Ambient Air Pollution and Adverse Birth Outcomes: A Natural Experiment

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ABSTRACT

Radical regulations to improve air quality were implemented prior to and during the Beijing Olympics Games of 2008, and consequently ambient concentrations of multiple pollutants were reduced in a distinct and short window of time, which presents an excellent opportunity to test the relationship between ambient air pollution and adverse birth outcomes as a natural experiment.

We used the birth outcome data from 50,874 live births delivered between January 1, 2006 and December 31, 2010 at the Beijing Haidian Maternal and Child Health Hospital and air monitoring data on ambient concentrations of nitrogen dioxide ($NO_{2)}$, carbon monoxide (CO), sulfur dioxide ($SO_{2)}$, and particular matter 10 micrometers or less ($PM_{10)}$ during the same period obtained from the Beijing Municipal Environmental Monitoring Center. We used multi-pollutant models to estimate the effect of each of the four pollutants during three trimesters of gestation on preterm birth status among all live births and on birth weight among term babies.

Results from single-pollutant models show that each ten-unit increase (10 ppm) in ambient concentration of SO_2 in the first (OR=1.03; 95% CI: 1.01 to 1.06; p=0.021) and third trimester of gestation (OR=1.05, 95% CI: 1.02 to 1.08; p=0.003) was associated with a higher risk of preterm birth. Each one-unit increase (1 ppm) in ambient concentration of CO in the third trimester of gestation (OR=1.16, 95% CI: 1.03 to 1.30; p=0.013) was associated with a higher risk of preterm birth. In multi-pollutant models, only the concentration of SO_2 in the first trimester predicted a higher risk of preterm birth (OR=1.09, 95% CI: 1.02 to 1.16; p=0.007). Among term babies, concentrations of all pollutants were negatively associated with birth weight, but only SO2 predicted lower birth weight when controlling for other pollutants. Each increment of 10 ppm SO2 in the first trimester predicted a 7.02 g (95% CI:-13.14 to -0.90; p=0.025) decrement in birth weight.

These findings suggest that exposure to ambient air pollution during certain period of pregnancy may increase the risk of preterm birth and decrease birth weight, but the effect size is small.

INTRODUCTION

Adverse pregnancy and birth outcomes, including preterm birth and low birth weight, are an important global public health issue. Fifteen million babies are born preterm (less than 37 weeks) worldwide each year (Fund, 2004). Low birth weight (less than 2,500 grams at birth) is caused by preterm or intrauterine growth restriction (IUGR), and affects more than 20 million infants worldwide, representing 16% of all births (Fund, 2004). China contributes to 7.8% of all global preterm births, which is more than of any other country except for India (Zhao, 2012). There was also a 14% increase in the number of preterm births in China between 2005 and 2009 (Zhao, 2012). In the U.S. in 2011, the preterm birth rate was 11.73% of all births (approximately 3.95 million births), and the rate of low birth weight was 8.10% of all births, or about 1 in every 70 infants (Martin, 2013). Low birth weight is an important predictor of health and is associated with compromised health outcomes including fetal and neonatal morbidity and mortality, inhibited organ development and function and higher rates of chronic disease in adulthood (Barker, 1992). In the U.S., the annual economic burden of preterm birth is $26.2 billion, of which 65% was due to medical care (Behrman, 2007).

To identify risk factors of adverse birth outcomes is therefore of major public health significance. In addition to nutrition, genetic defects, and health behaviors, ambient air pollution has gained increasing attention of scientists and policy makers. It is an urgent issue for newly industrialized countries such as China, where the surge in economic growth and rapid urbanization has led to an increased presence of ambient air pollutants such as carbon monoxide (CO), nitrogen dioxide (NO_2) and particulate matter less than 10 (PM_{10}) and 2.5 microns ($PM_{2.5}$) (EPA, 2007). In China's mega cities, on 10-30 percent of days, the concentration of air pollutants exceeds the Chinese National Ambient Air Quality Standard (CNAAQS) of Grade-II (Chan, 2008).

Many previous studies commonly linked birth outcomes, usually from birth certificates, of populations in different geographic areas with residence-based measurements of maternal exposure to ambient air pollution during pregnancy. In such a design, variation in air pollution between areas and across seasons is usually used. Unfortunately confounding variables likely pose serious threats to both sources. For example, residential areas close to industrial zones and highways typically have more affordable housing, but are also generally more polluted. Such areas are typically occupied by residents with lower socio-economic status, who tend to engage in riskier behaviors such as smoking and invest less in personal health, which may confound the association of residential air pollution and adverse birth outcomes. In addition, seasonality may be highly correlated with pollutants and thus directly controlling for seasonality may result in col-linearity problems with analysis, while controlling for other proxies, such as food availability, may miss important confounding factors that are not measured or observed (Woodruff, 2009).

To address these concerns, in the absence of randomized controlled trials on humans, an optimal alternative is a natural experiment design that examines changes in air pollution levels caused by external forces such as environmental regulations; There are only a small number of studies using such a design to address the common confounding factors including residential self-selection and seasonality (Slama, 2008; Currie, 2009). For example, using the introduction of electronic tolls in New Jersey and Pennsylvania as a quasi-experiment, a study found that the consequent reduction in automobile-generated pollutions near toll plazas substantially reduced prematurity and low birth weight in those areas (Currie, 2009).

The Beijing Olympic Games of 2008 presents such a quasi-experiment. Beijing, one of the largest metropolises with a population of over 15 million and more than 3 million vehicles, has been heavily polluted (Hao, 2005). Air pollution in Beijing was characterized historically by high concentrations of particulate matter and sulfur dioxide, with an increasing significance of ozone pollution caused by vehicular emissions (Hao, 2005; Wang, 2009).In an attempt to host the Beijing Olympic Games of 2008 with acceptable air conditions, the Chinese Government implemented aggressive regulations and measures to reduce pollution levels, mainly by closing down factories with emissions and halting constriction projects in Beijing and surrounding regions. In particular, more aggressive actions, including an alternate-day driving policy, were enforced between July 20 and September 20, 2008, to improve the air quality during the Olympic Games (August 8-24, 2008) and the subsequent Paralympic Games (September 6-17, 2008). These measures, which were relaxed after the game, resulted in a rapid and significant improvement in air quality (Wang, 2010). Previous studies reported that the reduction in air pollution during this period was associated with acute changes in biomarkers of inflammation and thrombosis and measures of cardiovascular physiology in healthy young people (Rich, 2012). The lower concentrations of black carbon (BC) and particulate matter with an aerodymanic diameter of less than or equal to 2.5 µm ($PM_{2.5}$) were also found to have reduced exhaled nitric oxide (eNO), an acute respiratory inflammation biomarker in children (Lin, 2011) and reduced levels of traffic-related $PM_{2.5}$ were also associated with heart rate variability (HRV), a marker of cardiac autonomic function (Wu, 2010).

In this study, we utilized the rapid changes of air quality during the 2008 Beijing Olympic Games as a natural experiment to examine the potential effects of ambient air pollution on adverse birth outcomes. The objectives were twofold: 1) to determine which of the standard pollutants affects preterm birth and low birth weight, and 2) to investigate whether such potential effects are time-sensitive, or which trimester of gestation is most vulnerable to exposure to air pollution in relation to preterm birth and low birth weight outcomes.

DADA

Ambient air pollution

We used data from 24 air quality monitoring sites in the Beijing metropolitan area across urban districts and suburban counties, which were operated by the Beijing Municipal Environmental Monitoring Center. At each site, the PM_{10} concentrations were measured hourly by a tapered element oscillating microbalance (TEOM) (model 1400a, Rupprecht and Patashnick, now Thermo Scientific). Hourly SO_2 and NO_2 concentrations were measured by a pulsed fluorescence gas analyzer (TE43C, Thermo Scientific) and chemiluminescence technology (TE42C, Thermo Scientific), respectively. Hourly CO concentrations were measured by a gas filter correlation analyzer (TE48C, Thermo Scientific). The hourly measurements at each site were averaged to daily levels, and these daily values from all the sites were combined and averaged to obtain citywide daily levels. The arithmetic mean of the citywide daily levels was then reported as the average citywide monthly level.

Study population

The maternal data were obtained from the Beijing Haidian Maternal & Child Health Hospital (HMCHH), which provides maternal and child health care to residents of Beijing, primarily those in the Haidian district and performs medical exams on approximately ten thousand newborns delivered at HMCHH annually. Data on birth date, education, household restriction status, and fertility history of women were collected at admission. Birth weight was measured within 24 hours after delivery. Gestational age (GA) was determined from the date of the mother's last menstrual period. We included all newborns (n=50,874) delivered at HMCHH between January 1, 2006, and December 31, 2010.

ANALYTICAL STRATEGY

We applied multi-pollutant models to investigate the effects of exposure to several pollutants in different trimesters of gestation on birth outcomes. Similar models were presented elsewhere (Currie, 2009). We illustrated the model with birth weight of term children as outcome below:

$$Birth_{iym} = \sum_{t=1}^{3} (PM_{10}{}^{t}\beta_{(pm_{10})}{}^{t} + SO_{2}{}^{t}\beta_{(SO_2)}{}^{t} + NO_{2}{}^{t}\beta_{(NO_2)}{}^{t} + CO^{t}\beta_{(CO)}{}^{t})$$

$$+ VX_{iym}\alpha + \varepsilon_{iym}$$

$Birth_{ijm}$ refers to the birth weight of infant *i* who was born in the year *y* and the month *m*, and ambient pollutions levels in each of the first, second, and third trimester of the pregnancy was denoted by *t*. For example, $PM_{10}{}^{1}$ refers to concentration of PM_{10} in the first trimester and $SO_2{}^{2}$ refers to concentration of SO_2 in the second trimester. VX stands for a variety of characteristics of the infant measured in the data, including sex, the household registration (*Huji*) of the family (*urban Fuji of Beijing, rural Huji of Beijing*, *urban Huji of other province*, or *rural Huji of other province*), maternal age at delivery,), and parity (1 VS 2 and above). Because seasonality of birth or conception is associated with both socio-economic factors and birth outcomes (Slama, 2008), We controlled for seasonal effect by including dummy variable of month of conception. We also included daily precipitation and daily minimum and maximum temperatures averaged over each trimester of gestation month of birth in the model. In addition, to examine the crude effect of each individual pollutant, we produced a series of single-pollutant models for PM_{10}, SO_2, NO_2, and CO. All analyses were performed with the software package SAS, version 8.2 (SAS Institute, Inc., Cary, North Carolina).

RESULTS

Table 1 shows the monthly average concentration and correlation coefficients of ambient air pollutants (SO_2, NO_2, CO, PM_{10}) in Beijing from 2006 – 2010. The monthly average concentration of CO, at 1.73 ppm, was the lowest of the four pollutants sampled and the monthly average concentration of PM_{10}, at 134.72 ppm was the highest The concentrations of SO_2, NO_2, CO, and PM_{10} were positively correlated with each other ($0.45<r<0.87$). As shown in Figure 1, concentrations of air pollutants in Beijing exhibited a significant seasonal pattern. In general, highest concentrations of all pollutants were measured in the winter. In particular, the restriction of pollutant emissions prior to and during the Games led to a significant reduction in concentration of all four pollutants, in particular PM_{10} and NO2.

6.3% of the newborns delivered at HMCHH were born preterm (GA less than 37 complete weeks). 54.7% of the infants were born to parents whose household registration (*huji*) was registered as "Beijing Urban (*Cheng Qu*)", followed by 27.2 % born to parents registered as "urban *huji* of other province". The average maternal age at delivery was 29.2 years with a standard deviation of 3.6. As a result of the strictly enforced family planning policy in urban China, the majority (87.9%) of the newborns were firstborns, although the statistics on gestation times suggest that 54.4% of the mothers had previous pregnancy experiences. Table 2 further displays the characteristics of the newborns and relevant maternal characteristics by both sex of the newborns and their gestational status. For example, the mean birth weight of the preterm sample, which was 2,581.4 g for males (n=1,784) and 2,477.2 g for females (n=1,387), was less than the mean birth weight of the term sample (3,453.7 g for males [n=24,842] and 3,331.4 g for females [n=22,600]).Missing data were rare and the regression analysis excluded cases with missing values.

<u>Ambient air pollution and preterm status</u>

Table 3 presents the estimates of the correlation between the concentrations of ambient air pollutants and preterm status. The first column shows the results of the single pollutant model for the concentration of SO_2. When compared with exposure to SO_2 during the second trimester (P=0.286), exposure to SO_2 during the first and third trimester of gestation predicted a higher risk of preterm status. Each ten-unit increment in SO_2 in the first and third trimester was associated with a 1.03 (95% CI: 1.01 to 1.06; p=0.021) and a 1.05 (95% CI: 1.02 to 1.08; p=0.003) higher odds of preterm delivery, respectively. Similarly, the concentration of CO in the third trimester predicted a higher risk of preterm delivery. Each one-unit (per ppm) increment in the concentration of CO was associated with 1.16 higher odds (95% CI: 1.03 to 1.30; p=0.013) of preterm delivery. Further analysis with multi-pollutant models suggested that with adjustments for other pollutants, only the concentration of SO_2 in the first trimester of gestation predicted preterm delivery, with each ten-unit increment in SO_2 predicting a 1.09 higher odds (95% CI: 1.02 to 1.16; p=0.007) of preterm delivery. Neither the concentration of NO_2 nor PM_{10} predicted the risk of preterm delivery, with or without adjustment for the concentration of other pollutants.

Ambient air pollution and birth weight

Table 4 presents the correlation of concentrations of ambient pollutants and birth weight among infants born full term. The first four columns present results from single-pollutant models in which only one of the pollutants (SO_2, NO_2, CO, or PM_{10}) was included. As shown, higher concentrations were associated with lower birth weight for all the pollutants. Specifically, the concentrations of SO_2 in both the first trimester and the second trimester of gestation were negatively associated with birth weight. Each ten-unit increment (per 10 ppm) in SO_2 concentration reduced birth weight by 6.24 g (95% CI: -8.99 to -3.49; p<0.0001) in the first trimester and by 4.23 g (95% CI: -5.94 to -2.52; p<0.0001) in the second semester.

For NO_2, only the concentrations in the first trimester of gestation predicted birth weight, each ten-unit increment reduced birth weight by 10.30 g (95% CI: -15.36 to -5.23; p<0.0001). For CO, higher concentrations in both the first trimester and the second trimester of gestation predicted lower birth weight. Each one-unit (per ppm) increment in CO in the first and second trimester reduced birth weight by 26.01 g (95% CI: -37.28 to -14.73; p<0.001) and 8.55 g (95% CI: -16.10 to -0.90; p=0.029), respectively. PM_{10} concentrations in all three trimesters were negatively associated with birth weight. Each ten-unit increment (per 10μ g/m^3) in PM_{10} in the first trimester, the second trimester, and the third trimester reduced birth weight by 6.20 g (95% CI: -8.78 to -3.62; p<0.0001), 7.10 g (95% CI: -10.31 to -3.89, p<0.0001), and 3.56 g (95% CI: -6.15 to -0.96; p=0.007), respectively.

The last column presents the estimates of the multi-pollutant models where the effect of each single pollutant was estimated with adjustment for other pollutants. As shown, when controlling for other pollutants, concentrations of SO_2 in the first and second trimester were negatively associated with birth weight, and each ten-unit increment reduced birth weight by 7.02 g (95% CI: -13.14 to -0.90; p=0.025) and 10.17 g (95% CI: -16.37 to -3.98; p=0.001), respectively. Higher concentrations of NO_2 in the first trimester of gestation also predicted lower birth weight, with each ten-unit increment in NO2 predicting a 15.14 g reduction (95% CI: -29.18 to -1.10; p=0.035) in birth weight. These effects are all small in terms of effect size. For example, the effect size of concentrations of NO_2 in the first trimester of gestation is less than 0.1, which is considered small [19].

DISCUSSION

The 2008 Beijing Olympic Games provided a natural experiment setting, in which the strict environmental regulations implemented by the Chinese government resulted in a substantial improvement in air quality. This enabled us to examine the effects of exposure to ambient air pollution on adverse birth outcomes. We observed small-magnitude associations between a number of ambient air pollutants and premature delivery and birth weight. Specifically, after adjusting for other pollutants, the concentration of SO_2 in the first trimester of gestation predicated a higher risk of a preterm birth. Among term newborns, concentrations of all ambient air pollutants were negatively associated with birth weight. However, only SO_2 predicted a lower birth weight when controlling for other pollutants.

There is evidence that an adverse intrauterine environment elevates the risk for chronic disease development later in life (Barker, 1998), and that air pollution plays a role in pregnancy outcomes (Woodruff, 2009).However, the strength of the evidence varies depending on the air pollutants and outcomes examined due to the heterogeneity among previously conducted studies (Stieb, 2012; Saram, 2005). Several studies have examined fetal growth and exposure to ambient air pollution by trimester, although the findings have been widely varied, rendering conclusions difficult to draw (Woodruff, 2009).Some studies have found an association between fetal growth and first-trimester exposure to PM_{10}(Dugandzic,2006; Hansen, 2006; Mediro, 2005), while another study found an association with second-trimester exposure (Mannes, 2005), and a final study found an association with third-trimester exposure (Bell et al, 2007). The data is similarly conflicting for other pollutants. For example, several studies found an association between fetal growth and first-trimester exposure to CO (Mediros, 2005; Bell et al., 2007; Gouveia et al., 2004; Salam, 2005; Wilhelm and Ritz, 2005), while others found an association during the third trimester (Bell et al., 2007; Wilhelm and Ritz, 2005).Data is similarly variable for exposure to the pollutants NO_2 and SO_2, and thus further research on air pollution and birth outcomes by exposure window is needed.

Although air pollution plays a role in pregnancy outcomes, the biological mechanism is not completely understood (Stieb, et al., 2012).Ambient air pollutants may induce oxidative stress and inflammation, as well as alter blood coagulation and hemodynamic responses for the fetus and placenta (Kannan, 2007). Such changes could affect nutrient intake by the fetus, potentially leading to preterm births or impairing fetal growth (Kannan, 2007). In non-pregnant individuals, exposure to PM have also been associated with endothelial function and plasma viscosity (Pope, 2006). It has been hypothesized that such alterations in artery vascoconstriction could affect maternal-placental exchanges and thus affect fetal growth (Slam et al, 2008). A fetuses' vulnerability to environmental toxicants may also result in the abnormal development of organ systems during this critical window of growth (Calabrese, 1986).

Experimental studies in laboratory animals have found evidence of changes in reproductive function after exposure to air pollution (Slama et al., 2008; Archibong et al., 2002; Mohallem, 2005; Rocha et al., 2008), however the relevance of these findings for human reproduction is uncertain (Carter, 2007). Further research of these effects on laboratory animals and studies on pregnant women using biomarkers may provide further insight on the biological mechanism (Slama et al, 2008).

There are several limitations to the study. First, this study extrapolated information from citywide measurements of ambient air pollution, and we were unable to draw conclusions based on exposures to air pollutants at the individual level. Certain uncontrolled factors such as occupation and mobility may have affected each individuals' level of exposure to ambient air pollutants. Second, smoking exposure, which significantly increased risk of preterm birth and low birth weight of newborns and may amplify the adverse effect of exposure to ambient air pollution during pregnancy is not controlled for. This concern may be mitigated because smoking among women, in particular, pregnant women is very rare in China, though the possibility can't be excluded that women are likely to have exposed to second hand smoking in China where smoking is common among men. Future studies may benefit from a perspective cohort research design allowing use of biomarkers of exposure at individual level and collection of detailed information on characteristics of study subjects including behaviors when budget is permitted (Slama, Darrow, & Parker et al, 2009). Third, we can't exclude a hypothetical "event effect" such that a mega event such as Olympic Games *per se* may affect psychological and physical health of residents in the host city. Future studies may address this concern by including residents who are exposed to different levels of ambient air pollution but experienced the same event. Lastly, because of data limitation, we are unable to test the possible biological mechanisms underlying the observed associations between exposure to amine air pollution during pregnancy and adverse birth outcomes.

Nevertheless, our study, based on a natural experiment approach, provided further evidence that ambient air pollution may be associated with an increase in likelihood of preterm births and in a reduction in birth weight although the effect sizes are small, which are in general consistent with previous studies based on other design. If such association is proved to be causal, Future studies should further investigate regulatory interventions as they pertain to ambient air pollution because of their potential role in preventing short and long term health consequences of preterm births and low birth weight infants.As previously mentioned, there have been other studies that examined the effects of the changes in ambient air pollution during the 2008 Beijing Olympics on health outcomes including two studies on ambient air pollution and cardiovascular health (Rich, 2012; Wu, 2010) and one on ambient air pollution and acute respiratory inflammation (Lin, 2011). However, to our knowledge this was the first study to examine ambient air pollution and birth outcomes during the 2008 Beijing Olympics.

FIGURE 1. Monthly average concentration of ambient pollutants in Beijing between 2006 and 2010; Note: Numbers for CO exhibited in the Figure are at a 0.1 ppm scale.

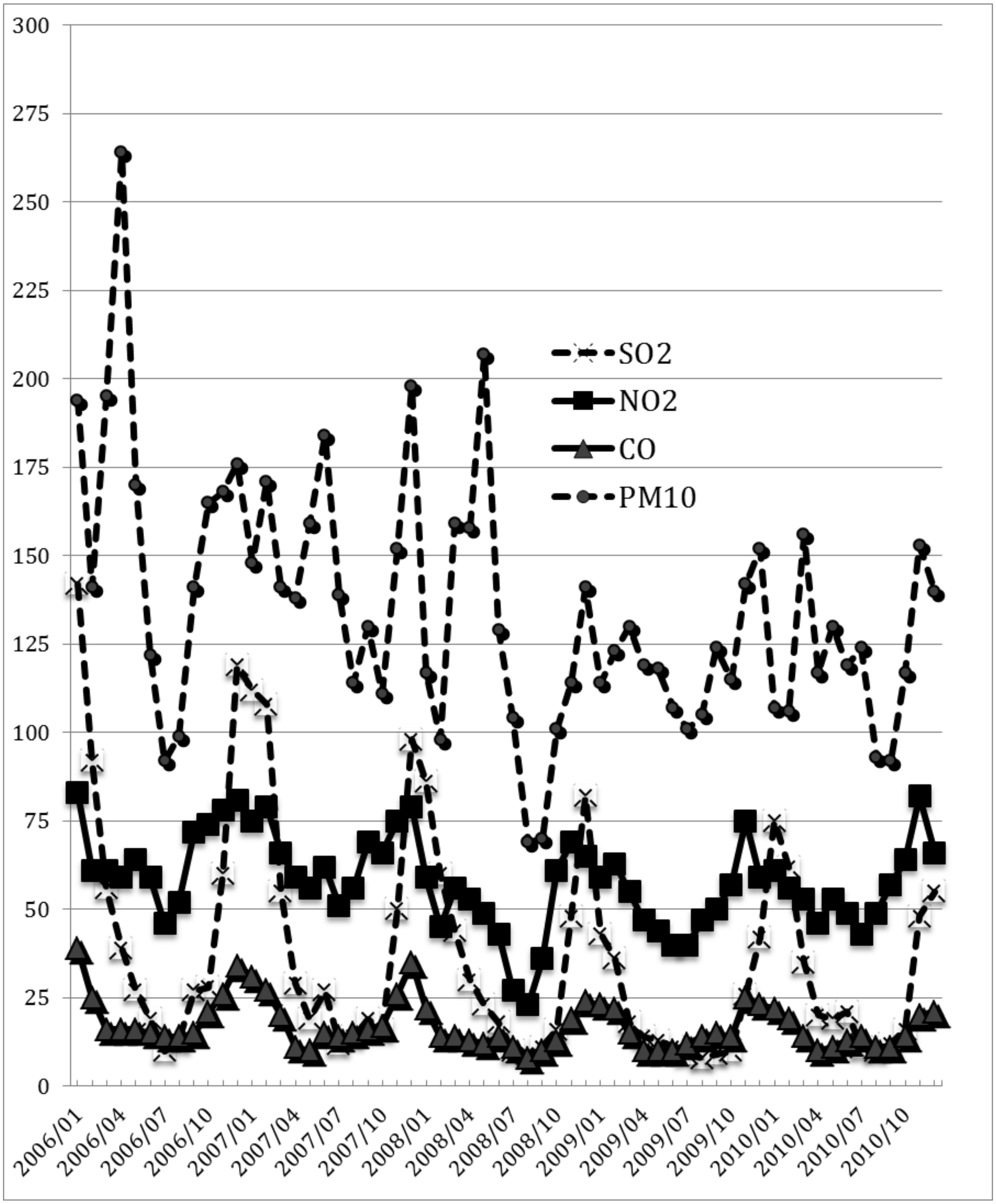

TABLE 1. Characteristics and correlations of monthly average concentration of ambient pollutants at Beijing during 2006-2010

Pollutants	Concentration				Correlation coefficients				
	Mean	Std Dev	Min	Max		SO2	NO2	CO	PM10
SO2 (ppm)	37.52	32.03	8.00	142.00	SO2	1.00	0.64	0.87	0.45
NO2 (ppm)	58.07	13.10	23.00	83.00	NO2	0.64	1.00	0.78	0.55
CO (ppm)	1.73	0.68	0.80	3.90	CO	0.87	0.78	1.00	0.45
PM10 (ppm)	134.72	35.16	69.00	264.00	PM10	0.45	0.55	0.45	1.00

TABLE 2. Characteristics of the mothers and newborns delivered at Beijing Haidian Maternal and Child Health Hospital between January 1, 2006 and December 31, 2010.

Characteristics	**Term sample** (N=47,671)		**Preterm sample** (N=3203)	
	Male (N=24,843)	Female(N=22,600)	Male (N=1,784)	Female (N=1,387)
Birth weight (grams) (Std Dev)	3453.7 (415.1)	3331.4 (402.8)	2581.4 (523.9)	2477.2 (513.6)
Birth Year				
2006	6.63	6.25	6.00	6.49
2007	23.81	23.99	21.69	23.22
2008	23.60	23.81	27.19	24.44
2009	24.97	24.62	26.23	25.67
2010	21.00	21.33	18.89	20.19
Household Registration (*Huji*)				
Urban Huji of Beijing	54.82	55.89	48.71	49.53
Rural Huji of Beijing	1.82	1.84	1.85	1.95
Other province, urban	27.33	27.44	26.51	26.03
Other state, rural	15.91	14.73	22.65	22.42
Missing	0.12	0.11	0.28	0.07
Maternal age at delivery				
Mean (STD)	29.2 (3.7)	29.2 (3.6)	29.3 (4.2)	29.3 (4.3)
Pregnancy history				
1	44.98	46.78	44.84	45.35
2	30.66	30.37	27.30	27.97
3+	24.25	22.77	27.86	26.68
Missing	0.10	0.08	0	0
Parity				
1	87.58	89.99	80.55	84.21
2+	12.41	9.98	19.34	15.65
Missing	0.02	0.03	0.11	0.14

TABLE 3. Effects of concentrations of ambient air pollutants on preterm delivery

Variables	Single pollutant models								Multi-pollutants Model	
	SO2 (per 10 ppm)		NO2 (per 10 ppm)		CO (per ppm)		PM10 (per 10 ug/m3)			
	OR(95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value	AOR (95% CI)	P-value
SO2, 1st trimester	1.03 (1.01, 1.06)	0.021							1.09 (1.02, 1.16)	0.007
SO2, 2nd trimester	1.01 (0.99, 1.03)	0.286							1.00 (0.94, 1.06)	0.932
SO2, 3rd trimester	1.05 (1.02, 1.08)	0.003							1.00 (0.93, 1.08)	0.921
NO2, 1st trimester			1.00 (0.95, 1.05)	0.974					1.01 (0.88, 1.16)	0.927
NO2, 2nd trimester			1.00 (0.97, 1.04)	0.839					0.88 (0.77, 1.00)	0.051
NO2, 3rd trimester			1.02 (0.97, 1.08)	0.384					0.89 (0.76, 1.04)	0.150
CO, 1st trimester					1.11 (0.99, 1.24)	0.076			0.96 (0.62, 1.48)	0.842
CO, 2nd trimester					1.04 (0.97, 1.12)	0.293			1.61 (0.99, 2.60)	0.055
CO, 3rd trimester					1.16 (1.03, 1.30)	0.013			1.62 (0.91, 2.89)	0.102
PM10, 1st trimester							1.00 (0.97, 1.02)	0.800	0.98 (0.94, 1.03)	0.503
PM10, 2nd trimester							0.98 (0.95, 1.01)	0.282	0.95 (0.89, 1.02)	0.177
PM10, 3rd trimester							1.01 (0.99, 1.04)	0.266	1.00 (0.92, 1.08)	0.968

Note: OR, Odds Ratio; AOR, Adjusted Odds Ratio

TABLE 4. Effects of concentration of ambient air pollutants on birth weight of infants born full term

Variables	Single pollutant models								Multi-pollutants Model	
	SO2 (per 10 ppm)		NO2 (per 10 ppm)		CO (per ppm)		PM10 (per 10 ug/m3)			
	Change of birth weight	P-value	Change of birth weight	P-value	Change of birth weight	P-value	Change of birth weight	P-value	Change of birth weight	P-value
SO2, 1st trimester	-6.24 (-8.99, -3.49)	<0.0001							-7.02 (-13.14, -0.90)	0.025
SO2, 2nd trimester	-4.23 (-5.94, -2.52)	<0.0001							-10.17 (-16.37, -3.98)	0.001
SO2, 3rd trimester	-2.54 (-5.49, 0.41)	0.091							3.30 (-4.18, 10.79)	0.387
NO2, 1st trimester			-10.30 (-15.36, -5.23)	<0.0001					-15.14 (-29.18, -1.10)	0.035
NO2, 2nd trimester			-3.69 (-7.49, 0.12)	0.058					-12.22 (-25.64, 1.22)	0.075
NO2, 3rd trimester			2.21 (-3.12, 7.54)	0.417					3.91 (-12.25, -20.06)	0.635
CO, 1st trimester					-26.01 (-37.28, -14.73)	<0.0001			12.81 (-31.08, 56.71)	0.567
CO, 2nd trimester					-8.55 (-16.10, -0.90)	0.029			14.51 (-34.21, 63.23)	0.559
CO, 3rd trimester					-3.33 (-15.16, 8.49)	0.581			-55.06 (-112.24, 2.12)	0.059
PM10, 1st trimester							-6.20 (-8.78, -3.62)	<0.0001	0.75 (-4.36, 5.58)	0.775
PM10, 2nd trimester							-7.10 (-10.31, -3.89)	<0.0001	7.65 (0.71, 14.59)	0.031
PM10, 3rd trimester							-3.56 (-6.15, -0.96)	0.007	8.12 (-0.10, 16.34)	0.053

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