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# Association between ambient fine particulate matter and preterm birth or term low birth weight: An updated systematic review and meta-analysis☆

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ABSTRACT

An increasing number of studies have been conducted to determine a possible linkage between maternal exposure to ambient fine particulate matter and effects on the developing human fetus that can lead to adverse birth outcomes, but, the present results are not consistent. A total of 23 studies published before July 2016 were collected and analyzed and the mean value of reported exposure to fine particulate matter ($PM_{2.5}$) ranged from 1.82 to 22.11 We found a significantly increased risk of preterm birth with interquartile range increase in $PM_{2.5}$ exposure throughout pregnancy (odds ratio (OR) = 1.03; 95% conditional independence (CI): 1.01–1.05). The pooled OR for the association between $PM_{2.5}$ exposure, per interquartile range increment, and term low birth weight throughout pregnancy was 1.03 (95% CI: 1.02–1.03). The pooled ORs for the association between $PM_{2.5}$ exposure per 10 increment, and term low birth weight and preterm birth were 1.05 (95% CI: 0.98–1.12) and 1.02 (95% CI: 0.93–1.12), respectively throughout pregnancy. There is a significant heterogeneity in most meta-analyses, except for pooled OR per interquartile range increase for term low birth weight throughout pregnancy. We here show that maternal exposure to fine particulate air pollution increases the risk of preterm birth and term low birth weight. However, the effect of exposure time needs to be further explored. In the future, prospective cohort studies and personal exposure measurements needs to be more widely utilized to better characterize the relationship between ambient fine particulate exposure and adverse birth outcomes.


## 1. Introduction

The fundamental causes of adverse birth outcomes are not well understood, despite growing evidence that environmental factors may play an important role. Air pollution is one of the most concerned environmental factors; evidence of adverse health effects of ambient air pollution has rose dramatically (West et al., 2016). The World Health Organization (WHO) estimated that in 2013, 87% of the global population lived in communities that exceeded the WHO's air quality guideline of a maximum mean ambient fine particulate matter ($PM_{2.5}$) of 10 (Brauer et al., 2016). The Global Burden of Disease (GBD) rated ambient fine particulate matter exposure as the seventh most important risk factor contributing to global mortality (Forouzanfar et al., 2015). Recently, an increasing number of studies have shown that maternal exposure to air pollution can affect the developing fetus, resulting in adverse birth outcomes such as infant death, still birth, term low birth weight

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(TLBW), preterm birth (PTB), and small for gestational age (Lee et al., 2013; Vinikoor-Imler et al., 2014; Dibben and Clemens, 2015). Furthermore, air pollution is also related to adverse respiratory and cardiovascular outcomes in clinical, epidemiological and toxicological studies (Ritz and Wilhelm, 2008; Yang et al., 2013; Rappazzo et al., 2014).

The effects of adverse birth outcomes can persist for a person's entire life, according to Developmental Origins of Health and Disease (Barker et al., 1990, 1993; Hanson and Gluckman, 2011). PTB is the main cause of death in newborn babies, and is associated with a high risk of childhood disability (Howson et al., 2013). Birth weight is an important indicator of fetal growth, development, and nutritional status; low birth weight is also related to low economic and social development of the given country or region. Considered a chronic disease, low birth weight is one of the major risk factors associated with global disease burden (Symanski et al., 2014).

Fine particulate matter refers to a heterogeneous mixture of substances that sometimes includes accumulated heavy metals and toxic organic pollutants such as polycyclic aromatic hydrocarbons (Dejmek et al., 2000); fine particulate matter may affect birth outcomes directly or indirectly. Laurent et al. related TLBW with primary particle concentrations by source and composition, and showed that increased risk of TLBW is associated with several major sources of $PM_{2.5}$ (especially gasoline, wood burning, and commercial meat cooking), and chemical composition in $PM_{2.5}$ (elemental and organic carbon, potassium, iron, chromium, nickel, and titanium, but not lead or arsenic) (Laurent et al., 2014). Basu et al., in California, USA, showed similar results; heavy metal elements, sulfur, sulfate, bromine, and ammonium are associated with reductions in birth weight and an increased risk of TLBW (Basu et al., 2014). Over the past decade, a number of recent studies estimated the association between $PM_{2.5}$ exposure during pregnancy in whole or part and TLBW or PTB. The results are inconsistent and controversial. Some studies found that air pollutants significantly impact birth outcomes, while others failed to find such associations (Laurent et al., 2013; Vinikoor-Imler et al., 2013; Brown et al., 2015; Huang et al., 2015). Huynh et al. executed a matched case–control study of the relationship between PTB and level of $PM_{2.5}$ exposure throughout pregnancy in California from 1999 to 2000. After controlling for demographic factors, the odds ratio (OR) of PTB per 10 of $PM_{2.5}$ was 1.15 (95%; CI: 1.07–1.24). Wu et al. conducted a retrospective cohort study in California from 1997 to 2006, examining the effect of air pollution levels throughout pregnancy on PTB risk in a cohort of 81186 singleton births, and found an association between PTB and $PM_{2.5}$, per 10 μg/m3, was 1.24 (95%; CI: 1.08–1.42). Pereira et al. saw a positive but non-significant association between $PM_{2.5}$ exposure and PTB (OR = 1.01, 95 CI %: 0.93–1.09) in Connecticut, USA. Wilhelm et al., in California, USA, did not find a consistent concentration-dependent relationship between ambient fine particulate matter and PTB (OR = 0.73, 95; CI % = 0.67–0.08). All of the aforementioned studies were conducted in the USA, yet the results of these studies were not consistent. Due to the varied compositions of ambient fine particulate matter, and the limitations of these studies' researching approaches, there is not yet sufficient evidence to establish causality.

To further understanding of the association between air pollution and birth outcomes, we have collected all data presently available and conducted a quantitative meta-analysis on the relationship between $PM_{2.5}$ exposure and term low birth weight or preterm birth. Of note, the pooled ORs include both 10 increases and interquartile range (IQR) incremental increases in $PM_{2.5}$ exposure. Data from more recent studies allowed us to assess the effect by gestational period, to conduct meta-regression and sensitivity analyses, to valuate publication bias, and to measure heterogeneity.

## 2. Materials and methods

### 2.1. Inclusion criteria and search strategy

From December 2015 to July 2016, we conducted a search on PUBMED and Cochrane, as well as on China National Knowledge Infrastructure (CNKI) and Wanfang Data Knowledge Service Platform to collect local data from Chinese studies. We limited our search to papers published in English or Chinese. We searched the following terms on PUBMED, based on the terminology used in recent reviews of the subject: "air pollution", "air pollutants", "particular matter", "fine particular matter", "pregnancy outcome", "birth outcomes", "infant, newborn", "birth weight", "infant, low birth weight", "low-birth-weight infant", "premature birth", "infant, premature" and "obstetric labor, premature". Meanwhile, to obtain additional publications, we manually searched the references of each primary study. Publications were also identified in the same manner from review articles.

### 2.2. Selection criteria

To choose the related articles, we first filtered the titles and abstracts of all studies. Studies were excluded if they were not related fine particulate matter to with low birth weight or preterm birth. Then, from the identified papers, we selected studies meeting the following eligibility criteria: a) inclusion of $PM_{2.5}$ exposure during pregnancy and single live births, b) clear definition of maternal exposure to $PM_{2.5}$ and of birth outcomes, c) pregnancy outcomes of TLBW or PTB, d) low birth weight defined by the World Health Organization as a birth weight of a liveborn infant of 2,499 g or less, including TLBW and preterm low birth weight (however we only included TLBW in this study) e) preterm birth determined as a less than 37 weeks gestational age at delivery, and f) presentation of sample sizes and ORs with 95% confidence intervals for each 10 or IQR increment increase of $PM_{2.5}$ exposure. If more than one study was determined for a given population, only the study that included either the most recent population data or the most up-to-date information (or both) was selected. Studies that met all of the above inclusion criteria were short listed for inclusion in the review.

### 2.3. Data extraction

Two investigators processed the data from each eligible study independently, using consistent strategy. If a study provided associations between $PM_{2.5}$ exposure and PTB or TLBW, both throughout pregnancy and in trimester-specific periods, all association data was extracted. A number of studies evaluated $PM_{2.5}$ exposure based on multiple sources of air pollution data (Stieb et al., 2016a,b; Kloog et al., 2012, Hannam et al., 2014; Fleischer et al., 2014; Coker et al., 2015; Lavigne et al., 2016; Hyder et al., 2014). We chose estimations based on remote sensing data because this increased sample size and decreased selection bias. Data was extracted systematically from each study using a predesigned standard data collection form. We collected the following information from all of the studies: author(s), date of publication, study period, location, study design, air pollution sources, exposure measurement, sample size, exposure range, outcome assessment, exposure period, Newcastle-Ottawa Scale (NOS) grade, Agency for Healthcare Research and Quality (AHRQ) grade, and the ORs and 95% CIs used during statistical analyses. The selection process of this study is showed in detail in Fig. 1.