



Maternal exposure to fine particulate matter from a coal mine fire and birth outcomes in Victoria, Australia

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ABSTRACT

Introduction: The Hazelwood coal mine fire was an unprecedented event in Australian history that resulted in the surrounding towns in regional Victoria being covered in plumes of smoke and ash for six weeks in 2014. Evidence concerning adverse reproductive impacts associated with maternal exposure to ambient air pollution is expanding. Gaps remain regarding the relative impact of acute changes in outdoor air quality lasting days to months, such as that resulting from coal mine fires.

Methods: Routinely collected perinatal data was used to define a complete cohort of singleton babies born within the affected region. Maternal average, and peak, fine particulate matter (PM_{2.5}) was assigned to residential address at time of delivery using a chemical transport model. Maternal, infant, meteorological and temporal variables were adjusted for in final linear and log-binomial regression models.

Results: There were a total of 3591 singleton livebirths during the study period; 763 of which were in utero during the coal mine fire. Average PM_{2.5} exposure was 4.4 µg/m³ (median 1.9; IQR 2.1 µg/m³) and peak was 45.0 µg/m³ (median 30.4; IQR 35.1 µg/m³). There was no association between coal mine fire-attributable PM_{2.5} and fetal growth or gestational maturity outcomes. However, there was weak evidence that gestational diabetes mellitus was an effect modifier in the relationship between maternal PM_{2.5} exposure and birth weight. Babies born to exposed gestational diabetic mothers were 97 g heavier per 10 µg/m³ increase in average PM_{2.5} exposure (95%CI 74, 120 g). No association was observed among mothers without gestational diabetes.

Conclusion: Maternal exposure to fine particulate matter resulting from the 2014 Hazelwood coal mine fire did not appear to adversely effect fetal maturity. However, there was weak evidence of a trophic response among babies born to exposed mothers with gestational diabetes, a possible susceptibility that requires further exploration.

1. Introduction

Coal mine fires are widespread and thousands are currently burning, especially in India, China, and the USA. The number of coal mine fires has increased dramatically since the Industrial Revolution as a result of human activity such as land clearing, mining and anthropogenic climate change (Melody and Johnston, 2015). The health harms associated with exposure to air pollution resulting from coal mine fires is poorly characterised (Melody and Johnston, 2015). The paucity of evidence concerning discrete periods of poor air quality hinders the emergency and public health responses to such events, as was highlighted during the Hazelwood coal mine fire in Victoria, Australia. For six weeks in February and March 2014, the Hazelwood coal mine fire covered the town of Morwell and the surrounding region in smoke and

ash. The fire was an unprecedented event that produced some of the most extreme concentrations of fine particulate matter (PM_{2.5}; particulate matter < 2.5 µm in diameter) ever measured in Australia (Parliament of Victoria, 2014). As outlined by a parliamentary enquiry into the response to the fire, the lack of available evidence regarding short- and long-term health harms associated with coal fire smoke exposure considerably hindered the public health response (Parliament of Victoria, 2014).

Maternal exposure to ambient air pollution is a well-recognised risk factor for adverse neonatal and obstetric outcomes, including fetal growth restriction, gestational maturity, hypertensive disorders of pregnancy and gestational diabetes mellitus (GDM) (Li et al., 2017; Zhu et al., 2015; Fleisch et al., 2016; Pedersen et al., 2014). Many previous studies have explored this association by gestational month or trimester

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(Li et al., 2017). However, relatively little is understood about the impact of maternal exposure to short- to medium-term periods of air pollution (days to months) resulting from severe smoke events, such as that caused by coal mine fires, wildfires or agricultural fires, on birth outcomes.

A handful of studies have explored the impact of maternal exposure to short- to medium-term episodes of poor air quality resulting from wildfires, agricultural fires, deforestation fires and particulate air pollution from volcanic eruptions, on neonatal outcomes such as birth weight, low birth weight, preterm birth and gestational length. Synthesising findings from these studies is challenging, owing to the limited number of studies and their heterogeneous classifications of exposure and/or outcome. However, findings suggest an adverse association with fetal growth and possibly preterm birth. Exposure in the second and third trimester appeared to be of greatest relative importance (Prass et al., 2012; O'Donnell and Behie, 2015; Jayachandran, 2009; Balsa et al., 2016; Candido da Silva et al., 2014; Holstius et al., 2012; Rangel and Vogl, 2016).

The need to characterise the relationship between short- to medium-term severe smoke events on neonatal outcomes is exemplified by the current lack of knowledge to inform emergency and public health responses to such events, as well as projections of increased frequency and severity of fires with a changing climate (Fried et al., 2008; Stracher and Taylor, 2004). The primary aim of this study was to explore the association between maternal exposure to coal-mine fire attributable PM_{2.5} and neonatal outcomes, including fetal growth and gestational maturity. The secondary aim was to determine whether any subgroups within the pregnant population were more susceptible to adverse neonatal outcomes in association with coal mine fire smoke exposure, such as extremes in reproductive age, gestational diabetes mellitus, hypertensive disorders of pregnancy, maternal smoking in pregnancy or infant sex.

2. Methods

Ethics approval for this study was obtained from the Tasmania Human Research Ethics Committee (ref H0015033).

2.1. Data

2.1.1. Pregnancy and delivery data

We analysed liveborn, singleton births to mothers resident in the Latrobe Valley from 1st March 2012 to 31st December 2015 that were recorded in the Victorian Perinatal Data Collection (VPDC). The VPDC is a statutory collection of information about all births occurring in Victoria, Australia. The VPDC comprises data on maternal characteristics, pregnancy care, birth and neonatal outcomes collected for all births of > 20 weeks gestation or at least 400 g if the gestation is unknown, usually by a midwife. Validation against medical records indicates birth weight, and estimated date of confinement, are recorded accurately for 95.8%, and 91.5%, of records respectively (Flood et al., 2017).

The outcomes of interest were fetal growth and maturity, namely birth weight, term low birth weight (tLBW), small for gestational age (SGA), large for gestational age (LGA), gestational maturity and preterm birth (PTB). Continuous outcomes included birth weight, which was measured in grams, and gestational age which was measured as completed weeks of pregnancy. Dichotomous terms included term low birth weight, which was defined as birth weight < 2500 g at > 37 weeks gestation. SGA was defined as a birth weight < 10th percentile for gender and gestational age, and LGA was defined as a birth weight > 90th percentile for gender and gestational age. 'Appropriately' grown infants were defined as those with a birth weight ≥ 10th and ≤ 90th percentile for gender and gestational age. Birth weight percentiles were defined using published Australian percentiles (Dobbins et al., 2012). Preterm birth was defined as birth occurring

before 37 weeks of gestation. All outcomes were dichotomous, with the exception of birth weight and gestational age, which were continuous outcomes.

2.1.2. Exposure data

For the purposes of this analysis, the Hazelwood coal mine fire lasted from 9 February to 31 March 2014 (51 days). Although the fire was declared safe on 26 March 2014, small amounts of smoke emissions continued into the following week, so exposure modelling was continued until 31 March 2014. Average daily concentration of particulate matter with an aerodynamic diameter < 2.5 μm (PM_{2.5}) directly attributable to the mine fire was the primary exposure metric of interest. Peak PM_{2.5} was the secondary exposure metric, which represents the highest 24-h average PM_{2.5} exposure during the coal mine fire period.

The average and peak daily PM_{2.5} concentrations for the 51-day period were determined using a chemical transport model developed by collaborators at the Commonwealth Scientific and Industrial Organisation (CSIRO) Oceans & Atmosphere Flagship. The model is a high resolution exposure model that estimates PM_{2.5} at an hourly time step and a one-by-one kilometre spatial resolution (Emmerson et al., 2016). The full model included background PM_{2.5} from natural sources, vehicular and power station emissions, landscape fires and the mine fire. The difference between the CSIRO model run with, and without, emissions from the mine fire was used to determine the concentration of PM_{2.5} specific to the mine fire. No air pollution data was available for the first week of the fire, when air quality was the poorest. The modelled estimates in the first week rely on a number of data sources, including mass of coal burnt, fire activity and emission factors. Modelled exposure correlated well with ground-based empirical monitoring implemented in the second week of the fire. Quantile-quantile plots of modelled versus observed hourly PM_{2.5} showed good correlation. Full details and validity of the model is published elsewhere (Emmerson et al., 2016). Exposure was assigned by first determining babies who were in utero during the coal mine fire period. The estimated date of conception was calculated by subtracting 266 days from the estimated date of confinement. Babies that were not in utero at all during the coal mine fire, included those born before the fire started on 9 February 2014 or conceived after smoke impacts of the fire ended on 31 March 2014. Babies in this group were assigned an average and peak daily smoke-derived PM_{2.5} value of zero. Those who had partial exposures due to conception or birth during the fire event were only assigned PM_{2.5} exposure estimates PM_{2.5} for the days during the fire period that they were in utero. Trimester at the beginning of the coal mine fire, when air quality was the poorest, was also determined to assess for potential sensitive windows of exposure.

Exposure was assigned according to maternal residence at delivery at the geographically detailed level of Statistical Area Level 1 (SA1), as per the 2011 Australian Bureau of Statistics Australian Standard Geographical Classification. SA1s are the smallest geographical classification and contain approximately 400 individuals. SA1s aggregate directly into SA2s, which are medium-sized geographical classifications representing communities that interact socially and economically (Australian Bureau of Statistics, 2016).

2.1.3. Weather and other controls

We obtained minimum and maximum daily temperature data from the Australian Government Bureau of Meteorology for the Morwell station; the single station that serves the Latrobe Valley region (Location 38.23°S, 146.41°E). The 24-h mean temperatures were calculated. We calculated trimester-specific averages: the first trimester ran from conception to day 84, trimester two ran from day 85 to day 113 and trimester three ran from day 114 to birth. Season of conception and year of conception were also determined to capture underlying temporal and seasonal trends in birth outcomes.

We addressed potential confounding by considering a priori several maternal, pregnancy-related, infant, meteorological and temporal

Table 1
Descriptive statistics by exposure to coal mine fire.

	Total cohort N = 3591	In utero during coal mine fire N = 763	Not in utero during coal mine fire N = 2828
	n (%)	n (%)	n (%)
Infant characteristics			
Female gender	1768 (49.2)	371 (48.6)	1397 (49.4)
Aboriginal and/or Torres Strait Islander	157 (4.4)	34 (4.5)	123 (4.4)
Admitted to special care nursery	792 (22.1)	179 (23.5)	613 (23.7)
Admitted to neonatal intensive care unit	43 (1.2)	5 (0.67)	38 (1.3)
Neonatal death prior to discharge	7 (0.19)	1 (0.13)	6 (0.2)
Maternal characteristics			
Maternal smoking in early pregnancy (< 20 weeks)	897 (25.0)	199 (26.1)	698 (24.7)
Maternal smoking in late pregnancy (> 20 weeks)	638 (17.8)	159 (20.8)	479 (16.9)
Country of birth Australia	3236 (90.1)	691 (90.6)	2545 (90.0)
Aboriginal and/or Torres Strait Islander	119 (3.3)	24 (3.2)	95 (3.4)
Pregnancy and labour characteristics			
Nulliparous	1417 (39.5)	305 (40.0)	1112 (39.3)
Spontaneous onset of labour	1638 (45.6)	328 (43.0)	1310 (46.3)
Caesarean section birth	956 (26.6)	223 (29.2)	742 (26.2)
Hypertensive disorder of pregnancy	169 (4.7)	27 (3.5)	142 (5.0)
Gestational diabetes mellitus	228 (6.4)	61 (8.0)	167 (5.9)
Birth outcomes			
tLBW	71 (2.0)	10 (1.3)	61 (2.2)
SGA	313 (8.8)	58 (7.6)	255 (9.0)
LGA	434 (12.1)	95 (12.5)	339 (12.0)
PTB	294 (8.2)	66 (8.7)	228 (8.1)
PTB – spontaneous onset	159 (4.4)	32 (4.2)	127 (4.5)
PTB – iatrogenic onset ^a	135 (3.8)	34 (4.5)	101 (3.6)

Abbreviations: LGA, large for gestational age; PTB, preterm birth; SGA, small for gestational age; tLBW; term low birthweight.

^a Iatrogenic preterm birth defined as birth occurring before 37 weeks completed gestation and labour type coded as ‘induced’ or ‘no labour.’

characteristics. Maternal characteristics included mother's age (high-risk (≤ 19 years and ≥ 35 years old) vs. low risk (20 to 34 years old)) and maternal socioeconomic position (Australian Bureau of Statistics Index of Relative Socioeconomic Disadvantage quintile assigned to the maternal residence at the level of SA1). Pregnancy-related characteristics included: parity (nulliparous, 1–2, 3 and above); hypertensive disorder during pregnancy (pre-existing maternal hypertension complicating pregnancy, pregnancy-induced hypertension, hypertension, preeclampsia, eclampsia; ICD10AM codes O10-16); diagnosis of GDM (yes/no; ICD10AM code O24); smoking in early pregnancy (first 20 weeks; yes/no), smoking in late pregnancy (last 20 weeks; yes/no); method of birth (Caesarean section, vaginal delivery) and labour onset (spontaneous, iatrogenic). Infant characteristics included infant sex (male, female, indeterminate) and Aboriginality (Aboriginal and/or Torres Strait Islander, non-Aboriginal, unknown). Meteorological characteristics included the mean daily temperature ($^{\circ}\text{C}$) for each trimester. Temporal characteristics included season of conception (winter, spring, summer and autumn) and year of conception.

We included singleton livebirths in our analysis, as pregnancies characterised by multiple births are systematically different from singleton births. We were not able to distinguish multiple pregnancies within the study period to the same mother; therefore, eligible births may include more than one pregnancy to the same woman.

2.1.4. Missing data

Missing data were handled using multiple imputation by chained equations (MICE package in R). Given the low proportion of missing data, twenty imputed datasets were considered adequate (White et al., 2011). Covariates included in the multivariable regression models were used as imputer variables. Regression models were fitted using the imputed data.

2.1.5. Statistical analysis

The association between maternal exposure to coal-mine fire attributable $\text{PM}_{2.5}$ and continuous outcomes, including birth weight and

gestational maturity, were estimated using multivariable linear regression. The relative risk associated with maternal exposure to coal-mine fire attributable $\text{PM}_{2.5}$ and dichotomous outcomes, including SGA, LGA, tLBW and PTB, were estimated using multivariable log-binomial regression. Covariates that were included in the model were chosen if there was robust a priori evidence and/or if there was evidence that the covariate was associated with exposure, associated with the outcome and adjustment for the covariate altered the coefficient by $> 10\%$. Effect modification was explored for covariates where there was biological plausibility, including maternal age, smoking in pregnancy, gestational diabetes mellitus, hypertensive disorders of pregnancy, season of conception and infant sex, and a p -value of the interaction term in the model < 0.10 . Our model took the form:

$$Y = f(\alpha + \beta\text{PM}_{2.5} + \delta X + \kappa Y + \gamma Z + \theta \text{Qt})$$

where Y is birth weight (grams), gestational maturity (weeks), tLBW, SGA, LGA and PTB. And $f(\cdot)$ is a linear function where the outcome is birth weight or gestational maturity and a log-binomial function when analysing tLBW, SGA, LGA and PTB. The vector X represents maternal variables, Y represents fetal variables, Z represents temperature variables in each trimester and Qt represents indicator variables for season and year of conception. Residuals of continuous outcomes used in linear regression were assessed for normality, and the outcome transformed if required. We set the statistical significance level (α) at 0.05. Sensitivity analyses were conducted to examine the robustness of the main results, including different classification of maternal age and inclusion of stillbirths in the analysis. Marginal effects of regression models which included interaction terms were calculated and plotted using `gg effects` package (Ludecke, 2018). Marginal effects are useful for understanding and plotting the relationship between the exposure and the outcome at different levels of the interaction term. Statistical analysis was conducted using R (v 3.4.0) (R Core team, 2017).

3. Results

A total of 3591 singleton livebirths were included in the analysis; 763 (21%) of which were in utero during the coal mine fire. Table 1 outlines the descriptive statistics for the infant and maternal characteristics by exposure category. The median birth weight was 3460 g. Among term births, 2.0% were low birth weight. The proportion of preterm births for the full cohort was 8.2%. Median maternal age was 28 years. Approximately 6% of mothers had a diagnosis of GDM and 5.0% had a hypertensive disorder of pregnancy. Just under a quarter of mothers smoked in the first 20 weeks of pregnancy, and approximately one-fifth smoked in the latter half of pregnancy. There was minimal missing data; variables with the highest proportion of missing data were those relating to maternal smoking in early and late pregnancy; missing for 4.4% and 1.4% of the cohort respectively. Missing smoking data was imputed using MICE (see methods). A significant temporal trend was observed for birth weight and gestational age at birth during the study period, whereby birth weight and gestational length decreased with each study year (Supplementary Table 1). Associations of birth outcomes with infant, maternal and pregnancy-related variables, that are well-recognised as risk factors for adverse neonatal outcomes in the existing literature, were identified in our cohort. These included smoking in pregnancy, maternal socioeconomic disadvantage and Aboriginality (Supplementary Table 2). There was no evidence that maternal age, smoking in pregnancy, hypertensive disorders of pregnancy, season of conception or infant sex were effect modifiers of the relationship between the exposure and the outcomes of interest (data not shown).

The mean daily PM_{2.5} exposure attributable to smoke from the coal mine fire was 4.4 µg/m³ (median 1.9; IQR 2.1 µg/m³). The mean peak PM_{2.5} exposure was 45.0 µg/m³ (median 30.4; IQR 35.1 µg/m³) (Fig. 1). Of the 763 babies in utero during the fire, 227 had partial exposures; including 91 who were conceived during the fire and 136 who were born during the fire.

3.1. Continuous PM_{2.5} analysis

There was no evidence of an association between maternal exposure to coal mine fire-attributable PM_{2.5} and birth weight, tLBW, SGA, LGA, completed gestational weeks or PTB in both unadjusted and adjusted analyses (Table 2). Findings are also presented per IQR increase in Supplementary Table 3.

There was weak evidence that GDM was an effect modifier in the relationship between maternal PM_{2.5} exposure and birth weight (GDM*average PM_{2.5} *p* value = 0.044 and GDM*peak PM_{2.5} *p* value = 0.094) (Table 3). Among pregnant women with a diagnosis of GDM, 10 µg/m³ increases in average fire-attributable PM_{2.5} was associated with a 97 g increase in birth weight (95%CI 74, 120 g). Similarly, 10 µg/m³ increases in peak fire-attributable PM_{2.5} were associated with a 107 g increase in birth weight (95%CI 74, 141 g). Among pregnant women without a diagnosis of GDM, average and peak fire-attributable PM_{2.5} were not significantly associated with birth weight. Fig. 2 demonstrates the independent association between particulate matter exposure and birthweight by GDM status (Fig. 2).

3.2. Categorical PM_{2.5} analysis

To understand whether a dose-response relationship was present, average and peak PM_{2.5} exposure were categorised into quartiles of exposure. Similar to findings for the continuous PM_{2.5} analysis, there were no associations between quartile increases in average or peak PM_{2.5} and birth weight, tLBW, SGA, LGA, completed gestational weeks or PTB (Table 4). However, when considering GDM as an effect modifier of the relationship between coal mine fire attributable PM_{2.5} and birth weight, there was evidence for an effect at the highest quartile of exposure for both average and peak exposure (GDM*Quartile 4 average

PM_{2.5} *p* = 0.04 and GDM*Quartile 4 peak PM_{2.5} *p* = 0.04) (Table 5). Among women with GDM, the highest quartile of average PM_{2.5} exposure was associated with a 293 g increase in birth weight (95%CI 109, 479 g) compared to the lowest quartile of exposure. Similarly, among women with GDM, the highest quartile of peak PM_{2.5} exposure was associated with a 284 g increase in birth weight (95%CI 105, 462 g) compared to the lowest quartile of exposure (Fig. 3). In women without GDM, quartile increases in average and peak PM_{2.5} were not associated with birth weight, nor was a trend evident.

3.3. Trimester-specific analysis

To determine whether there were any sensitive exposure windows, we examined whether the relationship between coal mine fire attributable PM_{2.5} and neonatal outcomes varied by trimester at the start of the fire. There was no significant relationship between timing of exposure and the neonatal outcomes of interest. However, there was a trend that did not attain statistical significance, whereby exposure to increasing average and peak PM_{2.5} exposure in the first trimester was associated with decrements in birth weight (Supplementary Fig. 1).

3.4. Sensitivity analysis

In our main analysis, we adjusted for maternal age as a dichotomous outcome (high-risk (≤ 19 years and ≥ 35 years old) vs. low risk (20 to 34 years old)). As a sensitivity analysis, we considered maternal age as a continuous outcome and as a three-level categorical factor (19 and younger; 20 to 24; and 35 years and older) and repeated the adjusted analyses. Re-classification of maternal age in this way did not alter the findings. In the main analysis, we excluded stillbirths due to difficulty in determining timing of outcome in relation to exposure. There were a total of 21 stillbirths in the cohort (0.6%). As a sensitivity analysis, we repeated the analyses with stillbirths included, which did not alter the findings.

4. Discussion

This is the first study to explore the association between maternal exposure to coal mine fire attributable PM_{2.5} and fetal growth and gestational maturity outcomes. In our cohort, well-characterised risk factors for adverse neonatal outcomes, including smoking in pregnancy, Aboriginality and socioeconomic disadvantage were identified. We observed no clear association between maternal exposure to fine particulate matter resulting from the coal mine fire and fetal growth and maturity outcomes. However, there was some evidence that maternal exposure to average coal mine fire-attributable PM_{2.5} was associated with increases in birth weight among women with GDM.

There is increasing evidence outlining an association between ambient PM_{2.5} air pollution and diabetes mellitus (Bowe et al., 2018) and to a lesser extent, GDM (Malmqvist et al., 2013). Large cohort studies have reported an association between maternal exposure to ambient PM_{2.5}, nitrogen oxide, ozone and sulphur dioxide and increased odds of GDM or impaired glucose tolerance (Malmqvist et al., 2013; Hu et al., 2015; Robledo et al., 2015; Fleisch et al., 2014). Fleisch et al. (2016) found the odds of GDM associated with ambient PM_{2.5} exposure was age-specific, observed in teenage pregnant women only (Fleisch et al., 2016). No study to date has reported maternal GDM as an effect modifier of the relationship between air pollution and birth weight.

Babies born to mothers with GDM are at an increased risk of macrosomia, the risk directly proportional to maternal hyperglycaemia (HAPO Study Cooperative Research Group, 2008). Although not yet described elsewhere, it is biologically plausible that GDM may act as an effect modifier for the relationship between air pollution and birth weight. It has been proposed that air pollution alters glucose tolerance and homeostasis by causing endothelial dysfunction, immune response alterations in visceral adipose tissues, alterations in insulin

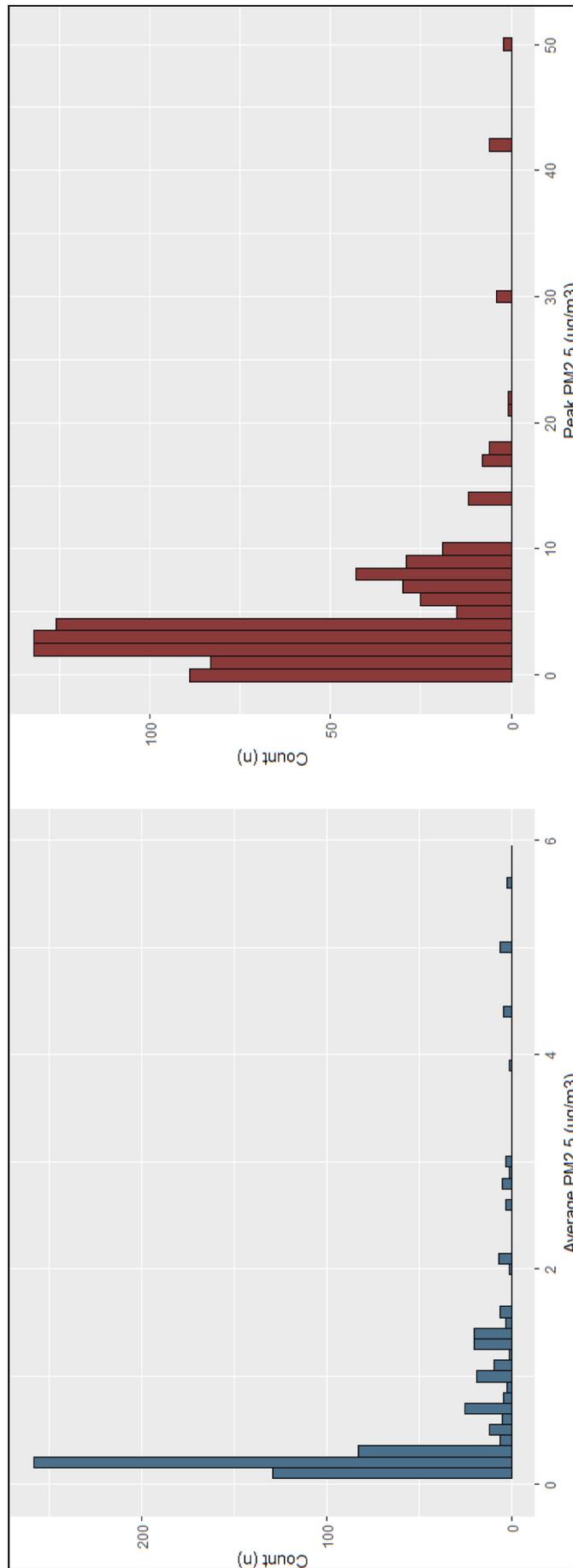


Fig. 1. Average and peak coal mine fire-attributable PM_{2.5} exposure among those in utero during the fire.

Table 2
Association between maternal exposure to coal mine fire-attributable PM_{2.5} and neonatal outcomes.

Outcome	Average PM _{2.5} (per 10 µg/m ³)		Peak PM _{2.5} (per 10 µg/m ³)	
	Crude mean difference (95%CI); <i>p</i> value	Adjusted ^a mean difference (95%CI); <i>p</i> value	Crude mean difference (95%CI); <i>p</i> value	Adjusted ^a mean difference (95%CI); <i>p</i> value
Birth weight (grams)	−27.5 (−77.1, 22.1); 0.27	6.81 (−42.58, 56.21); 0.79	−2.8 (−9.0, 3.3); 0.37	1.42 (−4.80, 7.63); 0.66
Completed gestational weeks	−2.34 (−4.17, 2.55); 0.37	0.96 (−3.36, 3.63); 0.88	−0.79 (−1.45, 0.93); 0.41	0.48 (−1.15, 1.33); 0.77
	Crude RR (95%CI); <i>p</i> value	Adjusted ^a RR (95%CI); <i>p</i> value	Crude RR (95%CI); <i>p</i> value	Adjusted ^a RR (95%CI); <i>p</i> value
tLBW	1.14 (0.72, 1.80); 0.57	0.98 (0.58, 1.63); 0.93	1.00 (0.93, 1.07); 0.95	0.99 (0.92, 1.06); 0.71
SGA	1.14 (0.92, 1.41); 0.23	1.06 (0.86, 1.31); 0.57	1.01 (0.98, 1.04); 0.47	1.00 (0.97, 1.03); 0.89
LGA	1.09 (0.91, 1.31); 0.36	1.14 (0.90, 1.44); 0.29	1.01 (0.98, 1.03); 0.56	1.01 (0.98, 1.04); 0.43
PTB	1.04 (0.81, 1.35); 0.74	0.97 (0.75, 1.27); 0.85	1.01 (0.97, 1.04); 0.72	1.00 (0.96, 1.03); 0.86

Abbreviations: LGA, large for gestational age; PTB, preterm birth, RR, relative risk; SGA, small for gestational age; tLBW, term low birth weight.

^a Adjusted for infant sex, infant aboriginality, maternal smoking in early pregnancy, maternal smoking in late pregnancy, maternal socioeconomic status, maternal age, season of conception, year of conception, mean ambient temperature in Trimester 1, 2 and 3.

transduction, increasing sympathetic nervous system activity and increasing insulin sensitivity (Eze et al., 2015). Women with GDM may be more susceptible to such challenges to glucose homeostasis, leading to further insulin resistance and hyperglycemia, which in turn are somatotropic to the developing fetus. While the evidence for effect modification in our study was modest, the relatively low number of women exposed to the highest quartiles of fine particulate matter may have limited our power. This possible relationship deserves further exploration.

Few studies have explored maternal exposure to a severe smoke event of medium-term duration and fetal growth outcomes. Among published studies exploring abrupt changes in ambient air quality, birth weight is the most commonly reported outcome and overall findings suggest air pollution is associated with decrements in birth weight. A study of Californian wildfires of 20 days duration in 2003 found infants in utero in their second or third trimester during the event, were between 7 and 9.7 g lighter than those not in utero in contemporaneous years (Holstius et al., 2012). Similarly, maternal exposure to Amazon deforestation fires was associated with reduced birth weight in male infants (Prass et al., 2012). Conversely, two studies have reported significant increases in birth weight in association with maternal exposure to severe smoke events, the mechanism of which has been unclear (Balsa et al., 2016; O'Donnell and Behie, 2015). Balsa et al. (2016)

found that maternal exposure to PM₁₀ elevations resulting from volcanic eruptions in the second trimester was associated with an increase in birth weight of 13.1 g (95%CI 4.07, 22.13) per 10 µg/m³ increase (Balsa et al., 2016). Similarly, a study exploring the association between maternal residence in areas severely affected by wildfires in Canberra, Australia, found that male infants born to mothers in severely affected areas were an average of 197 g heavier than those born to mothers resident in moderately affected areas (*p* < 0.003) (O'Donnell and Behie, 2015). Similarly, studies exploring tLBW have reported mixed findings (Balsa et al., 2016; Candido da Silva et al., 2014). All studies have a number of important limitations, including possible residual confounding and non-differential exposure misclassification. To date, no study has examined the association between maternal exposure to a severe smoke event of medium-term duration and SGA or LGA.

We did not observe a relationship between maternal exposure to coal mine fire-attributable to PM_{2.5} and gestational maturity outcomes, including completed gestational weeks or PTB. At odds with our findings, Balsa et al. (2016) found exposure to PM₁₀ elevations resulting from volcanic eruptions in the third trimester was associated with increased odds of PTB (OR 1.10; 95%CI 1.03, 1.19 per 10 µg/m³ increase in PM₁₀). However, consistent with our findings, an Australian study of bushfire exposure found no relationship between maternal residence in severely affected areas and gestational length (O'Donnell and Behie,

Table 3
The relationship between average and peak maternal PM_{2.5} exposure and birth weight with maternal Gestational Diabetes status as an interaction term.

	Birth weight Mean difference (95%CI); <i>p</i> value
Birth weight~β ₀ + AveragePM _{2.5} + AveragePM _{2.5} *GDM + covariates	
Intercept	3556.81 (2973.27, 4140.34); < 0.0001
Average PM _{2.5} (10 µg/m ³)	−16.54 (−75.67, 42.60); 0.58
GDM	−41.94 (−122.32, 38.45); 0.31
Interaction term: Average PM _{2.5} *GDM	113.77 (2.95, 224.60); 0.04
Birth weight~β ₀ + PeakPM _{2.5} + PeakPM _{2.5} *GDM + covariates	
Intercept	3568.85 (2982.58, 4155.11); < 0.0001
Peak PM _{2.5} (10 µg/m ³)	−0.87 (−8.64, 6.90); 0.83
GDM	−41.96 (−123.20, 39.29); 0.31
Interaction term: Peak PM _{2.5} *GDM	11.60 (−1.96, 25.16); 0.09

Adjusted for infant sex, infant aboriginality, maternal smoking in early pregnancy, maternal smoking in late pregnancy, maternal socioeconomic status, maternal age, season of conception, year of conception, mean ambient temperature in Trimester 1, 2 and 3. Abbreviations: GDM, Gestational Diabetes Mellitus.

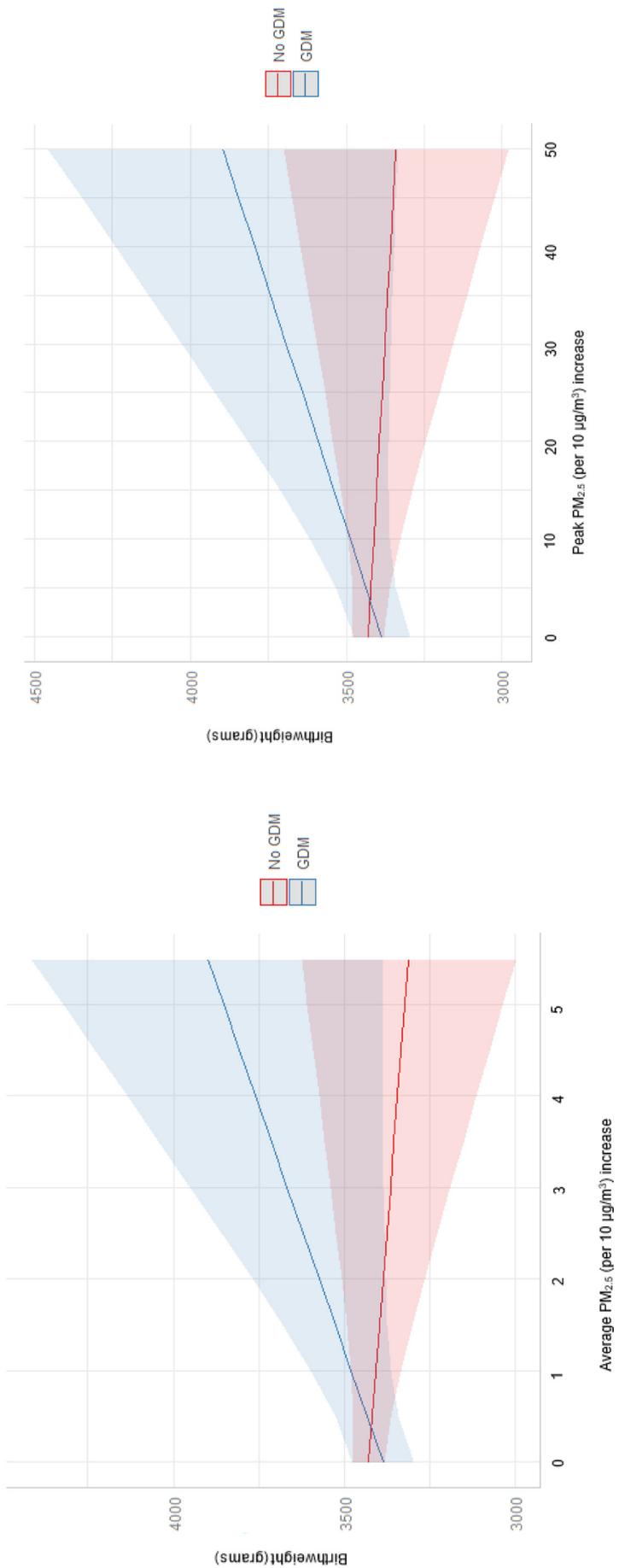


Fig. 2. Maternal PM_{2.5} exposure and birth weight by maternal gestational diabetes mellitus status.

Table 4
The relationship between quartile range increases in average PM_{2.5} and neonatal outcomes.

	Birth weight (grams)	Completed gestational weeks	tLBW	SGA	LGA	PTB
	Mean difference (95%CI); p value	Mean difference (95%CI); p value	RR (95%CI); p value	RR (95%CI); p value	RR (95%CI); p value	RR (95%CI); p value
Quartile 1 (< 0.89 µg/m ³)	Ref	Ref	Ref	Ref	Ref	Ref
Quartile 2 (0.89 to < 1.92 µg/m ³)	74.76 (-13.41, 162.94); 0.09	4.38 (-1.66, 6.41); 0.09	0.81 (0.25, 2.64); 0.72	0.55 (0.30, 1.03); 0.06	0.97 (0.63, 1.48); 0.87	0.67 (0.38, 1.19); 0.17
Quartile 3 (1.92 to < 3.00 µg/m ³)	13.06 (-77.32, 103.44); 0.78	2.01 (-4.30, 5.15); 0.73	0.36 (0.05, 2.66); 0.32	0.79 (0.46, 1.34); 0.38	1.08 (0.72, 1.62); 0.71	1.01 (0.60, 1.69); 0.97
Quartile 4 (≥ 3.00 µg/m ³)	1.04 (-85.72, 87.80); 0.98	2.20 (-4.10, 5.14); 0.66	1.32 (0.55, 3.18); 0.53	1.19 (0.80, 1.78); 0.40	0.97 (0.64, 1.47); 0.88	0.96 (0.60, 1.55); 0.87

Adjusted for infant sex, infant aboriginality, maternal smoking in early pregnancy, maternal smoking in late pregnancy, maternal socioeconomic status, maternal age, season of conception, year of conception, mean temperature in Trimester 1, 2 and 3.

Abbreviations: LGA, large for gestational age; PTB, preterm birth, RR, relative risk; SGA, small for gestational age; tLBW, term low birth weight.

Table 5
Relationship between quartile increases in average and peak maternal PM_{2.5} exposure and birth weight with maternal Gestational Diabetes status as an interaction term.

	Birth weight (grams) Mean difference (95%CI); p value
Birth weight~β ₀ + AveragePM _{2.5} Quartile + AveragePM _{2.5} Quartile*GDM + covariates	
Intercept	3696.16 (3099.6, 4292.70); < 0.0001
Quartile average PM _{2.5}	
Q2	70.48 (-20.75, 161.70); 0.13
Q3	29.15 (-65.78, 124.07); 0.55
Q4	-24.68 (-114.94, 65.59); 0.59
GDM	-41.85 (-129.48, 45.78); 0.35
Interaction term: Average PM _{2.5} Q2*GDM	94.79 (-231.27, 420.86); 0.57
Interaction term: Average PM _{2.5} Q3*GDM	81.38 (-245.54, 408.30); 0.63
Interaction term: Average PM _{2.5} Q4*GDM	318.31 (17.91, 618.71); 0.04
Birth weight~β ₀ + Peak PM _{2.5} Quartile + PeakPM _{2.5} Quartile*GDM + covariates	
Intercept	3590.85 (2970.80, 4150.90); < 0.0001
Quartile Peak PM _{2.5}	
Q2	18.00 (-70.84, 106.85); 0.69
Q3	39.76 (-53.31, 132.83); 0.40
Q4	-26.68 (-119.08, 65.73); 0.57
GDM	-44.78 (-131.95, 42.40); 0.31
Interaction term: Peak PM _{2.5} Q2*GDM	238.11 (-139.22, 615.44); 0.21
Interaction term: Peak PM _{2.5} Q3*GDM	67.92 (-249.15, 384.99); 0.67
Interaction term: Peak PM _{2.5} Q4*GDM	310.52 (16.87, 604.48); 0.04

Adjusted for infant sex, infant aboriginality, maternal smoking in early pregnancy, maternal smoking in late pregnancy, maternal socioeconomic status, maternal age, season of conception, year of conception, mean temperature in Trimester 1, 2 and 3.

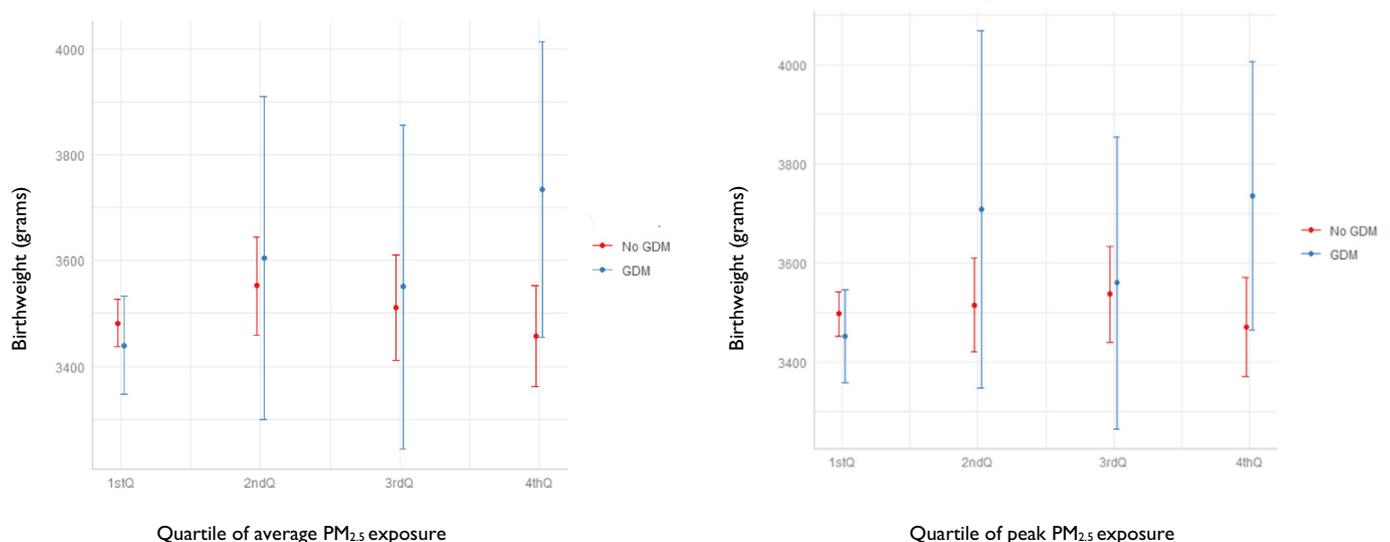


Fig. 3. Quartile increases in maternal PM_{2.5} exposure and birth weight by maternal gestational diabetes mellitus status.

2015).

Strengths of this study include the complete nature of the cohort through the use of routinely collected data that have been previously validated (Flood et al., 2017). Exposed pregnancies were compared to those to women living in the same area before and after the coal mine fire. Additionally, while we were unable to assign exposure at residential address, we did assign exposure using a relatively small geographical unit (SA1). SA1s are small geographical units that contain approximately 400 individuals and in the town of Morwell, where air quality was the worst, span an average of 0.30 km² (Australian Bureau of Statistics, 2016). This use of a small geographical unit, rather than address, may have introduced an element of exposure misclassification. While coal smoke is a complex mix of pollutants, we focused on fine particulate matter as it is a useful marker of exposure and has a number of well-established health harms (Melody and Johnston, 2015). Limitations include that we were unable to account for residential mobility during the coal mine fire. However, the importance of residential mobility during pregnancy in introducing bias remains unclear. In a previous study of ambient air pollution, there was negligible benefit in accounting for residential mobility (Pereira et al., 2016). However, this may differ for an event such as the Hazelwood coal mine fire, which caused substantial community concern and distress and may have led some people to relocate for some or all of the event. Additionally, we were unable to account for the effect of maternal stress on birth outcomes as a potential confounder of the studied relationship. Pregnancy-specific stress has been demonstrated to be associated with adverse neonatal growth and maturity (Lobel et al., 2008). As we were interested specifically in PM_{2.5} attributable to the fire, we did not include background air pollution in our exposure estimates, which are largely driven by traffic and industrial activities. Ambient PM_{2.5} concentrations were steady during the fire and on average approximately 6 µg/m³ (Emmerson et al., 2016). We did not have data on PM composition, and are therefore unable to ascertain specific health effects relating to composition. Additionally, the power of our study may be limited by the relatively small size of the cohort, as well as by the relatively modest mean and peak PM_{2.5} exposure for a subset of our cohort. However, as a study exploring a fire event in a regional setting, our sample size is fixed and utilising an administrative dataset attempts to minimise the sample size limitation by capturing the majority of the population. We were unable to adjust for potentially important covariates, including maternal pre-pregnancy BMI or height, as accurate and complete data for these variables were not available in the routinely collected data. Additionally, the diagnostic threshold for GDM was lowered across Australia during the study period, leading to an increased overall prevalence of GDM in the population. Timing of the adoption of the new diagnostic criteria varied by health service and provider and, as such, it is difficult to adjust for this change entirely. However, we have adjusted for year of birth to account for temporal patterns in the data. Timing of onset and severity of GDM were not recorded and therefore it was not possible to determine timing of GDM onset relative to coal mine fire exposure. Finally, it is possible that we did not observe an association between exposure to fine particulate matter emissions from the coal mine fire and fetal growth and maturity outcomes due to a lack of statistical power; our sample size was relatively small but represents a complete capture of the affected region.

5. Conclusion

We found no evidence of an association between maternal exposure to fine particulate matter resulting from a coal mine fire and fetal growth and maturity outcomes. Additionally, there was no clear evidence that the timing of exposure was important. However, women with GDM appeared to be more susceptible to possible trophic effects of exposure. Further work is required to explore GDM as a possible effect modifier of the relationship between maternal exposure to air pollution and birth weight. Characterising this relationship further would assist

in informing public health responses to severe smoke events in the future.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.envint.2019.03.028>.

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