing the traffic-related PM pollution.

In BMA method used in Study II, we only included the uncertainty from knots selection. In the future, we will address more emphasis on covariates and confounders selections that are also major sources of the uncertainty in estimation. Furthermore, although it is an easy and frugal way of using non-informative priors in Bayesian inference, after obtaining more information about the data, we may try informative priors to further test the sensitivity of the estimations. We will also address measurement errors by employing a more elaborate simulation framework in the future.

We mainly explored the non-accidental and respiratory deaths in current studies, some further exploration on cause-specific mortality with multi-pollutant interaction association are needed for both method optimization purpose and public health concerns.

# 9 FUNDING

The work of this thesis was supported by the Strategic Grant of Karolinska Institutet, the Junior Faculty Grant of the Institution of Environmental Medicine, Karolinska Institutet, the KID-funding of Karoalnska Institutet, and the Joint China-Sweden Mobility Grant of the Swedish Foundation for International Cooperation Research and Education.

# 10 ACKNOWLEDGEMENTS

I would like to express my sincere gratitude to everyone who has supported me throughout the work for this thesis, in particular:

To my principal supervisor *Yang Cao* for his wisdom, guidance, and supporting during these years. Thank you for all you have taught me about biostatistics, epidemiology, and scientific methodology, and for always being enthusiastic about my ideas and encouraging me through every step of this thesis.

To my co-supervisors *Fang Fang* and *Matteo Bottai* for introducing me to the field of research and encouraging me to write this thesis. Thank you *Fang* for sharing your great knowledge about epidemiology. Thank you *Matteo* for contributing with your expertise in statistics and for all the work you have put into our studies.

To *Andrea Discacciati*, *Paolo Frumento*, *Erin Gabriel*, *Celia Garcia Pareja*, *Ulf Hammar*, *Jonas Höijer*, *Michael Sachs*, and *Michele Santacatterina* from the Unit of Biostatistics, Institute of Environmental Medicine, and Biostatistics Core Facility, Karolinska Institutet for your support and the warm atmosphere created for working and being around.

To Chinese colleagues from the College of Resources and Environment, University of Chinese Academy of Sciences, and the Department of Epidemiology and Biostatistics, Institute of Basic Medicine Sciences, Chinese Academy of Medical Sciences & School of Basic Medicine, Peking Union Medical College for sharing your valuable data and being very supportive, patient and kind to me.

To Chinese colleagues *Bo Fang*, *Chunfang Wang*, and *Tian Xia* from the Shanghai Municipal Center for Disease Control and Prevention for offering the data and providing the opportunity to work with you , and for your inspiring discussion and insightful input.

To Chinese colleagues *Zhijun Zhou*, *Chunhua Wu*, *Xiuli Chang*, *Jiming Zhang*, *Jianqiu Guo*, *Xiaojuan Qi*, and *Yubin Zhang* from the School of Public Health, Key Laboratory of Public Health Safety of Ministry of Education, Collaborative Innovation Center of Social Risks Governance in Health, Fudan University for being such a wonderful host during my visits in Shanghai, and for the cheering talks over lunches and dinners.

To *Qing Shen* and *Tiansheng Shi* for your friendship and companionship inside and outside Karolinska Institutet.

To all the coauthors of this thesis and coworker of the studies or others not included for your valuable efforts and professional excellence.

To every one of my colleagues in the Institute of Environmental Medicine, Karolinska Institutet, for everything I have learned from you and for making me laugh every day at work.

I would also like to thank my family and friends for being such a great sources of energy in my life.

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