HEALTH EFFECTS OF AMBIENT AIR POLLUTION

- - A REVIEW OF RECENT EPIDEMIOLOGICAL EVIDENCE

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Abstract

High level of exposure to air pollution can cause a variety of adverse health outcomes. Air quality in developed countries has been generally improved over the last three decades. However, many recent epidemiological studies have consistently shown positive associations between exposures to relatively low levels of air pollution and health outcomes. Thus, adverse health effects of air pollution, even at relatively low levels, remain a public concern. This paper aims to provide an overview of current epidemiological evidence on this important issue and to identify future research opportunities of air pollution epidemiological studies.

1. Introduction

It is well known that exposure to high levels of air pollution can adversely affect human health. A number of air pollution catastrophes occurred in industrial countries between 1950s and 1970s, such as the London smog of 1952 [1]. Air quality in western countries has significantly improved since the 1970s. However, adverse health effects of exposure to relatively low level of air pollution remain a public concern, motivated largely by a number of the recent epidemiological studies that have shown positive associations between air pollution and health outcomes using sophisticated time-series designs [2].

This review highlights findings from major epidemiological studies designs (including time-series, case-crossover or case-control, panel, and cohort study designs) in estimating the associations of exposures to ambient air pollution with health outcomes over the last two decades, and identifies future research opportunities. We do not intend for this to be a formal systematic literature review or meta-analysis, but to discuss issues we feel are vitally important based on recent literature and our experience. This literature is divided into two parts. We first summarize findings from each of these major epidemiological study designs. Then, we discuss future research opportunities for air pollution epidemiological studies.

2. Health effects of ambient air pollution

2.1 Time-series studies

There are a large number of time-series studies on the short-term health effects of air pollution, with the emphasis on mortality and hospital admissions by means of fitting Poisson regression models at a community level or ecological level. This type of time-series design is a major approach to estimating short-term health effects of air pollution in epidemiological studies for the last two decades. Many studies have found associations between daily changes in ambient particulate air pollution and increased cardiorespiratory hospital admissions [3-6], along with cardiorespiratory mortality [7-9] and all cause mortality [10]. Because numerous air pollution time-series studies show that exposure to air pollution is associated with different kinds of human health outcomes, it is impossible to list results from all studies. Table 1 only selects major time-series studies on short-term health effects of PM_{10} and ozone from different countries around the world published over the last two decades. Early findings have been systematically and thoroughly reviewed by other authors [11-12].

Single-site time-series studies have been criticized because of exposure measurement errors, substantial variation of the air pollution effects and the heterogeneity of the statistical approaches used in different studies [13]. Recently, several multi-site time-series studies have been conducted in Europe and the United States. Two large collaborative air pollution projects in Europe and U.S. are summarised below.

In Europe, the APHEA (Air Pollution and Health: a European Approach) studies have provided many new insights. Initial studies were based on older data (APHEA-1) [14] and a new series of studies (APHEA-2) used data of the PM_{10} fraction since the late 1990s [15]. The APHEA-2 mortality studies covered over 43 million people and 29 European cities, which were all studied for more than 5 years in the 1990s. The combined effect estimate showed that all-cause daily mortality increased by 0.6 % (95 % CI: 0.4 %, 0.8 %) for each 10µg/m^3 increase in PM_{10} from data involving 21 cities. It was found that there was heterogeneity between cities with different levels of NO_2. The estimated increase in daily mortality for an increase of 10 µg/m^3 in PM_{10} were 0.2 % (95 % CI: 0.0 %, 0.4 %), and 0.8 % (95 % CI: 0.7 %, 0.9 %) in cities with low and high average NO_2, respectively [16]. The APHEA-2 hospital admission study involved 38 million people living in eight European cities. Hospital admissions for asthma and chronic obstructive pulmonary disease (COPD) increased by 1.0 % (95 % CI: 0.4 %, 1.5 %) per 10µg/m^3 PM_{10} increment among people older than 65 years [15].

In the United States, the National Morbidity, Mortality and Air Pollution Studies (NMMAPS) focused on the 20 largest metropolitan areas in the USA, involving 50 million inhabitants, during 1987-94 [2]. All-cause mortality was increased by 0.5 % (95 % CI: 0.1 %, 0.9 %) for each increase of 10µg/m^3 in PM_{10}. The estimated increase in the relative rate of death from cardiovascular and respiratory disease was 0.7 % (95 % CI: 0.2 %, 1.2 %). Effects on hospital admissions were studied in ten cities with a combined population of 1 843 000 individuals older than 65 years [17]. The model used considered simultaneously the effects of PM_{10} up to the lag of 5 days and effects of PM_{10} on chronic obstructive pulmonary disease admissions to be 2.5 % (95 % CI: 1.8 %, 3.3 %) and on cardiovascular disease admissions to be 1.3 % (95% CI: 1.0 %, 1.5 %) for an increase of 10 $\mu g/m^3$ in PM_{10}. Bell et al. [18] analysed the 95 NMMAPS community data to examine the association between ozone concentrations and mortality, showing that a 10-ppb increase in the previous week's ozone was associated with a 0.5 % (95 % posterior interval [PI], 0.3 %, 0.8 %) increase in daily mortality and a 0.64 % (95 % PI, 0.31 %, 0.98 %) increase in cardiovascular and respiratory mortality. The effect estimates of the exposure over the previous week were larger than those considering only a single day's exposure. Recently, Dominici et al. [13] examined the short-term association between fine particulate air pollution and hospital admissions and found that exposure to $PM_{2.5}$ was associated with different health outcomes. The largest association was observed for heart failure, viz., and a 10 $\mu g/m^3$ increase in $PM_{2.5}$ was found to be associated with a 1.3 % (95 % PI: 0.8 %, 1.8 %) increase in hospital admissions from heart failure on the same day.

Although time-series studies have shown that day-to-day variations in air pollutant concentrations are associated with daily deaths and hospital admissions, it is still unclear how many days, weeks or months of air pollution have brought such events forward. Harvesting or mortality/morbidity displacement means that some cases are occurring only in those to whom it would have happened in a few days anyway [19]. If so, the increase in cases during and immediately after exposure would be offset by a deficit in daily deaths a few days later [19, 20]. If air pollution has harvesting or long term effects, normal time-series models are unable to estimate the effects due to the issues of collinearity and statistical power. The distributed polynomial model [21] and the time-scale model [19] have been adopted to explore whether air pollution has harvesting or displacement effects on daily deaths or hospital admissions. While recent studies have not found obvious evidence of harvesting, they have found that estimated effects increase when longer lags of air pollution are included [19, 20].

Another type of time-series design is to fit logistic regression models or linear regression models at individual level, which is often used by birth outcome studies emerging in recent years. This type of study design is somewhat similar to the traditional case-control study based on statistical methods. Birth outcome studies define outcomes as low birth weight, preterm delivery as categorical variables, birth weight as a continuous variable, and other biomarkers such as birth defect and ultrasound measures of head circumference. Many studies have shown that there are significant associations between birth outcomes and exposures to ambient air pollutants [22-29]. For example, Liu et al.[23] estimated the associations between exposures to ambient air pollution and health outcomes in Vancouver, Canada. They found that 5-ppb increase of sulfur dioxide was associated with 11 % (95 % CI: 1 %, 22 %) increase of low birth weight (< 2500 grams) during the first month pregnancy and with 9 % increase of preterm delivery. A 1.0 ppm increase of carbon monoxide during the last month pregnancy was associated with 8 % increase of preterm delivery. Hensan et al. [28] examined the associations of exposures to ambient air pollution during early pregnancy with fetal ultrasonic measurements during mid-pregnancy in Australia. They found that a reduction in fetal abdominal circumference was associated with O_3 during the days 31-60 (-1.42 mm, 95% CI: -2.74, -0.09), SO2 during 61-90 (-1.67mm, 95 % CI: -2.94, -0.40), and PM_{10} during days 90-120 (-0.78mm, 95 % CI: -1.49, -0.08).

2.2 Case-crossover studies

Case-crossover study design is an alternative approach to estimating short-term health effects of air pollution in epidemiological studies. In the last two decades, the case-crossover design has been applied in a large number of studies of air pollution and health [30-33]. For example, Neas et al. [32] used a case-crossover study design to estimate the association between air pollution and mortality in Philadelphia and found a 100 µg/m³ increment in the 48 hours mean level of TSP was associated with increased all-cause mortality [odd ratio (OR) = 1.06 (95 % CI: 1.03, 1.09)]. A similar association was observed for deaths in individuals over 65 years of age (OR: 1.07 (95 % CI: 1.04, 1.11)). Levy et al. [33] estimated the effect of short-term changes in exposure to particulate matter on the rate of sudden cardiac arrest. The cases were obtained from a previously conducted population-based case-control study and were combined with ambient air monitoring data. The results did not show any evidence of a short-term effect of particulate air pollution on the risk of sudden cardiac arrest in people without previously recognised heart disease. Schwartz [31] conducted a case-crossover study to examine the sensitivity of the association between ozone and mortality when adjusted for temperature and found that 10-ppb increase of maximum hourly ozone was associated with 0.23 % (95 % CI: 0.01 % ~ 0.44 %) increase in daily deaths after adjusting for temperature in 14 US cities. Barnett et al. [30] examined the association between air pollution and cardio-respiratory hospital admissions in Australia and New Zealand cities. The results show that air pollution arising from common emission sources was significantly associated with cardiovascular health outcomes in the elderly. For example, for a 0.9-ppm increase in CO, there were significant increases in elderly hospital admissions for 2.2 % (95 % CI: 0.9 %, 3.4 %) increase of total cardiovascular disease and 2.8 % (95 % CI: 1.3 %, 4.4 %) increase of all cardiac disease.

2.3 Panel studies

Many air pollution panel studies have been conducted, including several large longitudinal studies of air pollution and health effects such as the Southern California Children's Health Study [34-35], in which children from grades 4, 7, and 10 residing in twelve communities near Los Angeles were followed annually. The results indicated that exposure to ambient particles, NO_2, and inorganic acid vapour was associated with reduced lung function in children. Another large panel study, the Pollution Effects on Asthmatic Children in Europe (PEACE), was designed to examine the relationship between short-term changes in air pollution and lung function, respiratory symptoms and medication use [36]. This project was conducted in 14 centres using a common protocol in the winter of 1993-1994. Each PEACE centre involved an urban and a rural panel of symptomatic children and followed at least seventy-five 6-12 year old children [36]. The pooled estimates of two literature reviews which were separately conducted about the PEACE study and showed that no clear relation could be established for changes in PM_{10}, black smoke, SO_2 and NO_2 and changes in respiratory health. The non-significant effects were thought to be possibly due to the short observation period. Ward and Ayres [37] reviewed 22 panel studies published in the 1990s to estimate the overall effects of ambient particles on children. Results show that the majority of identified panel studies indicated an adverse effect of particulate air pollution. Several recent panel studies also show that particulate air pollution is associated with human health [38-43].

2.4 Cohort studies

Compared to time-series and case-crossover studies, there are only a few large cohort studies. About a dozen cohort studies have been conducted in the United States [44-50], Europe [51-54] and Australia [55]. A cohort study conducted by Dockery et al. [45] in six U.S. cities shows that there was a statistically significant and robust association between air pollution and mortality. The adjusted mortality rate ratio for the most polluted city was 1.26 (95 % CI: 1.08-1.47) compared with the least polluted city. Air pollution was also associated with deaths from lung cancer and cardiopulmonary diseases. Abbey et al. [44] conducted a cohort study during 1973-1992 to estimate effect of exposure to long-term ambient concentrations of PM_{10} and other air pollutants, and show that PM_{10} was strongly associated with mortality from respiratory disease for both sexes adjusting for a wide range of potentially confounding factors. The relative risk (RR) for an interquartile range (IQR) difference of PM_{10} was 1.18 (95 % CI: 1.42, 3.97). Ozone was strongly associated with lung cancer mortality for males for the IQR difference (RR: 4.19; 95 % CI: 1.81, 9.69). Sulphur dioxide was also strongly associated with lung cancer mortality for both sexes. Pope et al. [50] conducted one cohort study in the US to examine the long-term effect of exposure to fine particulate air pollution. They found that fine particulate and sulphur oxide-related pollution were associated with all-cause, lung cancer and cardiopulmonary mortality. A $10\mu g/m^3$ increase in fine particulate air pollution was associated with an increase of 4 %, 6 %, and 8 % for all-cause, cardiopulmonary, and lung cancer mortality, respectively. Hoek et al. [54] investigated a random sample of 5000 people and 489 of 4492 (11 %) died during 1986-1994 in the Netherlands fining that cardiopulmonary mortality was associated with living near a major road with relative risk of 1.95 (95 % CI: 1.09-3.52). A cohort study conducted by Filleul et al. [53] in France found that urban air pollution to be associated with increased mortality over 25 years in France. Frostad et al. [53], in a 30-year follow-up cohort study in Norway, found that respiratory symptoms were a significant predictor of mortality from all causes. In Australia, Jalaludin et al.[55] enrolled a cohort of primary school children with a history of wheeze (n=148) in an 11-month longitudinal study to examine the association between ambient air pollution and respiratory morbidity. They found that PM_{10} and NO_2, but not ozone, were significantly associated with doctor visits for asthma.

2.5 Implications of weak health effects of air pollution

Even though the association of air pollution with health outcomes is weak, it still has strong public health implications. One reason is that air pollution affects the whole population. Another reason is that residents are continuously and permanently exposed to air pollution, which may have both short- and long-term effects on population health. Some intervention studies have shown that the reduction in air pollution has resulted in improvements in public health [51, 56]. For example, Hedley et al. [56] reported that cardiovascular, respiratory and all cause mortality reduced by 2.0 % ($p < 0.05$), 3.9 % ($p < 0.05$) and 2.1 % ($P < 0.05$) respectively in the first 12 months after an introduction of the restrictions on sulphur content of fuel in Hong Kong.

3. Current methodological issues

Air pollution epidemiologic research is challenged by the complexity of human exposure to environmental agents and by the difficulty of accurately measuring exposure. Residents are usually ubiquitously exposed to air pollution. In order to detect small effects of air pollution, both high statistical power and sophisticated study design are required. In addition, the characteristics of air pollutants vary and their concentrations change both spatially and temporally. Although everyone is susceptible to high concentrations of air pollutants, concentrations are not evenly distributed across populations. Due to such complexities, there are still many research questions to be addressed by future air pollution epidemiological studies. The following section discusses these issues.

3.1 Shape of the exposure response curve

The shape of the exposure and response curve is very important. A key question for attention is whether a threshold exists below which a certain air pollutant has no effect on population health. If such a threshold could be identified, public-health benefits would be expected from bringing the air pollutant concentrations below this level. Theoretical and empirical work has been done to shed light on this issue [57-58]. In the analysis of NMMAPS data, no threshold evidence was found for relationship between PM_{10} and daily all-cause and cardiorespiratory mortality [58]. By contrast, a threshold of about 50 μg/m³ was indicated for non-cardiorespiratory causes of death, i.e., below this point, PM_{10} had little influence on non-cardiorespiratory mortality. This issue remains to be clarified.

3.2 Mortality displacement

Although time-series studies have shown a link between daily air pollution concentrations and daily health outcomes, it may be that increases in air pollution only hasten the deaths of individuals in a small, frail subset of the population whose longevity is short even in the absence of air pollution. This hypothesis has been termed mortality displacement or harvesting. While earlier studies have included air pollutant(s) using lag-specific or lag-averaged measurements (e.g. lag 0 or mean of lags 0–1, 0-2 or 0-3), recently distributed lag models (DLM) have been employed to evaluate delayed effect and possible harvesting [19, 59, 60]. However, a simulation study shows that DLM coefficients can have large bias when the mean lifetime of individuals in the frail subset of the population is more than a few weeks, and that the magnitude of this bias increases as the mean lifetime of individuals in the frail subset of the population increases [61].

3.3 Model uncertainty and bias

The process of model selection includes how to select covariates (eg, meteorological variables and co-pollutants), lag structure for air pollutants and the number of degrees of freedom for smoothing functions to adjust for long-term trend, short fluctuation, seasonality, other covariates and the determination of referent in case-crossover design. Studies have shown that the model choice will impact on estimates of relative risk [62]. As a result, many authors attempted to estimate the effects using the best single lag or combination of lags for meteorological and air pollutants and to identify the best degree of freedom for smoothing to adjust for different potential confounders. Some types of data can use several different models. For example, when we estimate associations between exposure to air pollution and recurrent asthma episodes, based on different assumptions, at least five survival cox models could be applied to estimate the associations between exposure to air pollution and asthma episodes [63]. Different assumptions or models often result in different estimates.

Results presented by the "best" final models are likely to cause publication bias because stronger estimates tend to be submitted for publications and negative results are usually not presented or published. Multi-site time series design in which all data are analysed using the same model is one way to partly solve this problem. However, model uncertainty still exists in a multi-site study to some extent due to the model choice. Some studies have used Bayesian Model Averaging (BMA) to take into account uncertainties in model choice when making inference [62]. BMA uses hierarchical models. The predictions and inferences are based on multiple models rather than a single model. Predictions are obtained by forming weighted averages of predictions over the different models where weights depend on the degree to which the data support each model.

Measurement errors of exposures to air pollution and potential confounders usually exist in air pollution epidemiological studies and it is impossible to be solved in most air pollution studies (64). Due to spatial and temporal variations, data obtained in air pollution central monitors are not well representative of individual exposures. Some models are used to assess individual exposure to air pollution, but they could efficiently adjusted for the measurement errors (64).

Both times-series designs using Poisson regression model and case-crossover designs in a community level can efficiently adjust for some measured and unmeasured time-invariant characteristics of the subjects (such as gender, age, smoking status and spatial characteristics) are matched and therefore the potential confounding originating from those unmeasured characteristics is minimised [65-66]. However, other study designs lack the ability to efficiently adjust for this kind of confounders. For example, time-series design with logistic regression models at individual level used by birth outcome studies are vulnerable to this bias originating from spatial characteristic variation. Both individuals and air pollution are related to some geographic characteristics, such as land use, forest and public infrastructure. These geographic characteristics are also related to individual social and economic behaviours. This issue causes little attention so far and few birth outcome studies adjusted for the geographic characteristics although some studies adjusted for social economic status at some extents [22-29]. In general, the stronger reported associations might be partially able to attribute to this kind of bias. Similar situation may also exist to cohort study designs. A key design consideration for air pollution cohort studies is to identify a cohort with sufficient exposure variation in cumulative exposure, particularly when ambient air pollution measurements use data obtained central monitoring stations [50]. However, in maximizing the geographical variability of exposure the relative risk estimates from cohort studies are likely to be confounded by area-specific characteristics [67].

3.4 Interaction between temperature and air pollution

In many locations, patterns of air pollution are driven by weather. Therefore, concentrations of air pollutants may be associated with temperature. Therefore, it may be possible that temperature and air pollution interact to affect health outcomes. Although effect modification has important public health implications [68], this issue has so far received limited attention, probably because of methodological complexity and the difficulty in data interpretation. Several studies examined whether or not ambient air pollution and temperature interact to affect human health outcomes, but they produced conflicting results [69-72]). For example, Samet et al. [72] investigated the sensitivity of the particulate air pollution mortality effect estimate to alternative methods of controlling weather and did not find any evidence that weather conditions modified the associations of particulate air pollution and sulphur dioxide with mortality, regardless of approaches of synoptic weather conditions. Katsouyanni et al. [69] used a multiple linear regression to investigate the interaction between air pollution and high temperature during a heat wave in Athens in July 1987. They found that while the main effects of air pollution index were not statistically significant, there was statistically significant synergistic effect between high levels of sulphur dioxide and high temperature ($P<0.05$). Roberts [71] found evidence that the effect of particulate air pollution on mortality might depend on temperature but the synergistic effect was sensitive to the number of degrees of freedom used in confounder adjustments. Recently, we found that temperature and particulate matter symmetrically enhanced the effect [70]. Since then, several multiple-site studies have found evidence that temperature and air pollutants interacted to impact human health [73-74]. Thus, further research is needed to examine the interactive effects between air pollutants and temperature on mortality and morbidity, especially in spatial modification variation.

4. Conclusions

Many times-series, case-crossover and panel studies have shown that there are consistent short-term effects of air pollution on health outcomes (hospital visits or deaths). Some cohort studies have also shown that there were long-term health effects of air pollution. In spite of the weak associations of air pollution with human morbidity or mortality, its public health implications are strong because exposure to air pollution is ubiquitous and widespread. However, there are several challenges in the estimation of the health effects of low level exposure to air pollution, such as shape of the exposure response curve, harvesting effects, threshold of air pollution, interactive effects of air pollution and weather and potential bias.

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Table 1 Time-series studies of short-term health effects of air pollution after 2000

Study	Pollutant	Population	Methodology	Main findings
Czech Republic and rural region in Germany [75]	TSP	Mortality 1982-1994	Poisson regression (GAM)	Czech Republic: 3.8 % increase (95 % CI: 0.8 %, 9.6 %) per 100 µg/m³; No evidence for association in the rural area in German at the Czech border.
10 US cities [76]	PM_{10}	Mortality 1986-1993	Poisson regression (GAM)	0.67 % increases for a 10µg/m³ (95 % CI: 0.52 %, 0.81 %). No difference between summer and winter.
New Zealand [77]	PM_{10}	Mortality Jun 1988-Dec 1993	Poisson regression (GAM)	1% increase for all-cause mortality (95 % CI: 0.5 %, 2.2 %); 4 % increase for respiratory diseases (95 % CI: 1.5 %, 5.9 %)
10 US cities [21]	PM_{10}	Mortality 1986-1993	Distributed lag model (GAM)	1.4 % (95 % CI: 1.15 %, 1.68 %) increase for 10µg/m³ on a single day using a quadratic distributed lag model; 1.3 % increase (95 % CI: 1.04 %, 1.56 %) using an unstrained lag model
20 US cities [2]	PM_{10}, O_3, SO_2, CO, NO_2	Mortality 1987-1994	Poisson regression (GAM)	PM_{10}: 0.51 % increase (95 % CI: 0.07 %, 0.93 %) per 10 µg/m³ for all causes; 0.68 % increase per 10 µg/m³ for cardiovascular and respiratory diseases (95 % CI: 0.20 %, 1.16 %) O_3: weaker evidence during the summer; Other pollutants: no evidence
Hong Kong [78]	PM_{10}, SO2	Morality 1995-1998	Poisson regression (GAM)	Significant associations were found between mortalities for all respiratory diseases and ischaemic heart diseases (IDH). The increases for all respiratory mortalities (for a 10 µg/m³ increase in the concentration) are 0.8 % (95 % CI: 0.1 %, 1.4 %) for $PM_{10}$and 1.5 % (95 % CI: 0.1 %, 2.9 %) for SO_2 ; the increases for IDH are 0.9 % (95 % CI: 0.0 %, 1.8 %) for O_3 and 2.8 % (95 % CI: 1.2 %, 4.4 %) for SO_2.

Study	Pollutant	Population	Methodology	Main findings
Seoul Korea[79]	PM_{10}	Mortality 1995-1999	Poisson regression (GAM)	3.7 % increase (95 % CI: 2.1 %, 5.4 %) for non-accident causes, 13.9 % increase (95 % CI: 6.8 %, 21.5 %) for respiratory disease, 4.4 % increase (95 % CI: -1.0 %, 9.0 %) for cardiovascular disease and 6.3% increase (95 % CI: 2.3 %, 10.5 %) for cerebrovascular disease per IQR increase of PM_{10} (43.12μg/m³)
Shanghai, China [80]	PM_{10}, SO_2, NO_2	Mortality Jun 2000 to Dec 2001	Poisson regression (GAM)	0.3 % increase (95 % CI: 0.1 %, 0.5 %) for PM_{10}, 1.4 % increase (95 % CI: 0.8 %, 2.0 %) for SO2 and 1.5 % increase (95 % CI: 0.8 %, 2.2 %) for NO_2 per 10μg/m³
Brisbane, Australia [81]	BSP, O_3, SO_2, NO_2	Hospital admission 1987-1994	Poisson regression (GLM)	BSP: 1.5 % increase (95 % CI: 0.6 %, 2.3 %) for respiratory diseases per 24-hr 10^{-5}/m increase. O_3: 2.3 % increase (95 % CI: 0.6 %, 2.3 %) for respiratory disease per 8-hr unit increase. SO_2: 8.0 % increase (95 % CI: 3.0 %, 13.1 %) for respiratory disease per 24-hr unit increase. NO_2: -0.1 % increase (95 % CI: -0.3 %, 0.2 %) for respiratory disease per 1-hr-max unit increase.
Brazil [82]	PM_{10}, O_3, SO_2, CO, NO_2	Respiratory disease Hospital admission 1993-1997	Distributed lag model	9.4 % increase (95 % CI: 7.9 %, 10.9 %) for 2 or less years old group and 7.0 % (95 % CI: 5.7 %, 8.2 %) for all age group per IQR PM_{10} increase (35μg/m³); 1.6 % increase (95 % CI: 0.1 %, 3.0 %) for 2 or less years old group and 0.8 % (95 % CI: -7.5 %, 9.2 %) for all age group per IQR O_3 increase (46μg/m³); 5.9 % increase (95 % CI: 4.5 %, 7.4 %) for 2 or less years old group and 4.5 % (95 % CI: 3.3 %, 5.8 %) for all age group per IQR SO_2 increase (14μg/m³);

Study	Pollutant	Population	Methodology	Main findings
				5.0 % increase (95 % CI: 3.3 %, 6.8 %) for 2 or less years old group and 4.9 % (95 % CI: 3.5 %, 6.4 %) for all age group per IQR CO increase (3ppm); 9.4 % increase (95 % CI: 6.2 %, 12.6 %) for 2 or less years old group and 6.5 % (95 % CI: 3.3 %, 9.7 %) for all age group per IQR NO_2 increase (80µg/m³);