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Long-term exposure to low concentrations of air pollutants and hospitalisation for respiratory diseases: A prospective cohort study in Australia

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ABSTRACT

Background: Short- and long-term spatiotemporal variation in exposure to air pollution is associated with respiratory morbidity in areas with moderate-to-high level of air pollution, but very few studies have examined whether these associations also exist in areas with low level exposure.

Objectives: We assessed the association between spatial variation in long-term exposure to $PM_{2.5}$ and NO_2 and hospitalisation for all respiratory diseases, asthma, chronic obstructive pulmonary disease (COPD), and pneumonia, in older adults residing in Sydney, Australia, a city with low-level concentrations.

Methods: We recorded data on hospitalisations for 100,084 participants, who were aged > 45 years at entry in 2006–2009 until June 2014. Annual NO_2 and $PM_{2.5}$ concentrations were estimated for the participants' residential addresses and Cox proportional hazards regression was used to model the association between exposure to air pollutants and first episode of hospitalisation, controlling for personal and area level covariates. We further investigated the shape of the exposure-response association and potential effect modification by age, sex, education level, smoking status, and BMI.

Results: NO_2 and $PM_{2.5}$ annual mean exposure estimates were 17.5 $\mu g \cdot m^{-3}$ and 4.5 $\mu g \cdot m^{-3}$ respectively. NO_2 and $PM_{2.5}$ was positively, although not significantly, associated with asthma. The adjusted hazard ratio for a 1 $\mu g \cdot m^{-3}$ increase in $PM_{2.5}$ was 1.08, 95% confidence interval 0.89–1.30. The adjusted hazard ratio for a 5 $\mu g \cdot m^{-3}$ increase in NO_2 was 1.03, 95% confidence interval 0.88–1.19. We found no positive statistically significant associations with hospitalisation for all respiratory diseases, and pneumonia while negative associations were observed with COPD.

Conclusions: We found weak positive associations of exposure to air pollution with hospitalisation for asthma while there was no evidence of an association for all respiratory diseases.

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1. Introduction

Epidemiological studies consistently find associations between short-term temporal variation and long-term spatial variation in exposure to air pollution and mortality or morbidity (WHO 2013). Globally, ambient particulate matter pollution was the fifth-ranking risk factor for premature death in 2015. Exposure to particulate matter (PM) with aerodynamic diameter < 2.5 μm ($PM_{2.5}$) was estimated to cause 4.2 million premature deaths representing 7.6% of total global premature deaths (Cohen et al. 2017).

Over the last decades, ambient air pollutant concentrations have decreased significantly in developed countries (Brauer et al. 2016). Nevertheless, an epidemiological study found adverse health effects of exposure to air pollution at levels well below current WHO air pollution standards (Crouse et al. 2012). To date, due to the very limited number of epidemiological studies of long term exposure to air pollution at low concentrations, little evidence is available on whether there is any specific threshold below which the adverse health effects of air pollution do not occur (Burnett et al. 2014). In order to inform future risk assessments and regulation, it is important to know whether adverse effects continue to be observed at lower concentrations of air pollution.

The prevalence of respiratory diseases has significantly increased worldwide (Eder et al. 2006; Gibson et al. 2010; Murray et al. 2013; Sunyer 2001). In adults, tobacco smoking is established as the main risk factor, however, the increasing prevalence of respiratory diseases suggests a possible role of environmental factors such as air pollution (Eder et al. 2006; Kim et al. 2015; Sunyer 2001; WHO 2013). Exposure to air pollution has adverse acute respiratory effects (Künzli et al. 2010), including short-term decreases in lung function, respiratory symptoms, and increases in hospitalisation and death due to respiratory causes (Brunekreef and Holgate 2002; Zanobetti et al. 2008). The extent to which long-term exposure to air pollution contributes to respiratory disease is less clear (Schikowski et al. 2014b).

A cross-sectional European study of around 650,000 participants aged ≥20 years (Cai et al. 2017) found that 10 $\mu g \cdot m^{-3}$ increases in nitrogen dioxide (NO_2) and particulate matter with aerodynamic diameter < 10 μm (PM_{10}) were associated with 1.9 and 2.8% higher lifetime asthma prevalence respectively. Previous cohort studies have found associations between long-term exposure to air pollution with first hospitalisation, self-reported diagnosis/symptoms, development and persistence of asthma and chronic obstructive pulmonary disease (COPD) in Europe, US, and Australia (Andersen et al. 2011; Andersen et al. 2012; Bowatte et al. 2018; Fisher et al. 2016; Jacquemin et al. 2015; Young et al. 2014), while others did not observe any associations (Atkinson et al. 2015; Schikowski et al. 2014a; Weichenthal et al. 2017).

As summarised above, several studies have studied the associations between exposure to air pollution and respiratory diseases, however, evidence on the effects of long-term exposure to air pollution on respiratory health is inconsistent. Furthermore, most of these studies have been conducted in areas with relatively high levels of air pollution, with mean annual $PM_{2.5}$ concentrations > 10 $\mu g \cdot m^{-3}$, while annual average $PM_{2.5}$ in Sydney, Australia's largest city, was around 5.5 $\mu g \cdot m^{-3}$ in 2011 (source: New South Wales Government air pollution data).

Despite the need for studies of exposure-response relationships at lower pollutant concentrations, to our knowledge, there have been very few studies conducted on the long-term effects of exposure to low-levels of air pollution on respiratory morbidity. To address this gap in knowledge we investigated the associations between long-term exposure to low levels of air pollution and hospitalisation for respiratory diseases in an Australian cohort of adults over 45 years of age.

2. Methods

2.1. Design and health outcome

We obtained data on 266,969 adults aged above 45 years and over, living in the state of New South Wales (NSW), who were recruited to the Sax Institute's 45 and Up Study. The prospective participants were sampled from the Department of Human Services enrolment database. Each participant joined the study by completing a questionnaire at baseline (2006–2009) and giving signed consent for follow-up and linkage of their information to routine health databases. Questionnaire included information on demographic and social characteristics, personal health behaviours, and general health-related data (45 and Up Study Collaborators 2008). The data were linked by the Centre for Health Record Linkage to hospitalisation data (NSW Admitted Patient Data Collection) and mortality data (NSW Registry of Births Deaths and Marriages (RBMD)). Study participants for this analysis comprised participants who resided in a 100 km × 100 km grid centred on Sydney Airport (Sydney Metropolitan Region), due to availability of pollutant exposure estimates, resulting in a sample size of 99,317 participants. 45 and Up Study has ethical approval from the University of NSW Human Research Ethics Committee (HREC) and we have also obtained ethical approval from University of Sydney HREC for this study.

Only unscheduled hospitalisations were included in the analyses. Primary diagnosis was used to identify hospitalisation for all respiratory diseases (International Classification of Diseases, 10th revision (ICD-10): J00–J99 excluding J95.4 to J95.9, R09.1, R09.8), asthma (ICD-10: J45–J46), COPD (ICD-10: J40–J44), and pneumonia (ICD-10: J12–J18). Participants with a record of hospitalisation for the same diagnosis before the baseline were removed from the primary analysis. The first hospitalisation between baseline and 30 June 2014 was defined as the main outcome.

2.2. Exposure assessment

Ambient concentrations of NO_2 were estimated using a validated satellite-based land use regression (LUR) model that has been described in detail elsewhere (Knibbs et al. 2014; Knibbs et al. 2016). Briefly, the satellite-based LUR uses satellite observations of NO_2 and land-use variables to predict the annual average NO_2. This model explained around 80% (RMSE = 1.4 ppb) of spatial variation in annual ambient NO_2 concentrations during 2006–2011.We used this model to estimate annual average NO_2 concentration at mesh blocks across Sydney in 2007. Mesh blocks are the smallest geographical area defined by Australian Bureau of Statistics and contains around 30–60 dwellings. Participants' exposure to annual average NO_2 in 2007 was calculated at the mesh block centroid closest to their residential addresses.

Ambient $PM_{2.5}$ concentrations were estimated using a chemical transport model blended with fixed site monitor data (Physick et al. 2007). Using elliptical influence functions, this model blends computed air pollutant fields from a meteorological and air quality model with observations from the air quality network. This model estimated the 07/2010–07/2011 annual average $PM_{2.5}$ concentrations across Sydney at 1 km^2 resolution and has been described elsewhere (Broome et al. 2016). Estimated $PM_{2.5}$ and NO_2 concentrations were assumed to reflect the concentrations at baseline.

2.3. Statistical analyses

Cox proportional hazards models were used to assess the association between exposure to NO_2 and $PM_{2.5}$ and first hospitalisation for respiratory disease. Age was treated as underlying time and was left truncated at the age at recruitment and right censored at the first admission post recruitment, death or end of follow-up (30 June 2014), whichever came first. Following an approach similar to the ESCAPE study (Beelen et al. 2014), the effects of exposure to NO_2 and $PM_{2.5}$