Chronic Obstructive Pulmonary Disease in adults exposed to fine particles from a coal mine fire

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Abstract

In 2014 the Hazelwood open cut coal mine burned for six weeks, exposing nearby residents to fine particulate matter (PM2.5). The long-term health consequences are being evaluated as part of the Hazelwood Health Study (HHS). These analyses explore the association between PM2.5 and chronic obstructive pulmonary disease (COPD).

A sample of 346 exposed, and 173 unexposed, adults participated in the longitudinal Respiratory Stream of the HHS. Participants underwent spirometry and gas transfer measurements and answered validated respiratory questionnaires 3.5-4 years after the fire. Individual level mine fire-related PM2.5 exposure was modelled. Multivariate linear regression and logistic models were fitted to analyse associations between mean and peak PM2.5 exposure and clinical outcomes, stratified by smoking status.

A 10 μg/m³ increase in mean PM2.5 exposure was associated with a 69% (95%CI: 11% to 158%) increase in odds of spirometry consistent with COPD amongst non-smokers and increased odds of chest tightness (odds ratio [OR] 1.30, 95%CI 1.03 to 1.64) and chronic cough (OR 1.24, 95%CI 1.02 to 1.51) in the previous 12 months in all participants. For current smokers, increased mean PM2.5 exposure was associated with higher odds of chronic cough in the preceding 12 months (OR 2.18, 95%CI 1.28 to 3.71) relative to other participants.

More than three years after a six-week period of coal fire PM2.5 exposure, we identified a dose-response association between exposure and COPD in non-smokers. With climate change a likely contributor to increased risk of landscape fires, the findings will inform policy decisions during future sustained smoke events.

NOTE: This preprint reports new research that has not been certified by peer review and should not be used to guide clinical practice.
Introduction

The industrial era, largely fuelled by coal, has seen an increase in fires occurring within coal seams and at coal mines in association with human activity and changes in climate patterns [1]. Prominent examples of coal mine fires occurring in close proximity to human settlements have raised concerns about risks to human health around the world [2, 3]. Fires at the Jharia Coalfield in India and under the town of Centralia in Pennsylvania, illustrate instances where coal mine fires have led to mass relocation of residents arising from health and environmental effect concerns [1, 4].

The Centralia coal mine fire started in 1962 after local officials set fire to refuse in an abandoned coal pit. The fire then spread along an underground seam to tunnels beneath Centralia [5]. Emission of noxious gases and surface destabilization eventually made the town uninhabitable, with most residents evacuating between 1985 and 1991 [1, 5]. A health study comparing local residents with those of a nearby town suggested an increase in reported respiratory diseases in men and residents aged 40-79 years relative to their comparators [6]. Two years later a lower rate of diagnosed respiratory disease in relocated residents suggesting some attenuation of effects after exposure to the fire ceased [7].

Whilst coal mine fires near communities are widely reported, there remains limited peer reviewed literature on human health effects [1-3]. Analogous emissions from wildfires provide some insights into likely effects of exposure to smoke from coal mine fires [1]. Many of these studies assessed exposure to fine particulate matter with an aerodynamic diameter of less than 2.5 µm (PM2.5)[8]. A review of the health impacts of wildfire smoke in 2016 identified consistent evidence of smoke related respiratory morbidity, particularly asthma and chronic obstructive pulmonary disease (COPD) [8]. Wildfire smoke exposure was associated with COPD related physician visits [9, 10], emergency department presentations [11, 12], hospitalisations [13, 14] as well as medication dispensing [9, 15]. However, almost all of the existing studies used administrative health records to evaluate short term smoke exposure effects. Clinical testing, including lung function measurements, to ascertain effects of bushfires or coal mine fire exposure was lacking.

In 2014, prolonged air pollution was generated from a fire at the Hazelwood open-cut brown coal mine in the Latrobe Valley in south-eastern Australia. Concerns were raised regarding the health of local residents, particularly in the nearby town of Morwell where smoke was visible for 6 weeks. The Hazelwood Health Study (HHS) was established to investigate potential longitudinal health outcomes in people who were exposed to smoke from the Hazelwood mine fire (www.hazelwoodhealthstudy.org.au). The HHS Hazelinks Stream which utilises administrative health datasets, has previously reported more COPD related emergency department presentations [16], medications dispensed for respiratory conditions [17] as well as visits to specialist respiratory services [18] during the mine fire period. The HHS Adult Survey, carried out 2.5 years after the mine fire, also identified higher risks of self-reported respiratory symptoms associated with individual-level mine fire PM2.5 exposure [19]. The aim of this analysis was to evaluate clinical respiratory outcomes more than 3.5 years after the fire, particularly the risk of COPD and related respiratory symptoms, and their association with individual-level coalmine fire PM2.5 exposure.
Methods

Study design and setting

This analysis examined cross-sectional data from the Hazelwood Health Study’s Respiratory Stream, a longitudinal follow-up sub-study of the Adult Survey (see the methodology outlined elsewhere; [20]. Clinical testing was conducted in Morwell (exposed) between August and December 2017, and in Sale (unexposed) between January and March 2018. Study data were collected and managed using REDCap (Research Electronic Data Capture) [21] electronic data capture tools hosted at Monash University (Victoria, Australia).

Participants

The Respiratory Stream participants were drawn from the Adult Survey cohort which comprised residents of Morwell or Sale who were aged at least 18 years at the time of the mine fire [20]. Adult Survey cohort members were excluded from eligibility to participate in the Respiratory Stream if they had specified no further contact, had unknown age, sex or were aged over 90 years. Potential participants were also excluded if they had a contraindication to spirometry, such as recent surgery, myocardial infarction, pneumothorax, pulmonary embolus, open pulmonary tuberculosis or known aneurysms [22]. A target sample size of 339 from Morwell and 170 from Sale was derived based on the ability to detect a 5ml/year or greater FEV1 decline in exposed compared with non-exposed residents using a two-sample t-test with a two-sided p-value of 0.05 and 80% power. A weighted random sample (to correct for lower response rate in some subgroups of participants, such as young people) of 1,346 Adult Survey cohort members were selected for invitation into the Respiratory Stream, with those who had reported an asthma attack or taking asthma medication oversampled (40%) for further evaluation in an asthmatic sample (see Figure 1). Invitation to participate was by mail, email and/or SMS, and recruitment continued until the target sample size was achieved.

Participant characteristics

For each participant, demographic characteristics, such as age, sex, ethnicity, employment status, educational background and occupational exposure (working in dusty or polluted environments, such as coal mines, farms or driving diesel trucks) were drawn from the previously completed Adult Survey. Physical characteristics, including height and weight, were measured by trained staff during clinical testing, and body mass index (BMI) was calculated [23]. Smoking history was taken and participants were classified as current smokers, ex-smokers (current non-smokers with >100 cigarettes in their lifetimes) or non-smokers (< 100 cigarettes in their lifetimes) [24].

Exposure

Due to the lack of ground-level air pollution monitoring from the start of the fire, mine fire-related PM2.5 concentrations were retrospectively modelled by the Australian Commonwealth Scientific and Industrial Research Organisation (CSIRO) Oceans & Atmosphere using a chemical transport model that incorporated information on air monitoring, coal combustion and weather conditions [25]. The modelled 12-hourly concentrations were mapped to 12-hourly time-location diaries completed by participants as part of the Adult Survey, to estimate the level of exposure to mine-fire related PM2.5 for each individual. Two exposure metrics were considered: mean and peak daily mine fire-related PM2.5 exposure. Mean exposure was obtained by averaging the cumulative PM2.5 exposure across all the locations that participants visited over the exposure period (9 February - 31 March 2014). Peak
exposure was obtained by assigning the highest 12-hourly PM$_{2.5}$ level from all locations, regardless of the time that the participant spent in that location.

Outcomes

Questionnaires

Self-reported respiratory health was assessed with standardised questionnaires, adapted from the European Community Respiratory Health Survey II (ECRHSII) [26] and administered by trained interviewers.

Respiratory function tests

Trained investigators conducted objective measurements of respiratory function. Standardisation was achieved through the use of Standard Operating Procedures (SOPs), validated equipment, temperature-controlled rooms and utilisation of the same staff and equipment at both clinic sites. Preparation instructions were provided to participants at the time of booking the clinic visit.

Respiratory function was measured using the EasyOne Pro™ LAB Respiratory Analysis System (ndd Medical Technologies AG, Zürich, Switzerland). Spirometry was performed according to American Thoracic Society/European Respiratory Society (ATS/ERS) guidelines [27]. Parameters measured included FEV$_1$, FVC and FEV$_1$/FVC. Z-scores for FEV$_1$, FVC and FEV$_1$/FVC were calculated using the Global Lung Initiative (GLI) 2012 spirometry reference equations [28]. This analysis focussed on spirometry measurements performed ten minutes after administration of 300 µg Salbutamol via pressurised Metered Dose Inhaler and spacer (pMDI)[29].

Carbon monoxide transfer factor (T$_{LCO}$) was measured using the single-breath testing technique according to ATS/ERS guidelines [30]. T$_{LCO}$ values were adjusted for haemoglobin (Hb) using standard equations from ATS/ERS guidelines [30]. Z-scores for T$_{LCO}$ were calculated using the GLI 2017 reference equations [31].

Definition of COPD and abnormal T$_{LCO}$

COPD was defined by post bronchodilator FEV$_1$/FVC $<$5th percentile of predicted (lower limit of normal with FEV$_1$/FVC z-scores<-1.645) and abnormal T$_{LCO}$ was defined as haemoglobin adjusted T$_{LCO}$ $<$5th percentile of predicted (T$_{LCO}$ z-scores<-1.645). A similar definition for COPD was used in a recent population-based study on air pollution, lung function and COPD [32].

Statistical methods

Descriptive statistics were used to summarise characteristics and clinical outcomes for the low, medium and high exposure groups in Morwell (tertiles of mean PM$_{2.5}$ exposure in Morwell) as well as the non-exposed Sale group. Crude statistical significance was assessed using Pearson chi-squared tests for categorical and t-tests for continuous measures. Multivariate linear regression models were used to analyse the association between mean and peak PM$_{2.5}$ exposure (controlling for key confounders) on continuous clinical outcomes. Logistic regression models were used for binary clinical outcomes. Oversampling of the asthmatic participants was corrected using the weighting method. Since smoking is the strongest risk factor for developing COPD, we tested whether the associations between PM$_{2.5}$ exposure and outcomes differed between smoking groups by including an
interaction between exposure and participants’ smoking status (non-smoker, ex-smoker and current smoker) for all the outcome variables. Whether there was an overall interaction effect was tested using a Wald test of all interaction terms equal to zero. Sensitivity analyses were performed with unweighted and complete case models. Multiple imputation by chained equation (MICE) was used to deal with missing data. Statistical analyses were performed using Stata version 15 (Stata Corporation, College Station, Texas 2015).

Ethical considerations

The Monash University Human Research Ethics Committee (MUHREC) approved the Hazelwood Health Study: Cardiovascular and Respiratory Streams (approval number 1078). All participants provided written informed consent.

Results

As shown in Figure 1, 519 (39%) adults participated in the Respiratory Stream clinics; 346 from Morwell and 173 from Sale. Their characteristics were comparable across exposure groups (tertiles) and unexposed participants in terms of age, ethnicity, highest educational qualification, smoking status, years of smoking (for current and ex-smokers), occupational exposure and respiratory medication use in last 3 months, see Table 1. Distributions of exposure level for each group are provided in Supplementary Figure S1. However, there were higher proportions of male and obese participants and a lower proportion of employed participants in the higher exposure group compared with lower exposure group. Table 2 displays lung function and respiratory symptoms for participants in exposure groups. There were no substantial differences in post-bronchodilator spirometry or TLco between groups. However, respiratory symptoms in the last 12 months, including wheezing without an upper respiratory tract infection (URTI), chest tightness and chronic cough, were more prevalent in the higher exposure groups.

Adjusted associations between PM$_{2.5}$ exposure with respiratory symptoms and lung function are displayed in Table 3. A 10 µg/m$^3$ increase in mean PM$_{2.5}$ exposure was associated with a 30% (95% CI: 3% to 64%) increase in the odds of chest tightness in the last 12 months as well as a 24% (95% CI: 2% to 51%) increase in odds of chronic cough in the last 12 months. Figure 2 presents the results from logistic regression models for respiratory symptoms when interactions between exposure and smoking status were included. For ease of interpretation, we report the estimated OR associated with exposure (a 10 µg/m$^3$ increase in mean PM$_{2.5}$ or a 100 µg/m$^3$ increase in peak PM$_{2.5}$ exposure) in each smoking group separately. For chest tightness in the last 12 months, a dose-response relationship existed in non-smokers and current smokers, but not in ex-smokers. For chronic cough, there was strong evidence for a dose-response relationship in current smokers, but weaker evidence among non-smokers. There was also some evidence suggesting a dose response relationship among non-smokers for other respiratory symptoms including wheeze without URTI and chronic phlegm in the last 12 months (see Figure 2 and Table S1 in Supplementary Material).

Dose-response relationships between PM$_{2.5}$ exposure and post BD spirometry and TLco were not observed in the main model, however an interaction effect between exposure and smoking status was identified for spirometric COPD and post BD FEV$_1$/FVC z score but not TLco (see Figure 3 and Table S2 in the Supplementary Material). Among non-smokers, the interaction models estimated a 69% (95% CI: 11%, 158%) increase in the odds of spirometric COPD and a 0.13 (95% CI: 0.01, 0.26) reduction in post BD FEV$_1$/FVC z score per every 10 µg/m$^3$ increase in mean exposure to PM$_{2.5}$, but no exposure effect was observed in smokers and ex-smokers (see Figure 3 and Table S2).
Discussion

This analysis found that COPD, as defined by a post bronchodilator FEV1/FVC ratio less than the lower limit of normal, was associated with both mean and peak PM$_{2.5}$ exposure from a coal mine fire in non-smoking individuals over three years after exposure. An association was also observed between mine-fire related PM$_{2.5}$ exposure and respiratory symptoms (chest tightness and chronic cough) consistent with airflow obstruction in all participants. Effect modification by smoking was apparent for the associations between respiratory symptoms and PM$_{2.5}$ exposure. This was clearest for chronic cough in the last 12 months, as current smokers had twice the odds of this symptom in association with increasing mean PM$_{2.5}$ exposure.

The exposure-response relationship between PM$_{2.5}$ and COPD in non-smokers in this study was consistent with findings from the European Studies of Cohorts for Air Pollution Effects (ESCAPE) which reported a positive association between proximity to traffic intensity and the incidence of GOLD-defined COPD in never smokers [33]. There are several possible explanations for this finding. Individuals more susceptible to the adverse effects of smoke may be less likely to continue cigarette smoking and may subsequently display a greater physiological response to smoke [34]. In addition, studies of lung cancer and cardiovascular disease provide evidence that relevant biological pathways for cardiovascular disease may be activated at low levels of PM$_{2.5}$ exposure and that further increasing exposure demonstrates a “saturation phenomenon”. Diversely, a more linear relationship is found for lung cancer [34]. It is also possible that in smokers, ambient PM$_{2.5}$ exposure has an attenuated effect on spirometric COPD compared to non-smokers, although the biological pathways require further elucidation.

The lack of an effect on spirometry for smokers and ex-smokers exposed to PM$_{2.5}$ may equally relate to concurrent inhaled medication use, with these individuals potentially more likely to have used such medications compared to non-smokers. Lung function studies of asthmatics after a wildfire event have suggested a counter-intuitive preservation of lung function compared to non-asthmatics, with the possibility of a protective effect from the use of medications in this population [8]. Studies of COPD in non-smokers suggest a lower prevalence of respiratory symptoms, including chronic cough, reducing the likelihood of medication-seeking in this population [35].

From an epidemiological perspective, a quarter to a third of COPD occurs in non-smokers, with the proportion greater in low-middle compared to high income countries [35]. This may relate to an important role for indoor air pollution in the pathogenesis of COPD in non-smokers, with 45% of non-smokers reported to be exposed to biomass and 73% to coal smoke [35].

In general, there are limited data on the effects of particulate matter from coal mine fires on spirometry and our study provides a valuable addition to knowledge. Whilst comparison to other studies of coal mine fires is difficult for this reason, the similar emission profile between forest and coal mine fires allows comparison with the landscape fire literature [1]. Studies on the health impacts of wildfire smoke have found increasing evidence of a link with COPD using data on hospitalisations, physician visits and reliever medications [8]. However there were little data on effects on spirometry, with the exception of declines in peak expiratory flow among non-asthmatic children associated with wildfire exposure [8]. There was also little literature available on wild-fire smoke exposure lasting for up to six weeks, like the Hazelwood mine fire exposure. Wildfires often tend to be episodic and short in duration, and exposed populations from individual events are often small [8]. However, climate change may be contributing to increasing incidence of catastrophic wildfires globally, such as the
recent megafires in Australia which burned over a six month period and exposed more than 10 million people [36].

Declines in lung function (particularly FEV₁) after smoke exposure are commonly reported from studies of cross shift and cross season variations in wildfire fire fighters [37]. One study reported an association between levoglucosan (a woodsmoke marker) and decline in FEV₁ among wildland firefighters [38]. However, another study found no association between a decline in lung function and smoke components such as PM₃.₅, acrolein, formaldehyde or carbon monoxide exposure [39]. The role of wildfire smoke causing sustained changes in lung function among adult fire fighters is unclear with contradictory results from existing studies [37] In some children with asthma, peak expiratory flow rates have been measured to assess response to wildfires [8]. One small study measured FEV₁ and peak flow prior to, and 1 month after, wildfires with high PM₂.₅ levels and found stable lung function, but also elevated sputum eosinophils in two subjects tested during the fires, suggesting an acute inflammatory effect [40].

**Strengths & Limitations**

A major strength of our study was the measurement of lung function through spirometry, to enable an objective definition of COPD. To our knowledge, there were no comparable data available from other populations exposed to coal mine fires. Wildfire studies have largely focused on hospital and primary care presentations or medication dispensing [8]. This stream achieved the required sample size. The findings build upon previously reported respiratory health findings which have utilised administrative health datasets and self-reported symptoms.

Not relying on participants recalling their smoke exposure levels, an additional strength of our study was the estimation of individual exposures to PM₂.₅ from a combination of detailed time-location diaries and spatially and temporally resolved modelled PM₂.₅ concentrations using a chemical transport model. Whilst it is possible that some participants may have had difficulty recalling their precise locations and dates more than two years after the fire, considerable effort was made to manually review any detected inconsistencies in participant’s time-location diaries.

However, a limitation of the study includes that it was essentially a cross-sectional analysis and it was not possible to imply causation between PM₂.₅ exposure and COPD in non-smokers.

**Conclusions**

Our study found an association in non-smokers exposed to PM₂.₅ from an open cut brown coal mine fire and increased risk of spirometry defined COPD. Conversely, we also found a pronounced association between respiratory symptoms and PM₂.₅ exposure in smokers. These findings have important public health implications, as a better understanding of the exposure-response relationships across a range of PM₂.₅ exposure levels and durations would help inform policy decisions including evidence-based exposure reduction strategies for communities. These may be particularly important in the event of future large-scale landscape fires similar to those recently in Australia and the United States. Our study also highlighted the importance of objective measurement of pulmonary impairment through spirometry, given that reliance on symptoms alone does not reliably identify disease, particularly in non-smokers. Long term followup of this exposed cohort may provide valuable insights into the incidence and prognosis of COPD in coal-mine fire PM₂.₅ exposed non-smokers.
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| Characteristics                              | Sale (no exposure) | Morwell low exposure | Morwell medium exposure | Morwell high exposure | p-value |
|---------------------------------------------|--------------------|----------------------|-------------------------|-----------------------|---------|
| | N=173 | N=109 | N=113 | N=124 | |
| **Age group, n (weighted %)**               |                    |                      |                         |                       |         |
| 18-44 years                                 | 44 (22%)           | 36 (26%)             | 36 (30%)                | 35 (25%)              | 0.74    |
| 45-64                                       | 74 (42%)           | 43 (44%)             | 43 (34%)                | 50 (37%)              |         |
| 65+                                         | 55 (36%)           | 30 (29%)             | 34 (34%)                | 39 (38%)              |         |
| **Age, weighted mean (SD)**                 | 57.3 (20.0)        | 54.7 (14.3)          | 54.5 (15.3)             | 56.7 (14.7)           | 0.50    |
| **Male, n (weighted %)**                    | 62 (36%)           | 43 (46%)             | 46 (43%)                | 62 (56%)              | 0.023   |
| **Caucasian / White, n (weighted %)**       | 171 (99%)          | 108 (99%)            | 112 (100%)              | 123 (99%)             | 0.92    |
| **Employment status, n (weighted %)**       |                    |                      |                         |                       |         |
| Employed                                    | 89 (47%)           | 44 (38%)             | 46 (40%)                | 50 (35%)              | 0.021   |
| Retired                                     | 57 (38%)           | 32 (32%)             | 33 (30%)                | 37 (37%)              |         |
| Unable to work                              | 10 (6%)            | 15 (16%)             | 8 (9%)                  | 15 (12%)              |         |
| Other (unemployed, studying, home duties and other) | 17 (9%)   | 18 (13%)             | 26 (24%)                | 22 (16%)              |         |
| **Highest educational qualification, n (weighted %)** |                    |                      |                         |                       |         |
| Secondary up to year 10                     | 34 (17%)           | 28 (21%)             | 29 (22%)                | 28 (19%)              | 0.79    |
| Secondary year 11-12                        | 31 (19%)           | 24 (23%)             | 27 (24%)                | 21 (17%)              |         |
| Certificate (trade/apprenticeship/technical) | 73 (42%)           | 34 (37%)             | 38 (37%)                | 53 (48%)              |         |
| University or other Tertiary Institute degree | 34 (22%)           | 22 (19%)             | 16 (17%)                | 21 (16%)              |         |
| **BMI, n (weighted %)**                     |                    |                      |                         |                       |         |
| Underweight/Normal(BMI<25 kg/m^2)           | 40 (24%)           | 23 (20%)             | 21 (18%)                | 15 (11%)              | 0.06    |
| Overweight (25≤BMI<30 kg/m^2)               | 66 (38%)           | 35 (33%)             | 31 (29%)                | 35 (30%)              |         |
| Obese (BMI≥30 kg/m^2)                       | 67 (38%)           | 51 (47%)             | 61 (53%)                | 74 (59%)              |         |
| **Smoking status, n (weighted %)**          |                    |                      |                         |                       |         |
| Non-smoker                                  | 82 (49%)           | 58 (52%)             | 60 (54%)                | 49 (36%)              | 0.10    |
| Ex-smoker                                   | 66 (39%)           | 35 (33%)             | 34 (33%)                | 51 (47%)              |         |
| Current smoker                              | 25 (12%)           | 16 (15%)             | 19 (13%)                | 24 (17%)              |         |
| **Years of smoking among current and ex-smokers (N=270), weighted mean (SD)** |             |                      |                         |                       | 0.54    |
| Occupational exposure, n (weighted %)       | 64 (37%)           | 43 (44%)             | 44 (39%)                | 54 (46%)              | 0.47    |
| Use any SAMA/SABA* in the last 3 months, n (weighted %) | 64 (31%) | 51 (33%) | 53 (36%) | 60 (38%) | 0.82 |
| LAMA/LABA and/or ICS† use in the last 3 months, n (weighted %) | 9 (4%) | 7 (3%) | 9 (6%) | 8 (6%) | 0.87 |

* SAMA=short-acting muscarinic agonist, SABA=short-acting beta-agonist
† LAMA=long-acting muscarinic agonist, LABA=long-acting beta-agonist, ICS=inhaled corticosteroids
Table 2. Lung function and respiratory symptoms by exposure groups (tertiles of mean PM$_{2.5}$ exposure in Morwell vs. Sale)

| Outcome variables                  | Sale (no exposure) | Morwell low exposure | Morwell medium exposure | Morwell high exposure | p-value |
|------------------------------------|--------------------|----------------------|-------------------------|-----------------------|---------|
|                                    | N=173              | N=109                | N=113                   | N=124                 |         |
|                                    | n (weighted%)      | n (weighted%)        | n (weighted%)           | n (weighted%)         |         |
| Spirometric COPD                   | 24 (14%)           | 9 (6%)               | 14 (9%)                 | 12 (9%)               | 0.27    |
| Abnormal T$_{co}$                  | 18 (11%)           | 9 (7%)               | 15 (10%)                | 14 (12%)              | 0.50    |
| Spirometric COPD & abnormal T$_{co}$| 7 (4%)            | 2 (1%)               | 6 (4%)                  | 6 (5%)                | 0.27    |
|                                    | Weighted mean (SD) | Weighted mean (SD)   | Weighted mean (SD)      | Weighted mean (SD)    |         |
| Spirometry - post BD              |                    |                      |                         |                       |         |
| FEV$_1$, Litres                    | 2.9 (1.1)          | 3.0 (0.8)            | 2.9 (0.8)               | 2.9 (0.7)             | 0.86    |
| FEV$_1$ z score                    | 0.0 (1.5)          | 0.0 (1.0)            | -0.3 (1.1)              | -0.2 (1.0)            | 0.22    |
| FEV$_1$ %Predicted                 | 99.3 (22.2)        | 99.5 (13.9)          | 95.9 (16.3)             | 97.0 (24.9)           | 0.29    |
| FVC, Litres                        | 3.7 (1.3)          | 3.8 (1.1)            | 3.7 (1.0)               | 3.8 (0.8)             | 0.94    |
| FVC z score                        | 0.2 (1.2)          | 0.0 (0.9)            | -0.1 (0.9)              | -0.1 (0.8)            | 0.10    |
| FVC %Predicted                     | 102.6 (18.4)       | 100.7 (13.3)         | 98.7 (13.5)             | 99.2 (12.0)           | 0.13    |
| FEV$_1$/FVC                        | 76.5 (12.7)        | 78.7 (7.0)           | 77.2 (9.2)              | 77.0 (8.5)            | 0.20    |
| FEV$_1$/FVC z score                | -0.3 (1.4)         | -0.1 (0.9)           | -0.3 (1.0)              | -0.3 (1.0)            | 0.48    |
| T$_{co}$                           |                    |                      |                         |                       |         |
| T$_{co}$ z score                   | -0.2 (1.8)         | -0.2 (1.0)           | -0.2 (1.1)              | -0.2 (1.2)            | 0.99    |
| T$_{co}$ %Predicted                | 98.6 (25.6)        | 97.6 (15.0)          | 97.8 (17.7)             | 98.2 (19.8)           | 0.98    |
| T$_{co}$ Hb corrected z score      | -0.2 (1.8)         | -0.2 (0.9)           | -0.2 (1.1)              | -0.2 (1.2)            | 0.99    |
| T$_{co}$ Hb corrected %Predicted   | 99.4 (25.5)        | 98.2 (14.3)          | 98.5 (17.6)             | 99.0 (18.9)           | 0.96    |
| Respiratory symptoms in the last 12 months | | | | | |
| Wheeze                             | 66 (34%)           | 53 (41%)             | 52 (38%)                | 71 (50%)              | 0.08    |
| Wheeze and breathlessness          | 46 (23%)           | 43 (30%)             | 36 (25%)                | 46 (31%)              | 0.47    |
| Wheeze without URTI                | 49 (23%)           | 38 (27%)             | 36 (23%)                | 61 (43%)              | <0.001  |
| Chest tightness                    | 28 (15%)           | 22 (15%)             | 30 (19%)                | 36 (27%)              | 0.036   |
| Dyspnoea at rest                   | 26 (13%)           | 20 (16%)             | 22 (14%)                | 28 (19%)              | 0.60    |
| Dyspnoea after exercise            | 76 (42%)           | 65 (54%)             | 49 (38%)                | 68 (52%)              | 0.049   |
| Woken with dyspnoea                | 12 (6%)            | 17 (12%)             | 20 (14%)                | 16 (10%)              | 0.20    |
| Woken with cough                   | 56 (29%)           | 52 (45%)             | 42 (34%)                | 54 (39%)              | 0.11    |
| Chronic cough                      | 55 (29%)           | 47 (39%)             | 52 (45%)                | 67 (48%)              | 0.040   |
| Chronic phlegm                     | 25 (13%)           | 14 (13%)             | 21 (16%)                | 28 (22%)              | 0.22    |
Table 3. Adjusted associations (Odds Ratios and 95% Confidence Intervals) between PM$_{2.5}$ exposure, respiratory symptoms and lung function

| Respiratory symptoms in the last 12 months | Mean exposure model (10 µg/m$^3$) | Peak exposure model (100 µg/m$^3$) |
|-------------------------------------------|----------------------------------|----------------------------------|
|                                           | Adj OR (95% CI) | p-value          | Adj OR (95% CI) | p-value          |
| Wheeze                                    | 1.13 (0.89,1.43) | 0.31             | 1.00 (0.89,1.13) | 0.99             |
| Wheeze and breathlessness                  | 1.00 (0.76,1.32) | 1.00             | 0.92 (0.80,1.06) | 0.26             |
| Wheeze without URTI                        | 1.19 (0.96,1.48) | 0.11             | 1.07 (0.96,1.20) | 0.22             |
| Chest tightness                            | 1.30 (1.03,1.64) | 0.026            | 1.08 (0.96,1.21) | 0.22             |
| Dyspnoea at rest                           | 1.02 (0.77,1.33) | 0.91             | 1.02 (0.87,1.19) | 0.84             |
| Dyspnoea after exercise                    | 1.08 (0.87,1.34) | 0.48             | 0.99 (0.89,1.11) | 0.88             |
| Woken with dyspnoea                        | 0.84 (0.63,1.12) | 0.23             | 0.92 (0.78,1.08) | 0.29             |
| Woken with cough                           | 0.97 (0.77,1.22) | 0.78             | 0.95 (0.84,1.07) | 0.39             |
| Chronic cough                              | 1.24 (1.02,1.51) | 0.035            | 1.06 (0.95,1.18) | 0.33             |
| Chronic phlegm                             | 1.23 (0.93,1.62) | 0.15             | 1.02 (0.88,1.17) | 0.83             |

| Lung function†                             | Adj OR (95% CI) | p-value          | Adj OR (95% CI) | p-value          |
|-------------------------------------------|----------------|-----------------|----------------|-----------------|
| Spirometric COPD                           | 0.92 (0.67,1.26) | 0.60            | 1.02 (0.86,1.20) | 0.82            |
| Abnormal TcO                               | 1.16 (0.83,1.61) | 0.39            | 1.05 (0.89,1.23) | 0.58            |
|                                           | Adj β (95% CI) | p-value          | Adj β (95% CI) | p-value          |
| Post BD FEV1 z score                       | 0.02 (-0.09,0.13) | 0.68           | 0.03 (-0.03,0.08) | 0.30           |
| Post BD FEV1 %predicted                    | 0.04 (-1.71,1.78) | 0.97           | 0.28 (-0.56,1.11) | 0.51           |
| Post BD FEV1/FVC z score                   | 0.04 (-0.06,0.13) | 0.44           | 0.00 (-0.05,0.05) | 0.99           |
| Corrected TcO z score                      | -0.05 (-1.18,0.08) | 0.46           | 0.02 (-0.05,0.09) | 0.59           |

* Adjusted for smoking status, location of the participant (Morwell vs. Sale), BMI category, work place exposure, nasal allergies/hayfever, employed or not and having a certificate, university or other tertiary institute degrees.

† Adjusted for smoking status, location of the participant (Morwell vs. Sale), BMI category, employed or not and having a certificate, university or other tertiary institute degrees.
Figure 2. Forest plots of the estimated effects of PM$_{2.5}$ exposure on respiratory symptoms in the past 12 months for each smoking group. 

*Note:* The OR were estimated using multivariate logistic regression with an interaction between exposure and smoking status. All models were also adjusted for age, gender, location of the participant (Morwell vs. Sale), BMI category, workplace exposure, nasal allergies/hayfever, employed or not and having a certificate university or other tertiary institute degrees. * indicates evidence of an overall interaction effect (p-value <0.1 from Wald test of all interaction terms equal to zero.

Figure 3. Forest plots of the estimated effect of PM$_{2.5}$ exposure on lung function in each smoking group estimated using multivariate linear regression. 

*Note:* All models were adjusted for location of the participant (Morwell vs. Sale), BMI, workplace exposure, employment and higher education. * indicates evidence of an overall interaction effect (p-value <0.1 from Wald test of all interaction terms equal to zero.)
Adult Survey participants  

**n=4056**

- Morwell = 3096
- Sale = 960

Participants eligible for Respiratory Stream  

**n=3846**

- Morwell = 2948
- Sale = 898

Weighted random sample invited (40% with asthma)  

**n=1346**

- Morwell = 842
- Sale = 504

Target sample size was 339 Morwell and 170 Sale  
Recruitment continued until target achieved.

Non participants: 398 declined, 4 deceased, 423 no response.

Respiratory Stream participants (first round)  

**n = 519**

- Morwell = 346
- Sale = 173
