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# Maternal air pollution exposure and preterm birth in Wuxi, China: Effect modification by maternal age

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ABSTRACT

*Background:* Numerous studies have investigated prenatal air pollution and shown that air pollutants have adverse effect on birth outcomes. However, which trimester was the most sensitive and whether the effect was related to maternal age is still ambiguous.
*Objectives:* This study aims to explore the association between maternal air pollution exposure during pregnancy and preterm birth, and if this relationship is modified by maternal age.
*Methods:* In this retrospective cohort study, we examine the causal relationship of prenatal exposure to air pollutants including particulate matters, which are less than 10 µm ($PM_{10}$), and ozone ($O_3$), which is one of the gaseous pollutants, on preterm birth by gestational age. A total of 6693 pregnant women were recruited from Wuxi Maternal and Child Health Care Hospital. The participants were dichotomized into child-bearing age group (< 35 years old) and advanced age group (> = 35 years old) in order to analyze the effect modification by maternal age. Logistic and linear regression models were performed to assess the risk for preterm birth (gestational age < 37 weeks) caused by prenatal air pollution exposure.
*Results:* With adjustment for covariates, the highest level of $PM_{10}$ exposure significantly increased the risk of preterm birth by 1.42-fold (95% CI: 1.10, 1.85) compared those with the lowest level in the second trimester. Trimester-specific $PM_{10}$ exposure was positively associated with gestational age, whereas $O_3$ exposure was associated with gestational age in the early pregnancy. When stratified by maternal age, $PM_{10}$ exposure was significantly associated with an increased risk of preterm birth only in the advanced age group during pregnancy (OR:2.15, 95% CI: 1.13, 4.07). The results suggested that $PM_{10}$ exposure associated with preterm birth was modified by advanced maternal age ($OR_{interaction}$ = 2.00, 95% CI: 1.02, 3.91, $P_{interaction}$ = 0.032).
*Conclusion:* Prenatal air pollution exposure would increase risk of preterm birth and reduced gestational age. Thus, more attention should be paid to the effects of ambient air pollution exposure on preterm birth especially in pregnant women with advanced maternal age.

## 1. Introduction

Babies born less than 37 weeks usually defined preterm birth, which is one of the most common birth outcomes among livebirths (Vogel et al., 2017). World Health Organization reported the incidence of preterm birth has risen annually and affected 15 million neonates in 2016 (WHO, 2017). Preterm birth is prevalent in China, affecting approximately 10% of newborns (Blencowe et al., 2012; Liu et al., 2016). It is not only a leading cause of neonatal mortality, but also the second leading cause of death in children under five years old after pneumonia (Horvath et al., 2017). The impact of preterm birth is far-reaching which could result in the adverse effects on children's development such as impairment of vision (Leung et al., 2017), hearing (Franck et al., 2017; Wroblewska-Seniuk et al., 2017) and even

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intelligence (Arhan et al., 2017; Sharp et al., 2017). Potential biological mechanisms related to preterm birth remain unclear. Identifying the underlying causes of preterm birth is an urgent and important matter in the field of public health.

Polluted air is a threat to human health of all ages. Exposure to air pollution has been associated with cardiovascular disease, stroke, diabetes mellitus, hypertension, asthma, cognitive disorder and even carcinogenesis (Alvarez-Pedrerol et al., 2017; Castner et al., 2017; Chiu et al., 2017; Mazidi and Speakman, 2017; Sorensen et al., 2017; Wing et al., 2017; Zhou et al., 2017). On a global scale, an estimated 7 million deaths have been attributed to air pollution exposure (Cohen et al., 2017). In addition, women and children appear more susceptible to this environmental threat (Collaborators, 2017). Many studies across countries and regions have been conducted recently to investigate the association between ambient air pollution during pregnancy and adverse birth outcomes using cohort and case-control studies. Some studies concluded that exposure to particulate matter ($PM_{10}$ and $PM_{2.5}$) from polluted air in pregnant women increased the risk of preterm birth (Pereira et al., 2014; Zhao et al., 2015), while the relationship has not been found in other studies (Gray et al., 2014). Moreover, whether PM exposure related to preterm birth was trimester-specific is still inconsistent. Some studies indicated that first trimester might be the most sensitive exposure window (Gehring et al., 2011; Lee et al., 2013), whereas others proposed that second or third trimester is more sensitive (Arroyo et al., 2016; Estarlich et al., 2016; Johnson et al., 2016).

The trend that women tend to delay their pregnancy has become more pronounced in recent years, due to the changes in the society, the priority of career and education also among women, and the economic stress resulting in the need for two incomes and a higher female work participation (Jefferson et al., 2015). The definition of advanced maternal age is childbearing in a woman over 35 years of age (Martin et al., 2013). It was reported that the prevalence of advanced maternal age has increased by 9% in United Kingdom from 1990 to 2004 (Wongtaylor et al., 2012). Increased maternal age have been associated with decreased fertility and fecundity and with adverse perinatal birth outcomes (Carolan and Frankowska, 2011). It was reported that an increased risk of stillbirth, miscarriage, fetal growth restriction (FGR), preterm birth, and gestational complications such as preeclampsia and gestational diabetes in pregnant women with advanced maternal age (Lean et al., 2017; Ogawa et al., 2017; Wang et al., 2017). However, data is scarce on the association between air pollution and gestational age or preterm birth, especially how maternal age at pregnancy could influence these relationships.

In this study, we recruited 6693 pregnant women in Wuxi Maternal and Child Care Hospital to evaluate the association between air pollution and preterm birth as well as gestational age. Furthermore, whether maternal age could modify the effect on association between $PM_{10}$ and preterm birth was also investigated.

## 2. Methods

### 2.1. Study population

A retrospective cohort study was conducted to investigate the association between maternal exposure to ambient air pollution and the risk of preterm birth or gestational age. We collected birth data from 2014 to 2016 in Wuxi Maternal and Child Care Hospital and 7142 pregnant women in obstetrics department were voluntarily recruited to our study. Birth registry data was retrieved to obtain information about mothers and their neonates (e.g. maternal age, family address, gestational age, the date of delivery, birth weight and neonatal sex). A previous selection criteria of study population was referred in current study (Hannam et al., 2014). Study population was confined to local residents in Wuxi, singletons, live birth and maternal age between 15 and 50 years. Neonates with birth weight less than 500 g were excluded in our study due to low survival rate (Hannam et al., 2014). After a series of inclusion/exclusion standards, a final population of 6693 (93.7%) pregnant women were included in the present study (Fig. 1). We obtained written consent from all participants. The study protocol was approved by the institute review board of Nanjing Medical University and complied with the principle outlined in the Helsinki Declaration.

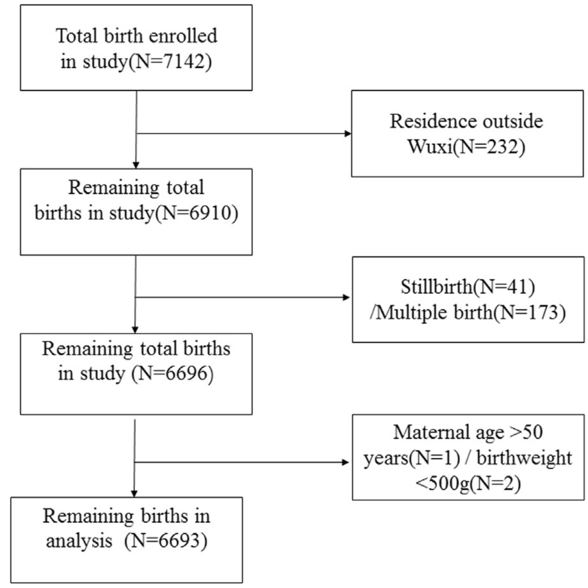


**Fig. 1.** Flow chart of study population.

### 2.2. Exposure assessment

Data on the air pollutants of $PM_{10}$ (aerodynamic diameter less than 10 μm), Ozone ($O_3$) and meteorological factors including apparent temperature and relative humidity were collected from January 1st, 2013 to December 31st, 2016 in Wuxi CDC (Centers for diseases control). We processed air pollutant values and meteorological value averagely in 24-h except for $O_3$ (measured in 8-h mean). The data of meteorology were based on monitoring in the whole city area. There are eight air monitor stations in Wuxi, namely Xuelang, Caozhang, Shibei, Dongting, Qitang, Wangzhuang, Rongxiang, Yanqiao. And the study population was uniformly distributed in the central city of Wuxi.

We used inverse distance weighting (IDW) approach to calculate exposure values at individual level. The IDW was a popular spatial interpolation method used in the measurements of pollutants concentration (Allshouse et al., 2017). According to the air pollutants concentration measured daily from monitoring stations, we estimated the pollutant concentration individually based on the distance between maternal address and monitoring station. First, we obtained the date of conception through linking the date of birth in hospital-based birth records to gestational age. According to classification referred by previous study (Wu et al., 2009), the first trimester was defined as conception date to 13 weeks, mid-trimester as 14–27 weeks and the third trimester as 28 weeks to birth. Based on this classification, exposure value was calculated averagely by trimester. Each maternal residential address at the time of pregnancy registered in the medical records were converted into longitudinal and latitudinal coordinates using Google Maps software. The map coordinates of the eight air monitoring stations were also converted to coordinates by a geographic information system (ARCGIS, version 10.3; ESRI, Redlands, CA, USA).

### 2.3. Covariates

Covariates that could be potential confounders were extracted from the hospital record registry, including maternal age at delivery, parity