

Review

# Ambient PM<sub>2.5</sub> Human Health Effects—Findings in China and Research Directions

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**Abstract:** Exposure to fine particulate matter (PM) results in adverse health outcomes. Although this is a global concern, residents of China may be particularly vulnerable due to frequent severe air pollution episodes associated with economic growth, industrialization, and urbanization. Until 2012, PM<sub>2.5</sub> was not regulated and monitored in China and annual average concentrations far exceeded the World Health Organizations guidelines of 10 µg/m<sup>3</sup>. Since the establishment of PM<sub>2.5</sub> Ambient Air Quality Criteria in 2012, concentrations have decreased, but still pose significant health risks. A review of ambient PM<sub>2.5</sub> health effect studies is warranted to evaluate the current state of knowledge and to prioritize future research efforts. Our review found that recent literature has confirmed associations between PM<sub>2.5</sub> exposure and total mortality, cardiovascular mortality, respiratory mortality, hypertension, lung cancer, influenza and other adverse health outcomes. Future studies should take a long-term approach to verify associations between exposure to PM<sub>2.5</sub> and health effects. In order to obtain adequate exposure assessment at finer spatial resolutions, high density sampling, satellite remote sensing, or models should be employed. Personal monitoring should also be conducted to validate the use of outdoor concentrations as proxies for exposure. More research efforts should be devoted to seasonal patterns, sub-population susceptibility, and the mechanism by which exposure causes health effects. Submicron and ultrafine PM should also be monitored and regulated.

**Keywords:** PM<sub>2.5</sub>; health effects; risks; air pollution; China

## 1. Introduction

Air quality is a global concern. Particulate matter (PM) has been identified as having a significant impact on human health. Fine particles, specifically, particles with a diameter of 2.5 micrometers and smaller (PM<sub>2.5</sub>) have been established to be more detrimental than those equal to or less than 10 micrometers (PM<sub>10</sub>) [1,2]. Fine and ultrafine particles are also carriers of harmful metals [3]. PM<sub>2.5</sub> has been associated with adverse health outcomes including acute and chronic respiratory illnesses such as pneumonia and chronic bronchitis, cardiovascular diseases such as coronary heart disease, congestive heart failure, and premature death [4–6]. Many epidemiological studies have confirmed the relationship between increased mortality or morbidity and PM<sub>2.5</sub> concentrations [5,6]. A recent US study found that long-term exposure to ambient PM<sub>2.5</sub> is associated with elevated risks of mortality in the nationwide adult cohorts [7]. It was recently estimated that worldwide, approximately 1 million premature deaths each year are attributed to atmospheric fine particle pollution [8]. An estimated 3.5 million cases of chronic obstructive pulmonary disease (COPD) and 220,000 lung cancer mortalities are caused by anthropogenic PM<sub>2.5</sub> annually [9].

Due to rapid economic growth, industrialization, and urbanization, China is experiencing severe air pollution leading to increased risks for the exposed populations. Among 61 cities with annual

PM<sub>2.5</sub> concentrations greater than 80 µg/m<sup>3</sup>, 10 of these cities were in China [10]. Over 1.3 million adult premature mortalities were attributed to PM<sub>2.5</sub> exposure in 2013 [11]. Beijing, with a population of 21.7 million (2015) and an area of 16,411 km<sup>2</sup> [12], is amongst the most polluted cities in the country, frequently experiencing a gray haze across the city [13] and attracting global attention due to high pollutant concentrations. The estimated premature deaths attributable to PM<sub>2.5</sub> exposure in the capital city were 10,204 for cardiovascular disease and 1228 for lung cancer in 2005 [8].

Several studies have demonstrated a relationship between exposure to fine atmospheric particles and risk to human health in China [14–16]. Although air pollution in China has been the focus of numerous studies, these have typically focused on PM<sub>10</sub>, SO<sub>2</sub>, and NO<sub>2</sub> with less attention paid to PM<sub>2.5</sub> [17–19]. This is because until 2012, PM<sub>2.5</sub> was not listed as a criteria pollutant in the Chinese Ambient Air Quality Standards and, therefore, was not routinely monitored [20]. Some recent research has focused on PM<sub>2.5</sub> concentrations [21,22], source apportionment [22–24], and more recently health risks attributed to PM<sub>2.5</sub> exposure in Beijing [20,25,26]. Although research is now being compiled, there are still many shortcomings to address such as the limited time periods that these studies have covered and the limited ground-based measurements which may not be representative of residential, or even city-wide, exposures.

A review of PM<sub>2.5</sub> measurements and health effects in China, which included four PM<sub>2.5</sub> health outcome studies that took place in Beijing between 2004 and 2009, was published recently [20]. This previous review identified strategies and highlighted the need for urgent action in order to address the air pollution problem in China. Since the time that these studies took place, the Ambient Air Quality Standards for PM<sub>2.5</sub> in China were released in 2012 [27] as well as a number of pollution control measures have been implemented such as switching coal-fired burners to cleaner fuels, eliminating outdated vehicles, and switching from coal residential heating to electricity [28]. Furthermore, many more studies have been published as it becomes more evident that PM<sub>2.5</sub> concentrations in Beijing are potentially putting residents at risk and, therefore, a review of the most recent studies is warranted.

Risk assessment methods can generally be classified as either health endpoint studies (morbidity and mortality) [6,15,26] or risk based, either carcinogenic or non-carcinogenic, using exposures and unit risk (UR) or slope factors (SF) [29,30]. Both types will be included in this review. The scope of the recent findings concerning PM<sub>2.5</sub> health effects in Section 2 is limited to Beijing due to elevated concentrations and high population density there [31,32]. The major focus of this article is to evaluate and present high priorities for future work on the topic of PM<sub>2.5</sub> and its health effects, based on a literature review.

## 2. Beijing PM<sub>2.5</sub> Air Quality, Regulations, Major Sources, and Health Effects

### 2.1. PM<sub>2.5</sub> Air Quality and Regulation

Although the Chinese government has instituted policies and regulations aimed at improving air quality, PM<sub>2.5</sub> concentrations in Beijing are still far above the WHO Air Quality guidelines [33] of 10 µg/m<sup>3</sup> (annual) or 25 µg/m<sup>3</sup> (daily) (Table 1). Before the commencement of PM<sub>2.5</sub> monitoring at the 12 long-term government stations since 2013 [34], PM<sub>2.5</sub> concentrations were primarily collected at a few research sites (e.g., Peking University [25]) and at the US Embassy [29,35]).

In 2012, the Chinese government released the Ambient Air Quality Standards (AAQCs) for ambient PM<sub>2.5</sub> for the first time [13,27]. The standards have two grades which apply to different areas. Grade I standards, which apply to areas such as national parks, set 24-h and annual average limits of 35 and 15 µg/m<sup>3</sup>, respectively. Grade II standards, which apply to general areas limit daily and annual averages to 75 and 35 µg/m<sup>3</sup>, respectively (Table 1). All studies compiled for this review reported that PM<sub>2.5</sub> concentrations were well exceeding these standards. The annual average PM<sub>2.5</sub> concentration in 2001 was 110 µg/m<sup>3</sup> [36]. Guo et al. [25] reported an average PM<sub>2.5</sub> concentration of 122 µg/m<sup>3</sup> between 2004 and 2005 at the Peking University site. Annual mean concentrations ranged from 85 to

105  $\mu\text{g}/\text{m}^3$  during 2008–2013 at the US Embassy site in Beijing, and there were only 328 days out of 1746 that met the standard [29]. More recently, Batterman et al. [13] reported a two-year average concentration of 83  $\mu\text{g}/\text{m}^3$  from 2013–2015, still well above Chinese and International standards (Table 1).

**Table 1.** Ambient air quality standards of  $\text{PM}_{2.5}$ .

Averaging Time	China [27]		USEPA [37]	WHO [33]	EU [38]
	Grade-I	Grade-II			
Annual ( $\mu\text{g}/\text{m}^3$ )	15	35	15	10	25
Daily ( $\mu\text{g}/\text{m}^3$ )	35	75	35	25	N/A

## 2.2. Sources of $\text{PM}_{2.5}$

In order to target reduction it is important to understand the origination of the pollution. For this purpose, source apportionment studies have been conducted and examples are summarized in Table S1. It is clear that secondary PM (range 26–33%), coal burning (7–29%), dust (9–23%), vehicles exhausts (3–26%), industrial emissions (6–28%), and biomass burning (6–13%) are consistently major contributors to  $\text{PM}_{2.5}$  concentrations in Beijing [22–24,36,39–41]. Jin et al. [24] also reported a large contribution from the construction industry (23.3%). Significant contributions from household biofuel and open biomass burning to  $\text{PM}_{2.5}$  concentrations was also recently confirmed by Zhang and Cao [42].

Many studies have based their analysis on determining the mechanisms of exposure and on where reductions efforts should be focused. An intake fraction study of  $\text{PM}_{2.5}$  and  $\text{NO}_x$  concluded that the intake fraction values from vehicle emissions were several times higher than those from industry emissions in China [43]. This supports the controlling of vehicle emissions as top priority for protection of human health.

## 2.3. $\text{PM}_{2.5}$ Human Health Effect Studies

A summary of the health effects studies to be discussed in this section is provided in Table S2. A review study on  $\text{PM}_{2.5}$  in China, including health effects, was recently provided by Pui et al. [20]. In this review, four  $\text{PM}_{2.5}$  health effects studies in Beijing were highlighted and are summarized here. Significant increases in total mortality, cardiovascular mortality, and respiratory mortality with 10  $\mu\text{g}/\text{m}^3$  increases in  $\text{PM}_{2.5}$  concentrations between 2007 and 2008 were reported by Chen et al. [26]. Furthermore, significant associations between elevated levels of  $\text{PM}_{2.5}$  and emergency room visits for cardiovascular disease events between 2004 and 2006 were reported by Guo et al. [25]. The daily average  $\text{PM}_{2.5}$  concentration during this study was 122  $\mu\text{g}/\text{m}^3$ . The same authors reported significant associations between  $\text{PM}_{2.5}$  exposure and emergency hospital visits for hypertension in Beijing in 2007 [44]. Lastly, Li et al. [6] reported significant associations between respiratory mortality and morbidity and  $\text{PM}_{2.5}$  exposure from 2004–2009, over which period the mean  $\text{PM}_{2.5}$  concentration was 76  $\mu\text{g}/\text{m}^3$ . Specifically, the authors reported an elevation in respiratory mortality and morbidity up to 4.6 and 4.5% respectively, corresponding to a 10  $\mu\text{g}/\text{m}^3$  increase in  $\text{PM}_{2.5}$  concentrations. Average increases were 0.69% and 1.32%, respectively, which are still significant. This study demonstrated that adverse effects were observed with lags ranging from 0 to 8 days and, furthermore, were still significant after controlling for variables such as time trend, seasonality, and meteorological factors. The authors also reported that cool and dry weather increased the effects of  $\text{PM}_{2.5}$  on human health, whereas warm and humid weather decreased the effects.

Long-term exposure to  $\text{PM}_{2.5}$  in Beijing between 2001 and 2012 was investigated by Zheng et al. [30]. This study applied concentration-response functions to estimate yearly mortality attributable to  $\text{PM}_{2.5}$  by ischemic heart disease, cerebrovascular disease, chronic obstructive pulmonary disease, and lung cancer among the population older than 30 years and due to acute lower respiratory infection among the population less than five years old. Based on this analysis, the authors estimated

total mortality to be 6382 deaths per year in Beijing central area, which would extrapolate to approximately 22,000–30,000 deaths per year attributable to PM<sub>2.5</sub> concentrations for the city of Beijing. This warrants urgent initiatives to reduce PM<sub>2.5</sub> concentrations.

Studies have also focused on the health impacts of acute high pollution events. In January 2013, Beijing experienced continuous haze, with mean daily PM<sub>2.5</sub> concentrations ranging from 98–228 µg/m<sup>3</sup>. Maximum daily concentrations were greater than 270 µg/m<sup>3</sup> at all 16 districts; and greater than 500 µg/m<sup>3</sup> in 10 of 16 districts. Hourly concentration was as high as 900 µg/m<sup>3</sup>. It was reported that 479 premature deaths were due to high PM levels [45]. Analysis of four-year medical data from a hospital 3 km from a PM<sub>2.5</sub> monitor found increased risks for all-cause, cardiovascular, and respiratory emergency visits, and respiratory outpatient visits during the 11–13 January episode [46].

Significant association between ambient PM<sub>2.5</sub> peak concentrations and an increase in human influenza cases has been reported [29]. Hourly PM<sub>2.5</sub> concentration data from the US Embassy site in Beijing were collected between 2008 and 2013 and influenza case data were collected from the National Infectious Disease Reporting System for Beijing. Using wavelet analysis, the authors demonstrated a correlation between peak monthly PM<sub>2.5</sub> concentrations and increased cases of influenza, with a time lag of one to two months between the two. In other words, there was a delayed effect of PM<sub>2.5</sub> on influenza cases.

The conclusion above was further supported by Feng et al. [47] who observed significant positive associations across all age categories between exposure to PM<sub>2.5</sub> and influenza-like illness risk during the flu season in their time-series analysis. They also noted a short term delay of effects, with the two-day moving average of PM<sub>2.5</sub> concentrations being the best predictor.

#### 2.4. Discussion

Although uncertainties still exist surrounding the main sources of PM<sub>2.5</sub>, the mechanisms by which exposures can cause adverse effects, and spatial and temporal variabilities, there is clear evidence that PM<sub>2.5</sub> concentrations in Beijing remain much higher than Chinese and International standards and that exposure to these concentrations is resulting in adverse health effects. Since the release of AAQCs in 2012, concentrations have decreased from annual values exceeding 100 µg/m<sup>3</sup> in 2001 [36] to a reported two-year average of 83 µg/m<sup>3</sup> in 2013–2015 [13]. Although this trend is encouraging, the values are still significantly higher than WHO guidelines (Table 1) and are contributing to adverse health impacts for residents.

There exist significant challenges in comparing and evaluating PM<sub>2.5</sub> exposure and health risk study outcomes. Researchers use different study designs and modeling approaches and different regions present different relative risks [6] as shown in Table 1. Studies also reported varying exposure lag effects [29,47].

Many researchers have been reviewing PM<sub>2.5</sub> health outcomes data in other countries along with current PM<sub>2.5</sub> concentration levels in China to urge action on systematic research on these linkages in China [48]. Although some comparisons may be helpful, it is important to keep in mind that air pollution mixture in Beijing is different from that of cities in North America and Europe. Recent studies have demonstrated acute and chronic effects of PM<sub>2.5</sub> exposure at levels much lower than Beijing is experiencing. Shi et al. [49] reported associations between both short-term and long-term PM<sub>2.5</sub> exposure and all-cause mortality at exposures (PM<sub>2.5</sub> < 10 µg/m<sup>3</sup>) below the standards established for the United States (12 µg/m<sup>3</sup> of annual average PM<sub>2.5</sub>, 35 µg/m<sup>3</sup> daily, Table 1) and by the WHO (Table 1) in the New England area of the U.S. This finding of low concentration PM<sub>2.5</sub> mortality effects suggests that the much higher concentrations in China are highly likely to have an adverse impact on residents.

Interestingly, several researchers have noted that the exposure response relationships in China are lower than in the US or Europe. China, with much greater concentrations, has lower relative risks. For example, for a 10 µg/m<sup>3</sup> increase in PM<sub>2.5</sub>, Chen et al. [26] estimated a relative risk of 0.66% in Beijing, whereas for the same increase in concentration, relative risks of 2.2% [50], 6.38% [51], and

11% [52] have been reported in California (US), Las Palmas (Canary Islands, Spain), and Ontario (Canada), respectively. It has been suggested that this may be due to population sensitivity to PM and more so, due to different particle components [53,54]. These are important findings in themselves. Because PM composition is variable, study results in one region cannot be extrapolated to another based on PM mass concentrations alone. Although these comparisons are helpful and may urge action, Hu and Jiang [48] made a great point by suggesting that rather than time being spent on verifying western countries' research, for China, the focus should be on controlling PM<sub>2.5</sub> concentrations and researching prevention of adverse health outcomes. The authors state that "China needs to take action without further delay".

Taken together, these above-mentioned studies have demonstrated associations between exposure to PM<sub>2.5</sub> and a number of adverse health outcomes in Beijing. Increases in total mortality, cardiovascular mortality, respiratory mortality, cardiovascular disease emergency room visits, influenza-like illnesses were reported. This is clear evidence that the residents of Beijing are at risk due to the current concentrations levels of PM<sub>2.5</sub>. Protection of human health should be top priority.

Furthermore, the costs associated with pollution-related health effects are substantial. Some cost estimates have been reported in the literature and summarized by Zhang et al. [55]. The health impacts due to PM related pollution between 2000 and 2004 had associated costs equal to 6.55% of Beijing's GDP [55]. A recent study estimated the economic effects of ambient PM<sub>2.5</sub> due to the increased lung cancer incidence rate and mortality rate in selected Chinese cities and on the national level. Beijing, with the highest ambient PM<sub>2.5</sub> concentration among the eight cities, was estimated to have a 26% increase in the incidence rate of lung cancer. The total economic loss, including increased social expenditure and forgone labor output, was approximately 4 billion RMB¥ (6.8 RMB¥ ≈ 1 US\$) in 2015 alone, which equates to 0.18% of the city's GDP, and more than 5% of the nationwide loss of 79.2 billion RMB¥ [32].

Novel approaches to measuring welfare loss caused by air pollution have been developed [56–58]. Health and economic impacts have been shown to be substantial in Chinese provinces with high PM<sub>2.5</sub> concentrations [59]. Recent analysis has estimated that China will experience a 2% GDP loss and 25.2 billion USD in health expenditures from PM<sub>2.5</sub> pollution in 2030 [59]. It was also recently estimated that exposure to PM<sub>2.5</sub> in China resulted in a nationwide welfare loss of US\$248 billion in the year 2015 alone, with over the half the cost attributed to mortalities associated with chronic exposure [60]. These same studies have suggested a combination of integrated air pollution control strategies and climate policies to improve welfare and reduce economic costs of air pollution health effects.

In their "Atmospheric Pollution Prevention and Control Action Plan", The Legislative Affairs Office of China's State Council has set a target of reducing PM<sub>2.5</sub> to 60 µg/m<sup>3</sup> in Beijing by the end of 2017 [61]. A recent announcement confirmed that the capital city met this target in 2017, with a reported annual PM<sub>2.5</sub> concentration of 58 µg/m<sup>3</sup>. This is down 35.6% from the 2012 value [62]. Although still much higher than the Chinese standards and WHO guidelines (Table 1), this is a step in the right direction for the city. China can look to the U.S. and other countries as an example on how to map a route towards substantial reduction of PM<sub>2.5</sub>. The USEPA credits their substantial reductions in PM<sub>2.5</sub> concentrations (33% reduction between year 2000–2012) to several factors, including effective nation-wide sampling, accurate mass and chemical composition measurements and source apportionment, establishment of voluntary and mandatory emission controls, and establishment of partnerships between federal, state, and local governments, as well as with academic, industry, and environmental groups [63]. In the future, Beijing could be an example to other countries who are facing rapid economic growth and industrial expansion, and through proactive measures, could possible prevent residents from being exposed to high levels of air pollutant concentrations.

### 3. Identifying Next Steps and Prioritizing Future Research

Although it can clearly be concluded that PM<sub>2.5</sub> concentrations are high in Beijing and many other cities worldwide with potentially dangerous implications for the residents, much more work is

needed. Previous studies provide preliminary results and directions, however, due to inconsistencies in study designs, cannot yet provide clear conclusions on the levels of PM<sub>2.5</sub> and their associated effects. Spatial resolutions vary from one monitor [25,29] to high density sampling campaigns [64]. The bias in exposure estimates will be high for residents who are far removed from the monitors. Furthermore, most studies do rely on outdoor measurements, however, exposures depend on indoor and outdoor concentrations and the proportion of time spent in these environments. Previous studies have also taken place for varying lengths of time, varying from less than a month [45] to up to four years [29]. At shorter time periods, the observed concentrations may not be representative of lifetime exposures or even annual averages. With these challenges in mind, researchers have identified important next steps for future studies aimed at understanding the impacts of ambient PM<sub>2.5</sub> on human health. The objectives of these next steps are to develop methods and policies to decrease concentrations and better understand the human health implication.

### 3.1. The Need for Long-Term Studies

Several studies identified the need for longer term studies to verify some of the associations [22,47,55,65]. The PM<sub>2.5</sub> exposure-response relationships in China will have a greater reliability now because 4-year data are available since the governments began routinely monitoring for PM<sub>2.5</sub> in China in 2013. Data from this newly established national network in over 300 cities is being made available [66,67]. The first full year of data (April 2014–April 2015) showed annual average PM<sub>2.5</sub> concentrations ranging from 16 to 119 µg/m<sup>3</sup> [42], with the highest annual concentration observed in in the Beijing-Tianjin-Hebei (BTH) region. The national PM<sub>2.5</sub> database has been employed in a number of health effect studies (e.g., [31,66]). The estimated premature mortality attributable to PM<sub>2.5</sub> was 652,000 in 161 cities, accounting for approximately 7% of total deaths in 2015 [31]. With the network in place to monitor PM<sub>2.5</sub> concentrations across China, long term datasets can be analyzed and correlated with health outcomes.

### 3.2. Evaluating the Assumption of Ambient Outdoor Concentrations as a Proxy for Exposure

Many studies acknowledge that a limitation of their research is the use of outdoor fixed station measurements as a proxy for personal exposure [25,26,29,47,64,68]. However, it may not be reasonable to use the fixed station outdoor concentration as a proxy for personal exposure due to two concerns, (1) the lack of an adequate spatial resolution, and (2) outdoor concentrations may not be a suitable proxy to personal exposure.

#### 3.2.1. Spatial Resolution

Reliance on a single monitoring station has frequently been stated as a limitation of past studies [25,47]. Furthermore, Zhang et al. [55] point out that their study assumes that the entire population, across urban areas of Beijing, are exposed to a city-wide average concentration levels. The authors suggest the use of atmospheric diffusion models to obtain concentrations at finer spatial resolutions. Some possible options for improving spatial resolution are discussed below.

Deployment of low-cost PM sensors allows for higher spatial resolution in human exposure assessment. Those low-cost sensors rely on either nephelometry, which measures particle light scattering of an ensemble of aerosol, or optical particle counting which measures particle size and number of individual particles [69]. Although these techniques do not directly measure particle mass, they are statistically related to particle mass concentrations measured by a reference measurement. The cost of those sensors is a fraction of the instruments employed in stationary government monitoring stations. Furthermore, those sensors are smaller in size, and weight, and with lower power consumption. Thus, they are suitable for deployment at a neighbourhood-scale to provide insight into spatial and/or temporal air quality patterns [69].

Another solution to address the limitation of sparse measurement data in PM exposure studies is to estimate ground-level PM<sub>2.5</sub> using satellite remote sensing. In this technique, satellite sensors provide

aerosol optical depth (AOD), which is a quantitative measure of PM abundance in the atmospheric column [70]. Using regression models, quantitative relationships have been established between AOD and PM<sub>2.5</sub> [71,72] allowing for evaluation of spatial and temporal characteristics of PM<sub>2.5</sub> over large geographic regions. Until recently, a lack of ground level PM<sub>2.5</sub> measurements for calibration limited the development of models outside of North America [73]. The newly established national monitoring network in China is now allowing for models to be developed in China (e.g., [73–75]), some with a high resolution of 1 km × 1 km [76]. Ma et al. [73] estimated daily PM<sub>2.5</sub> concentrations in China with fused satellite AOD as the primary predictor to successfully provide estimates of national-scale PM<sub>2.5</sub> in China to areas that are not covered by the ground-level monitoring network. Model estimates from 2013 indicated that 96% of the Chinese population live in areas with PM concentrations exceeding the Chinese National Ambient Air Quality Level 2 Standard of 35 µg/m<sup>3</sup>. Satellite-derived PM datasets can fill in data gaps by providing adequate resolution of PM<sub>2.5</sub> concentrations. This could alleviate the spatial coverage restraint surrounding epidemiologic studies in some countries, including China.

Geographic information system (GIS) techniques have been used to estimate concentrations of air pollutants including PM. This was recently explored using the ordinary kriging method to estimate spatial characteristics of PM<sub>10</sub> across Beijing during 2008–2009 [19]. The spatially resolved estimates were then used to investigate the effects of ambient PM<sub>10</sub> on the cause-specific respiratory mortality in Beijing, which identified significant associations between exposure and increased risk of mortality. Similar GIS techniques could be applied to investigate PM<sub>2.5</sub>. A promising approach is land use regression (LUR). Predictor variables include land use, road traffic, population density, weather conditions, altitude, topography, and distance to road, industrial facility or the ocean [77]. Application of LUR techniques has been reported worldwide. Models were built to produce high resolution (1 km × 1 km) annual concentration maps of nitrogen dioxide (NO<sub>2</sub>), PM<sub>10</sub>, ozone, sulphur dioxide (SO<sub>2</sub>) and carbon monoxide (CO) across the European Union [77]. In a recent US study of mortality risk and PM<sub>2.5</sub> air pollution with nationwide adult cohorts, the 10-year (1999–2008) exposures to PM<sub>2.5</sub> at the metropolitan statistical area of residence were estimated using GIS models with traffic indicators [7]. More accurate exposure assessment is expected with incorporation of innovative approaches, such as machine learning [78].

### 3.2.2. Outdoor Concentrations as Proxies for Exposure

Outdoor concentrations are routinely used as proxies for exposure. In reality, human exposure to PM<sub>2.5</sub> is influenced by indoor and outdoor exposures as well as personal activities such as smoking, owning a pet, or simply moving throughout the home causing resuspension of particles [79]. Personal monitoring studies allow for apportioning of exposure of different age groups in different environments and improve the identification of health risks [3]. However, personal monitoring of a large sample is often cost prohibitive. An extensive exposure assessment study was conducted in Windsor, Ontario, Canada to examine the relationships between indoor and outdoor concentrations and personal exposures to, amongst other pollutants, PM<sub>2.5</sub> [79]. This study demonstrated PM concentrations obtained from personal environmental monitors were 52% (winter) and 26% (summer) higher than those obtained from the fixed sites, highlighting the importance of addressing the assumption of ambient outdoor concentrations as proxies for personal exposure. Although Du et al. [80] reported mean personal PM<sub>2.5</sub> exposure concentration (102.5 µg/m<sup>3</sup>) being very close to the mean fixed-site concentration (118.5 µg/m<sup>3</sup>), and a strong correlation ( $r = 0.81$ ) between those two concentrations in Beijing, more research is needed to evaluate and refine this assumption. With this in mind, Hodas et al. [81] evaluated and refined an outdoor-to-indoor transport model for PM<sub>2.5</sub>. Models such as these can improve the use of outdoor PM<sub>2.5</sub> concentrations to estimate residential exposure. This can lead to reduced exposure misclassification in epidemiologic studies. Moreover, source components will differ between indoor and outdoor environments and the effects of this should be considered in risk assessment and health effect investigations.

### 3.3. Investigating the Mechanism by Which Exposures Cause Adverse Human Health Effects

Association between exposure and health outcomes may not indicate a causal relationship. Researchers have stressed the need for further studies to understand the mechanisms underlying the observed associations as well as public health and environmental policy implications [29,47].

Preliminary evidence for mechanisms between PM<sub>2.5</sub> and increased mortality, such as increased blood pressure, reduced lung function, and others has been established in the literature [82–84]. The USEPA recently proposed a mechanism for the biological mechanism by which PM affect human health [85]. The hypothesized mechanism is through the induction of pulmonary inflammatory responses mediated through the generation of reactive oxygen species (ROS). The researchers propose that particle-induced ROS generation is a major mechanism for adverse effects of PM in the respiratory, cardiovascular, immune, and neural systems. Interactions with ROS within these systems causes cellular oxidative stress, resulting in altered function and disease [85]. This mechanism was linked to airway inflammation, allergic airway inflammation, heart rate variation, hypertension, and inflammation in the brain. The authors point out the importance of continued acute and long-term mechanistic research focusing on the inflammatory responses in these affected systems. In addition, they mention the need to identify new biomarkers and outcomes to support epidemiological studies. Researchers are now identifying specific genes and regulatory mechanisms. Liu et al. [86] presented the first evidence of epigenetic changes with air pollution induced inflammatory responses.

Furthermore, it is important to mention that, in reality, exposures are rarely limited to a single air pollutant or a single component. Air pollution is made up of multi-pollutant mixture and the mechanisms and extent to which these mixtures impact human health prove more challenging to fully understand. Future research on the effects of multipollutant mixtures, including PM, is warranted [85,87].

### 3.4. Identification of Seasonal Patterns and Sub-Population Susceptibilities

Seasonal factors can impact both PM concentrations and the effects of exposure. Previous research has demonstrated that characteristics of particle mixtures change throughout the year [6,88,89]. Seasonally variable factors such as temperature and humidity have also been shown to affect estimates of the effects of PM exposure on respiratory morbidity and mortality differently in different seasons [5,6,90,91]. Higher PM<sub>2.5</sub> concentrations were reported on hot and humid days than on cool and dry days in Beijing [6], however cool and dry weather increased the effect of PM<sub>2.5</sub> on respiratory health. The conclusion that fine particles have a greater effect on respiratory health in warmer seasons is consistent with previous studies in Shanghai, China [92] and Wuhan, China [91].

More work is needed to further evaluate and conclusively identify seasonal patterns of PM<sub>2.5</sub> because meteorological conditions can alter the effect of PM<sub>2.5</sub> exposures [6]. In light of the evidence of seasonal variability in PM<sub>2.5</sub> concentrations and effects of exposure, it is beneficial to conduct sampling campaigns in multiple seasons in order to reduce exposure misclassification. It is also important to consider seasonality when interpreting the results of health studies based on a single season.

Adverse effects have also been reported to vary in severity depending on the population. For example, elderly and females were identified as being more vulnerable to PM exposures in recent studies (e.g., [19]). The USEPA PM center based research studies have demonstrated that estimates of health effects of PM vary substantially across communities and seasons [85]. This heterogeneity is partially due to differences in sources and composition (discussed below).

### 3.5. Determination of Sources and Chemical Compositions

PM<sub>2.5</sub> composition varies with location, climate, season, land use, and extent of mobile emissions [93]. It is important for future studies to focus on characterizing the chemical constituents and sources of PM<sub>2.5</sub> [47,65], because previous studies have suggested that some specific PM<sub>2.5</sub> components are responsible for the majority of health effects, especially toxic trace metals [94]. The majority of toxic

trace metals (some are carcinogenic) in the air such as Cr, Pb, As, Cd, and Ni are in the form of fine particulates [94]. Some previous studies have estimated the health risks attributable to specific elements in Beijing and other regions in China [95,96], as well as in Washington, D.C., USA [94]. The relative toxicity of trace metals can be compared by considering the slope factor of these elements. Slope factors provide an estimate of the increased cancer risk from exposure to a dose of 1 mg/kg-d for a lifetime [97]. An exposure assessment in Cincinnati, Ohio employed LUR models to estimate elemental components of PM<sub>2.5</sub> [78]. In addition to trace metals, polycyclic aromatic hydrocarbons (PAHs), are components of organic carbon on PM and have toxic, mutagenic, and carcinogenic potentials. PAH inhalation exposure has been associated with an estimated 6.5 million cases of lung cancer in China each year [98]. Toxic equivalency factors (TEF) have been used to estimate inhalation cancer risk associated with exposure to PAHs. TEFs related the toxicity of individual PAHs to an equivalent concentration of benzo(a)pyrene, a known carcinogen. Higher TEF values indicate higher toxicity of individual PAHs. In addition to investigating associations between PM<sub>2.5</sub> mass concentrations and health outcomes, future studies should analyze for specific effects of trace metals and PAH components.

A recent study in Xi'an, China, a similarly high population, high pollution mega city, evaluated the constituents of PM<sub>2.5</sub>, including organic carbon, elemental carbon, 10 water soluble ions and 15 elements, and mortality [68]. A high degree of heterogeneity amongst the constituents is observed. Specifically, the influence from PM<sub>2.5</sub> constituents that were associated with fossil fuel combustion demonstrated significantly greater positive associations with mortality outcomes compared to common crustal elements. This demonstrates the importance of understanding the chemical constituents of PM<sub>2.5</sub> rather than relying only on PM<sub>2.5</sub> mass and is particularly important when comparing studies from different geographical areas.

An understanding of chemical composition of PM<sub>2.5</sub> is especially essential in developing countries because of changes in their energy sourcing for economic, environmental or health based reasons. For example, the release of Chinese Ambient Air Quality Standards for PM<sub>2.5</sub> in 2012 led to some switching of energy sources. In Beijing, changes in energy sources related to pollution control measures include switching coal-fired burners to cleaner fuels such as natural gas, eliminating outdated vehicles, and replacing residential coal heating with electricity [28]. This calls for the need for new studies on source apportionment and chemical composition and the effects of these changes on the magnitude of the health outcomes that have been identified. Zhang and Cao [42] point out the need for simultaneous investigation of real-time chemical composition of PM<sub>2.5</sub> and meteorological conditions at a fine spatial temporal resolution to obtain a more comprehensive picture of source and PM<sub>2.5</sub> formation mechanisms.

Furthermore, there is a need to differentiate the effects of exposure to primary versus secondary PM<sub>2.5</sub>. Most studies focus on health effects of exposure to primary PM, largely originating directly from anthropogenic activities. Emissions of other pollutants, including sulfur oxides, nitrogen oxides, ammonia, and volatile organic compounds, undergo physicochemical transformations, leading to formation of secondary particles. Researchers have begun to elucidate the impacts of exposure to secondary particles. Studies indicate that processes involved in the aging of particles produces oxidized ROS and secondary particles are more toxic than the primary ones [85]. This underlines the importance of investing the health impacts of secondary PM in future research.

### *3.6. Determination of Impacts from Exposure to Ultrafine Particles*

Although the focus of this review is on PM<sub>2.5</sub>, future work should also address the impacts from exposure to particles in nanoscale size range, also known as ultrafine particles (UFPs) (<100 nm). UFPs in the atmosphere can originate from several sources, however, the predominant source is traffic emissions [3]. The mechanism by which UFP exposure can pose potentially adverse impacts differs from that of PM<sub>2.5</sub> or PM<sub>10</sub> due to the greater potential for the smaller particles to be deposited to the lungs and translocated to other parts of the body [99]. Some studies have established linkages between exposure to ultrafine PM and adverse health outcomes. For example, Leitte et al. [64] demonstrated

associations between exposure to particles in the 50–100 nm range and respiratory emergency room visits in Beijing. However, the impacts of exposure to UFPs has not been extensively studied and health outcomes are largely unknown. Further, the World Health Organization suggests that exposure to UFPs may have greater potential for adverse health impacts compared to larger particles [100]. This is particularly important for Asian cities as a recent study suggests that exposure to outdoor UFPs in these cities is approximately four times larger than that in European cities [3]. UFPs are likely to continue to increase in Asian cities due to the increasing traffic volumes. For these reasons, submicron and ultrafine PM should be included in the monitoring networks and be regulated. Additionally, more policy and research efforts should be devoted to UFPs.

#### 4. Conclusions

There has been growing attention to ambient PM<sub>2.5</sub> concentrations in Beijing as well as China and the recent studies that point to adverse health effects and increased risks due to exposure. A review of recent literature confirms the associations between PM<sub>2.5</sub> exposure and adverse health outcomes including total mortality, cardiovascular mortality, respiratory mortality, hypertension, lung cancer, COPD, and influenza. There is clear evidence that the residents of Beijing are at risk due to high concentration levels of PM<sub>2.5</sub>.

Impressive progress has been made since the release of PM<sub>2.5</sub> air quality standards in 2012, with a 36% deduction in annual concentrations at Beijing, from 90 µg/m<sup>3</sup> in 2012 to 58 µg/m<sup>3</sup> in 2017 [62], however, still well above Chinese and International standards (Table 1). Our comprehensive review of previous studies has identified the following priorities for future research on PM<sub>2.5</sub> health effects in China:

- conducting long-term studies to verify exposure-health effect associations;
- employing high density sampling campaigns or application of satellite remote sensing and/or spatial models to obtain exposures at finer spatial resolutions;
- carrying-out personal monitoring studies to evaluate the use of outdoor concentration as a proxy for exposure;
- investigation of the mechanisms by which exposure results in adverse health outcomes, especially in a multipollutant context;
- identification of seasonal patterns and sub-population susceptibilities;
- evaluation of the impact of chemical composition of PM on health outcomes;
- regulation and monitoring of ambient PM<sub>1</sub>; and
- determination of impacts from exposure to ultrafine PM.

The solution to environmental and public health protection in China should be a multi-faceted long-term approach that includes government regulations, public awareness and involvement, and industrial compliance. Ultimately, public health recommendations need to balance protection from adverse effects and practicality. The implications of this review should highlight a critical need for public health and environmental protection policies to be reviewed or tightened. Although progress is underway, there is still a long way to go for China to optimize its economic and energy structure [101]. With a focus on these suggestions for future research and regulations, this work can help to inform China as well as other countries who will go through the same transitions in the future, to strives for a balance between economic growth and environmental protection.

**Supplementary Materials:** The following are available online at <http://www.mdpi.com/2073-4433/9/11/424/s1>. Table S1: Major sources of PM<sub>2.5</sub> in Beijing by receptor modeling. Source contribution (%) in parentheses (columns 4–10) when available. Table S2: Summary of health effects studies, including PM<sub>2.5</sub> concentrations measured, health outcomes investigated, approaches, and major findings.

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