



Air pollution and emergency department visits for respiratory diseases: A multi-city case crossover study

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ABSTRACT

Increasing evidence suggests that ambient air pollution is a major risk factor for both acute and chronic respiratory disease exacerbations and emergencies. The objective of this study was to determine the association between ambient air pollutants and emergency department (ED) visits for respiratory conditions in nine districts across the province of Ontario in Canada. Health, air pollutant (PM_{2.5}, NO₂, O₃, and SO₂), and meteorological data were retrieved from April 2004 to December 2011. Respiratory diseases were categorized as: chronic obstructive pulmonary disease (COPD, including bronchiectasis) and acute upper respiratory diseases. A case-crossover design was used to test the associations between ED visits and ambient air pollutants, stratified by sex and season. For COPD among males, positive results were observed for NO₂ with lags of 3–6 days, for PM_{2.5} with lags 1–8, and for SO₂ with lags of 4–8 days. For COPD among females, positive results were observed for O₃ with lags 2–4 days, and for SO₂ among lags of 3–6 days. For upper respiratory disease emergencies among males, positive results were observed for NO₂ (lags 5–8 days), for O₃, (lags 0–6 days), PM_{2.5} (all lags), and SO₂ (lag 8), and among females, positive results were observed for NO₂ for lag 8 days, for O₃, PM_{2.5} among all lags. Our study provides evidence of the associations between short-term exposure to air pollution and increased risk of ED visits for upper and lower respiratory diseases in an environment where air pollutant concentrations are relatively low.

1. Background

Ambient air pollution plays an important role in a large spectrum of health disorders. The World Health Organization estimates that 22% of global death and disability can be attributed to environmental factors (Prüss-Ustün et al., 2016). Ambient air pollution accounts for an estimated 8% of the portion of disease burden for respiratory infections and 9% for chronic obstructive pulmonary disease (COPD) (Prüss-Ustün et al., 2016). Human activities (including burning of fossil fuels, such as coal, oil, natural gas, and gasoline to produce electricity and power vehicles) are a major source of environmental air pollutants sulphur dioxide (SO₂), nitrogen dioxide (NO₂), ozone (O₃), and particulate matter (PM).

Many studies have found positive associations between air pollution and mortality, morbidity, hospitalizations and emergency department (ED) visits for respiratory diseases (Stieb et al., 2009; Kousha and Rowe, 2014; Burnett et al., 1994; Barnett et al., 2005; To et al., 2016; Penard-Morand et al., 2005; Pope, 1989; Schwartz et al., 1991; Chen et al.,

2017), and especially asthma (Stieb et al., 2009; Szyszkowicz, 2008; Villeneuve et al., 2007; Gasana et al., 2012; Choi et al., 2011; Peel et al., 2005; Linaker et al., 2000; McConnell et al., 2003; To et al., 2013). Individuals with pre-existing respiratory disease, such as chronic obstructive pulmonary disease (COPD), demonstrate increased susceptibility to the adverse health effects of ambient air pollution (Lim et al., 2012; Cohen et al., 2017), particularly for older adults (Chen et al., 2004). In addition, there is evidence of gender differences in ambient air pollution exposures and ED visits for conjunctivitis (Szyszkowicz et al., 2016), otitis (Kousha and Castner, 2016), and several respiratory disorders (de Torres et al., 2005; Martinez et al., 2007; Szyszkowicz and Kousha, 2014; Malig et al., 2016). There is a paucity of evidence on gender differences in the association between air pollution and ED use for upper respiratory conditions, such as sinusitis, pharyngitis, and infection. Furthermore, gender-related trends in COPD, lower respiratory diseases intricately linked to environmental exposure, warrant ongoing research. Historically, men have demonstrated higher rates of morbidity and mortality from COPD compared with women; these higher

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rates were frequently associated with personal smoking behaviors (Aryal et al., 2013). More recently, COPD morbidity and mortality in women have dramatically increased (Aryal et al., 2013). Therefore, to address the aforementioned knowledge gaps and evolving trends, this current study focuses on the health outcomes of both upper respiratory diseases and COPD ED visits, stratified by sex.

Evidence supporting the association between ambient air pollution and respiratory health effects is inconsistent, possibly due to differences in study design, statistical method, sample size, air pollution concentrations and estimates of exposure. Ecological studies using time series or time-stratified analyses to estimate short-term air health effects have generally found positive associations between daily increases in air pollution and daily increases in morbidity and mortality from respiratory diseases (Stieb et al., 2009; Kousha and Rowe, 2014; Barnett et al., 2005; Choi et al., 2011). However, some cohort studies have not demonstrated significant effects of long term air pollution exposure on respiratory mortality (Hoek et al., 2013; Dimakopoulou et al., 2014). While there are several single-site investigations, replication with multi-city studies strengthens the body evidence and enhances the potential for reproducibility and reliability of the findings (Malig et al., 2016). Studies of ambient air pollution and respiratory health outcomes have been conducted around the globe, often with a focus on regions with the highest concentrations of air pollution (Barnett et al., 2005; Chen et al., 2017; Chan-Yeung et al., 2004). Alternatively, in global estimates of air pollution levels, Canada generally demonstrates lower concentrations of pollutants compared to other parts of the world (Lim et al., 2012). Recent evidence indicates there may be no threshold value below which a low level of exposure to pollutants, such as fine particulate matter, does not affect human health (Di et al., 2017). Furthermore, lower PM_{2.5} concentrations have been associated with an even steeper dose-response concentration curve for overall mortality than higher exposure concentrations (Chen et al., 2017). To strengthen the body of evidence on ambient air pollution exposure and ED visits for COPD and upper respiratory conditions, the present study was designed as a multi-location analysis in Canada.

The aim of this present study was to investigate the associations between ambient air pollution and ED visits for respiratory diseases in nine districts and urban areas in the province of Ontario in Canada. This study is one of the largest multi-city studies correlating air pollutants with ED visits for respiratory disease by pooling results from nine individual cities and districts.

2. Methods

A case-crossover design (Maclure, 1991) was used to evaluate the potential association between ED visits for respiratory conditions and ambient air pollution from April 2004 to December 2011 in nine urban areas and districts across the province of Ontario, Canada: Algoma, Halton, Hamilton, Middlesex, Ottawa, Peel, Toronto, Essex and York. These urban areas and districts represent a major cross-section of Ontario. Algoma is located in Northeastern Ontario. Ottawa is in South-eastern Ontario. Toronto is Ontario's most populated metropolitan area, with Halton, Peel, and York as municipalities and Hamilton located immediately to the south. The remaining locations of Middlesex (London) and Essex (Windsor) line the southernmost portion of Ontario.

The ED visit, as the level of analysis, was used to represent health outcomes. If the same individual was represented by multiple ED visits, each visit was treated as a separate, individual observation. We utilized the daily mean values of air pollutant concentrations, temperature and relative humidity. Analyses were conducted separately for males and females. Additional sub-analyses were conducted for warm and cold seasons and some by age groups.

A p-value less than 0.05 was considered statistically significant in all presented statistical results. Results are reported as odds ratios (ORs) and 95% confidence intervals (CI) associated with an increase in interquartile range (IQR) of the air pollutants.

3. Health data

Health data were retrieved from the National Ambulatory Care Reporting System (NACRS). The NACRS database contains data from participating hospital and community-based ambulatory care services such as day surgery, outpatient clinics and ED visits which are collected at time of service. (For more information, see Canadian Institute for Health Information (CIHI) website: www.cihi.ca).

We retrieved ED visits for the period of April 2004 to December 2011 from the ICD-10 using the *International Classification of Diseases*, Tenth revision (ICD-10). For this study the following categories were considered: 1) COPD and bronchiectasis (codes J41-J44, J47), and 2) upper respiratory diseases (codes J00-J06, J30 and J31). Supplemental analyses were also conducted using related conditions of (1) acute lower respiratory diseases (codes J10-J18, J20-J22, and J96), and (2) asthma (using a subset of J45 codes to represent acute exacerbation). The analysis for COPD focused on adults at least 55 years old (based on age distribution for the ED visits). Upper respiratory emergencies were analyzed for the entire population.

4. Environmental data

The environmental data were obtained from Environment Canada's National Air Pollution Surveillance program. (See NAPS Web site: <https://www.ec.gc.ca/rnsps-naps/>). To obtain data on ambient air pollution, NAPS stations within 35 km of each patient's residential 3-digit postal codes (i.e. Forward Sortation Area (FSA): all postal codes that start with the same three characters are together considered an FSA) were selected and identified. See Supplemental Fig. S3 for a map of the ambient air monitor locations. The daily average values of O₃, NO₂, SO₂, and PM_{2.5} (PM of the diameter no greater than 2.5 µm) were calculated by averaging over all the stations within this 35 km radius.

Hourly data for relative humidity and temperature for all cities were retrieved from Environment Canada. We calculated the daily levels for these weather parameters by averaging hourly data over 24-h periods. In case of weather data, stations within 100 km of patient's 3 digit postal code (FSA) were considered. If more than one station was available for a patient, the daily values of all stations were averaged.

5. Statistical analysis

Two stages of statistical analysis were performed using a time-stratified case-crossover design, then pooling the estimates across the nine cities/districts using a fixed-effects model (Janes et al., 2005; Bateson and Schwartz, 1999). The method of case-crossover is an adaptation of the case-control design in which cases act as their own controls on a set of predefined control days, usually the days around the time of ED visit (Bateson and Schwartz, 1999). This statistical design is now recognized as being useful approach in studies of air pollution as it avoids confounding by individual characteristics and adjusts for longer time-varying covariates such as trends and seasonal effects (Maclure, 1991; Janes et al., 2005; Bateson and Schwartz, 1999).

In the first stage, single pollutant models were fit with the emergency (case) day outcome, controlling for temperature, relative humidity, and an indicator for days with influenza. By nature of the case-crossover design, comparisons for pollution levels non-emergency days are referred to as controls. Slopes (betas) for O₃, NO₂, PM_{2.5} and SO₂ were calculated separately for each city by using conditional logistic regression realized by applying the PROC PHREG procedure in SAS (Enterprise Guide, version 4.2). Several different time lags for air pollutants and meteorological factors were modeled, from same-day exposure (i.e., 0 day lag) to exposure 8 days before admission (i.e., 8 day lag). In order to reduce bias, the control periods were selected from the same day of the week as the case's hospital visit, in the same month and year; thus 3 or 4 controls were selected for each individual case (Bateson and Schwartz, 1999).

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