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Ambient air pollution and preterm birth: A prospective birth cohort study in Wuhan, China

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ABSTRACT

Importance: Although studies in western countries suggest that ambient air pollution is positively associated with adverse pregnancy outcomes, the upper levels of pollutant exposures have been relatively low, thus eroding confidence in the conclusions. Meanwhile, in Asia, where upper levels of exposure have been greater, there have been limited studies of the association between air pollution and adverse pregnancy outcomes.
Objective: The primary objective was to evaluate whether high levels of pollution, including particulate matter pollution with a mass median aerodynamic diameter of less than 2.5 μm ($PM_{2.5}$) and 10 μm (PM_{10}), sulfur dioxide (SO_2), nitrogen dioxide (NO_2), ozone (O_3), and carbon monoxide (CO) are related to increased occurrence of preterm birth (PTB).
Methods: We conducted a population-based study in Wuhan, China in a cohort of 95,911 live births during a two-year period from 2011 to 2013. The exposure was estimated based on daily mean concentrations of pollutants estimated using the pollutants' measurements from the nine closest monitors. Logistic regressions were performed to determine the relationships between exposure to each of the pollutants during different pregnancy periods and PTB while controlling for key covariates.
Results: We found 3% (OR = 1.03; 95% CI: 1.02, 1.05), 2% (OR = 1.02; 95% CI: 1.02, 1.03), 15% (OR = 1.15; 95% CI: 1.11, 1.19), and 5% (OR = 1.05; 95% CI: 1.02, 1.07) increases in risk of PTB with each 5-μg/m^3 increase in $PM_{2.5}$ and PM_{10} concentrations, 100-μg/m^3 increase in CO concentrations, and 10-μg/m^3 increase in O_3 concentrations, respectively. There was negligible evidence for associations for SO_2 and NO_2. The effects from two-pollutant models were similar to the estimated effects from single pollutant models. No critical exposure windows were identified consistently: the strongest effect for PTB was found in the second trimester for $PM_{2.5}$, PM_{10}, and CO, but for SO_2 it was in the first trimester, second month, and third month. For NO_2 it was in the first trimester and second month, and for O_3, the third trimester.
Conclusion: Findings reveal an association between air pollutants and PTB. However, more toxicological studies and prospective cohort studies with improved exposure assessments are needed to establish causality related to specific pollutants.

1. Introduction

There were 12.9 million preterm births (9.6% of total birth) worldwide and approximately 85% of these occurred in Asia and Africa (Beck et al., 2010). Babies born preterm are at an increased risk for both short-term and long-term health effects (Chernausek,

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2012; Verrips et al., 2012; Stoll et al., 2004). PTB infants are at increased risk of neurodevelopmental impairment and respiratory and gastrointestinal complications (Baraldi and Filippone, 2007). PTB births are also associated with the development of type-2 diabetes, hypertension, and cardiovascular disease in adulthood (Saigal and Doyle, 2008). It is not clear why the PTB rate is so high; as causation appears to be complex and is poorly understood, but interrelated biological, physical, psychological, and social factors are thought to play a significant role.

An increasing number of studies have examined the effects of air pollution on PTB, including studies in China (Zhao et al., 2015), South Korea (Seo et al., 2010), Japan (Kashima et al., 2011), the United States (Vinikoor-Imler et al., 2014), Canada (Brauer et al., 2008; Liu et al., 2003), England (Dolk et al., 2010), the Netherlands (Gehring et al., 2011), Norway (Madsen et al., 2010), Australia (Hansen et al., 2007), and the Czech Republic (Bobak, 2000). Despite the fact that most published studies have reported that various air pollutants are related to PTB, variability exists in the nature of the studied pollutants and associated pregnancy outcomes. Heterogeneous associations including negative associations and effects of small magnitude have also been observed (Laurent et al., 2013).

There has been a lack of toxicological data to provide guidance on selecting the most relevant vulnerable exposure windows during pregnancy (Glinianaia et al., 2004). Previous investigations used a broad range of exposure windows (i.e., weeks, months, trimesters) to determine the temporal relationships between air pollution and adverse pregnancy outcomes (Hansen et al., 2007). Some studies reported that exposure during the first trimester was associated with an increased risk of PTB (Bobak, 2000). Other studies suggest that third trimester exposures had greater effects (Ritz and Yu, 1999; Wang et al., 1997). It is still unknown whether or not the peak effect period differs across populations and pollutants. As such, it is challenging to synthesize the temporality of exposure to specific pollutants and determine which contribute most to PTB (Woodruff et al., 2009).

The primary objective of this study was to evaluate whether high pollution levels of $PM_{2.5}$, PM_{10}, SO_2, NO_2, O_3, and CO are related to increased occurrence of PTB in a cohort of 95,911 neonates born in the seven inner-city districts of Wuhan, China during a two-year period from June 10, 2011 to June 9, 2013. The specific aims were to test two research questions (1) are elevated ambient concentrations during vulnerable pregnancy periods associated with increased PTB when adjusting for major risk factors? (2) Are the associations confounded by co-pollutants?

2. Materials and methods

2.1. Study area

Wuhan, the capital of Hubei Province, is the largest city in Central China, and is located in the middle of the Yangzi River delta, at 29°58′–31°22′ North latitude, 113°41′–115°05′ East longitude. Its population is approximately 10 million people and approximately 6.4 million of them reside in seven urban core districts. Wuhan occupies a land area of 8494 km^2. Wuhan has a subtropical, humid monsoon climate with hot and humid summers every year. Its daily average temperature in July is 37.2 °C, and the maximum daily temperature often exceeds 40 °C. Because of its hot summer, Wuhan has been called an "oven" city in China.

The lowest daily average temperature in January is lower than 1.0 °C. The major industries in Wuhan include ferrous smelters, chemical plants, power plants, and machinery plants. Wuhan is one of the biggest hubs for land, water, and air transportation in China. The major sources of air pollution in the city are motor vehicles and the use of coal for industrial processes. With high concentrations of pollutants and a relatively stable population, Wuhan provides a unique opportunity to examine the effects of air pollution on adverse pregnancy outcomes.

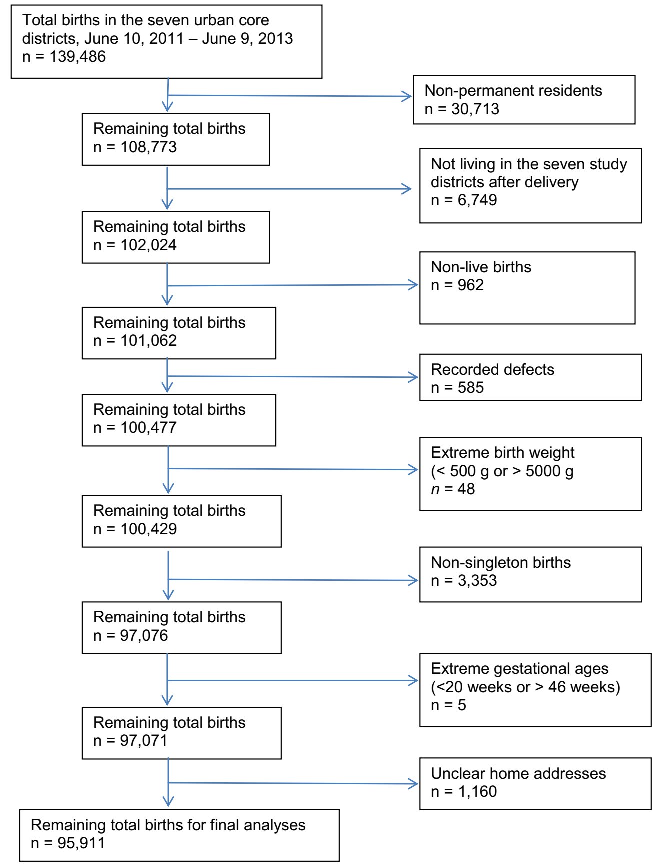

Fig. 1. Flow chart of the cohort study population selection.

2.2. Study population

This is a population-based prospective cohort study. We followed the 95,911 pregnant women living in the seven inner-city districts in Wuhan from August 19, 2010 to September 9, 2013. All pregnant women living within the targeted districts of Wuhan receive their prenatal care from and deliver through the Wuhan Medical and Health Center for Women and Children. This system uses a single integrated information system and we collected data from this electronic record for the first prenatal care visit, delivery, and postnatal period. The Institutional Review Board of Saint Louis University approved the study protocol.

We collected data for 139,486 births in the city of Wuhan in this study (Fig. 1). We applied the similar inclusion and exclusion criteria to the study populations in order to facilitate comparisons between the magnitude of the effects from our study and those published in the literature. These restrictions were applied in previously published work (Bell et al., 2007; Ritz et al., 2007). After excluding 30,713 non-permanent residents of the city and 6749 births not living in the seven urban core districts, we had an initial pool of 102,024 births. Further exclusions were made for 962 nonviable births, 585 recorded birth defects, 48 births with extreme birth weights (<500 g or >5000 g), 3353 non-singleton births, five with extreme gestational ages (<20 weeks or >46 weeks), and 1160 births with unclear home addresses. In some cases, a single birth met multiple exclusion criteria. From the 102,024 with qualified residential history in the study area, these exclusions left 95,911 births (94.0%) for analyses.