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Fine particulate air pollution, nitrogen dioxide, and systemic autoimmune rheumatic disease in Calgary, Alberta

Sasha Bernatsky [a,b,*], Audrey Smargiassi [c,d], Markey Johnson [e], Gilaad G. Kaplan [f], Cheryl Barnabe [f,g,h,i,j], Larry Svenson [g,h,i,j], Allan Brand [c,d], Stefania Bertazzon [k], Marie Hudson [a,l], Ann E. Clarke [a,m,o], Paul R. Fortin [n], Steven Edworthy [f,g,h,i,j], Patrick Bélisle [b], Lawrence Joseph [a,b]

[a] Department of Medicine, McGill University, Montreal, Quebec, Canada
[b] Division of Clinical Epidemiology, McGill University Health Centre, Montreal, Quebec, Canada
[c] Département de Santé Environnementale et de Santé au Travail, Université de Montréal, Montreal, Quebec, Canada
[d] Institut National de Santé Publique du Québec, Montréal, Canada
[e] Air Health Science Division, Health Canada, Ottawa, Ontario, Canada
[f] Department of Medicine, University of Calgary, Calgary, Alberta, Canada
[g] Department of Community Health Sciences, University of Calgary, Canada
[h] Surveillance and Assessment, Alberta Ministry of Health, Canada
[i] Department of Community Health Sciences, Cumming School of Medicine, University of Calgary, Calgary, Albert, Canada
[j] University of Alberta, School of Public Health, Edmonton, Alberta, Canada
[k] Department of Geography, University of Calgary, Calgary, Alberta, Canada
[l] Division of Rheumatology, Jewish General Hospital, Montréal, Quebec, Canada
[m] Division of Allergy and Clinical Immunology, McGill University Health Centre, Montreal, Quebec, Canada
[n] Division of Rheumatology, Department of Medicine, Université Laval, Quebec city, Quebec, Canada
[o] Department of Epidemiology, Biostatistics and Occupational Health, McGill University, Montreal, Quebec, Canada

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ABSTRACT

Objective: To estimate the association between fine particulate ($PM_{2.5}$) and nitrogen dioxide (NO_2) pollution and systemic autoimmune rheumatic diseases (SARDs).
Methods: Associations between ambient air pollution ($PM_{2.5}$ and NO_2) and SARDs were assessed using land-use regression models for Calgary, Alberta and administrative health data (1993–2007). SARD case definitions were based on $\geq$2 physician claims, or $\geq$1 rheumatology billing code; or $\geq$1 hospitalization code (for systemic lupus, Sjogren's Syndrome, scleroderma, polymyositis, dermatomyositis, or undifferentiated connective tissue disease). Bayesian hierarchical latent class regression models estimated the probability that each resident was a SARD case, based on these case definitions. The sum of individual level probabilities provided the estimated number of cases in each area. The latent class model included terms for age, sex, and an interaction term between age and sex. Bayesian logistic regression models were used to generate adjusted odds ratios (OR) for NO_2 and $PM_{2.5}$. pollutant models, adjusting for neighbourhood income, age, sex, and an interaction between age and sex. We also examined models stratified for First-Nations (FN) and non-FN subgroups.
Results: Residents that were female and/or aged >45 had a greater probability of being a SARD case, with the highest OR estimates for older females. Independently, the odds of being a SARDs case increased with $PM_{2.5}$ levels, but the results were inconclusive for NO_2. The results stratified by FN and non-FN groups were not distinctly different.
Conclusion: In this urban Canadian sample, adjusting for demographics, exposure to $PM_{2.5}$ was associated with an increased risk of SARDs. The results for NO_2 were inconclusive.

1. Introduction

Systemic autoimmune rheumatic diseases (SARDs) are complex chronic inflammatory disorders (such as systemic lupus, SLE) characterized by multi-system inflammation (Callaghan et al.,

* Corresponding author at: Division of Clinical Epidemiology, McGill University Health Centre, Montreal, Canada. Fax: +1 514 934 8293.
E-mail address: sasha.bernatsky@mcgill.ca (S. Bernatsky).

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2007; Bernatsky et al., 2009; Aghdassi et al., 2011) and high disease burden (Panopalis et al., 2007). Although there is some evidence that SARDs may be triggered by environmental factors (Cooper et al., 1999; Cooper and Stroehla, 2003; Ballestar, 2010; Shapira et al., 2010) there remain considerable knowledge gaps regarding mechanisms through which the environment may trigger these autoimmune diseases. Fine particulate matter ($PM_{2.5}$) enters the body through airways and can trigger a systemic inflammatory response (van Eeden et al., 2001). This mechanism may be important in driving some of air pollution's effects in cardiovascular disease (van Eeden et al., 2012) and diabetes (Anderson et al., 2012; Chen et al., 2013). However, other components of air pollution, such as nitrogen dioxide (NO_2) are also pro-inflammatory and may also be of interest, and NO_2 has been linked to adverse health outcomes, including asthma (Cai et al., 2014), cardiac disease (Zhao et al., 2014), and diabetes (Eze et al., 2014). A very few studies have examined the association between air pollution and SARDs. We have previously estimated levels of $PM_{2.5}$ across Alberta, using satellite imagery (Bernatsky et al., 2014). However, satellite remote sensing estimates air pollution concentrations over larger geographic areas (10 km grids) increasing the possibility of exposure misclassification. The goal of this study was to examine associations between air pollution and SARDs at a finer spatial scale. Our objective was also to estimate the degree to which a diagnosis of SARDs was associated not only with ambient $PM_{2.5}$ levels, but also NO_2 levels. The current analyses focused on Calgary, the largest city in Alberta (almost 1.3 million residents, representing almost 40% of the province's population).

2. Methods

We examined associations between local-scale ambient NO_2 and $PM_{2.5}$ in Calgary, Alberta using land use regression (LUR) models and administrative health data. The LUR modelling approach has been widely used for research estimating individual exposure to ambient air pollution (Johnson et al., 2013). Land-use regression models are built by including predictor variables, such as traffic, topography, and other geographic variables, in multivariable regression using monitored pollution levels as the outcome. Subsequently, levels of pollution may then be estimated for any point, using the parameter estimates derived from the regression model. This method has been identified as a preferred approach to estimating small area variations in air pollution effectively, when household level monitoring data are not available (Ryan and LeMasters, 2007; Health Effects Institute, 2010).

We used comprehensive (physician billing and hospitalization) administrative provincial health data from Alberta (1993–2007) and focussed our analyses on Calgary, since LUR estimates for $PM_{2.5}$ and NO_2 were available for this region of Alberta, only. In Canada, each province maintains linkable databases on all residents who are recipients of a comprehensive health plan which covers physician visits and hospitalizations. In the Alberta health administrative databases, information on First Nations (FN) status is also available, at the individual level. The FN variable is defined by whether or not an individual's health premiums are paid by the First Nations and Inuit Health Branch (Health Canada) at any time point since 1994, thus indicating Treaty Status as per the Indian Act (Alberta Health and Wellness, 2004).

The databases record one physician billing code per visit (in Alberta, up to three diagnosis codes are allowed, but use of more than one code is infrequent), and all hospitalizations (with up to 25 diagnostic codes per hospitalization in Alberta). The SARD case definition was based on three algorithms: two or more physician billing claims with the International Classification of Diseases (ICD)-9 code 710 (within 2 years but at least 2 months apart); at least one such billing code by a rheumatologist; or at least one hospitalization with an ICD-10 diagnostic code corresponding to a SARD diagnosis (M32.1, M32.8–32.9, M33–M34, M35.0, M35.8–35.9, M36.0). These diagnostic codes include SLE, Sjogren's Syndrome, scleroderma, polymyositis, dermatomyositis, and undifferentiated connective tissue disease. Within the ICD-9 classification system, in provinces where billing data are only limited to three digits, it is impossible to differentiate between these conditions (SLE, Sjogren's Syndrome, scleroderma, polymyositis, dermatomyositis, and undifferentiated connective tissue disease). Rheumatoid arthritis (and systemic vasculitis, by the way) fall under separate ICD-9 categories (714.x and 446.x respectively) and we were unable to include these groups in the current study.

Residents of Calgary could meet one or more of the three SARDs case definitions. Bayesian hierarchical latent class regression models (which do not assume any case definition to be a perfect gold standard) (Bernatsky et al., 2005) were used to estimate the probability that any given Calgary resident was a SARD case, based on their results relative to the three case definitions. For example, a resident who never fulfilled any of the case definitions would have an estimated probability of being a SARD that was much smaller then someone who fulfilled all three case definitions, the former near zero (but not exactly zero) and the latter nearer to 1 (but not exactly 1). Residents with one or two case definitions would have estimated probabilities between these extremes. The latent class approach to case definition within administrative data (as opposed to assuming chart review or anything else as a perfect gold standard), where individuals are not assigned a case status per se, but rather are provided with an estimated probability of being a case, has been shown to useful across several diseases and jurisdictions (Prosser et al., 2008).

The individual level probabilities estimated were summed to estimate the total number of SARD cases according to groups characterized by age (dichotomized to less than or equal to 45 years of age, or older than 45), sex, and dissemination area, DA (the smallest standard geographic area for which all Canadian census data are disseminated, generally representing between 400 and 700 persons). The DA associated with the residence of each Calgary subject was obtained through overlay of Calgary postal code centroids on a geographic layer of the Calgary dissemination areas. To obtain SARD prevalence rates for each DA, for each age and sex group, we divided the estimated number of SARD cases by the appropriate regional Calgary population figures obtained from the Canadian Census 2006.

We then used the case definition results as outcome data in a logistic regression model that estimated odds ratio (OR), estimates for sex, age group, and pollution levels (explained below), across all dissemination areas in Calgary. The model also included an interaction term between age and sex. Around our point estimates of the odds ratios (ORs) generated from the model are Bayesian 95% credible intervals (CrI). Regional income information was obtained from the Canadian Census 2006 for Alberta.

Long-term exposure to ambient NO_2 and $PM_{2.5}$ was estimated using the LUR model results developed for Calgary dissemination block areas. The LUR is based on data from two-week summer and winter air monitoring campaigns (held in August 2010 and January 2011). NO_2 LUR model data were based on data from 46 sites in summer and 47 sites in winter, while $PM_{2.5}$ models were based on data from 25 sites in summer and 29 sites in winter. NO_2 was modelled using a geographically weighted land-use regression model to address spatial non-stationarity and autocorrelation (Beratazzon et al., 2011; Elikan et al., 2011). $PM_{2.5}$ was modelled using traditional linear regression LUR methods, because the $PM_{2.5}$ spatial non-stationarity and autocorrelation do not have a lot of impact on $PM_{2.5}$ estimates. Some examples of important predictors of NO_2 and $PM_{2.5}$ in the LUR models included traffic and