Author/s:
Holt, NR;Gao, CX;Borg, BM;Brown, D;Broder, JC;Ikin, J;Makar, A;McCrabb, T;Nilsen, K;Thompson, BR;Abramson, MJ

Title:
Long-term impact of coal mine fire smoke on lung mechanics in exposed adults

Date:
2021-09-01

Citation:
Holt, N. R., Gao, C. X., Borg, B. M., Brown, D., Broder, J. C., Ikin, J., Makar, A., McCrabb, T., Nilsen, K., Thompson, B. R. & Abramson, M. J. (2021). Long-term impact of coal mine fire smoke on lung mechanics in exposed adults. Respirology, 26 (9), pp.861-868. https://doi.org/10.1111/resp.14102.

Persistent Link:
https://hdl.handle.net/11343/298685

Holt Nicolette (Orcid ID: 0000-0003-2122-8381)
Ikin Jillian (Orcid ID: 0000-0003-0794-0129)
Thompson Bruce (Orcid ID: 0000-0002-5885-0652)
Abramson Michael (Orcid ID: 0000-0002-9954-0538)

Editorial Office Notes:

RES-20-1523.R2

ORIGINAL ARTICLE

Received 14 December 2020

Accepted 2 June 2021

Associate Editor: Alexander Larcombe

Senior Editor: Lutz Beckert

Publication fee waiver: YES

Volume: 26.6-12

Long term impact of coal mine fire smoke on lung mechanics in exposed adults

Nicolette R Holt BSc, MBBS[1,2], Caroline X. Gao BEng, MBiostats, PhD[1,3], Brigitte M Borg BAppSc CRFS ACP[1,4], David Brown BComp, GradDipEd, AssocDipAppSc[1], Jonathan C Broder BPsychSc, MAppSc(Stat&OpRes)[1], Jillian Ikin BA (Psych), PhD[1], Annie Makar BBiomedSc[4], Thomas McCrabb BBiomedSc[4], Kris Nilsen BSc, BEng(Hon), PhD[4], Bruce R Thompson BAppSci, PhD[5], Michael J. Abramson MBBS (Hons), BMedSc (Hons), PhD[1]

[1] School of Public Health & Preventive Medicine, Monash University, Melbourne, Australia

[2] Peter MacCallum Cancer Centre, Melbourne, Victoria 3000, Australia

[3] Centre for Youth Mental Health (Orygen), University of Melbourne

[4] Respiratory Medicine, The Alfred Hospital, Melbourne, Australia

[5] School of Health Sciences, Swinburne University of Technology, Hawthorn, Australia

Correspondence:

Professor Michael Abramson

School of Public Health & Preventive Medicine

Monash University

553 St Kilda Rd, Melbourne, Vic 3004

Australia

e-mail: michael.abramson@monash.edu

SUMMARY AT A GLANCE

Four years after a mine fire of 6 weeks duration, each 10 µg/m^3 increase in $PM_{2.5}$ exposure was associated with negative respiratory system reactance equivalent to 4.7 years of aging, and an increase in the area under the reactance curve equivalent to 3.9 years of aging, in exposed adults.

ABSTRACT

Background and objective In 2014, a six-week long fire at the Hazelwood coal mine exposed residents in the adjacent town of Morwell to high concentrations of fine particulate matter with an aerodynamic diameter <2.5μm ($PM_{2.5}$). The long-term health consequences are being evaluated as part of the Hazelwood Health Study.

Methods Approximately 3.5 to 4 years after the mine fire, adults from Morwell (n=346) and the comparison town Sale (n=173) participated in the longitudinal Respiratory Stream of the Study. Individual $PM_{2.5}$ exposure was retrospectively modelled. Lung mechanics were assessed using the forced oscillation technique (FOT), utilising pressure waves to measure respiratory system resistance (Rrs) and reactance (Xrs). Multivariate linear regression was used to evaluate associations between $PM_{2.5}$ and transformed Rrs at 5Hz, area under the reactance curve (AX5) and Xrs at 5Hz controlling for key confounders.

Results There were clear dose-response relationships between increasing mine fire $PM_{2.5}$ and worsening lung mechanics, including a reduction in post-bronchodilator Xrs5 and an increase in AX5. A 10 μg/m^3 increase in mine fire related $PM_{2.5}$ was associated with a 0.015 (95%CI: 0.004, 0.027) reduction in exponential(Xrs5) post bronchodilator, which was comparable to 4.7 years of aging. Similarly, the effect of exposure was associated with a 0.072 (0.005, 0.138) increase in natural log(lnAX5) post-bronchodilator, equivalent to 3.9 years of aging.

Conclusion This is the first study using FOT in adults evaluating long term respiratory outcomes after medium-term ambient $PM_{2.5}$ exposure to coal mine fire smoke. These results should inform public health policies and planning for future events.

SHORT TITLE: Coal fire exposure and lung mechanics

KEY WORDS: Particulate matter, environmental lung disease, coal mine fire, smoke, air pollution, respiratory, lung mechanics, forced oscillation technique

ABBREVIATIONS

AX5: area under the reactance in 5 seconds curve

BD: bronchodilator

COPD: chronic obstructive pulmonary disease

FEV_1: forced expiratory volume in 1 second

FOT: forced oscillation technique

Fres: resonant frequency

FVC: forced vital capacity

ln: natural log

$PM_{2.5}$: particulate matter less than 2.5 thousandths of a millimetre in diameter

Rrs: respiratory system resistance

Rrs5: respiratory system resistance in 5 seconds

SD: standard deviation

Xrs: respiratory system reactance

Xrs5: respiratory system reactance in 5 seconds

μm: micrometre or a thousandth of a millimetre

$\mu g/m^3$: micrograms per cubic metre of air

INTRODUCTION

Ambient air particulate matter (PM) exposure, from sources including vehicle exhaust, industry, biomass fuels and wildfires, collectively account for an estimated 7.5% of all deaths globally in 2016.[1] In particular, fine PM with an aerodynamic diameter < 2.5µm ($PM_{2.5}$) infiltrates deep into the peripheral lung. Short-term (days) exposure to $PM_{2.5}$ has been shown to be associated with cardiovascular and respiratory morbidity and mortality.[2, 3] Guo et al[4] showed in a large cohort study that long-term ambient $PM_{2.5}$ exposure was consistently associated with reduced lung function, accelerated annual lung function decline and an increased risk of developing chronic obstructive pulmonary disease (COPD) in adults. Similarly in a review, Li et al[5] showed an association with long-term exposure to ambient air pollution levels and increased incidence of respiratory symptoms in children.

The long-term sequelae of fine particle exposures on lung function, particularly from medium exposure episodes (weeks to months) such as landscape fires, have not been well characterised. Studies of wildfires predominantly use secondary data such as hospitalization and emergency presentations to identify respiratory associations.[6] Though long-term exposure to indoor coal burning has been found to be associated with worsening respiratory symptoms, reduced lung function and chronic obstructive pulmonary disease in adults - much remains unknown regarding the impact of coal mine fires on human lung health.[6] Addressing the gaps in the current available evidence is critical given the increasing incidence of catastrophic wildfires globally attributable to climate change.[7]

The forced oscillation technique (FOT) is a methodology used to measure lung mechanics. FOT may be able to detect early changes in peripheral airway function that spirometry cannot.[8] To our knowledge, no study has assessed the long-term impact of $PM_{2.5}$ from exposure to coal mine fires, wildfires, or biomass fuel smoke in adults using FOT.

In February 2014, embers from nearby bush fires started a fire in the Hazelwood open-cut brown coal mine, located in the Latrobe Valley, south-eastern Australia. It was an unprecedented event that generated significant air pollution from coal mine fire smoke over six weeks, particularly affecting residents in the adjacent town of Morwell. The most exposed population at the time numbered approximately 14,000.[9] This resulted in considerable community concerns about the potential long-term health effects of smoke exposure.

The Hazelwood Health Study (www.hazelwoodhealthstudy.org.au) was established to investigate potential health effects in people who were exposed to smoke from the mine fire. The Hazelinks stream of the Hazelwood Health Study utilised hospital emergency presentations and admissions data to show that hospitalisation for respiratory conditions increased during the first month of the mine fire.[10] The Adult Survey stream of the Hazelwood Health Study[11] compared self-reported health outcomes between the most exposed community and an unexposed sample more than two years after the event. The Adult Survey found increasing risks of respiratory symptoms, particularly cough, phlegm and wheeze, related to the mine fire exposure.[12] This analysis aimed to further investigate the association between exposure to mine fire smoke and long-term lung function as assessed by FOT, 3.5 to four years after the event.

METHODS

Study design and setting

The Respiratory Stream of the Hazelwood Health Study is a longitudinal follow-up study of selected participants from the Adult Survey.[11, 13] The study was conducted between August and December 2017 in Morwell (exposed), and between January and March 2018 in the nearby town of Sale (unexposed). Refer to Appendix S1 in the Supporting Information for an explanation of the selection of Sale as the comparator town. Study data were collected and managed using REDCap (Research Electronic Data Capture)[14] electronic data capture tools hosted at Monash University, Australia.

Participant recruitment and sample collection

Participants were eligible for the Respiratory Stream of the Hazelwood Health Study if they had completed the Adult Survey, were at least 18 years of age on 9 February 2014 and had lived in the study area at the time of the mine fire. Adult Survey participants were excluded from the Respiratory Stream if they had specified no further contact, were of unknown age or sex, or were aged over 90 years. Participants were further excluded where a contraindication to spirometry was identified – including recent surgery, myocardial infarction, pneumothorax, pulmonary embolism, open pulmonary tuberculosis or known aneurysms.[15]

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 forced expiratory volume in 1 second (FEV_1) decline in exposed compared with non-exposed participants 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 participants was invited for assessment of their respiratory function. Participants reporting an asthma attack or current asthma medication use in the Adult Survey were oversampled (40%) to provide ability for further evaluation in an asthmatic sample. Response bias was evaluated and corrected using statistical weighting (see Appendix S2 in the Supporting Information) and sensitivity analysis using unweighted data.

Invitation to participate was by mail, email and/or short message service (SMS), and recruitment continued until the target sample size was achieved (see **Figure 1**).

Participant characteristics

Participant characteristics such as age, sex, ethnicity, employment status and smoking history were collected via questionnaires. Participants were classified as non-smokers (<100 cigarettes in their lifetimes), ex-smokers (current non-smokers with >100 cigarettes in their lifetimes) or current smokers.[16] Height and weight were measured by trained personnel during the study visit. Education level and occupational exposures (employment in dusty or polluted environments for at least six months) were obtained from the Adult Survey.[11] Self-reported asthma status was captured via a modified European Community Respiratory Health Survey questionnaire.[17] Participants were identified as having spirometry consistent with COPD if post bronchodilator (BD) ratio of FEV_1 to forced vital capacity (FEV_1/FVC) < lower limit of normal (5^{th} percentile) using Global Lung Initiative spirometry reference values.[18]

Exposure assessment

Retrospective modelling of the spatial and temporal distribution of mine fire-related $PM_{2.5}$ concentrations by the Australian Commonwealth Scientific and Industrial Research Organisation Oceans & Atmosphere[19, 20] was used due to the absence of ground-level air pollution monitoring at the beginning of the mine fire. Please refer to Appendix S3 in the Supporting Information for a more detailed explanation of $PM_{2.5}$ modelling. Individual level mean daily $PM_{2.5}$ exposures over the mine fire period (51 days, between 9 February to 31 March, 2014) were estimated through linking time-location diary data (reported in the Adult Survey) with the modelled fire-related $PM_{2.5}$ exposure data as described by Johnson et al.[12]

Clinical outcome measures

Respiratory testing was performed by the same trained respiratory scientists at both sites using standard operating procedures in line with current respiratory measurement standards where available. Spirometry was measured using the EasyOne Pro Lab Respiratory Analysis System (ndd Medical Technologies AG, Zürich, Switzerland) in line with international standards.[21] Forced Oscillation Technique (FOT) parameters were measured using the Tremoflo C-100device (Thorasys, Montreal, Canada) in line with standards current at time of testing (see Appendix S4 in the Supporting Information for details).[22] Parameters reported for FOT included respiratory system resistance and reactance at a frequency of 5Hz (Rrs5 and Xrs5 respectively), the area under the reactance curve (AX5) and resonant frequency (Fres). Data were imputed[23] where acceptability criteria were not met or coherence <0.80 for 5Hz or <0.90 at 11 or 19Hz.[22] Tests were performed before and 10 minutes after administration of a short acting bronchodilator (300µg salbutamol). Bronchodilator use in the previous 24 hours was recorded, as bronchodilators were unable to be withheld prior to assessment due to ethical reasons.

Statistical analysis

Statistical weighting was developed and applied to all analyses to correct for over-sampling of asthmatics as well as possible attrition bias from the Adult Survey to clinical follow-up; see details in Appendix S2 in the Supporting Information. Descriptive statistics were used to compare patient characteristics and clinical outcomes between non-exposed Sale participants as well as the tertiles of $PM_{2.5}$ exposure level in Morwell (low, medium or high exposure). Crude statistical significance was assessed using Pearson chi-squared tests for categorical measures and t-tests for continuous measures.

Multivariate linear regression models were fitted to analyse the association between mean $PM_{2.5}$ exposure and outcomes, controlling for key confounders including age, height, weight, sex, smoking status, self-reported asthma and/or COPD, employment, education level and occupational exposure. Standardised z-scores and %predicted[24] for FOT outcome variables were not used in the analysis due to poor regression model fit and high proportions of participants outside of reference prediction range (mostly due to older age and heavier weight). Therefore, possible outcome transformation methods and nonlinear associations were explored using both Box-Cox transformation and fractional polynomial regression models. The best outcome transformation methods were identified as logarithmic transformations for Rrs5, AX5 and Fres and exponential transformation for Xrs5. Additional non-linearity was not observed between transformed outcomes and predicators such as age, weight and height. Missing data were addressed using multiple imputation using chained equations. Due to the lack of a low or no exposure sample in Morwell, as well as possible differences between Morwell and Sale participants, two sets of regression models were carried out for each outcome variable: Model 1 including a binary variable indicating township of participant (Morwell or Sale), and Model 2 excluding this variable. Sensitivity analyses were performed with unweighted and complete case models as well as models including only Morwell participants. Statistical analyses were performed using Stata version 16 (Stata Corporation, College Station, Texas 2016).

RESULTS

Participant characteristics and $PM_{2.5}$ exposure

This cross-sectional analysis included all participants in the first round of Respiratory Stream data collection, which comprised a total of 519 participants (346 from Morwell, and 173 from Sale). Refer to **Figure 1** for flow of participants.

Table 1 shows the participant characteristics by exposure level to mine fire smoke. The mean (standard deviation; SD) $PM_{2.5}$ exposure levels for non-exposed (Sale) and for Morwell (low, medium and high exposure groups) were 0.1 (0.4), 5.9 (1.8), 11.5 (1.5) and 27.8 (10.3) $\mu g/m^3$, respectively. There were differences between exposure groups for gender distribution and weight, with those in the high exposure group having a higher proportion of males and heavier weight. Other participant characteristics were comparable between exposure groups. Refer to **Table S1** in the Supporting Information for characteristics of participants versus non-participants.

$PM_{2.5}$ exposure and lung function

As Forced Oscillation Technique variables are dependent on sex, age, height and weight – unadjusted results were not included in the analysis. As shown in **Figure 2** and **Table S2** in the Supporting Information, all outcome variables were skewed and displayed slightly larger variation in baseline compared to post bronchodilator outcomes. A clear dose response pattern was observed between exposure level and FOT outcomes. Results from multivariate linear regression analysis (**Table 2**) revealed a negative association between increasing mine fire related $PM_{2.5}$ exposure and post bronchodilator reactance at 5Hz, with Morwell included or excluded as a predictor. With Morwell excluded as a predictor, a 10 μg/m^3 increase in mine fire related $PM_{2.5}$ was associated with 0.015 reduction in post bronchodilator exponential transformed Xrs5. This was equivalent to 4.7 years of aging estimated in the regression model (as shown in **Table S3** in the Supporting Information, the estimated effect of 10-years of aging was 0.032, therefore equivalent years of ageing was calculated as $0.015\times10/0.032=4.7$). When Morwell was excluded as a predictor, regression analysis suggested that increased exposure to mine fire related $PM_{2.5}$ was associated with increased area under the post bronchodilator reactance curve (AX5). The effect of exposure was associated with a 0.072 increase in ln(AX5) post-bronchodilator; being equivalent to 3.9 years of aging (see **Table S4** in the Supporting Information**,** effect of 10-years of aging was estimated to be 0.185). More detailed regression results for post bronchodilator Xrs5 and AX5 are shown in **Tables S3** and **S4** in the Supporting

Information. An association between increasing $PM_{2.5}$ exposure and bronchodilator response in exponential transformed Xrs5 was also seen (**Table 2** and **Table S5** in the Supporting Information for details). Sensitivity analyses (results not shown) suggest that results from un-weighted/un-imputed models and models including Morwell participants only were highly consistent with main findings.

DISCUSSION

Assessment of participants nearly four years after the Hazelwood coal mine fire revealed an association between medium term mine fire related $PM_{2.5}$ exposure and more negative respiratory system reactance (Xrs5), specifically measured after administration of bronchodilator. To the best of our knowledge, this represents the first study using FOT analysis in adults to evaluate longer term respiratory function after a medium term $PM_{2.5}$ exposure related to coal mine fire smoke.

The mechanism for the more negative reactance (a marker of the compliance of the respiratory system) is unclear. Previous studies of long-term exposure to air pollution and $PM_{2.5}$ have shown associations with increased respiratory morbidity and airflow obstruction.[4, 6, 25-27] Separately, it has been shown that measurements of reactance at 5-6Hz via FOT are sensitive to airway closure[28-31] and expiratory flow limitation[32-34] in subjects with obstruction. A possible mechanism for the association seen between medium term exposure $PM_{2.5}$ and Xrs5 in this study may be early peripheral airway changes that occur with airflow limitation or accelerated lung aging.

Interestingly, the association between $PM_{2.5}$ and Xrs5 was only observed in the post-bronchodilator data. A possible explanation for this finding is that participants were recruited from a general population with varying states of lung health and by assessing participants post-bronchodilator, variability of bronchomotor tone was minimised across participants[35-37] allowing assessment of fixed pulmonary abnormalities. That is, the assessment of the relationship between $PM_{2.5}$ and Xrs5 could be undertaken without the confounding effects of bronchomotor tone.

Importantly, these findings in adults are similar to the findings in children within the Hazelwood Health Study Early Life Followup Stream. Shao and colleagues (2020)[38] demonstrated that infant or *in utero* exposures to coal mine fire emissions were associated with long-term impairment of lung reactance, with increased average $PM_{2.5}$ being significantly associated with worsening area under the reactance curve - a complementary parameter in the evaluation of reactance.[24] Similarly, abnormalities in oscillometry parameters were found in subjects with lower respiratory symptoms, after acute exposure to pollution from the 911 terrorist attacks, where spirometry was insensitive.[39, 40]

The study has several strengths. Unlike observational studies that have used only secondary data (such as hospitalization) to assess respiratory health, this research has built upon previously collected hospitalisation[10] and self-reported symptom data[12] with the inclusion of objective measures of lung mechanics. A further strength of this study was the inclusion of individual estimates of $PM_{2.5}$ exposure utilising a combination of detailed time-location diaries and spatially and temporally resolved modelling of $PM_{2.5}$ concentrations based upon coal combustion and weather conditions.

However, the study also has some limitations. The study endeavoured to account for all relevant potential confounding factors in our analysis, such as age, gender, weight, BMI, education status, tobacco and occupational exposures, and included sampling weights to account for attrition bias. However, it is feasible that some of the observed results occurred by chance or were influenced by unknown confounding factors or factors influencing participation in the study. Furthermore, at this stage in the study, we only have cross-sectional data on lung mechanics. Future follow-up of the Hazelwood Health Study Respiratory Stream participants will better inform an investigation of the long-term implications of medium-duration coal mine fire-related smoke exposure on respiratory mechanics and lung health.

In conclusion, a clear dose response association was observed between medium-duration $PM_{2.5}$ exposure levels from ambient coal mine fire smoke and a more negative respiratory system reactance in this cohort. This study adds new findings to the literature on the lung health effects of medium term $PM_{2.5}$ exposure. These inform public health policy and planning for future coal mine fires or similar medium duration $PM_{2.5}$ generating pollution events such as the recent megafires in Australia and the United States. Longitudinal data are required to confirm the findings of this study and to better understand the association of coal mine fire smoke and altered respiratory system reactance and potential accelerated lung aging in exposed populations.

ACKNOWLEDGMENTS

We wish to thank Susan Denny, Kylie Sawyer, Shantelle Allgood and Kristina Thomas from the Monash University School of Rural Health, who assisted with the study. Most of all, the study team would like to acknowledge the contribution of all community members who have participated in the study to date.

Research funding: The Hazelwood Health Study is funded by the Victorian Department of Health & Human Services (Australia). However, this paper presents the views of the authors and does not represent the views of the Department.

CONFLICT of INTERESTS

This study was previously presented online at the virtual European Respiratory Society International Congress 2020.

Michael Abramson holds investigator initiated grants for unrelated research from Pfizer and Boehringer-Ingelheim. He has also undertaken an unrelated consultancy for Sanofi and received a speaker's fee from GSK. The other authors declare no conflicts of interest.

Human Ethics Approval Declaration:

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

Author contributions

NH led the drafting of the work and revising it critically, and contributed to interpretation of the data. BB contributed to the design of the work, the acquisition, analysis and interpretation of data, drafting the work and revising it critically. CG and JB contributed to the analysis and interpretation of data, drafting the work and revising it critically. DB contributed to the acquisition of data, drafting the work and revising it critically. JI contributed to the design of the work, the acquisition and interpretation of data, drafting the work and revising it critically. AM and TM contributed to the design of the work, the acquisition and interpretation of data, drafting the work and revising it critically. KN contributed to the interpretation of data, drafting the work and revising it critically. BT contributed to the conception and design of the work, the interpretation of data, drafting the work and revising it critically. MA contributed to the conception and design of the work, the acquisition, analysis and interpretation of data, drafting the work and revising it critically. All authors approved the final version and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work were appropriately investigated and resolved.

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Figure legends

Figure 1 Flowchart of recruitment from the Adult Survey to the Respiratory Stream

Figure 2 Box and whisker plots of FOT parameters Rrs5, Xrs5, AX and Fres by exposure group: (A) Untransformed (B) Transformed.

Table 1: Participant characteristics by exposure group.

Characteristic	Sale N=173	Morwell low exposure N=109	Morwell medium exposure N=113	Morwell high exposure N=124	p-value
	n (weighted %)	n (weighted %)	n (weighted %)	n (weighted %)	
Age group / years					
18-44	44 (22%)	36 (26%)	36 (30%)	35 (25%)	0.74
45-64	74 (42%)	43 (44%)	43 (37%)	50 (37%)	
65+	55 (36%)	30 (29%)	34 (34%)	39 (38%)	
Gender					
Male	62 (36%)	43 (46%)	46 (43%)	62 (56%)	0.02
Caucasian/white	171 (99%)	108 (99%)	112 (100%)	123 (99%)	0.92
Employed	89 (47%)	44 (38%)	46 (40%)	50 (35%)	0.34
Higher education*	107 (63%)	56 (57%)	54 (54%)	74 (64%)	0.39
BMI kg/m^2					
Underweight/Normal (BMI<25)	40 (24%)	23 (20%)	21 (18%)	15 (11%)	0.06
Overweight (25≤BMI<30)	66 (38%)	35 (33%)	31 (29%)	35 (30%)	
Obese (BMI≥30)	67 (38%)	51 (47%)	61 (53%)	74 (59%)	
Smoking status					
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%)	
Asthma and/or COPD[‡]	73 (37%)	58 (41%)	57 (40%)	63 (39%)	0.96
Historical occupational exposure	64 (37%)	43 (44%)	44 (39%)	54 (46%)	0.47
	Mean (SD)	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	
Age / years	57.3 (20.0)	54.7 (14.3)	54.5 (15.3)	56.7 (14.7)	0.50
Height / cm	166.5 (11.2)	166.0 (9.6)	166.4 (8.8)	167.1 (7.9)	0.86
Weight / kg	81.2 (24.4)	86.7 (22.7)	86.8 (20.2)	88.8 (17.0)	0.009

$PM_{2.5}$ exposure / μg/m^3	0.1 (0.4)	5.9 (1.8)	11.5 (1.5)	27.8 (10.3)

Abbreviations: BMI Body Mass Index; COPD chronic obstructive pulmonary disease; SD standard deviation

* Certificate, University or other Tertiary Institute degree

‡ Spirometric COPD and/or self-reported asthma attack in the last 12 months

Table 2. Summary of multivariate linear regressions of FOT parameters – regression coefficients (β) and 95% confidence intervals.

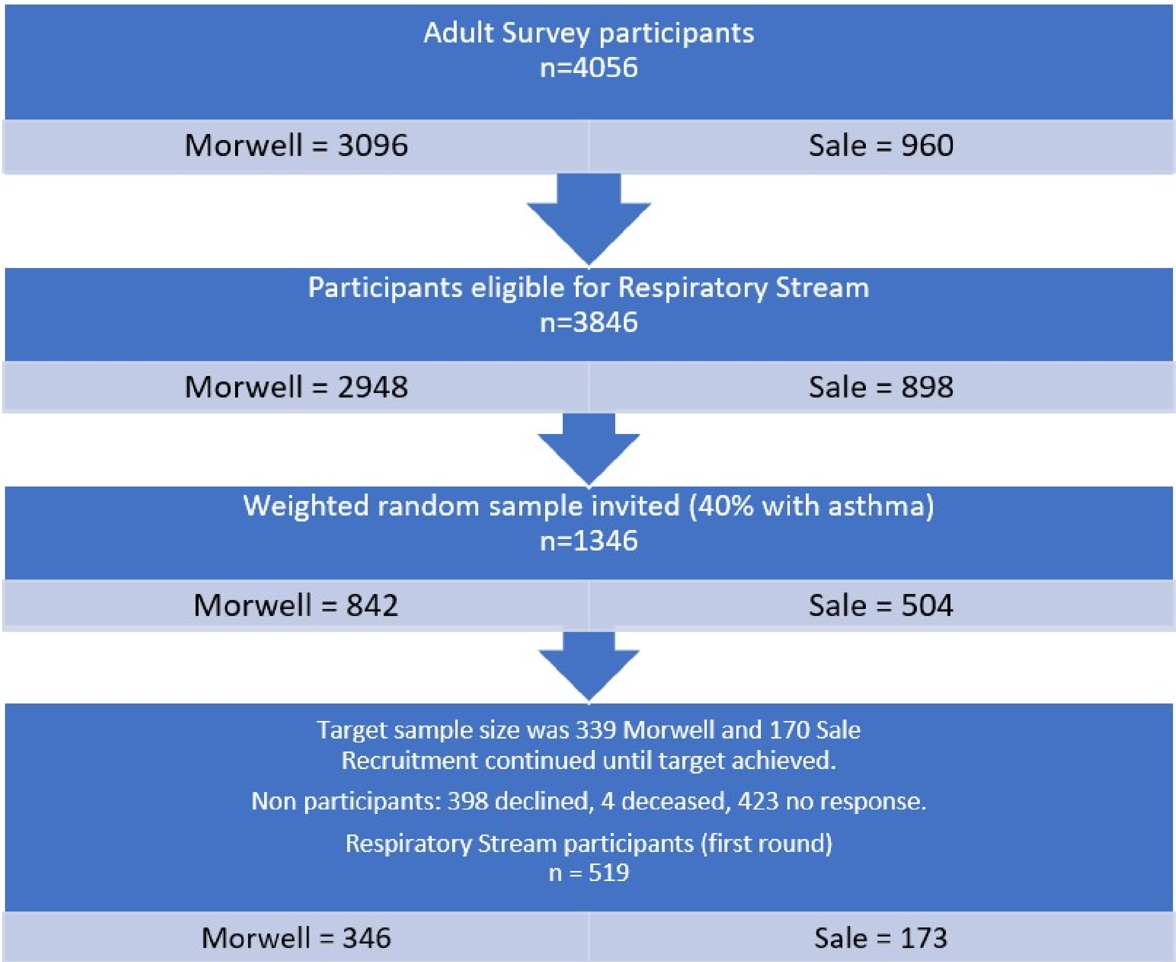
	Mean exposure model (10 µg/m³)			
	Model 1 (Including township as a confounder)		**Model 2 (Excluding township as a confounder)**	
	β-Coef (95% CI)	**p-value**	**β-Coef (95% CI)**	**p-value**
Baseline*				
Baseline ln(Rrs5)	-0.003 (-0.035, 0.029)	0.87	-0.001 (-0.028, 0.026)	0.95
Baseline exp(Xrs5)	-0.009 (-0.024, 0.006)	0.23	-0.008 (-0.020, 0.005)	0.23
Baseline ln(AX5)	0.030 (-0.056, 0.116)	0.50	0.038 (-0.034, 0.109)	0.31
Baseline ln(Fres)	0.001 (-0.030, 0.032)	0.97	0.006 (-0.019, 0.032)	0.62
Post BD‡				
Post BD ln(Rrs5)	0.011 (-0.018, 0.041)	0.45	0.012 (-0.013, 0.036)	0.34
Post BD exp(Xrs5)	**-0.018 (-0.032, -0.003)**	**0.015**	**-0.015 (-0.027, -0.004)**	**0.011**
Post BD ln(AX5)	0.063 (-0.017, 0.144)	0.12	**0.072 (0.005, 0.138)**	**0.034**
Post BD ln(Fres)	0.017 (-0.010, 0.045)	0.22	0.021 (-0.001, 0.044)	0.07
Difference between baseline and post BD				
Difference in ln(Rrs5)	0.012 (-0.010,0.034)	0.27	0.012 (-0.006,0.029)	0.20
Difference in exp(Xrs5)	**-0.009 (-0.018,0.000)**	**0.047**	**-0.008 (-0.015,-0.001)**	**0.032**
Difference in ln(AX5)	0.030 (-0.026,0.086)	0.30	0.032 (-0.013,0.078)	0.17
Difference in ln(Fres)	0.014 (-0.008,0.037)	0.21	0.013 (-0.005,0.032)	0.15

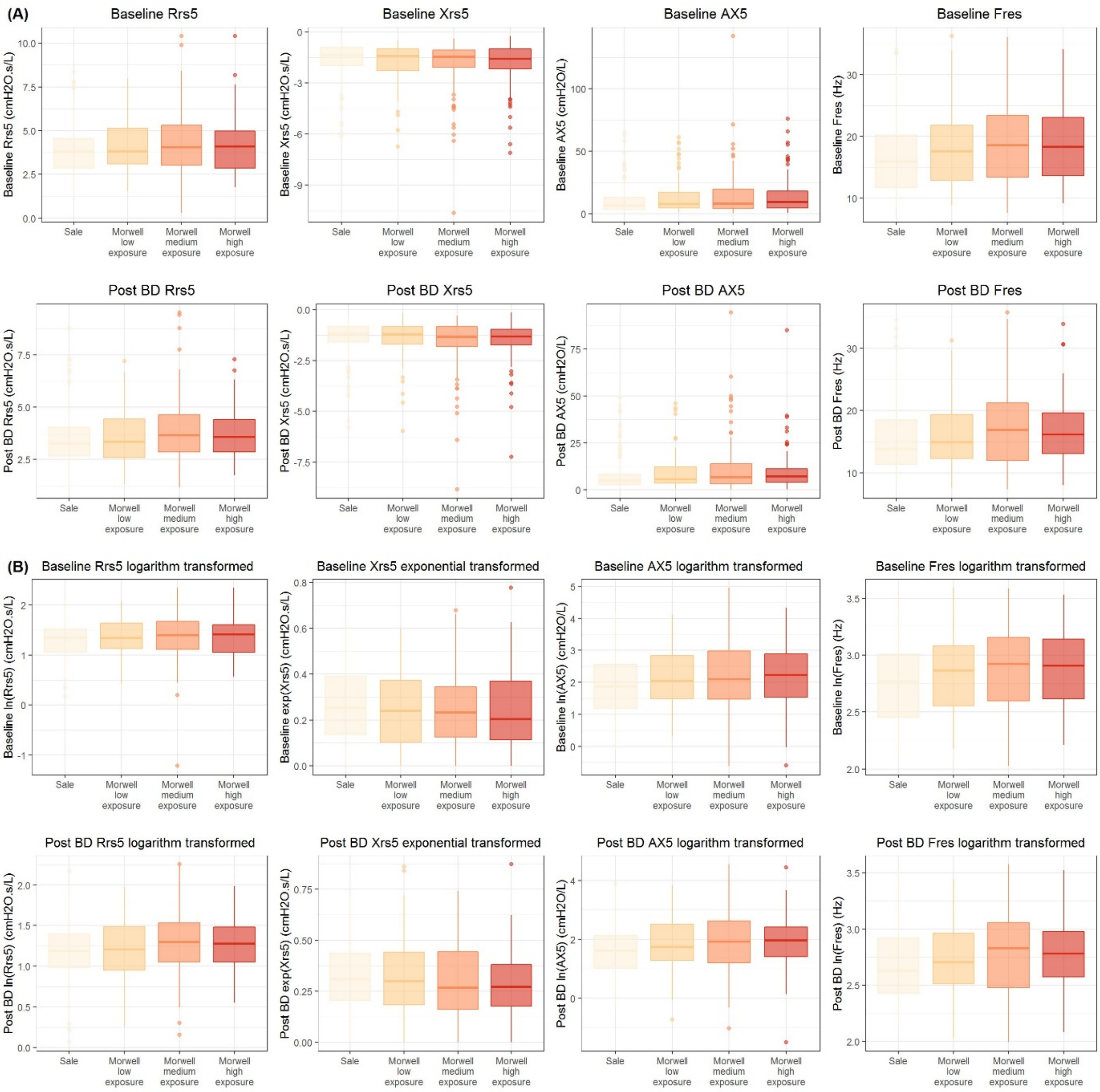
Abbreviations: BD bronchodilator; exp exponential; ln natural log; Rrs5 respiratory system resistance at 5Hz; Xrs respiratory system reactance at 5Hz; AX5 area under the reactance curve from 5Hz; Fres resonant frequency.

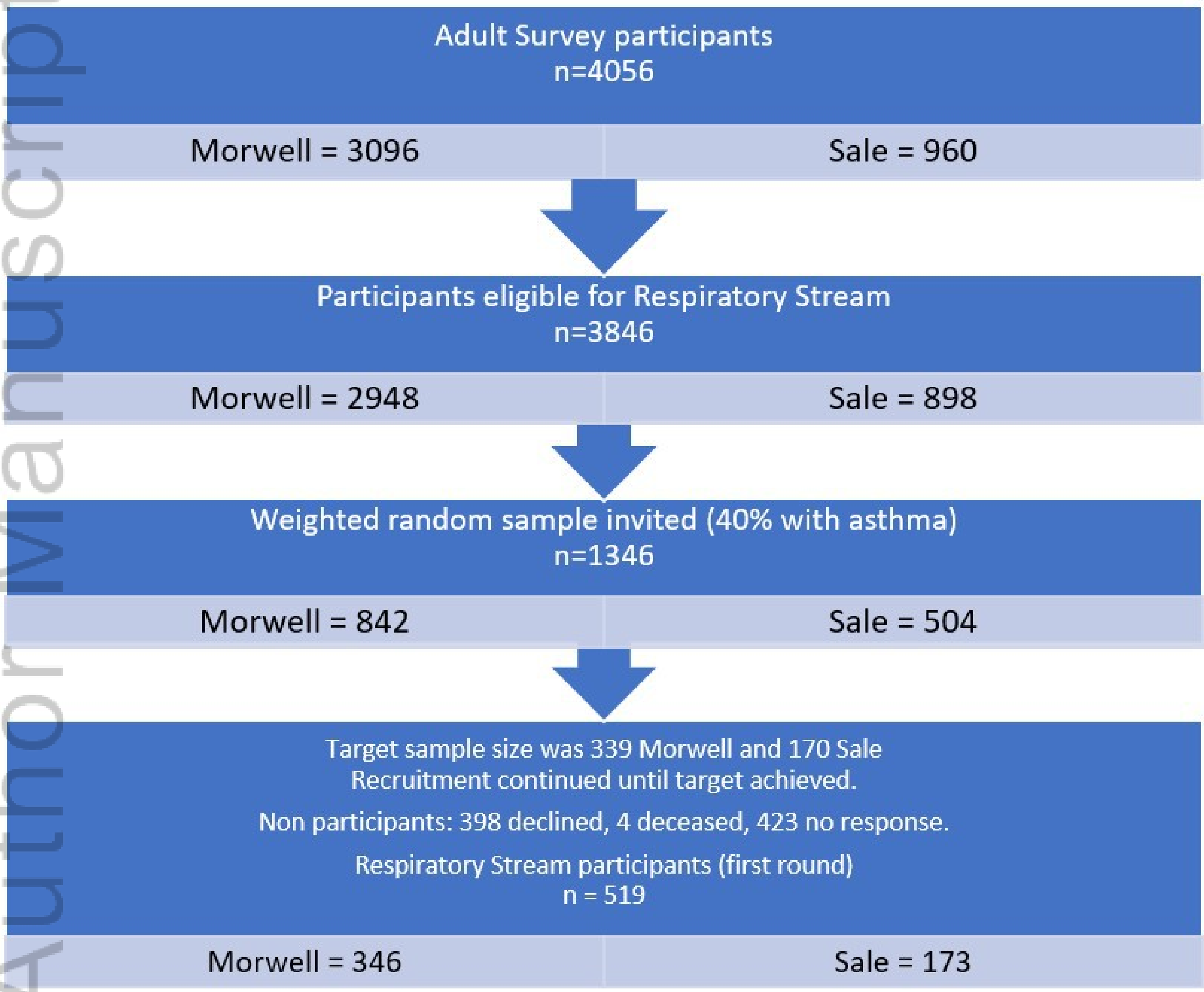
* Regression models adjusted for age, gender, height, weight, employment, education, smoking status, asthma and COPD status and work exposure and whether participants had bronchodilator prior to the

test. Missing data, including 44 records for baseline Rrs5, baseline Xrs5 and baseline AX5; 48 records for baseline Fres; 6 records for education level, were imputed using multiple imputation with chained equations.

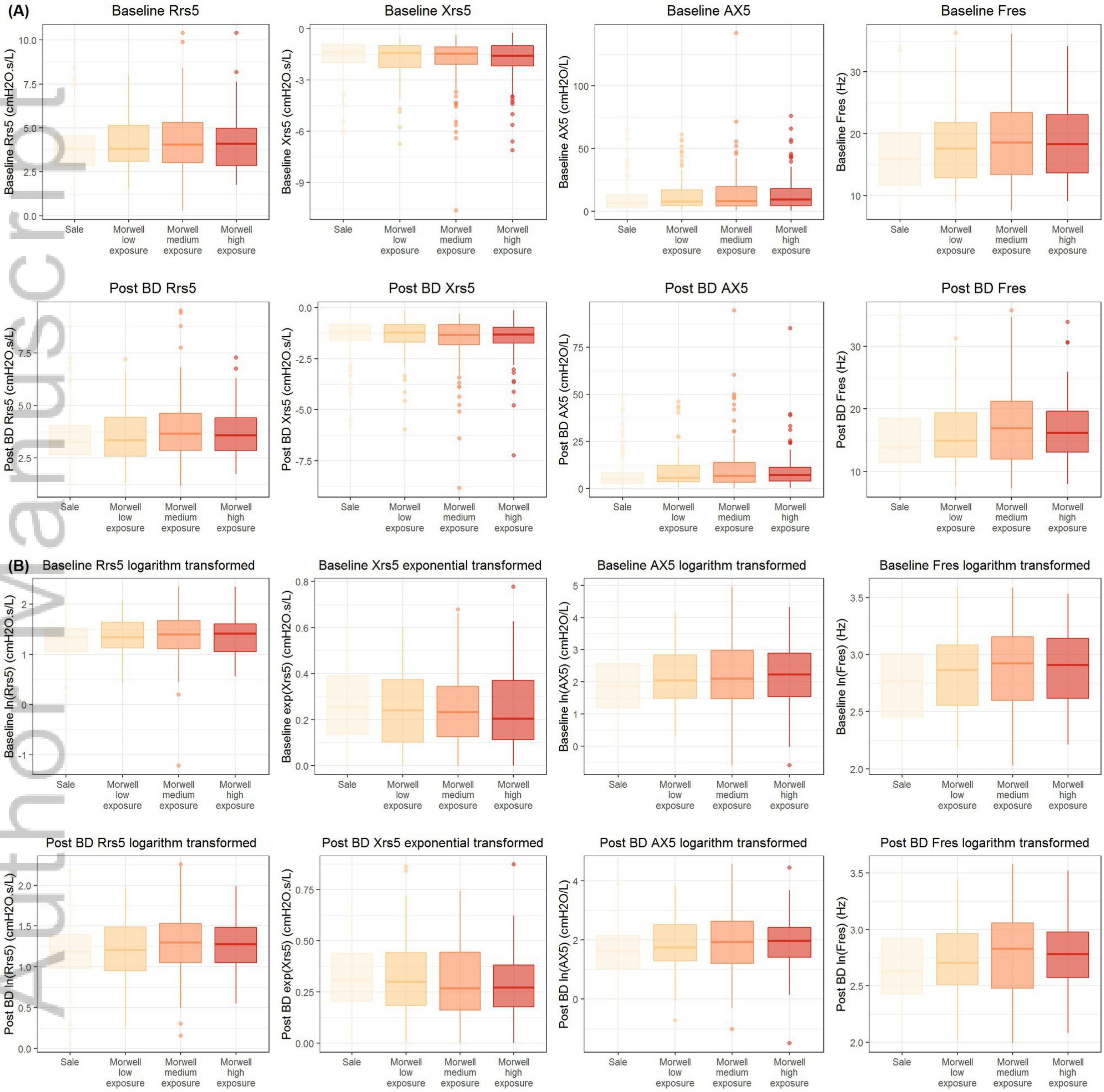
‡ Model 1 adjusted for age, gender, height, weight, employment, education, smoking status, asthma and COPD status, work exposure and township of the resident (Morwell or Sale). Whether the participants had taken a BD prior to their assessment was also controlled for in the models of FOT outcomes at baseline, as well as difference between baseline and post BD. Model 2: identical to Model 1 except township was not included as a confounder. Missing data, including 41 records for post BD Rrs5, post BD Xrs5 and post BD AX5; 42 records for post BD Fres; and 6 records for education level, were imputed using multiple imputation with chained equations.


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


(A)
Baseline Rrs5
Baseline Xrs5
Baseline AX5
Baseline Fres
Baseline Rrs5 (cmH2O.s/L)
Baseline Xrs5 (cmH2O.s/L)
Baseline AX5 (cmH2O/L)
Baseline Fres (Hz)
Post BD Rrs5
Post BD Xrs5
Post BD AX5
Post BD Fres
Post BD Rrs5 (cmH2O.s/L)
Post BD Xrs5 (cmH2O.s/L)
Post BD AX5 (cmH2O/L)
Post BD Fres (Hz)
(B)
Baseline Rrs5 logarithm transformed
Baseline Xrs5 exponential transformed
Baseline AX5 logarithm transformed
Baseline Fres logarithm transformed
Baseline ln(Rrs5) (cmH2O.s/L)
Baseline exp(Xrs5) (cmH2O.s/L)
Baseline ln(AX5) (cmH2O/L)
Baseline ln(Fres) (Hz)
Post BD Rrs5 logarithm transformed
Post BD Xrs5 exponential transformed
Post BD AX5 logarithm transformed
Post BD Fres logarithm transformed
Post BD ln(Rrs5) (cmH2O.s/L)
Post BD exp(Xrs5) (cmH2O.s/L)
Post BD ln(AX5) (cmH2O/L)
Post BD ln(Fres) (Hz)
Sale
Morwell low exposure
Morwell medium exposure
Morwell high exposure



RESP_14102_Fig 1 FOT recruitment.jpg



RESP_14102_Figure 2.jpg