ORIGINAL ARTICLE

Impact of ambient air pollution on birth weight in Sydney, Australia

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Background: Studies in Asia, Europe, and the Americas have provided evidence that ambient air pollution may have an adverse effect on birth weight, although results are not consistent.

Methods: Average exposure during pregnancy to five common air pollutants was estimated for births in metropolitan Sydney between 1998 and 2000. The effects of pollutant exposure in the first, second, and third trimesters of pregnancy on risk of ''small for gestational age'' (SGA), and of pollutant exposure during pregnancy on birth weight were examined.

Results: There were 138 056 singleton births in Sydney between 1998 and 2000; 9.7% of babies (13 402) were classified as SGA. Air pollution levels in Sydney were found to be quite low. In linear regression models carbon monoxide and nitrogen dioxide concentrations in the second and third trimesters had a statistically significant adverse effect on birth weight. For a 1 part per million increase in mean carbon monoxide levels a reduction of 7 (95% CI −5 to 19) to 29 (95% CI 7 to 51) grams in birth weight was estimated. For a 1 part per billion increase in mean nitrogen dioxide levels a reduction of 1 (95% CI 0 to 2) to 34 (95% CI 24 to 43) grams in birth weight was estimated. Particulate matter (diameter less than ten microns) in the second trimester had a small statistically significant adverse effect on birth weight. For a 1 microgram per cubic metre increase in mean particulate matter levels a reduction of 4 grams (95% CI 3 to 6) in birth weight was estimated.

Conclusion: These findings of an association between carbon monoxide, nitrogen dioxide, and particulate matter, and reduction in birth weight should be corroborated by further study.

E pidemiological studies addressing the relation between ambient air pollution and fetal development are accumulating worldwide. Studies conducted in China,[1] the Czech Republic,[2 3] Korea,[4] the UK,[5] Brazil,[6] and North America[7–11] have examined the link between ambient air pollution levels during pregnancy and reduction in birth weight or intrauterine growth retardation (IUGR). There is evidence to suggest that air pollutant exposure during pregnancy has an adverse impact on birth weight, although the findings are inconsistent; the effect of individual pollutants and the period(s) during pregnancy when pollutant levels are likely to have most impact on birth weight is not clear.

It is useful, then, to examine the impact of ambient air pollution and birth weight in a variety of different sites to clarify the nature of the relation. We examined this relation in Sydney as there is complete, routinely collected data available. In the present study we evaluated the effect of prenatal exposure (in early, mid, and late pregnancy) to five common urban air pollutants: particulate matter (PM_{10} and $PM_{2.5}$), carbon monoxide (CO), nitrogen dioxide (NO_2), and ozone (O_3) from routine air monitoring in the Sydney metropolitan area on birth weight.

METHODS

Information on all births in metropolitan Sydney between 1 January 1998 and 31 December 2000 was obtained from the Midwives Data Collection (MDC) at the New South Wales Department of Health. The MDC is a population based surveillance system covering all live births and stillbirths of at least 20 weeks gestation and at least 400 grams birth weight. Birth data includes maternal demographic factors (age, smoking status, country of birth, postcode of residence at time of delivery), pregnancy factors (date of the last menstrual period, gestational hypertension and diabetes,

parity, time of first antenatal visit to a healthcare provider), details about the delivery (type of delivery), and infant factors (birth weight, gestational age). Other known causes of low birth weight including multiple births, hypertension of pregnancy, and gestational diabetes were excluded.

We obtained daily air pollution data from the New South Wales Environment Protection Authority (EPA) and daily meteorological data from the Australian Bureau of Meteorology. Air pollution data included concentrations of PM_{10}, $PM_{2.5}$, NO_2, O_3, and CO recorded at 14 monitoring stations in metropolitan Sydney. Monitoring stations were excluded if less than 80% of readings were available for each pollutant. Pollutant concentrations were analysed as continuous variables.

For each birth, exposure to each air pollutant during gestation was estimated by calculating the average of each pollutant over 30 days (last month) and 90 days (third trimester) before birth, the mid 90 days of gestation (second trimester), and 90 days (first trimester) after the estimated date of conception. Pollutant concentrations from monitoring stations were averaged to provide an estimate for the whole of metropolitan Sydney, using an approach similar to the APHEA2 (Short-term Effects of Air Pollution and Health: A European Approach) studies.[12–14] The process was repeated

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Table 1 Characteristics of all singleton births in Sydney from 1998 to 2000 by "small for gestational age"

Variable	Small for gestational age (n = 13 402)		Not small for gestational age (n = 138 056)		Adjusted OR (95% CI)
	No.	%	No.	%	
Maternal age (years)					
<24	2762	20.6	19460	14.1	1.02 (0.97 to 1.08)
25–34*	8340	62.2	93828	68.0	1.00
35–44	2285	17.0	24639	17.8	1.01 (0.95 to 1.01)
>45	15	0.1	129	0.1	1.55 (0.84 to 2.84)
Maternal smoker					
Yes	2659	19.8	14254	10.3	1.97 (1.87 to 2.08)
No	10741	80.1	110375	79.9	
Sex of infant					
Female	6456	48.2	60381	43.7	1.01 (0.97 to 1.05)
Male	6946	51.8	64273	46.6	
Maternal Aboriginality		0.0		0.0	
Yes	117	0.9	806	0.6	1.03 (0.83 to 1.28)
No	13275	99.1	123758	89.6	
Gestation at first antenatal visit					
>20 weeks	1803	13.5	13854	10.0	1.12 (1.05 to 1.18)
⩽20 weeks	11486	85.7	110014	79.7	
Previous pregnancy					
No	7427	55.4	53102	38.5	0.57 (0.54 to 0.59)
Yes	5973	44.6	71517	51.8	
IRSD quintile					
5 (least disadvantaged; high SES)*	3843	28.7	58638	42.5	1.00
4	2857	21.3	27395	19.8	1.24 (1.17 to 1.13)
3	2374	17.7	19997	14.5	1.38 (1.30 to 1.46)
2	1684	12.6	13826	10.0	1.50 (1.41 to 1.61)
1 (most disadvantaged; low SES)	2644	19.7	18200	13.2	1.73 (1.63 to 1.83)
Season of birth					
Summer (Dec–Feb)*	3265	24.4	43727	31.7	1.00
Autumn (Mar–May)	3456	25.8	31109	22.5	1.05 (0.99 to 1.11)
Winter (Jun–Aug)	3375	25.2	31469	22.8	1.00 (0.95 to 1.06)
Spring (Sep–Nov)	3306	24.7	31751	23.0	0.99 (0.94 to 1.05)

*Referent group.
OR, odds ratio adjusted for other covariates; SD, standard deviation; SES, socioeconomic status.
Note that in Australia, autumn is in March, April, May; winter is in June, July, August; spring is in September, October, November; and summer is in December, January, February.

matching air pollution concentrations from each eligible monitoring station and births to mothers residing in postcodes within 5 km of the monitoring station.

The following covariates were included in regression models: sex of child, maternal age (in year groupings), gestational age (only included in linear regression models), maternal smoking (yes/no), gestational age at first antenatal visit (⩽20 weeks or >20 weeks), maternal indigenous status (whether mother identifies as being Aboriginal or Torres Strait Islander), whether first pregnancy, season of birth, and socioeconomic status (SES). SES was measured using the Index of Relative Socioeconomic Disadvantage (IRSD) of postcode of maternal residence. The Australian Bureau of Statistics (ABS) constructs the IRSD to classify geographical areas on the basis of social and economic information collected in the population census. Each postcode in New South Wales (population of approximately 1000–5000 people) is assigned an IRSD index. We then ranked the postcodes and divided the list into quintiles.

A variable "small for gestational age" (SGA) was calculated based on the Australian national birth weight centile for gestational age 1991–94.[15] SGA was defined as greater than two standard deviations below the mean birth weight according to gestational age as SGA. SGA was analysed as a categorical variable in logistic regression models using the SAS System for Windows v8.02. Linear regression models were also developed using birth weight as a continuous variable. Following the development of the basic model, air pollutants were then added to the model to determine the association between ambient air pollutants and birth weight. Single and multi-pollutant pollutant models were assessed and we investigated interactions between air pollution

variables and covariates. The impact of pollutant exposures in other pregnancy periods on key findings was also analysed.

RESULTS

There were 138 056 singleton births in Sydney between 1998 and 2000; 9.7% of babies (13 402) were classified as SGA. Mean (SD) birth weight for babies born in Sydney between 1998 and 2000 was 3418 (531) grams. After adjusting for other maternal and infant characteristics, SGA was significantly associated with maternal smoking, gestational age greater than 20 weeks at first antenatal visit, and first pregnancy (table 1). All SES variables exhibit a statistically significant association with SGA. Compared to the high SES category, there was increasing risk of SGA with decreasing SES.

Pollutant concentrations in Sydney from 1 April 1997 to 31 December 2000 are presented in table 2. A correlation matrix of air pollution variables is presented in table 3 to show correlations between pollutants. Correlation coefficients above 0.8 were observed between PM_{10} and $PM_{2.5}$. Correlation coefficients were also calculated to determine the correlations between air monitoring stations. Correlation coefficients between the 14 monitoring stations ranged from 0.68 to 0.85 for CO. Correlation coefficients between the 14 monitoring stations ranged from 0.46 to 0.85 for NO_2; from 0.53 to 0.94 for O_3; from 0.67 to 0.91 for PM_{10}; and from 0.66 to 0.93 for $PM_{2.5}$. All pollutants differed according to season (p < 0.01) and post hoc analysis revealed that all seasons were different to all others (p < 0.05). Concentrations of CO, NO_2, and $PM_{2.5}$ were highest in winter and lowest in summer. Concentrations of PM_{10} and O_3 were highest in summer and lowest in winter.

Table 2 Daily average pollutant concentrations for air monitoring stations in Sydney, 1 April 1997–31 December 2000

	Australian National Standard	Mean (SD)	Minimum	25th centile	Median	75th centile	Maximum
Pollutant							
PM$_{10}$ (μg/m^3)							
24 hour av	50 μg/m^3	16.8 (7.1)	3.8	12.3	15.7	19.9	104.0
PM$_{2.5}$ (μg/m^3)							
24 hour av	25 μg/m^3*	9.4 (5.1)	2.4	6.5	8.4	11. 2	82.1
CO (ppm)							
8 hour av	9.0 ppm	0.8 (0.7)	0.0	0.4	0.6	1.1	4.6
O$_3$ (ppb)							
1 hour max	100 ppb	31.6 (14.6)	3.2	22.7	27.7	36.3	126.7
NO$_2$ (ppb)							
1 hour max	120 ppb	23.2 (7.4)	56.2	18.0	23.0	27.5	59.4

*Advisory reporting standard from 2003.
ppb, parts per billion (10^{-9}); ppm, parts per million (10^{-6}); CO, carbon monoxide, 8 hour average in ppm; O$_3$, ozone, 1 hour max in ppb; PM$_{10}$, particulate matter less than 10 microns, 24 hour average in μg/m^3; PM$_{2.5}$, particulate matter less than 2.5 microns, 24 hour average in μg/m^3; NO$_2$, nitrogen dioxide, 24 hour average in ppb.

Citywide average air pollutant concentrations in the last month, third trimester, and first trimester of pregnancy had no statistically significant effect on SGA after adjusting for infant and maternal characteristics (table 4). Concentrations of PM$_{10}$, PM$_{2.5}$, and O$_3$ in the second trimester of pregnancy had a small but statistically significant adverse effect on SGA (OR 1.01, 95% CI 1.00 to 1.04; OR 1.03, 95% CI 1.01 to 1.05; and OR 1.01, 95% CI 1.00 to 1.01, respectively).

Eleven metropolitan air monitoring stations were eligible for inclusion in the analysis of babies born to women residing within 5 km of an air monitoring station (table 4). There were 51 460 eligible births in 1998–2000. Of these, 5985 (11.6%) were classified as SGA. NO$_2$ concentrations in the second and third trimesters and one month before birth had a statistically significant adverse effect on risk of SGA (ORs between 1.07 and 1.14) (table 4). The NO$_2$ effects were robust to controlling for exposures in other pregnancy periods (ORs between 1.1 (95% CI 1.0 to 1.2) and 1.1 (95% CI 1.0 to 1.2) for second and third trimesters respectively). Exposure to PM$_{10}$ in the second trimester of pregnancy had a small but statistically significant adverse effect on risk of SGA (OR 1.02, 95% CI 1.01 to 1.03) (table 4), although these findings were not robust to analysis when controlling for exposures to PM$_{10}$ in other periods of pregnancy (OR 1.01, 95% CI 0.99 to 1.02).

In multivariate linear regression models, the effect of pollutant concentrations on birth weight (in grams) was examined for all births in Sydney during the study period and for babies born to women residing within 5 km of an air monitoring station (table 5). Citywide average levels of PM$_{10}$ and PM$_{2.5}$ in the second trimester and last month of pregnancy had a small but statistically significant adverse effect on birth weight. When analysing only babies born to

women residing within 5 km of an air monitoring station, we observed a small adverse effect of PM$_{10}$ exposure during the second trimester on birth weight (regression coefficient −4.3, 95% CI −5.8 to −2.8). Thus, for every 1 μg/m^3 increase in 24 hour average PM$_{10}$ during the second trimester of pregnancy, a 4 gram reduction in birth weight was estimated. This finding persisted after controlling for exposures in other pregnancy periods and analysis in multi-pollutant models (table 6).

Citywide average levels of CO in the last month of pregnancy had a statistically significant adverse effect on birth weight, whereas the 5 km results reveal an adverse effect of CO exposure on birth weight for the second and third trimesters of pregnancy. Linear regression coefficients for the 5 km analysis ranged from −23 (95% CI −44.6 to −1.2) to −29 (95% CI −51.0 to −6.8); thus, for every 1 part per million increase in 8 hour average CO during pregnancy, a 23–29 gram reduction in birth weight was estimated. Analysis of second trimester CO findings in two and three pollutant models and controlling for exposures in other pregnancy periods are presented in table 6. CO findings in the second trimester did not remain statistically significant when analysed in multi-pollutant models.

Citywide average levels of NO$_2$ in the first and third trimesters of pregnancy resulted in a small but statistically significant adverse effect on birth weight, whereas the 5 km results reveal an adverse effect of NO$_2$ exposure on birth weight for all periods of pregnancy. Linear regression coefficients for the 5 km analysis ranged from −20 (95% CI −27.8 to −11.5) to −34 (95% CI −43.4 to −24.3). NO$_2$ findings in the second trimester remained when analysed in two pollutant models, but did not remain when analysed in the four pollutant model (table 6).

Table 3 Matrix of Pearson correlation coefficients of pollutant concentrations (averaged across all air monitoring stations) in Sydney, April 1997–December 2000, and birth outcomes for term births in Sydney, 1998–2000

Pollutant	Birth weight	CO	NO$_2$	O$_3$	PM$_{10}$	PM$_{2.5}$	Temp
Birth weight	1.00						
CO	0.00	1.00					
NO$_2$	0.01	0.57	1.00				
O$_3$	0.01	−0.20	0.29	1.00			
PM$_{10}$	0.01	0.26	0.47	0.52	1.00		
PM$_{2.5}$	0.01	0.53	0.66	0.36	0.81	1.00	
Temp	0.00	−0.42	−0.16	0.60	0.38	0.05	1.00

Temp, temperature; ppb, parts per billion (10^{-9}); ppm, parts per million (10^{-6}); CO, carbon monoxide, 8 hour average in ppm; O$_3$, ozone, 1 hour max in ppb; PM$_{10}$, particulate matter less than 10 microns, 24 hour average in μg/m^3; PM$_{2.5}$, particulate matter less than 2.5 microns, 24 hour average in μg/m^3; NO$_2$, nitrogen dioxide, 24 hour average in ppb.

Table 4 Association (OR point estimate, 95% CI) between pollutant concentrations in Sydney and risk of small for gestational age (SGA) for infants born in Sydney between 1998 and 2000 by exposure period

Pollutant	No. of infants (SGA/total)	Exposure period							
		One month before birth		Third trimester		Second trimester		First trimester	
		OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
All births									
PM_{10}	13402/138056	1.01	1.00 to 1.03	1.00	0.99 to 1.013	1.01	1.00 to 1.04	1.00	0.98 to 1.02
$PM_{2.5}$	13402/138056	1.01	0.99 to 1.03	0.99	0.97 to 1.02	1.03	1.01 to 1.05	0.99	0.97 to 1.01
CO	13402/138056	1.06	0.98 to 1.16	1.01	0.91 to 1.11	0.99	0.90 to 1.10	0.95	0.88 to 1.04
NO_2	13402/138056	1.00	1.00 to 1.01	1.01	1.00 to 1.02	1.00	0.99 to 1.01	1.00	0.99 to 1.01
O_3	13402/138056	1.00	0.99 to 1.01	1.00	1.00 to 1.01	1.01	1.00 to 1.01	1.00	1.00 to 1.01
5 km births									
PM_{10}	5391/44891	1.00	0.99 to 1.02	1.01	0.99 to 1.02	1.02	1.01 to 1.03	1.01	0.99 to 1.02
$PM_{2.5}$	1595/13855	1.01	0.97 to 1.04	1.00	0.95 to 1.05	1.00	0.96 to 1.05	0.99	0.94 to 1.04
CO	2892/22684	1.10	0.96 to 1.27	1.05	0.90 to 1.23	1.06	0.90 to 1.25	0.99	0.86 to 1.14
NO_2	5985/51460	1.07	1.00 to 1.14	1.13	1.05 to 1.21	1.14	1.07 to 1.22	1.06	0.99 to 1.14
O_3	5460/45730	1.01	0.97 to 1.06	1.01	0.96 to 1.07	1.00	0.95 to 1.06	0.99	0.93 to 1.03

OR estimates adjusted for: maternal age, maternal smoking, indigenous status, SES, gestational age at first antenatal visit, season of birth, and parity.
OR per 1 unit increase in pollutant concentration.
ppb, parts per billion (10^{-9}); ppm, parts per million (10^{-6}).
Units and averaging periods:
PM_{10} ($\mu g/m^3$): 24 hour av
$PM_{2.5}$ ($\mu g/m^3$): 24 hour av
CO (ppm): 8 hour av
O_3 (ppb): 1 hour max
NO_2 (ppb): 1 hour max

DISCUSSION

We examined associations between birth weight and exposure to air pollution concentrations at various stages of pregnancy across all of Sydney and for those infants born to women residing within 5 km of air monitoring stations. We showed a small effect of PM_{10} concentration in the second trimester of pregnancy, on birth weight in both linear and logistic regression models. We also showed that CO and NO_2 concentrations in the second and third trimesters of pregnancy (most pronounced in the second trimester), had a statistically significant effect on birth weight. The effect of NO_2 concentrations was only seen when examining births to women residing within 5 km of an air monitoring station. The effect of CO concentrations was only seen in the linear regression analysis and was most pronounced when examining births to women residing within 5 km of an air monitoring station.

There are a number of strengths to our study. We were able to investigate the association between low birth weight and pollutant concentrations for a large number of births in metropolitan Sydney between 1998 and 2000, and we were able to test this association using information on infants born to women residing within 5 km of an air monitoring station, again for a large number of births. We were also able to analyse the effect of five common air pollutants (PM_{10}, $PM_{2.5}$, CO, NO_2, and O_3), as these pollutants are routinely monitored at many air monitoring stations in metropolitan Sydney. One strength of this study is that we have been able to control for maternal smoking, indigenous status, gestational age at first antenatal visit, and parity among other potential confounders.

Although our analysis controlled for a number of important potential confounders, we did not have the information to adjust for some known risk factors for low birth weight; for example, maternal nutrition, maternal occupation, or pre-pregnancy maternal weight. Also, residual confounding by SES cannot be ruled out. Our SES estimate is a group level variable assigned to postcode of maternal residence at time of birth.

The most important source of bias in our study is due to measurement of exposure. By using air pollutant concentrations averaged across Sydney, we assume that ambient pollutant concentrations represent an individual's actual exposure to pollutants. This assumption does not account for time-activity patterns that may mediate exposure such as commuting habits, place or type of work, or time spent outdoors.

The use of citywide average exposure does not account for variations in pollutant concentrations across Sydney or even within the 5 km zone around an air monitoring station. It is likely that pollutants, particularly primary pollutants such as nitrogen dioxide and carbon monoxide, are not homogeneously distributed across Sydney. The distribution of primary pollutants will largely depend on the presence of combustion sources such as roads or industry. Thus we also examined the impact of pollutant concentrations only for births to women residing within 5 km of an air monitoring station to attempt to provide a better estimate of exposure for pollutants with large geographic variability. Analysis of the effect of CO and NO_2 shows a clear pattern of increased effect when examining only births to

Table 5 Changes in birth weight (in grams) for a 1 unit change in exposure to air pollutants (PM$_{10}$ and PM$_{2.5}$ in µg/m^3; CO in ppm; O$_3$, NO$_2$ in ppb) at each trimester, and last month of pregnancy; results of linear regression models adjusted for covariates

Pollutant	One month before birth Multiple linear regression coefficient	95% confidence limits		Third trimester Multiple linear regression coefficient	95% confidence limits		Second trimester Multiple linear regression coefficient	95% confidence limits		First trimester Multiple linear regression coefficient	95% confidence limits	
All births												
PM$_{10}$	−1.21	−2.31	−0.11	−0.95	−2.30	0.40	−2.05	−3.36	−0.74	−0.14	−1.37	1.09
PM$_{2.5}$	−2.48	−4.58	−0.38	−0.98	−3.74	1.78	−4.10	−6.79	−1.41	0.36	−2.29	3.01
CO	−15.28	−25.59	−4.97	−6.63	−18.57	5.31	−10.72	−23.09	1.65	1.86	−8.31	12.03
NO$_2$	−0.76	−1.72	0.20	−1.48	−2.70	−0.26	−0.95	−2.07	0.17	−1.07	−2.07	−0.07
O$_3$	−0.11	−0.56	0.34	−0.45	−1.08	0.18	−0.75	−1.38	−0.12	−0.09	−0.66	0.48
5 km births												
PM$_{10}$	−2.98	−4.25	−1.71	−3.84	−5.35	−2.33	−4.28	−5.79	−2.77	−2.57	−4.04	−1.10
PM$_{2.5}$	−2.70	−6.80	1.40	−2.83	−9.00	3.34	1.54	−4.59	7.67	1.89	−1.99	5.77
CO	−10.41	−30.03	9.21	−22.88	−44.58	−1.18	−28.87	−50.98	−6.76	−8.96	−28.60	10.68
NO$_2$	−19.68	−27.83	−11.53	−32.17	−41.81	−22.53	−33.85	−43.38	−24.32	−26.22	−35.41	−17.03
O$_3$	−0.65	−6.51	5.21	−2.00	−9.64	5.64	8.77	1.05	16.49	8.99	−0.59	18.57

ppb, parts per billion (10^{-9}); ppm, parts per million (10^{-6}).
Units and averaging periods:
PM$_{10}$ (µg/m^3): 24 hour av
PM$_{2.5}$ (µg/m^3): 24 hour av
CO (ppm): 8 hour av
O$_3$ (ppb): 1 hour max
NO$_2$ (ppb): 1hour max

women residing within 5 km of an air monitoring station. Ozone and PM$_{2.5}$ are secondary pollutants and thus should be more homogeneously distributed throughout metropolitan Sydney. The effects of concentrations of PM$_{2.5}$ and O$_3$ change little when analysing only births to women residing within 5 km of an air monitoring station.

Our findings of an adverse effect of particulates in the second trimester and of NO$_2$ and CO at various stages of pregnancy on birth weight have been replicated in previous studies. In a meta-analysis of studies examining the impact of particulate exposure on birth weight, Glinianaia and colleagues[16] concluded that in those studies where an effect of particulates in birth outcomes has been shown, there is considerable variability in the stage of pregnancy that the impact occurs.[16] The same can be said of those studies examining the impact of other pollutants on birth weight.

Chen and colleagues[9] examined the impact of ambient PM$_{10}$ and other pollutant concentrations on birth weight in Northern Nevada (USA) between 1991 and 1999, and found that exposure to PM$_{10}$ in the third trimester of pregnancy was negatively associated with birth weight in Nevada.[9] Gouveia and colleagues[6] examined the impact of O$_3$, CO, and PM$_{10}$ concentrations on birth weight in Sao Paolo, Brazil in 1997, and found that first trimester exposure to CO and PM$_{10}$ had an adverse affect on birth weight. No association between O$_3$ concentrations in any trimester and birth weight was observed.

IUGR, defined as birth weight below the 10th centile of recorded birth weight, was associated with exposure to PM$_{2.5}$ and PM$_{10}$ concentrations in the first trimester of pregnancy in Northern Bohemia.[3] In the Czech Republic, IUGR was not associated with exposure to sulphur dioxide (SO$_2$) and total suspended particulate (TSP) concentrations during pregnancy.[2] Bobak[2] also reported that exposure to SO$_2$, TSP, and oxides of nitrogen (NO$_x$) during pregnancy had no affect on risk of low birth weight, after adjusting for gestational age (as well as other maternal characteristics). Ha and colleagues[4] examined the effect of exposure to CO, NO$_2$, TSP, and SO$_2$ in the first trimester of pregnancy on low birth weight in Seoul, South Korea. For each inter-quartile increase in pollutant the relative risk of low birth weight was 1.08 for CO, 1.07 for NO$_2$, 1.06 for SO$_2$, and 1.04 for TSPs.[4] No effect of exposure to these pollutants in the third trimester of pregnancy was noted.

Liu and colleagues[11] examined the effect of SO$_2$, NO$_2$, CO, and O$_3$ concentrations on IUGR, low birth weight, and preterm birth in Vancouver, Canada. Low birth weight was associated with exposure to SO$_2$ during the first month of pregnancy (OR 1.1 for a 5 ppb increase). IUGR was associated with exposure to SO$_2$ (OR 1.1 for a 5 ppb increase), NO$_2$ (OR 1.1 for a 10 ppb increase), and CO (OR 1.1 for a 1 ppm increase) in the first month of pregnancy.

Last trimester exposure to CO in Los Angeles, USA was reported to result in an increased risk of low birth weight in term births after adjusting for maternal characteristics including commuting habits (OR = 1.22).[7] Maisonet and colleagues[10] reported an increased risk of term low birth weight due to exposure to CO and SO$_2$ in all trimesters of pregnancy in six cities in North Eastern United States. No effect of exposure to PM$_{10}$ was noted.[10] Concentrations of TSP and SO$_2$ in the last trimester of pregnancy were

associated with low birth weight in four residential areas of Beijing, China.[1]

In a recent study in Poland, Jedrychowski and colleagues[17] monitored individual exposure to fine particles over 48 hours during the second trimester of pregnancy of 362 women who gave birth between 34 and 43 weeks gestation. $PM_{2.5}$ exposures in this study averaged 43 µg/m³ (with a range of 10–147 µg/m³), thus were much higher than those observed in the present study. The authors observed an association between birth weight, birth length, and head circumference, and $PM_{2.5}$ exposure in the second trimester of pregnancy. A reduction in birth weight at an increased exposure from 10 to 50 µg/m³ of 140 grams was estimated.

The hypothesised effect of air pollutants on reproductive health relate to a decreased in utero oxygen supply, resulting from a reduction of oxygen carrying capacity induced by air pollution.[4] Another possibility is that the production of free radicals induced by air pollution might cause an inflammatory response, increasing blood viscosity.[18 19] Suboptimal placenta perfusion from blood viscosity changes may cause adverse pregnancy outcomes, including low birth weight and preterm birth.[20] The possible biological mechanisms involved in the reduction in birth weight associated with maternal exposure to air pollution are likely to vary according to the timing of this exposure. The implantation of the fetus and the formation of the placenta occur during the first trimester, while weight gain occurs predominantly during the third trimester. In the first trimester genetic mutations are generally considered the most important cause of placental abnormalities, and in the second and third trimesters complex vascular alterations are considered to be the main cause of placental abnormalities and consequent fetal growth retardation.[21] Pollutants are recognised as being able to have an effect on both dimensions.[21] The effect of air pollutant exposure during pregnancy on birth weight has a plausible biological basis; however, the reported studies fail to show consistency in pollutants and periods during pregnancy where an effect occurs.

The lack of consistency in findings may be due to difficulties distinguishing between pollutants. In this study, when examining multiple pollutant models it appears that NO_2 is the most important pollutant, despite the fact that NO_2 levels in Sydney are well below the national standard. The lack of consistency in findings among countries may also be accounted for by differences in pollutant levels and mix. Air quality in the Sydney metropolitan area is generally good. Concentrations of pollutants measured at air monitoring sites in Sydney are typically well below standards, although seasonal conditions can cause the occasional exceedence of the national air quality standards.[22] In Sydney, motor vehicles are a major source of air pollutants, although solid fuel heating for domestic purposes in winter and occasional bush fires in summer also add to the fine particle concentrations.[22] Given the number of comparisons made in this study, the positive findings may be spurious. It is important, then, to corroborate these finding with future research.

Future research should involve the formation of individual testable hypotheses to avoid the problem of multiple tests. Research should also focus on obtaining higher quality exposure data, for example, modelling air pollution concentrations to smaller geographical areas using emission inventory, traffic density, and meteorological data in the presence of improved time activity data.

In conclusion, we observed that CO and NO_2 concentrations, particularly in the second trimester of pregnancy, have an adverse effect on birth weight. We also observed that $PM_{2.5}$ and PM_{10} concentrations in the second trimester of pregnancy have a small adverse effect on birth weight. While the number of studies in this area is accumulating, a

Table 6 Key second trimester findings of multivariate linear regression analysis (multiple linear regression coefficients (SE)) using multi-pollutant models and controlling for pollutant exposures in other pregnancy periods for babies born to women residing within 5 km of an air monitoring station; birth weight is expressed in grams

	Single pollutant model	95% confidence limits	Two pollutant models (PM₁₀ and CO)	95% confidence limits	Two pollutant models (PM₁₀ and NO₂)	95% confidence limits	Two pollutant models (CO and NO₂)	95% confidence limits	Two pollutant models (PM₁₀ and O₃)	95% confidence limits	Four pollutant model	95% confidence limits	Controlling for exposures in other pregnancy periods	95% confidence limits
PM₁₀	−4.28	−5.79 −2.77	−3.72	−6.29 −1.15	−2.65	−4.32 −0.98			−5.47	−7.06 −3.88	−3.27	−7.05 0.51	−3.03	−4.85 −1.21
NO₂	−33.85	−43.38 −24.32			−26.21	−37.46 −14.96	−26.74	−45.75 −7.73			−9.91	−35.10 15.28	−25.26	−35.63 −14.89
CO	−28.87	−50.98 −6.76	−27.31	−55.30 0.68			−20.17	−43.12 2.78			−25.97	−54.15 2.21	−24.38	−47.33 −1.43
O₃	8.77	1.05 16.49							18.28	10.03 26.53	−14.81	−33.65 4.03	8.84	1.10 16.58

ppb, parts per billion (10^{-9}); ppm, parts per million (10^{-6}).
Units and averaging periods:
PM_{10} (µg/m³), 24 hour av
CO (ppm), 8 hour av
NO_2 (ppb), 1 hour max

consistent pattern of pollutants and exposure times is not emerging. Further research is required to corroborate our findings.

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