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Author/s:

Shao, J;Zosky, GR;Hall, GL;Wheeler, AJ;Dharmage, S;Melody, S;Dalton, M;Foong, RE;O'Sullivan, T;Williamson, GJ;Chappell, K;Abramson, MJ;Johnston, FH

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Shao Jingyi (Orcid ID: 0000-0003-0794-2810)
Zosky Graeme (Orcid ID: 0000-0001-9039-0302)
Hall Graham (Orcid ID: 0000-0002-6217-9494)
Dharmage Shyamali (Orcid ID: 0000-0001-6063-1937)
Abramson Michael (Orcid ID: 0000-0002-9954-0538)

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Early life exposure to coal mine fire smoke emissions and altered lung function in young children

Jingyi Shao¹, Graeme R. Zosky^{1,2}, Graham L. Hall³, Amanda J. Wheeler^{1,4}, Shyamali Dharmage⁵, Shannon Melody¹, Marita Dalton¹, Rachel E. Foong³, Tierney O'Sullivan¹, Grant J Williamson⁶, Katherine Chappell¹, Michael J. Abramson⁷, Fay H. Johnston¹

¹Menzies Institute for Medical Research, University of Tasmania, Hobart, Tasmania 7000, Australia; ²School of Medicine, Faculty of Health, University of Tasmania, Hobart, Tasmania 7000, Australia; ³Children's Lung Health, Telethon Kids Institute and School of Physiotherapy and Exercise Science Curtin University, West Perth, Western Australia 6872, Australia; ⁴Behaviour, Environment and Cognition Research Program, Mary MacKillop Institute for Health Research, Australian Catholic University, Level 5, 215 Spring Street, Melbourne, Victoria 3000, Australia; ⁵Allergy and Lung Health Unit, Melbourne School of Population and Global Health, University of Melbourne, Carlton, Victoria 3052, Australia; ⁶School of Biological Sciences, University of Tasmania, Hobart, Tasmania 7000, Australia; ⁷Department of Epidemiology and Preventive Medicine, School of Public Health and Preventive Medicine, Monash University, Melbourne, Victoria 3004, Australia.

Correspondence: A/Prof Fay H. Johnston, Menzies Institute for Medical Research, University of Tasmania, 17 Liverpool Street, Hobart, Tasmania 7000, Australia. E-mail: Fay.Johnston@utas.edu.au

Summary at a glance

We found modest evidence for an association between infant exposure to elevated particulate matter during a six-week coal mine fire and reduced respiratory system

reactance measured three years after the fire. The magnitude of the association was small, but of potential clinical importance in the most severely exposed children.

Abbreviations

PM_{2.5}, particulate matter with an aerodynamic diameter less than 2.5 micrometers

FOT, forced oscillation technique

Rrs₅, resistance at a frequency of 5 Hz

Xrs₅, reactance at a frequency of 5 Hz

AX, the area under the reactance curve

SES, socio-economic status

CI, confidence interval

IQR, interquartile range

SD, standard deviation

Latrobe ELF Study, the Latrobe Early Life Follow-up Study

HHS, Hazelwood Health Study

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Abstract

Background and objective: Long-term respiratory risks following exposure to relatively short periods of poor air quality early in life are unknown. We aimed to evaluate the association between exposure to a six-week episode of air pollution from a coal mine fire in children aged less than two years, and their lung function three years after the fire.

Methods: We conducted a prospective cohort study. Individual exposure to 24-hour average and peak concentrations of particulate matter less than 2.5 micrometers in diameter (PM_{2.5}) during the fire were estimated using dispersion and chemical transport modelling. Lung function was measured using the forced oscillation technique, generating standardized Z scores for resistance, reactance at a frequency of 5Hz (Rrs₅; Xrs₅) and area under the reactance curve (AX). We used linear regression models to assess the associations between PM_{2.5} exposure and lung function, adjusted for potential confounders.

Results: 84 of the 203 infants originally recruited, aged 4.3±0.5 years, completed FOT testing. Median [IQR] for average and peak PM_{2.5} were 7.9 [6.8, 16.8] and 103.4 [60.6, 150.7] µg/m³, respectively. The mean±SD Z scores were Rrs₅ 0.56±0.80, Xrs₅ -0.76±0.88 and AX 0.72±0.92. After adjustment for potential confounders including maternal smoking during pregnancy, a 10 µg/m³ increase in average PM_{2.5} was significantly associated with worsening AX (β-coefficient, 0.260; 95%CI 0.019, 0.502), while the association between a 100 µg/m³ increase in peak PM_{2.5} and AX was borderline (0.166; 95%CI -0.002, 0.334).

Conclusion: Infant exposure to coal mine fire emissions could be associated with long-term impairment of lung reactance.

Key words: long-term effects, outdoor smoke, particulate matter, preschool children, respiratory function tests

Short title: Infant smoke exposure and lung function

Introduction

Short-term health impacts associated with exposure to fine particulate matter, a major pollutant generated by fires^[1], have been well characterised. There is consistent evidence associating short-term smoke exposure with increased physician visits, emergency department presentations and hospitalizations for respiratory diseases^[2-3]. However, the long-term health risks from relatively short, that is days to weeks in duration, air pollution episodes have not been characterised, especially in children^[3]. This represents an important gap in the available evidence because severe episodic exposure to fire smoke is likely to increase with climate change^[4].

Infants and young children are more susceptible to the respiratory impacts of air pollution exposure due to their less developed airways and immune system, and faster breathing rates compared with adults^[5]. The first two years of life is a critical window for lung growth^[6]. There is a small but growing body of evidence suggesting that long-term exposure to air pollutants during infancy could result in measurable respiratory health impacts later in life. For example, exposure to traffic-related air pollution during the first year of life has been associated with impaired lung function in both children and adolescents^[7-8]. However, evidence of long-term respiratory impacts from relatively short durations of air pollution exposure during infancy is extremely limited^[9]. One study investigating the Great Smog in London suggested that exposure to the Great Smog during the first year of life could increase the risk of childhood asthma^[10].

The Hazelwood coal mine fire was ignited by embers from wildfires in February 2014 in the Latrobe Valley, Victoria, Australia and lasted for 45 days. In this mine fire episodes of moderate to extreme air pollution were experienced in several nearby towns for days to weeks. The peak 24-hour average concentration of particulate matter with an aerodynamic diameter less than 2.5 μm ($\text{PM}_{2.5}$) reached 731 $\mu\text{g}/\text{m}^3$ at the closest town of Morwell, dramatically higher than the national air quality standard of 25 $\mu\text{g}/\text{m}^3$ ^[11-12]. The health harms resulting from exposure to smoke from coal mine fires could be comparable to those from forest and peat fires. There is a similar spectrum of toxic components, especially in smouldering fires, and the temporal patterns of exposure are similar – often being time limited but severe^[3].

We investigated the infants aged less than two years who were exposed to smoke from the mine fire with the aim of evaluating the association between the magnitude of smoke exposure and lung function three years after the fire.

Methods

Recruitment

This study was based on a prospective cohort study of 571 children who were born between 01/03/2012 and 31/12/2015 and resided in the Latrobe Valley at the time of the fire (see Supplementary Figure S1)^[13]. At recruitment (February to September 2016), the participating parent/carer of each child completed a baseline questionnaire on

sociodemographic, health and family characteristics. Only the 203 members of the cohort who were ≤ 2 years old at the time of the fire were old enough to attempt respiratory function testing and invited to participate in this study [Figure S1 in Supplementary Information]

The Tasmanian Health and Medical Human Research Ethics Committee (reference H14875) approved this study. Additional approval was received from the Human Research Ethics Committees of Monash University, Monash Health, and the University of Melbourne. All parents or caregivers of the studied participants provided signed consent forms for both the baseline survey and the clinical testing.

Exposure estimate

Hourly PM_{2.5} concentrations during the fire period from 09/02/2014 to 31/03/2014 were estimated using meteorological, dispersion and chemical transport modelling at a spatial resolution of $1 \times 1 \text{ km}^{[14]}$. The model quantitatively calculated PM_{2.5} emission rates at an hourly timestep based on parameters such as how much coal was burned using maps of the area and estimated emission factors. Personal exposures were then calculated for 24-hour average and peak periods based on participants' day/night locations.

Clinical testing

Children's lung function was evaluated three years after the fire, (March to July 2017), using the forced oscillation technique (FOT) (TremoFlo C-100 device, Thorasys, Montreal,

Quebec, Canada) according to ATS/ERS guidelines^[15]. We reported standardized Z scores for baseline Rrs and Xrs at a frequency of 5 Hz (Rrs₅ and Xrs₅), and the area under the reactance curve (AX)^[16]. We excluded measurements with artefacts such as mouth or tongue movement, leakage, swallowing, glottal closure or talking and those having a coherence of <90% at one or more frequencies. Three to five acceptable measurements with a coefficient of variation <10% were obtained for each child. [Supplementary material].

Covariates

All covariates were selected *a priori* according to the existing literature^[17-22] [Supplementary material].

Statistical analysis

We used Pearson's Chi-square test and Welch's t test for the comparisons of characteristics between our studied participants and the full cohort. We calculated β -coefficients and 95% confidence intervals (CIs) from multiple linear regression models to evaluate the associations between infant PM_{2.5} exposure and lung function with or without adjustment for *a priori* selected covariates. We chose the increments of 10 $\mu\text{g}/\text{m}^3$ for average PM_{2.5} and 100 $\mu\text{g}/\text{m}^3$ for peak PM_{2.5} (close to the interquartile ranges (IQRs) of average and peak PM_{2.5} in this study) to enable comparison with other air quality studies suggesting decreased lung function in children after a 10 and 71 $\mu\text{g}/\text{m}^3$ increase in average and peak PM_{2.5} exposure^[23-24]. Five participants (6.0%) had missing values for covariates. We used multiple imputation by chained equations to estimate missing data for

covariates^[25][Supplementary Table S1]. We conducted sensitivity analysis by excluding the participants with imputed data. Additionally, maternal smoking status during pregnancy was assessed as an interaction term in the multivariable regression models. We conducted stratified analysis by gender to assess the different effects of fire smoke exposure on males and females. We performed statistical analyses using R 3.5.0 (the R Foundation, Vienna, Austria). A p -value <0.050 was considered statistically significant.

Results

Participants' characteristics

Of the 203 children eligible for the study, the parents/carers of 137 provided consent for later clinical follow-up. Of these, 101 children attended the clinic and 85 (84.2%) successfully completed FOT testing. We excluded one participant from data analysis due to the poor quality of the FOT measurements (Figure 1).

Almost one fifth (17.9%) of the participants were exposed to maternal tobacco smoking while *in utero*, and two fifths (39.3%) had mothers with ≤ 12 years of education, i.e. completion of secondary education or less. Nearly a quarter (23.8%) of children lived in a house with a current smoker. The mean $\pm$ standard deviation (SD) age of the children at the time of FOT testing was 4.3 ± 0.5 years. The mean annual background $\text{PM}_{2.5}$ concentration in this area ($6.7 \mu\text{g}/\text{m}^3$) was lower than the national air quality standard of $8 \mu\text{g}/\text{m}^3$ ^[12] (Table 1).

Our participants had comparable characteristics with the entire cohort ($n=571$) in terms of gestational age, birthweight, gender, maternal alcohol or tobacco use during pregnancy, primary carer's education level and smoking status, maternal stress and breastfeeding duration (Chi-square or t test $p > 0.050$ for all comparisons; Supplementary Table S2).

$\text{PM}_{2.5}$ exposure during the fire period

The median [IQR] of the average and peak PM_{2.5} levels during the fire period were 7.9 [6.8, 16.8] and 103.4 [60.6, 150.7] µg/m³, respectively (Table 1). Children were exposed to a wide range of PM_{2.5} during the fire period as indicated by the large IQRs.

Lung function measures and risk factors

The mean±SD Z scores of baseline Rrs₅, Xrs₅ and AX were 0.56±0.80, -0.76±0.88 and 0.72±0.92, respectively. Three of the 84 children had Z scores for Rrs₅ ≥2, nine had Z scores for Xrs₅ ≤ -2 and six had Z scores for AX ≥2.

After adjustment for PM_{2.5} and other covariates, maternal smoking during pregnancy was strongly associated with impaired lung reactance, indicated by a decreased Xrs₅ (-1.152; 95%CI -1.708, -0.597; *p*=0.000) and increased AX (0.739; 95%CI 0.101, 1.377; *p*=0.026), while lower maternal education was associated with higher Xrs₅ (0.459; 95%CI 0.063, 0.855; *p*=0.026). Other covariates were not associated with any of the outcomes.

Infant fire PM_{2.5} exposure and lung function

In univariable analysis, PM_{2.5} was associated with Xrs₅ and AX, but not with Rrs₅ (Table 2).

Multivariable model suggested a linear relationship with no threshold for AX. Each 10 µg/m³ increase in average PM_{2.5} was associated with increased AX (0.260; 95%CI 0.019, 0.502; *p*=0.038). Similarly, for every 100 µg/m³ increase in peak PM_{2.5}, we observed a borderline association with AX (0.166; 95%CI -0.002, 0.334; *p*=0.058), consistent with reduced lung function. However, the association between average or peak PM_{2.5} exposure

and Xrs_5 , seen in the univariable analysis, was no longer present (Table 3; Figure 2). There was no evidence that maternal smoking modified the association between mine fire $PM_{2.5}$ and lung function (Supplementary Table S3).

Stratified analysis

Stratified analysis in girls and boys did not show statistically significant associations, although boys tended to have stronger associations than girls for measures of reactance (Supplementary Table S4).

Sensitivity analysis

After excluding participants with imputed data ($n=5$), the results were very similar, although slightly stronger (Supplementary Table S5).

Discussion

At a three-year follow-up of an infant cohort, we observed an association between elevated concentrations of PM_{2.5} during the coal mine fire and worsening peripheral lung mechanics. These results suggest that exposure to mine fire smoke in early life may have influenced lung growth and development. The measured changes in lung function associated with the fire smoke exposure were small for each incremental increase in exposure but would be likely to be of clinical relevance in the most severely exposed children. Furthermore, reductions in lung function as assessed by FOT, and measured on a single occasion, do not necessarily mean that there is a clinical problem or that one might subsequently develop. A recent study suggested that infants with low lung function during the first year could recover in later childhood^[26].

We are not aware of other published studies evaluating early life exposure to smoke from fires, or other short to moderate duration episodes of air pollution, and lung function in preschool aged children. The only comparable study, in terms of exposure, was conducted in monkeys but not in humans. The California fires of 2008 caused degraded air quality for a period of three weeks in a primate research facility soon after the birth of 50 rhesus macaque monkeys, and their lung function was evaluated in adolescence^[27]. Unlike our results, these authors found moderate reductions in airway resistance in the exposed animals compared with the unexposed indicating better lung function. Increased lung stiffness was also observed in the exposed monkeys but only in females, while our study implied stronger effects in boys than in girls after coal mine fire smoke exposure, although

the results were not statistically significant. Future studies are needed to compare the effects of early life exposure to short duration of poor air quality on lung function by gender.

Epidemiological studies have evaluated the impact of exposure to different concentrations of constant background air pollution, as distinct from short-term pollution episodes, in early life and later lung function. One study evaluated the association between exposure to traffic-related air pollution during the first year of life and adolescent lung function using a similar approach to ours^[28]. The authors reported mixed results with some associations identified between reduced lung function and exposure to oxides of nitrogen, but not particulate matter. Studies evaluating exposure to traffic-related PM_{2.5} in infancy and lung function measured with spirometry at 7-10 years of age have reported both reduced^[29], or unchanged^[30] lung function. However, these comparisons should be considered with caution because of different populations, metrics, sources and durations of air pollution exposure that were investigated.

Consistent with current literature, we found that maternal tobacco smoking during pregnancy had negative effects on children's lung function. Many epidemiological studies have indicated an adverse effect of maternal tobacco smoking on the lung health of infants and children^[19, 31-37]. Our findings further highlight the need for smoking cessation support for parents, from the pre-conception period and onwards, to improve their children's respiratory health.

The direction of associations between lower maternal education and lung function in our study was unexpected and not consistent with the weight of existing evidence regarding SES and child health^[21, 38-40]. While we do not have a good explanation for these findings, it could be chance findings in the context of multiple comparisons or inaccurate measurement of maternal education. This finding should be interpreted cautiously because of the small number of children in the subgroups (e.g. n=33 for children with mothers without post-secondary qualifications).

A strength of the study was our ability to adjust for participants' activity patterns to estimate personal PM_{2.5} exposure estimates. Furthermore, we were able to use a simple, non-invasive and objective method of evaluating lung function outcomes suitable for young children^[15]. In addition, we conducted multiple imputation to deal with missing values, which could avoid the reduction of sample size and minimize bias^[41]. Sensitivity analysis of complete cases revealed similar results to the main findings, indicating that our results were robust.

However, our study has some limitations. First, while we were able to evaluate outcomes in children exposed across a wide range of PM_{2.5}, we did not include a group of children with no smoke exposure at all because children in this group were too young to do the FOT testing. Second, the exposure estimates were drawn from modelled air quality data because the monitoring conducted during the fire across the Latrobe Valley was absent during the first week of the fire. Furthermore, our exposure estimates relied upon parental recall of their whereabouts during the fire period and there is therefore, a risk of exposure

misclassification and recall error. While most respondents reported that they were confident of their recall of events during the fire, we were unable to test this objectively. However, there is evidence suggesting a strong correlation between confidence and accuracy of recall in eyewitness studies^[42-43]. Finally, although our study population were representative of the full cohort in terms of demographic and socioeconomic characteristics, a higher proportion of children with well-educated and non-smoking parents were recruited from the local population^[13], which might influence the generalisability of the study findings.

It is possible that the results were influenced by residual confounding. We adjusted for the most important factors such as maternal tobacco smoking, secondhand smoke exposure and maternal education. Education status is a widely used proxy for SES, but in our analysis, lower educational attainment was found to have an unexpected protective association. Therefore, maternal education might not have been the most appropriate marker of SES in our participants. For this reason, our analysis also included the index of socio-economic disadvantage by region^[44] for the residential location of each participant. However, inclusion of this marker did not appreciably change the results.

It has been shown that improvements in air quality were associated with improved lung function in children^[45-46]. Given that the mine fire episode was brief and air quality in the region is generally very good, the effects observed in this study might change as children grow. Therefore, it is important to continue to monitor lung function in this group, to identify if the differences persist. Further studies with a larger sample size and wider range

of exposures by including the *in utero* and no exposure groups at follow-ups would be important for confirming these initial findings.

In conclusion, early life exposure to short-term high intensity air pollution can possibly alter lung development in children. It will be important to continue to monitor children's lung function to investigate long-term outcomes.

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Disclosure statement

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Table 1. Characteristics of the participants

Characteristics	Mean±SD	Range
Birthweight* (kg)	3.4±0.6	1.4, 5.3
Gestational age (week)	39.5±1.9	33.0, 43.0
IRSD	3.3±2.8	1.0, 10.0
Background PM _{2.5} exposure (µg/m ³)	6.7±0.9	3.4, 8.3
Age at clinic visit (years)	4.3±0.5	3.4, 5.3
Height (cm)	106.8±6.2	94.5, 128.8
Weight (kg)	19.7±4.9	13.6, 48.5
	n (N) [‡]	%
Gender: Boys	41 (84)	48.8
Maternal alcohol use during pregnancy: yes	9 (83)	10.8
Maternal smoking during pregnancy: yes	15 (84)	17.9
Maternal education: secondary education or less	33 (84)	39.3
Maternal history of asthma: yes	22 (84)	26.2
Maternal stress during pregnancy: frequently stressed	12 (84)	14.3
Effect of coal mine fire on maternal stress: 'increased a lot'	31 (83)	37.3
Second hand smoke exposure: yes	20 (84)	23.8
Breastfeeding: ≤3 month	27 (83)	32.5
Respiratory medication use 24 hours before FOT testing: yes	11 (84)	13.1
Cold/flu-like illnesses in the past 3 weeks: yes	52 (84)	61.9
PM _{2.5} concentrations during the fire period (µg/m ³)	Median	IQR
24-hour average PM _{2.5}	7.9	6.8, 16.8
24-hour peak PM _{2.5}	103.4	60.6, 150.7

Abbreviations: SD, standard deviation; IRSD, Index of Relative Socio-economic Disadvantage; PM_{2.5}, particulate matter with an aerodynamic diameter less than 2.5 micrometers; IQR, interquartile range.

*Participants with complete data for birthweight (n=82).

[‡]n represents number of participants with specific characteristics, while N represents number of participants with completed data for the variable.

Table 2. Univariable analysis of infant coal mine fire PM_{2.5} exposure and other covariates on lung function

Univariable analysis (n=84)	β-coefficient (95%CI)		
	Z (Rrs ₅)	Z (Xrs ₅)	Z (AX)
Average PM _{2.5} (10 µg/m ³ increase)	0.176 (-0.004, 0.356)	-0.213 (-0.410, -0.017)*	0.241 (0.035, 0.447)*
Peak PM _{2.5} (100 µg/m ³ increase)	0.104 (-0.023, 0.231)	-0.120 (-0.260, 0.020)	0.163 (0.018, 0.308)*
Birthweight (1 kg increase)	0.058 (-0.238, 0.353)	0.034 (-0.291, 0.358)	0.104 (-0.237, 0.445)
Gestational age (per week increase)	0.042 (-0.048, 0.132)	-0.021 (-0.120, 0.079)	0.045 (-0.059, 0.149)
IRSD (per unit increase)	-0.041 (-0.103, 0.020)	0.044 (-0.023, 0.111)	-0.020 (-0.091, 0.051)
Background PM _{2.5} (1 µg/m ³ increase)	-0.030 (-0.219, 0.159)	0.098 (-0.109, 0.305)	-0.052 (-0.270, 0.166)
Maternal alcohol use during pregnancy: yes	0.163 (-0.395, 0.721)	-0.375 (-0.982, 0.231)	0.348 (-0.289, 0.986)
Maternal smoking during pregnancy: yes	0.358 (-0.084, 0.801)	-0.860 (-1.317, -0.402) [§]	0.613 (0.112, 1.115)*
Maternal education: secondary education or less	-0.010 (-0.362, 0.342)	0.265 (-0.118, 0.649)	-0.265 (-0.667, 0.138)
Maternal history of asthma: yes	-0.159 (-0.549, 0.230)	-0.117 (-0.547, 0.312)	0.096 (-0.356, 0.547)
Maternal stress during pregnancy: frequently stressed	0.141 (-0.350, 0.632)	-0.258 (-0.795, 0.280)	0.240 (-0.326, 0.805)
Effect of coalmine fire on maternal stress: 'Increased a lot'	0.092 (-0.264, 0.448)	0.042 (-0.350, 0.434)	0.009 (-0.402, 0.421)
Second hand smoke exposure: yes	0.309 (-0.090, 0.707)	-0.193 (-0.635, 0.249)	0.141 (-0.324, 0.607)
Breastfeeding duration: ≤3 months	0.229 (-0.139, 0.597)	-0.052 (-0.456, 0.353)	0.076 (-0.349, 0.502)
Recent cold/flu-like illness: yes	0.169 (-0.184, 0.521)	0.102 (-0.287, 0.491)	0.000 (-0.409, 0.410)
Respiratory medication use: yes	-0.036 (-0.546, 0.474)	0.271 (-0.287, 0.829)	-0.230 (-0.817, 0.356)

Abbreviations: CI, confidence interval; Z (Rrs₅), Z score for resistance at a frequency of 5 Hz; Z (Xrs₅), Z

score for reactance at a frequency of 5 Hz; Z (AX), Z score for the area under the reactance curve; PM_{2.5},

particulate matter with an aerodynamic diameter less than 2.5 micrometers; IRSD, Index of Relative Socio-economic Disadvantage.

* $P < 0.05$.

[§] $P < 0.001$.

Table 3. Multivariable analysis of infant coal mine fire PM_{2.5} exposure and other covariates on lung function

Multivariable analysis (n=84)	β-coefficient [‡] (95%CI)		
	Z (Rrs ₅)	Z (Xrs ₅)	Z (AX)
Average PM _{2.5} (10 µg/m ³ increase)	0.132 (-0.088, 0.351)	-0.184 (-0.394, 0.026)	0.260 (0.019, 0.502)*
Peak PM _{2.5} (100 µg/m ³ increase)	0.071 (-0.082, 0.224)	-0.082 (-0.230, 0.065)	0.166 (-0.002, 0.334)

Abbreviations: CI, confidence interval; Z (Rrs₅), Z score for resistance at a frequency of 5 Hz; Z (Xrs₅), Z score

for reactance at a frequency of 5 Hz; Z (AX), Z score for the area under the reactance curve; PM_{2.5}, particulate matter with an aerodynamic diameter less than 2.5 micrometers.

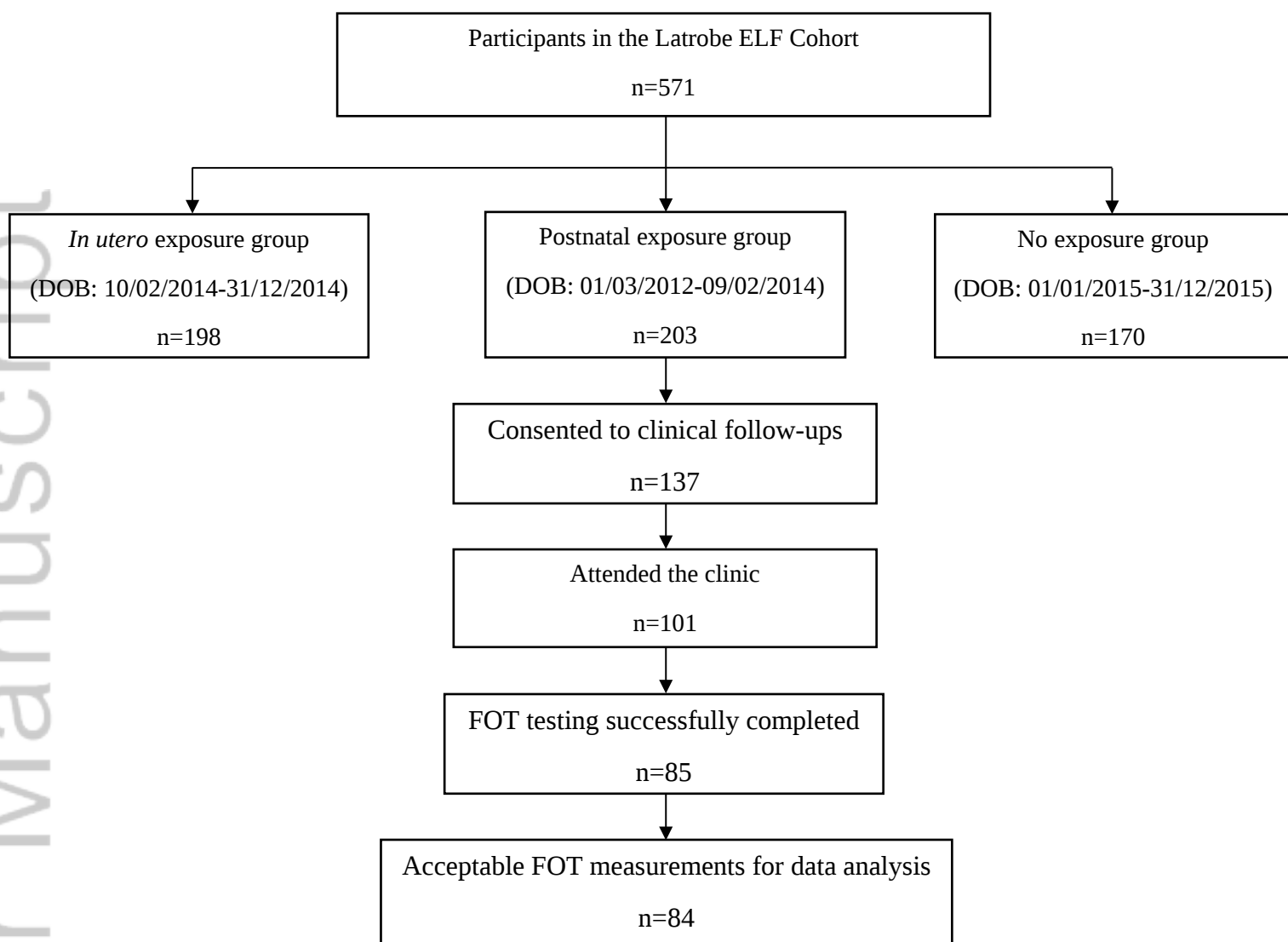
[‡]Models adjusted for birthweight, gestational age, IRSD, background PM_{2.5} exposure, breastfeeding duration, maternal alcohol use during pregnancy, maternal smoking during pregnancy, maternal education, maternal history of asthma, maternal stress during pregnancy or during the fire, secondhand smoke exposure, cold/flu-like illnesses in the past three weeks and respiratory medication use 24 h before FOT testing. Average and peak PM_{2.5} were modelled separately, and models included all covariates listed in the table.

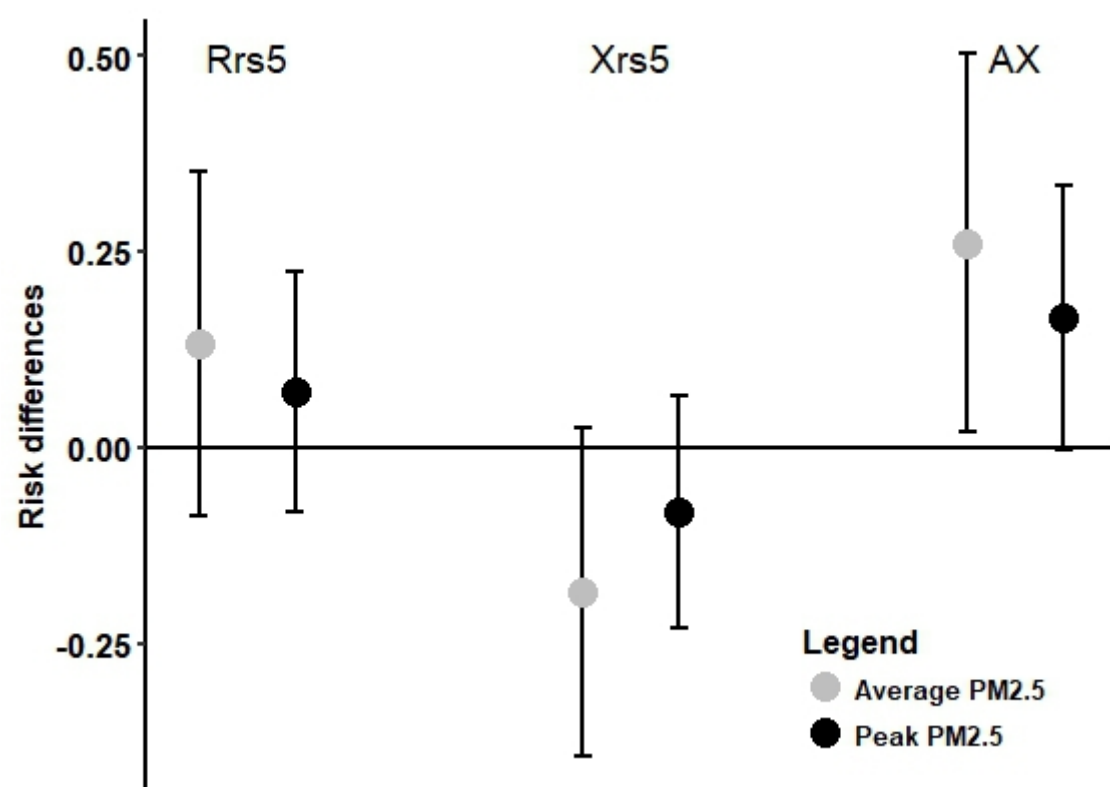
* $P < 0.05$.

Figure Legends

Figure 1. Flow chart of the children participating in this study. DOB, date of birth; FOT, forced oscillation technique.

Figure 2. Risk differences (points) and 95%CI (whiskers) for the associations between infant fire PM_{2.5} exposure and lung function. The risk difference presents the coefficients from multivariable linear regression analysis demonstrating the change in measures per incremental increase in exposure to fire-related PM_{2.5}. Rrs5, Resistance at a frequency of 5 Hz; Xrs5, Reactance at a frequency of 5 Hz; AX, the area under the reactance curve; PM_{2.5}, particulate matter with an aerodynamic diameter less than 2.5 micrometers.





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