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Fine particulate air pollution and systemic autoimmune rheumatic disease in two Canadian provinces

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ABSTRACT

Objective: To estimate the degree to which fine particulate (PM2.5) air pollution is associated with systemic autoimmune rheumatic diseases (SARDs).
Methods: We used population-based administrative data from Alberta (1993–2007) and Quebec (1989–2011). SARD algorithms included ≥ 2 physician billing codes, or ≥ 1 rheumatology billing code, or ≥ 1 hospitalization diagnostic 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 any given resident was a SARD case, based on the algorithms. Mean 2001–2006 residential ambient PM2.5 levels were assigned using satellite-derived data for dissemination area regions in Alberta and CLSC regions in Quebec. The sum of individual level probabilities provided the estimated total cases per region in each province, according to age, sex, urban-versus-rural residence, income, and PM2.5 levels. In Alberta, we ran separate models for First-Nations (FN) and non-First Nations subgroups. Bayesian logistic regression modeling generated odds ratio (OR) estimates for being a SARD case, accounting concurrently for demographics, as well as an interaction term between age and sex.
Results: Our data suggested that the probability of being a SARD case was higher among females versus males and for residents aged >45 versus younger, with the highest ORs for older females. Independently, the odds of being a SARDs case increased with PM2.5 levels in both provinces.
Conclusion: Our data suggest that PM2.5 exposure may be associated with an increased risk of SARDs.

1. Introduction

Systemic autoimmune rheumatic diseases (SARDs) are complex chronic inflammatory disorders (Callaghan et al., 2007; Bernatsky

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et al., 2009; Aghdassi et al., 2011; Panopalis et al., 2007). Some SARDs include systemic lupus erythematosus (SLE), scleroderma, primary Sjogren's syndrome, and polymyositis–dermatomyositis. These conditions are characterized by an over-reactive immune system and systemic inflammation that can result in a variety of manifestations, including organ damage like kidney failure in SLE. There is compelling evidence that SARDs may be triggered by environmental factors (Cooper et al., 1999; Cooper and Stroehla, 2003; Ballestar, 2010; Shapira et al., 2010) although there remain considerable knowledge gaps.

There is a growing interest in the role of air pollution on inflammation and disease, especially particulate matter (PM). Sources of PM from human activities include road vehicles and industrial emissions. Fine PM (with a median diameter $<2.5\ \mu m$) enter the body through airways and can trigger a systemic inflammatory response. van Eeden et al. (2001) studies have linked PM to systemic inflammation, in particularly in cardiovascular disease and diabetes (Anderson et al., 2012; Chen et al., 2013). However, very few studies have examined the association between PM and SARDs. One category of PM, diesel exhaust nanoparticles, has been shown to have pro-inflammatory effects on the cells of patients with systemic autoimmune rheumatic disease (Mastrofrancesco et al., 2014). In addition preliminary data has shown an association between road-traffic density and SLE prevalence in Montreal (Labrecque et al., 2010), found links between PM2.5 levels and SLE activity in a clinical SLE cohort (Bernatsky et al., 2011a,b), and suggested PM2.5 and SO_2 industrial emissions as triggers of autoimmunity (Bernatsky et al., 2015a,b).

Our objective was to provide more information regarding the effects of pollution on SARDs prevalence in two provinces in Canada.

2. Methods

We used population-based administrative health data from the provinces of Alberta (1993–2007) and Quebec (1996–2011). In Canada, each province maintains linkable databases on all residents who are recipients of a comprehensive health plan. The databases record one physician billing diagnosis code per visit (in Alberta, up to three diagnosis codes are allowed, but infrequently used), and all hospitalizations (with up to 25 diagnostic codes per hospital separation in Alberta, and 15 in Quebec). Use of administrative data to study rheumatic disease outcomes is often done, although billing and hospitalization diagnostic codes found in administrative data are not necessarily clinically confirmed. To address this, our methods take account the imperfect nature of these diagnostic codes, using a model that calculates the sensitivity and specificity of the billing and hospitalization diagnostic codes.

We considered three algorithms that could be helpful in identifying SARD cases: ≥ 2 physician billing claims with the International Classification of Diseases (ICD)-9 code 710.x (within 2 years but at least 2 months apart); ≥ 1 such billing code by a rheumatologist; or at ≥ 1 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). This includes systemic lupus erythematous, Sjogren's syndrome, scleroderma, polymyositis, dermatomyositis, and undifferentiated connective tissue disease.

The Alberta health data that we used contained the six digit postal code of the residence of the subjects. As dissemination areas are the smallest geographic areas available in the Canadian Census with socio-demographic information, the Canadian Census dissemination area associated with the residence of each Albertan subject was obtained through geographic overlay of postal code centroids on a geographic layer of the dissemination area (Statistics Canada, 2012). In Alberta, information on First Nation (FN) status is also available (Alberta Health and Wellness, 2014).

For the Quebec health file, we were only provided with the first three digits of the postal code, and the smallest geographic area that would include the polygons of the three digits postal codes and at which socio-demographic information was available was the area served by each Quebec 'local social and health service center' (CLSC). No reliable indicator of First Nations status is typically available in Quebec administrative data.

The population by age group and sex at the dissemination area level, as well as median regional income information, was obtained from the Canadian Census 2006 for Alberta (Statistics Canada, 2014). For Quebec, the demographic information used at the CLSC level was from Canadian Census data for the year 2011 (Ministère de la Santé et des Services Sociaux. Estimations de population, 2014), and median regional income information was from Canadian Census data for 2006. Mean 2001–2006 ambient fine particulate (PM2.5) levels derived from satellite imagery (Atmospheric Composition Analysis Group, 2014) were assigned to the dissemination area of each Alberta resident and the CLSC area of each Quebec resident. We linked to each DA or CLSC of residence, mean PM2.5 levels from 2001 to 2006 derived from satellite imagery by van Donkelaar et al. (2010). van Donkelaar et al. (2010) estimated PM2.5 levels with optical depth data from the MODIS (Moderate Resolution Imaging Spectroradiometer) and MISR (Multiangle Imaging Spectroradiometer) satellite instruments, and the GEOS-Chem global chemical transport model. This data is available at ⟨http://fizz.phys.dal.ca/~atmos/martin/?page_id=140⟩. Concentrations of PM2.5 (in $\mu g/m^3$) were estimated for a grid of 10 km by 10 km and the value of each grid was assigned to all DA that were found in it. In Quebec, when more than one $10\ km \times 10\ km$ cell of the PM2.5 data were intersecting the geographic area of a CLSC, a weighed mean based on the population density within these cells was computed.

Alberta and Quebec data were analyzed separately. In the first step of our analyses, Bayesian hierarchical latent class regression models were used to estimate the probability that any given resident of Alberta or Quebec was a SARD case, given the results for our three algorithms. At the first level of this model are the individual variables (age group, sex, urban versus rural residence). The only hierarchical second level variable is the intercept, which creates probabilities within each group of characteristics. Once can then considers the priors on the intercept distributions as a third level. The model estimates and adjusts for the imperfect sensitivity and specificity of the billing and hospitalization diagnostic code information (Broten et al., 2014). The individual level probabilities were summed (for all subjects who were still alive at the end of the period) to estimate the total number of cases according to groups characterized by age (dichotomized to less than or equal to 45, or older than 45 years), sex and urban-versus-rural residence.

We then used these as outcome data in multivariate hierarchical logistic regression models that estimated odds ratios (OR) for sex, urban-versus-rural location of residence (based on the postal code information that was recorded most proximal to the date of the first ICD diagnosis code for a SARD, from billing or hospitalization data), income level, and PM2.5 levels, across all regions. Statistics Canada median income values for each Alberta dissemination area and Quebec CLSC were categorized into quartiles.

The hierarchical nature of the logistic model in this final step allowed us to estimate, on the individual level, the effects on SARDs prevalence relative to age group and sex, and on a regional level, to estimate the effects of income and pollution levels on SARD prevalence rates. Around our point estimates of the ORs generated from the model, we produced 95% credible intervals (CrI).