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Research article

Long-term exposure to low air pollutant concentrations and hospitalisation for respiratory diseases in older men: A prospective cohort study in Perth, Australia

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ABSTRACT

Background: Acute exposure to ambient air pollution even at low concentrations has been associated with increased hospitalisation for respiratory diseases but the effects of long-term exposure are less certain. In this study, we investigated the associations between long-term exposures to $PM_{2.5}$, $PM_{2.5}$ absorbance and NO_2 and hospitalisation for asthma, chronic obstructive pulmonary disease and pneumonia in a cohort of older men living in Perth, Western Australia, a city where the levels of air pollutants are well below the world standards.

Materials and methods: The study population of 11,156 men with no prior hospitalisation for respiratory disease was drawn from the Health in Men Study (HIMS) cohort of men aged >65 years living in Perth, Western Australia between 1996-1999. $PM_{2.5}$, $PM_{2.5}$ absorbance ($PM_{2.5a}$) and NO_2 were measured across the Perth metropolitan area over three seasons in 2012. Land use regression (LUR) models were used to estimate annual concentrations of $PM_{2.5}$, $PM_{2.5}$ absorbance and NO_2 at the residential address of each participant from inception (1996) to 2015. Hospitalisation for respiratory disease between inception and 2015 was ascertained using the Western Australian Data Linkage System. The association between exposure to air pollution with hospitalisation for respiratory disease was examined using Cox regression analysis.

Results: No statistically significant associations were observed in the fully adjusted models. However, positive associations were observed with first hospitalisation for pneumonia (HR 1.08, 95% CI: 1.01–1.16) when adjusted for age, year of enrolment, smoking status, education, BMI and physical activity.

Conclusions: In this longitudinal study of older men we found no evidence of associations between increased long-term exposure to low-level air pollution with increased risk of hospitalisation for respiratory diseases in Perth, Australia. More studies on respiratory morbidity associated with exposure to low levels of air pollution are needed for more comprehensive understanding of the overall risk.

1. Introduction

Chronic respiratory illnesses led to an estimated 3.91 million deaths globally in 2017, accounting for 7% of all deaths (X. Li, Cao, Guo, Xie and Liu, 2020). The two most common of these diseases are chronic obstructive pulmonary disease (COPD) and asthma. COPD is the 7th leading cause of death globally (James et al., 2018), while asthma is ranked 28th (Dharmage et al., 2019). In Australia COPD was the 5th leading cause of death in 2018 (Australian Institute of Health and Welfare, 2020) with the prevalence estimated at 7.5% for persons aged 40 and over (Toelle et al., 2013). Asthma has been increasing in several high income countries and it is well recognised that changing environmental factors are important contributors to these increases (Dharmage et al., 2019).

The World Health Organization has identified ambient air pollution as a major risk factor for respiratory illness (World Health Organization,

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2016). Pollution from particulate matter (both household and ambient) accounted for 31% of COPD deaths globally, with ambient pollution contributing a greater proportion since 2002 (X. Li et al., 2020). Acute exposure to ambient air pollution has been shown to be associated with increased hospitalisation for respiratory diseases (J. Li et al., 2016; Orellano et al., 2017; Sharma et al., 2020; Zhang et al., 2016; Zheng et al., 2015) even at low concentrations (Hinwood et al., 2006). Lu P et al. (2020) also observed short-term exposures to PM_{10}, NO_2 and SO_2 were associated with hospital outpatient visits for asthma in China.

The evidence on the respiratory effects from long-term exposure is more limited and less consistent (Andersen et al., 2011; Atkinson et al., 2015; Salimi et al., 2018; Schikowski et al., 2014). Reduced lung function has been observed in a number of studies (Adam et al., 2015; Doiron et al., 2019; Edginton, O'Sullivan, King and Lougheed, 2019; Keidel et al., 2019). Baseline concentrations of $PM_{2.5}$, black carbon, Ozone and NO_x were significantly associated with increased risk of emphysema, but for exposure during follow-up only Ozone and NO_X were associated with emphysema (Wang et al., 2019). In a UK population, Doiron et al. (2019) found that $PM_{2.5}$ and NO_2 were associated with a higher COPD prevalence, with higher associations observed for obese, lower income, and non-asthmatic participants. Eguiluz-Gracia et al. (2020) in their review concluded that ambient air pollution is associated with higher asthma exacerbations and possibly higher asthma prevalence.

The 'Effects of Low-Level Air Pollution: A Study in Europe' (ELAPSE) study pooled data from three Danish and Swedish cohorts and found that long-term exposure to $PM_{2.5}$, NO_2, and black carbon is associated with the development of COPD (Liu et al., 2021). In a subset of participants exposed to air pollution levels below the EU and US limit values the hazard ratios were more pronounced. Further, findings from the Danish Nurses Cohort study reported that low levels of exposure to $PM_{2.5}$ were associated with higher risk of respiratory mortality (So et al., 2020). These findings suggest that there is no safe threshold level.

There have been few studies conducted in areas with low-levels of air pollution despite the need for information on the exposure-response relationships at lower concentrations.

In this study, we investigated the associations between long-term exposures to $PM_{2.5}$, $PM_{2.5}$ absorbance ($PM_{2.5a}$) (as a surrogate measure of black carbon) and NO_2 and hospitalisation for respiratory disease in the Health in Men Study (HIMS) cohort (Norman et al., 2008). This study was conducted in Perth, Western Australia. Perth is a coastal city with a population of approximately two million people and where the levels of air pollutants are well below the world standards.

2. Methods

2.1. Study population

The study population was drawn from the Health in Men Study (HIMS) (Norman et al., 2008), a cohort of older men living in Perth, Western Australia. Briefly, HIMS commenced as a randomised controlled trial of screening for abdominal aortic aneurysm and the study population included men aged 65 years and over. Of the 19,352 men invited to participate, 12,203 (63%) were recruited between April 1996–January 1999, with 11,727 living in the metropolitan Perth region. The participants completed a questionnaire at baseline and again every 2–4 years. Further follow up was also conducted using linked hospitalisation and mortality data from the Western Australia Data Linkage System (Norman et al., 2008). This study was approved by the Human Research Ethics Committee at The University of Western Australia and all men provided written informed consent prior to participating in the study.

2.2. Health outcomes

Information on respiratory hospitalisations was obtained using the Western Australian Data Linkage System. The main outcomes were defined as the first hospitalisation between recruitment and 30/06/2015 for (1) all respiratory conditions; (2) asthma, (3) COPD and (4) pneumonia. Principal diagnosis was used to identify hospitalisation for all respiratory diseases (International Classification of Diseases (ICD)9 (460–519) and ICD10 (J00 - J99 excluding J95.4 to J95.9, R09.1, and R09.8)), asthma (ICD9 (493) and ICD10 (J45 - J46)), COPD (ICD9 (490–492, 494–496) and ICD10 (J40–44, J47, J67)) and pneumonia (ICD9 (466, 480–486), ICD10 (J12-J18)). Data included a combination of ICD9 and ICD10, therefore, both have been used to classify the diagnoses. It was hypothesised that long term exposure to air pollution would affect the occurrence of hospitalisation and also reduce the time to the event. Similar hypothesis has been made in the literature (Andersen et al., 2011, 2012; Salimi et al., 2018; Jacquemin et al., 2015).

2.3. Exposure assessment

Long-term exposure to $PM_{2.5}$, $PM_{2.5a}$ and NO_2 were estimated at the residential address of the each cohort member using land use regression (LUR) models. The development of these models followed the European Study of Cohort for Air Pollution Effects protocol (http://www.escapeproject.eu/manuals/), and has been described previously (Mila Dirgawati et al., 2015, 2016). In short, in 2012, two week monitoring campaigns across three seasons (summer, autumn, and winter) over the Perth metropolitan area, plus continuous monitoring at one site were conducted. NO_2 and NO_x were measured at 43 sites and $PM_{2.5}$, and light absorbance of $PM_{2.5}$ at 20 sites. LUR models to predict the 2012 annual concentration for each pollutant were developed using land use and traffic related predictor variables, that were derived using Geographic Information System and entered into the model using forward regression.

Annual mean air pollutant concentrations from the year of recruitment (baseline) in the years 1996–1999 and for the follow-up period to 2011 were estimated through back extrapolation based on the LUR model (for the year 2012) and the fixed air monitoring sites in Perth Metropolitan region, maintained by the WA Department of Water and Environmental Regulation (DWER) using the ratio method. This method is described more fully elsewhere (Mila Dirgawati et al., 2016). Although $PM_{2.5}$ and NO_2 measures were available from the fixed monitoring sites over the study period, BC concentrations were not directly measured by DWER. To obtain BC concentration estimates, temporal NO_2 concentration ratios were used as a proxy for temporal changes to BC, as the concentration of BC and NO_2 were correlated ($r = 0.7$).

The models were used to predict annual pollutant concentrations at the HIMS participants' residence in 2012 and then back-extrapolated to estimate concentrations at baseline and over the follow-up period.

2.4. Statistical analyses

The associations between exposure to $PM_{2.5}$, $PM_{2.5a}$ and NO_2 and each outcome (hospitalisation for all respiratory disease, asthma, COPD and pneumonia) were assessed using Cox proportional hazard regression models. Exposure increments were determined by using the inter quartile range (2.1, 5.4, and 0.4 for $PM_{2.5}$, NO2, and $PM_{2.5a}$, respectively) and choosing the nearest whole number for their increments (2, 5, and 1 respectively).

Age was treated as underlying time and censoring was done at the first admission, death or end of follow-up (30/06/2015), whichever occurred first. The models were adjusted for potential confounders, determined a priori, in three steps following an approach similar to ESCAPE cohorts study protocol (Beelen et al., 2014). Model 1 included age (underlying time in years) and year of enrolment. Model 2 was further adjusted for smoking status at baseline (current, previous, or never smoker), education level at baseline (never attended school, primary school, some high school, completed high school, or completed any tertiary degree), body mass index at baseline (BMI; linear and squared term), and physical activity at baseline (sufficient or not). Sufficient physical activity is classified as participating in 150 min of physical activity per week (Sims et al., 2006). Model 3 was further adjusted for area

level socioeconomic status (SES) indicator. We used the Index of Relative Socioeconomic Disadvantage (IRSD) from the 2011 Census. This index summarises a range of information such as income and education. We grouped the IRSD score into quartiles where category 1 is the most disadvantaged and category 4 is the least disadvantaged.

All models were developed using the dataset with no missing exposure and covariates in model 3 (n = 11,665). Participants with a record of hospitalisation before the baseline for all respiratory diseases (n = 571), asthma (n = 102), COPD (n = 130) and pneumonia (n = 225) were excluded from the relevant analyses. However, a sensitivity analyses was undertaken where participants with a record of hospitalisation for the same diagnosis before the baseline were included. The shape of the association between the pollutants and the outcomes which showed statistically significant associations in model 2 or 3 were also studied. Exposure to pollutants were included as a natural cubic spline with four degrees of freedom in the model 3. The significance of the nonlinearity was tested by comparing the models' fit using likelihood ratio test.

Results are presented as hazard ratios (HR) with 95% confidence intervals (CI) using Survival package version 3.27 in R version 4.0.3 (R Core Team, 2020).

3. Results

HIMS participants were on average 72.1 years (SD = 4.38 years) at baseline. The characteristics of the HIMS participants at baseline are displayed in Table 1. Of the 11,156 men with no hospitalisation for respiratory diseases before baseline, 2,728 experienced a hospitalisation for a respiratory disease during the follow up period. The average length of follow-up was 12 years. Compared to men who were not hospitalized for a respiratory illness, men who had been hospitalized for a respiratory illness were more commonly current smokers, with lower levels of education and weekly physical activity (Table 1).

The average annual pollutant concentrations estimated at baseline for all participants were 5.05 μgm^{-3} for $PM_{2.5}$, 0.97 $\times$ 10^{-5} m^{-1} for $PM_{2.5a}$ and 13.4 μgm^{-3} for NO_2 (Table 2). The baseline pollutant concentrations were higher for participants who experienced a hospitalisation for all respiratory diseases compared with those who did not experience a hospitalisation for a respiratory disease during the study period, however, this difference was only significant for $PM_{2.5}$ and $PM_{2.5a}$.

The associations between an increase in exposure of 2 μgm^{-3} $PM_{2.5}$, 1 $\times$ 10^{-5} m^{-1} $PM_{2.5a}$ and 5 μgm^{-3} in NO_2 and first hospitalisation for all respiratory disease, asthma, COPD and pneumonia during the study period are displayed in Table 3.

A 2 μgm^{-3} increase in $PM_{2.5}$ was associated with a 12% increase in hazard of first hospitalisation for COPD (95%CI 1.03–1.24) when adjusted for age, year of enrolment, smoking status, education, BMI and physical activity (model 2) and an 8% increase (95%CI 0.98–1.2) when also adjusted for area level SES (model 3). A 1 $\times$ 10^{-5} m^{-1} increase in $PM_{2.5a}$ was associated with a significant increase in risk of first hospitalisation for COPD (HR 1.45 95%CI 1.13–1.87), when adjusted for age and year of enrolment only. The risk was attenuated to 18% percent increase and no longer significant when adjusted for other demographic and socio-economic factors (95% CI 0.91–1.53).

Exposures to $PM_{2.5}$ and $PM_{2.5a}$ were positively associated with first hospitalisation for all respiratory disease (HR and 95%CI: 1.10 (1.05–1.16) for $PM_{2.5}$ and 1.19 (1.03–1.37) for $PM_{2.5a}$) in the least adjusted model (model 1).

Positive associations were observed with first hospitalisation for pneumonia (HR and 95% CI: 1.08 (1.01–1.16)) in model 2. These associations were attenuated and no longer significant when adjusted for area level SES.

No association was observed for NO_2 exposure and respiratory hospitalisations. Exposures to $PM_{2.5}$, $PM_{2.5a}$ and NO_2 were not associated with first hospitalisations for asthma.

The associations were slightly more positive for all respiratory diseases and COPD when we included the subjects with previous hospitalisations (Supplementary Materials Table S1). The potential nonlinearity between exposure to $PM_{2.5}$ and hospitalisation for Pneumonia and COPD were investigated since their associations were statistically significant in both model 1 and 2. The results of the spline models showed that their associations did not differ significantly from a linear association.

Table 1. HIMS cohort characteristics at baseline grouped by post-baseline hospitalisation for all respiratory diseases.

	Not hospitalised for respiratory illness (N = 8,428)	Hospitalised for respiratory illness (N = 2,728)	Total (N = 11,156)	p value
Smoking status				<0.001
Current	829 (9.8%)	384 (14.1%)	1213 (10.9%)	
Never	2801 (33.2%)	610 (22.4%)	3411 (30.6%)	
Previous	4797 (56.9%)	1733 (63.5%)	6530 (58.5%)	
Missing (n)	1	1	2	
Education level				<0.001
Primary school or below	1757 (20.9%)	728 (26.7%)	2485 (22.3%)	
Some high school	3132 (37.2%)	1036 (38.0%)	4168 (37.4%)	
Completed high school	2058 (24.4%)	630 (23.1%)	2688 (24.1%)	
Completed any tertiary degree	1476 (17.5%)	332 (12.2%)	1808 (16.2%)	
Missing (n)	5	2	7	
BMI				<0.001
Underweight (<18.5 kgm^2)	40 (0.5%)	27 (1.0%)	67 (0.6%)	
Normal (18.5–24.9 kg/m^2)	2459 (29.2%)	867 (31.8%)	3326 (29.8%)	
Overweight (25.0–29.9 kg/m^2)	4429 (52.6%)	1302 (47.7%)	5731 (51.4%)	
Obese (≥ 30 kg/m^2)	1495 (17.7%)	531 (19.5%)	2026 (18.2%)	
Missing (n)	6	1	7	
Sufficient physical activity (> 150 min per week)				<0.001
Yes	5301 (63.1%)	1585 (58.3%)	6886 (61.9%)	
Missing (n)	26	8	34	

*Pearson's Chi-squared tests were performed to compare the distribution of the variables across the hospitalisation for respiratory diseases.

Table 2. Summary of $PM_{2.5}$, $PM_{2.5a}$, and NO_2 concentrations estimated at baseline for the HIMS participants grouped by hospitalisation for all respiratory diseases.

	Not hospitalised for respiratory illness (N = 8,428)	Hospitalised for respiratory illness (N = 2,728)	Total (N = 11,156)	p value*
$PM_{2.5}$ ($\mu g \cdot m^{-3}$)				<0.001
Mean (SD)	5.01 (1.70)	5.16 (1.64)	5.05 (1.69)	
Median (Q1, Q3)	5.31 (3.95, 6.25)	5.44 (4.19, 6.33)	5.35 (4.02, 6.26)	
Range	<0.56–10.02	<0.56–9.53	<0.56–10.02	
NO_2 ($\mu g \cdot m^{-3}$)				
Mean (SD)	13.38 (4.10)	13.50 (4.08)	13.41 (4.10)	0.197
Median (Q1, Q3)	13.13 (10.47, 16.12)	13.24 (10.72, 16.14)	13.16 (10.54, 16.12)	
Range	<3.8–27.22	<3.8–27.24	<3.8–27.24	
$PM_{2.5a}$ ($10^{-5}m^{-1}$)	323	116	439	
Mean (SD)	0.96 (0.27)	0.98 (0.26)	0.97 (0.27)	
Median (Q1, Q3)	0.97 (0.78, 1.14)	0.98 (0.80, 1.16)	0.97 (0.79, 1.15)	
Range	0.08–1.90	0.14–1.86	0.08–1.90	0.016

* Two-sample t-tests were performed to compare the distribution of the variables across the hospitalisation for respiratory diseases.

Table 3. Hazard ratios and 95% Confidence Intervals from Cox proportional Hazard Models with increasing covariate adjustments.

Outcome	Pollutant	Model	Population size	Number of cases	HR and 95% CI
All respiratory diseases	$PM_{2.5}$ per 2 $\mu g\ m^{-3}$	1	11,094	2,714	**1.10 (1.05–1.16)**
		2			1.04 (0.99–1.09)
		3			1.01 (0.96–1.06)
	$PM_{2.5a}$ per $10^{-5}m^{-1}$	1			**1.19 (1.03–1.37)**
		2			1.07 (0.92–1.24)
		3			1.06 (0.91–1.22)
	NO_2 per 5 $\mu g\ m^{-3}$	1			1.03 (0.98–1.08)
		2			1.00 (0.95–1.05)
		3			1.00 (0.95–1.05)
Asthma	$PM_{2.5}$ per 2 $\mu g\ m^{-3}$	1	11,563	55	1.04 (0.75–1.44)
		2			1.01 (0.72–1.41)
		3			0.88 (0.61–1.28)
	$PM_{2.5a}$ per $10^{-5}m^{-1}$	1			0.88 (0.32–2.40)
		2			0.82 (0.30–2.28)
		3			0.78 (0.28–2.16)
	NO_2 per 5 $\mu g\ m^{-3}$	1			0.96 (0.69–1.35)
		2			0.95 (0.68–1.33)
		3			0.93 (0.66–1.31)
COPD	$PM_{2.5}$ per 2 $\mu g\ m^{-3}$	1	11,535	875	**1.24 (1.14–1.36)**
		2			**1.12(1.02–1.22)**
		3			1.07 (0.97–1.17)
	$PM_{2.5a}$ per $10^{-5}m^{-1}$	1			**1.45 (1.13–1.87)**
		2			1.18 (0.91–1.53)
		3			1.16 (0.89–1.50)
	NO_2 per 5 $\mu g\ m^{-3}$	1			1.05 (0.97–1.14)
		2			0.99 (0.91–1.08)
		3			0.99 (0.91–1.08)
Pneumonia	$PM_{2.5}$ per 2 $\mu g\ m^{-3}$	1	11,440	1,443	**1.14 (1.07–1.22)**
		2			**1.08 (1.01–1.16)**
		3			1.06 (0.99–1.14)
	$PM_{2.5a}$ per $10^{-5}m^{-1}$	1			1.17 (0.96–1.43)
		2			1.07 (0.87–1.30)
		3			1.05 (0.86–1.29)
	NO_2 per 5 $\mu g\ m^{-3}$	1			1.01 (0.94–1.07)
		2			0.98 (0.92–1.05)
		3			0.98 (0.92–1.04)

Model 1: adjusted for age (underlying time).
Model 2: Model 1 plus smoking status, education level, body mass index (BMI; linear and squared term), and physical activity (sufficient or not).
Model 3: Model 2 plus area level socioeconomic status (SES) indicator.

4. Discussion

We found no statistically significant evidence of adverse associations between long-term exposure to low levels of $PM_{2.5}$ and $PM_{2.5a}$ in Perth, Australia and increased risk of hospitalisations for COPD. The observed null associations could be due to low statistical power, overadjustment or low levels of exposure.

Associations between $PM_{2.5}$ and pneumonia and all respiratory diseases and $PM_{2.5a}$ and all respiratory diseases were also observed but only in the least adjusted model (adjusted for age and year of enrolment only). The number of hospitalisations for asthma were very low (68 out of 11,226 participants), precluding an investigation into its relationship with the ambient air pollutants. No associations between NO_2 exposure and respiratory outcomes were observed.

The observed associations between exposure to air pollution and respiratory morbidity are generally in agreement with other similar studies. A systematic review of 247 articles investigating the health effects associated with $PM_{2.5}$ exposure, concluded that increased levels of $PM_{2.5}$ were associated with increased rates of respiratory morbidity (Sharma et al., 2020). Abramson, Wigmann, Altug, and Schikowski (2020) found $PM_{2.5}$ but not NO_2 and PM_{10} to be associated with Fraction of exhaled FeNO, a well-validated biomarker of airway inflammation. Requia et al. (2018) reviewed the evidence of the associations between exposure to air pollutants and cardiorespiratory related hospitalisation and mortality. They observed an increase of 2.7% in reported risk of respiratory disease for every 10 micro-grams per cubic meter change in $PM_{2.5}$.

Previous studies have also shown an association between exposure to $PM_{2.5}$ and increased risk of COPD. A systematic review of 13 studies (2010–2018) reported that a daily increase of 10 $\mu g/m^3$ $PM_{2.5}$ was associated with increased in COPD hospitalisations (OR and 95% CI: 1.025 (1.8–3.2). Weichenthal et al. (2017) in study of 1.1 million adults who resided in Toronto, Canada also found $PM_{2.5}$ (10.9 $\mu g/m^3$) to be associated with incident COPD cases (HR and 95% CI: 1.07 (1.06, 1.09), they also found COPD cases to be associated with ultrafine particles (<0.1 μm) and NO_2. They identified incident cases of COPD from the Ontario COPD Database available via the Institute for Clinical and Evaluative Sciences. An incident case of COPD was defined as having 'at least one health care interaction (emergency department visit, hospitalisation or physician visit) that is specific to COPD'. Their estimated long-term average air pollution concentrations at baseline for $PM_{2.5}$ was 10.9 $\mu g/m^3$, and in our study, it was 5.05 $\mu g/m^3$.

Further, Wang et al. (2019), in study of six metropolitan regions of the United States also found $PM_{2.5}$ (10.32 $\mu g/m^3$) at baseline to be associated with increased in emphysema (CT scan confirmed) risk of 0.58 percentage points per 10 years. In a cohort of older US persons (18.9 million) Pun et al. (2017) observed $PM_{2.5}$ exposure (12.5 (10.3–14.3) $\mu g/m^3$)was associated with a 10% increase in mortality from COPD (RR 1.10 (95% CI: 1.08, 1.12)) (Pun et al., 2017).

Salimi et al. (2018) also investigated the relationship between long-term exposure to $PM_{2.5}$ and NO_2 and respiratory hospitalisations in the New South Wales, Australia using the 45 and up cohort study. They did not observe associations between $PM_{2.5}$ (4.5 $\mu g\ m^{-3}$) and all respiratory outcomes or COPD but did observe a 10% increase in asthma hospitalisation risk, albeit non-significant. Their findings in relation to COPD and asthma differed to what we observed in this study despite similarities in study design, exposure levels and population demographics. Higher spatial resolution of the air pollution model of our study, longer follow up period, and an older male population may contribute to these differences.

The association between exposure to $PM_{2.5a}$ and increased risk of all respiratory and COPD hospitalisations reported in this study adds to the small body of literature investigating exposure to $PM_{2.5a}$ (a surrogate for black carbon) and health risks. Our findings are consistent with data from the ESCAPE cohort where long term exposure to black carbon was associated with increased hospitalisations for COPD (Liu et al., 2021).

While we were not able to investigate this relationship, exposure to black carbon was associated with increased risk of hospitalisation for asthma in the ELAPSE study (Liu et al., 2020) and in the ESCAPE cohort (Jacquemin et al., 2015). A meta-analysis of five ESCAPE cohort studies investigating exposure to air pollution and lung function did not find an association with exposure to $PM_{2.5a}$ (Adam et al., 2015), however, findings from a large Dutch population-based LifeLines Cohort Study reported an association that appeared to be stronger for participants who were female, had a higher BMI and had underlying respiratory diseases (de Jong et al., 2016). More work is required in this area.

We did not find an association with exposure to NO_2 and respiratory disease which is contradictory to some previous findings. A meta-analysis by Adam et al. (2015) reported long-term exposure to NO_2 was associated with reduced lung function in five European cohorts. This link has also been reported in an Australian cohort (Tasmanian Longitudinal Health Study (TAHS)) where higher NO_2 exposures over a 5 year period were associated with prevalent asthma, wheeze and impaired lung function in middle aged adults (Bowatte et al., 2017). Further studies are needed to assess this association.

There are several strengths in our study. The Health In Men Study is a large cohort with complete follow up of participants via data linkage. The participants are older men and are more vulnerable to the health effects of air pollution making them an appropriate study sample. Exposure to air pollution was estimated at the house hold level giving us individual exposure assessments. Cross validation methods of the LUR models for estimating pollutant concentrations supported the validity of LUR models for $PM_{2.5}$, $PM_{2.5a}$ and NO_2 in Metropolitan Perth (Mila Dirgawati et al., 2015, 2016).

On the other hand the results may not be inferred to younger or female populations. Exposure was assessed in 2012 and back extrapolated to estimate exposure at baseline and some men may have moved to a higher or lower polluted area. However 90% did not move during the study. Measuring exposure at one point in time limited our ability to investigate the exposure and hospitalisation relationship over time. Further, there was little variation in air pollution concentrations between baseline measures in 1996–1999 and 2012 (M. Dirgawati et al., 2019). The low numbers of asthma cases meant we did not have the power to investigate any associations with air pollutants. There may have been additional confounding factors that were not considered, leading to residual confounding. For example, we had only had measures of area-level SES rather than individual measures. The data on confounders were obtained at baseline, however, there may have been changes over time in smoking, BMI and physical activity.

Limited studies that have investigated the association between respiratory hospitalisations with low levels of air pollution, particularly in a cohort of older men, making comparing our results to those of other studies limited.

This study adds to the limited body of knowledge investigating the link between low levels of air pollution and respiratory morbidity. Long-term exposure to air pollution appears to be associated with adverse health outcomes even in geographical areas with low levels of pollution. These finding may have implications for the health of older adults and policies such as reduction of air pollution at low levels, and more acknowledgment of health risks due to air pollution in the chronic disease management plan. Further studies in this area, in particular large cohorts with power to detect differences, are needed to understand the overall risk.

Declarations

Author contribution statement

Farhad Salimi: Conceived and designed the experiments; Analyzed and interpreted the data; Wrote the paper.

Ania Stasinska; Geoffrey G. Morgan: Analyzed and interpreted the data; Wrote the paper.

Graeme J. Hankey; Osvaldo Almeida; Bu Yeap; Leon Flicker: Contributed reagents, materials, analysis tools or data; Wrote the paper.

Jane Heyworth: Conceived and designed the experiments; Contributed reagents, materials, analysis tools or data; Analyzed and interpreted the data; Wrote the paper.

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Data availability statement

The data that has been used is confidential.

Declaration of interest's statement

The authors declare no conflict of interest.

Additional information

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